Effect of nurse-led medication reviews - an interventional study

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ABSTRACTS

ISPOR 16TH ANNUAL EUROPEAN CONGRESS RESEARCH ABSTRACTS

RESEARCH PODIUM PRESENTATIONS – SESSION I
HEALTH CARE EXPENDITURE OR REIMBURSEMENT STUDIES – BIOLOGICS

BI1
ADHERENCE AND RESOURCE USE AMONG PATIENTS TREATED WITH BIOLOGICS. FINDINGS FROM THE BEETLE STUDY (BIOLOGICAL DRUGS: EVALUATION OF ECONOMICS, TREATMENTS, AND LABELING IN REAL-WORLD SETTING)

Degli Esposti L, Sangiorgi D, Buda S
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OBJECTIVES: Systemic administration of anti-TNF alpha leads to an anti-inflammatory and joint protective effect in pathologies such as rheumatoid arthritis, psoriasis, Crohn's disease. The aim of this study was to assess adherence to therapy and stay on treatment (no switches or interruptions) of patients treated with biologics according to therapeutic indication and to calculate health care resources consumption (drugs, outpatient services, hospitalizations). **METHODS:** An observational retrospective cohort analysis based on 5 Local Health Units administrative databases was conducted. Patients who filled at least one prescription for anti-TNF alpha between January 1, 2009-December 31, 2011 were included. Patients were followed-up for one year. Patients were defined as adherent if they had >80% of follow up period covered by drugs dispensation. **RESULTS:** A total of 1219 patients were analyzed, 47% male, age 49.6±14.6. Patients affected by rheumatoid arthritis were 36%, psoriasis 31%, Crohn's disease 10%, psoriatic arthritis 7%, ulcerative colitis 3%, ankylosing spondylitis 3%, diagnosis not available 11%; 420 (34%) were treated with Adalimumab, 615 (50%) Etanercept, 184 (15%) Infliximab. Among the 94% of patients who did not switch, patients treated with Infliximab seemed to have the highest rate of adherent patients across all indications: 51%, vs. 27% Etanercept and 23% Adalimumab; at the multivariable logistic regression model, Infliximab resulted a protective predictor of non adherence for all indications (OR ranged from 0.08 to 0.43). For patients who started a first-line biological drug, stay on treatment was 73% for Infliximab, 67% Etanercept, 64% Adalimumab. The mean annual expenditure for each patient in analysis was €11,120; in particular, non-pharmacological expenditure was €988 for adherent and €1,255 for non-adherent patients; at the multivariable generalized linear model, Infliximab was associated with the lowest cost for all indications. **CONCLUSIONS:** Patients treated with Infliximab were associated to higher adherence and stay on treatment and lower costs, as compared to Adalimumab and Etanercept.

BI2
WHAT ARE THE KEY DRIVERS OF REIMBURSEMENT FOR BIOSIMILARS? AN EXAMINATION OF REIMBURSEMENT PROCESSES AND RECOMMENDATIONS ACROSS NINE COUNTRIES

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Mapi, London, UK

OBJECTIVES: Biosimilars are biotherapeutic products that are similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product. The first biosimilar (Omnitrope) received EU regulatory approval in 2006; since then, 14 biosimilars have received marketing authorisation. This study examined the differences in the approaches to reimbursement of biosimilars in countries using HTA to inform decision-making. **METHODS:** Four biosimilar medicines were selected to provide sufficient documentation in seven European countries, South Korea and Australia. Regulatory approval and HTA reimbursement decision documents were identified and a qualitative analysis of the processes, recommendations by indication, evidence and key decision drivers was undertaken to explain differences in recommendations across countries. **RESULTS:** Twenty-one different indications were appraised; 90% of appraisals were 'recommended', 9% 'recommended with restrictions', and 1% were 'not recommended'. The Netherlands and Germany accepted 'clinical comparability' to the originator as sufficient evidence for automatic reimbursement. Sweden and France were the only countries to appraise and to recommend for all indications. Scotland and Wales recommended all biosimilars but restricted indications in some cases. Agencies accepted the notion of clinical comparability and extrapolation across indications when appraising the evidence. A cost-minimisation analysis and budget impact analysis were key economic decision drivers. A full cost-effectiveness analysis was only requested by NICE. Other factors influential in recommending reimbursement were: lobbying, dual reimbursement processes, and other reimbursement mechanisms. **CONCLUSIONS:** As the market for biosimilars continues to grow, it is imperative that specific HTA reimbursement processes are developed for assessing biosimilars. This includes further research on how different drug classes should be considered; especially pertinent due to the increase in biosimilars for monoclonal antibody-based drugs, which differ from the product classes (erythropoietin, white blood cell stimulators, growth hormone and insulins) currently dominating the market.

BI3
DIFFERENCES IN APPROACH TO BIOSIMILARS: NICE VERSUS SMC RECOMMENDATIONS

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OBJECTIVES: Several biosimilar products have been approved for marketing in the European Union, but their market penetration remains slow. Lack of clear reimbursement guidance could be one of the reasons for this slow penetration. This study examines how many, if any, biosimilar products have been assessed in the UK by NICE and by the SMC and to what extent recommendations by the two HTA organisations are consistent. **METHODS:** Secondary research was conducted, including a review of all NICE and SMC final guidance and of guidance in progress by NICE to compare the HTA process outcome and issues raised by the two HTA agencies. **RESULTS:** NICE has issued only one final guidance for a biosimilar product (Omnitrope) and has another guidance in progress (for epoetin including biosimilars). The SMC has issued guidance for 4 biosimilar versions of filgrastim (Ratiograstim, TevaGrastim, Zarzio and Nivestim), 2 biosimilar versions of epoetin (Binocrit and Retacrit) and 1 version of somatropin (Omnitrope). All SMC guidance for biosimilars issued to date has been positive. The NICE guidance for Omnitrope is positive despite some reservations about the economic model. **CONCLUSIONS:** Considering the limited overlap between NICE and SMC decisions (only one drug - Omnitrope - was considered by both agencies), it is difficult to assess consistency in the SMC approach compared to NICE's approach at this stage. Based on the biosimilars HTA guidance by NICE and the SMC to date, a cost-minimisation analysis may be acceptable for biosimilars even if such an approach - in the absence of a full cost-effectiveness model - might be rejected for an originator product. Both HTA agencies recommend that prescribing for biosimilars should be by brand name to avoid automatic substitution in the pharmacy.

BI4
IMPACT OF EXCLUSIVE HOSPITAL DISTRIBUTION OF BIOSIMILAR ON DRUG HEALTH CARE BUDGET

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OBJECTIVES: There is an increased trend in shifting biologics distribution to exclusive hospital pharmacy channel. Although it looks obvious that such process will generate savings through tenders at regional or national level such policy consequences were not clearly quantified. We used a model developed for EU commission to assess the consequences of such policies on biosimilars for selected EU countries (model developed for the European Commission for the project"EU Pharmaceutical expenditure forecast" http://ec.europa.eu/health/healthcare/key_documents/index.en.htm). **METHODS:** We built a model to assess policy scenarios impact on pharmaceuticals reference forecast for seven EU Member States (France, the UK, Germany, Poland, Portugal, Greece and Hungary). We tested the impact of shifting biosimilar distribution to hospital channel on pharmaceutical industry revenue, Health insurers budget and society cost. **RESULTS:** For the period 2012-2016 the savings of biosimilars (based in million Euros) for Health insurance will be for: UK 2,023; GE 1,127; FR 1,634; PL 200; GR 19; PO 272; HU 29. The extra savings by shifting of the biosimilars distribution to exclusive hospital pharmacy will be: for UK 353; GE 3,392; FR 1,684; PL 37; GR 206; PO 65; HU 176. The difference is relatively small for UK, although significant. However, it is considerable for Germany and France (around 3 and 2 time original saving). Similar figures (revenue loss) are seen for pharmaceutical companies. **CONCLUSIONS:** Although the impact of such policy varies from one country to one another based on initial proportion of biosimilar distributed through hospital and level of discount over branded products, this policy appears to have a substantial impact on drug expenditures and might contribute to sustainability of health insurance in EU countries. Germany and France might benefit dramatically from such policy.

CANCER OUTCOMES RESEARCH STUDIES

CA1
RESPONSIVENESS OF THE EQ-5D IN ONCOLOGY: A META-ANALYSIS

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OBJECTIVES: The EQ-5D is often employed in clinical trials to derive quality-adjusted life years for cost-utility analyses, and in comparisons of health-related quality of life across conditions. However, there are concerns that the EQ-5D is less

responsive to change particularly in oncology. Therefore the objective of this study was to determine the level of responsiveness of the EQ-5D in oncology. **METHODS:** A systematic review identified relevant articles reviewing responsiveness of the EQ-5D in adults (EMBASE, Medline). Effects sizes (ES) were calculated for the studies identified where not already reported. A meta-analysis was undertaken of the effect sizes: homogeneity of variance was assessed (fixed effects) and random effects models applied where there was significant heterogeneity. Responsiveness was also compared for improvement/deterioration in health status. Analyses were conducted in SPSS v18. **RESULTS:** Data were available from 12 studies (3 breast, 2 prostate, as well as ovarian, lung and renal cancers) each with EQ-5D data at a minimum of 2 time points leading to a total of 45 entries. The overall unweighted ES was -0.26 (95%CI: -0.31 to -0.21), however there was significant heterogeneity in terms of effect sizes ($Q(44) = 427.00$, $p<0.001$) which was accounted for using the random effects model ($Q(44) = 39.58$, $p>0.05$). The overall weighted effect size (ES) was -0.17 (95%CI: -0.33 to -0.01). The weighted ES for improvement was 0.08 (95%CI: -0.02 to 0.18), and -0.52 (95%CI: -0.64 to -0.41) for deterioration. **CONCLUSIONS:** There is considerable heterogeneity in the reported effect size of the EQ-5D. Responsiveness of the EQ-5D in oncology trials as measured by effect sizes is modest at best. The instrument appears to be more sensitive to deterioration in health status than to improvements. Further work will explore the ES of the EQ-5d in comparison with responsiveness of disease-specific measures and changes in health status.

CA2

THE BURDEN OF CAREGIVING IN CANCER: THE STATUS OF CLINICAL RESEARCH

Foster RE, Bardos JI, Wilson TJ, Hamerslag L, Kusel J
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OBJECTIVES: The responsibility of caring for cancer patients, often suffering from a magnitude of health problems, can result in a considerable burden for their caregivers, both physically and psychologically. The objective of this study was to assess the status and extent of clinical research into the burden of caregiving for cancer patients. **METHODS:** ClinicalTrials.gov was searched for all cancer trials that considered caregiver burden, using a matrix of search terms such as 'carer', 'burden of care' or 'caregiver'. The impact of geographical location or cancer type on the proportion of trials assessing caregiver burden, the outcome measures used and the proportion of trials including caregiver burden as an outcome over time were investigated. **RESULTS:** From a total of 36,184 cancer-focused trials documented worldwide, 1,596 (4%) assessed caregiver burden. Outcome measures included caregiver quality of life (QoL), satisfaction with care and mood states. The impact of caregiver burden in cancer trials within different world regions varied, with the highest proportion of trials that considered caregiver burden located in Mexico (23%) and Asia (14-22%). Trials for five major cancer types (breast, lung, prostate, colorectal, liver) assessed caregiver burden at similar frequency (4-5%). Evaluation of completed trials demonstrated that the proportion of cancer trials considering caregiver burden increased from <1% between 1997-2001 to 7% after 2012. **CONCLUSIONS:** Fewer than 5% of all cancer trials documented worldwide have evaluated the impact of caregiver burden, although geographical variation does exist. The equal assessment of caregiver burden across cancer types may suggest that no single cancer type is considered to have a higher degree of caregiver burden. Interestingly, while the number of total cancer trials evaluating caregiver burden documented to date is relatively low, the incidence has increased over the last 15 years, suggesting that the growing importance of caregiver burden is being recognised.

CA3

EMA APPROVAL OF DRUGS ON THE BASIS OF PIVOTAL NON-COMPARATIVE PHASE II TRIAL DATA

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HERON Health, London, UK

OBJECTIVES: The recent European Medicines Agency (EMA) approval of crizotinib has highlighted the potential for regulatory approval to be gained on the basis of pivotal non-comparative Phase II data. This research aims to determine the circumstances under which the EMA will approve submissions on this basis. **METHODS:** All publicly available European Public Assessment Reports (EPARs) were screened up to June 2013. Submissions that were based on pivotal Phase II data were identified and the acceptance decision, disease, and level of benefit were extracted. **RESULTS:** Eight drugs (bevacizumab, bortezomib, crizotinib, dasatinib, everolimus, gefitinib, imatinib, ofatumumab) across ten indications been submitted to the EMA on the basis of pivotal non-comparative Phase II data. All submissions were for entry indications except imatinib, which was also submitted for two further indications on this basis. All, except crizotinib, were for indications with no alternative therapies and all were for onology indications except everolimus which was for subependymal giant cell astrocytoma (SEGA). All, except crizotinib, were EMA designated orphan medical products for these indications. One submission was rejected (bevacizumab), one was restricted (ofatumumab), and eight were approved. Top-line supportive Phase III data was only available in two submissions (crizotinib and everolimus). Overall response rates (ORRs) were the primary endpoints in all submissions except imantinib and dasatinib in leukaemia indications and everolimus in SEGA. Rejected drugs had ORRs of 47% (ofatumumab, rejected subpopulation) and 38% (bevacizumab). Approved drugs had ORRs of 60% (crizotinib), 58% (ofatumumab, approved subpopulation), 40% (imatinib), and 35% (bortezomib). Despite low ORRs, imatinib was used to treat a disease with no licensed therapies (gastrointestinal stromal tumours), and bortezomib offered a 10% complete remission rate. **CONCLUSIONS:** Pivotal Phase II data can support EMA approval if it demonstrates substantial clinical benefits for small patient populations with severe diseases that lack therapeutic alternatives.

CA4

MEASURING THE COST OF LOST PRODUCTIVITY DUE TO PREMATURE CANCER-RELATED MORTALITY: A EUROPEAN OVERVIEW

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OBJECTIVES: To assess the economic burden of cancer by estimating years of potential productive life lost (YPPLL) and costs of lost productivity due to premature cancer-related mortality across Europe. **METHODS:** We derived the number of cancer deaths by sex for 23 of the most common cancer sites in 30 European countries from GLOBOCAN. YPPLL were calculated by multiplying the number of cancer-specific deaths for each productive age group (15-64) by standard life expectancy at the mid-point for each age group. Using the human capital approach, we multiplied standardised YPPLL for each individual by country- age- and gender-specific annual wages from age of death until retirement following adjustments for labour force participation and unemployment. Costs were expressed in 2008€. **RESULTS:** All cancer sites combined generated a total of €150.9 billion in premature mortality costs in Europe in 2008. Western Europe accounted for almost half of the total, followed by Northern (21%), Southern (21%) and Central & Eastern Europe (9%). Findings contrasted with YPPLL where Central & Eastern Europe had the highest burden. Male costs exceeded female costs by 88% in Europe as a whole (male: €98.4 billion; female: €52.5 billion) and across all European regions. Lung was the most expensive site (€34.7 billion; 23% of total costs), followed by breast cancer (€13.6 billion, 9%), colorectal cancer (€12.1 billion, 8%), brain & CNS (€9.1 billion, 6%) and pancreatic cancer (€7.5 billion, 5%). According to premature mortality cost per death, testicular cancer was the most expensive site (€2.5 million per death), followed by brain & CNS cancer (€481,512) and Hodgkin lymphoma (€474,559). **CONCLUSIONS:** Lost productivity costs due to cancer-related premature mortality are significant in Europe. Productivity costs provide an alternative perspective on the cancer burden on society and may inform cancer control policy decisions.

CONCEPTUAL PAPERS

CP1

INCREMENTAL COST PER QUALITY-ADJUSTED LIFE YEAR GAINED? THE NEED FOR ALTERNATIVE METHODS TO EVALUATE MEDICAL INTERVENTIONS FOR ULTRA-RARE DISORDERS

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OBJECTIVES: To critically appraise the problems posed by the systematic valuation of interventions for ultra-rare disorders using conventional health economic analysis methods. **METHODS:** An international group of clinical and health economic experts met in conjunction with the Annual European ISPOR Congress in Berlin/Germany, November 2012, to identify and deliberate underlying issues openly, adhering to the Chatham House rule. **RESULTS:** The group reached a broad consensus, including: The complexities of research and development new treatments for ultra-rare disorders (URDs) may require conditional approval and reimbursement policies, such as coverage with evidence development agreements, but should not be used as a justification for showing surrogate endpoint improvement only. As a prerequisite for value assessment, demonstration of a minimum significant clinical benefit should be expected within a reasonable timeframe. Regarding the economic evaluation of interventions for URDs, the currently prevailing logic of cost effectiveness (using benchmarks for the maximum allowable incremental cost per quality-adjusted year, QALY, gained) was considered inappropriate since it does not capture well-established social preferences regarding health care resource allocation. Such social preferences include, but are not limited to, a priority for care for the worse of (related to initial health state), for those with more urgent conditions (the so called "rule of rescue"), a relatively lower priority based upon capacity to benefit, and a dislike against "all or nothing" resource allocation decisions that might deprive certain groups of patients from any chance to access effective care. **CONCLUSIONS:** Alternative paradigms to establish the "value for money" conferred by interventions for URDs should be developed with high priority. Such methods should capture and reflect prominent societal value judgments, beyond efficiency as conventionally defined by QALY maximization under a budget constraint.

CP2

THE MULTIMODEL ENSEMBLE APPROACH TO REDUCING STRUCTURAL UNCERTAINTY IN DECISION ANALYTICAL MODELLING

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Decision analytical modelling represents an essential tool for undertaking health economic evaluation. Markov models provide a mathematical framework for such analyses, particularly in the context of assessing the cost-effectiveness of treatments for chronic diseases where economic outcomes are typically extrapolated beyond the duration of clinical trials. However, structural uncertainty is a key challenge, to methodologists and decision makers alike, that has hitherto attracted insufficient attention. Best practice guidelines advocate the testing of structural assumptions through alternative modelling approaches or conducting scenario analyses. It should be recognised, however, that structural differences in model design represent a strength, rather than limitation, of the modelling process and in fields such as climate modelling, multi-model comparisons and ensemble predictions have been used extensively as the basis for more robust policy decisions. Methods for combining models represents an emerging field in climate modelling, but the simplest approach is to treat all models equally and the mean of all model predictions has been shown to improve on the 'best' model predictions in numerous studies. A weighted multi-model approach may also be developed, but this remains an area of ongoing debate. To date, health economists have not fully embraced the potential of the multi-model paradigm to reduce structural uncertainty. In this work,

we illustrate how this approach may be developed to a) simultaneously and systematically compare health economic outcomes predicted by multiple Markov models; b) address the question of whether (and how) to weight different models within an ensemble based on different performance metrics and model skill scores; c) identify, quantify, and partition total uncertainty across a multi-model ensemble into different sources (for example, to highlight where future research priorities may optimally lie to further improve the robustness of policy recommendations through model improvement and data collection); and d) apply this approach to some real-world examples.

CP3

THE GROWING ROLE OF QUALITATIVE INTERVIEWS IN HEALTH OUTCOMES RESEARCH

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OBJECTIVES: Qualitative interviews, as tools for scientific evidence generation, are often excluded from consideration in health outcomes research. Lack of methodological rigour and the non-reproducibility and non-generalizability of results are often used to justify quantitative methodologies. Here we present an illustrative example of qualitative interviewing's value within health outcomes research. In a study aiming to measure patient and physician preferences for hepatitis C treatments, a discrete choice experiment was designed and a systematic literature review was conducted. **METHODS:** To assess the comprehensibility and relevance of the questionnaire as well as to estimate the value and preciseness of assumptions, pre-tests consisting of a questionnaire pilot followed by a semi-direct interview were conducted. The semi-direct interviewing followed rigorous methods, including defined themes assembled in a discussion guide and behavioural rules for the interviewer to promote axiological neutrality. Analytical methods using predefined codes for the interpretation enabled a systematic understanding of datasets. **RESULTS:** The qualitative component mostly validated but sometimes challenged the theoretical assumptions of the discrete-choice experiment, which had been previously developed on the basis of the systematic literature review. Interviews shed light on occasional complexity and lack of comprehensibility of some questions. The qualitative analysis provided insights to patients' and physicians' experience of their treatment selection process. It included socio-psychological dispositions, like the aversion for work absenteeism or the importance of social representation encouraging patients to prefer treatments which side effects would not affect their social capacities. **CONCLUSIONS:** This method provided in-depth and structured feedback from a small group of patients and physicians. As health outcomes studies increasingly require to expand their level of detail and sensitivity by entering subjective fields of personal preferences, patients' experiences and decision-making processes, there is a pressing need for conducting qualitative micro-level studies prior to supporting broader, field-based studies.

CP4

CONCEPTUAL AND PRACTICAL CONSIDERATIONS WHEN DEALING WITH MISSING UTILITY DATA IN LONGITUDINAL TRIALS, AND SUBSEQUENT USE IN COST-EFFECTIVENESS ANALYSES

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Patient preference-based health-related quality of life measures (utilities) are a critical input in cost-effectiveness analyses of pharmaceuticals and other health care technologies. Over recent years it has become more common for utility data to be collected alongside key clinical data within the pivotal Phase III trials. However, utility data are often not available for all patients throughout the entire course of the trial. The authors discuss the concept that there are unique characteristics of utility data that need to be considered when dealing with missing values, including the large inter-patient variability typically present at baseline. Missing data arise because i) patients become more ill and are less able to complete patient-reported instruments, ii) patients die during the course of the trial, or iii) patients are censored at later stages of the trial due to rolling recruitment. Whilst this is often a problem in oncology trials, it is also a consideration in other interventional and observational research designed to inform pharmacoeconomic evaluations. Situations where individual patient data are accessible and where only summary statistics are available are discussed. The practical considerations of how such re-analysed data should then be included within an economic model are discussed, given the manner in which utilities are incorporated will vary depending on the nature of the health states used.

RESEARCH ON METHODS – MODELING STUDIES

MO1

A GUIDE TO ADJUSTING SURVIVAL TIME ESTIMATES TO ACCOUNT FOR TREATMENT SWITCHING IN RANDOMISED CONTROLLED TRIALS

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OBJECTIVES: Treatment switching is a common issue in clinical trials of cancer treatments – often patients randomised to the control group are permitted to switch onto the experimental treatment at some point during follow-up. In such circumstances an intention to treat (ITT) analysis will result in biased estimates of the overall survival advantage – and therefore the cost-effectiveness – associated with the experimental treatment. Methods to adjust for switching have been used inconsistently and potentially inappropriately in health technology assessments (HTA). We present an analytical framework to guide analysts on the use of methods to adjust for treatment switching in the context of economic evaluations. **METHODS:** We conducted a review of methods used to adjust for treatment switching in HTA, and two rigorous simulation studies to assess the performance of adjustment methods in a range of realistic scenarios. We tested different simulated trial sample sizes, crossover proportions, treatment effect sizes, levels of administrative censoring, and data generating models. Combining the findings from our review and our simulation study, we made practical recommendations on the use of adjustment methods in HTA. **RESULTS:** Our review demonstrates that adjustment methods make important limiting assumptions. Our simulation studies show that the bias associated with alternative methods is highly associated with deviations from their assumptions. Our recommended analysis framework aims to help researchers find suitable adjustment methods on a case-by-case basis. The characteristics of clinical trials and the treatment switching mechanism observed within them, should be considered alongside the key assumptions of the adjustment methods. **CONCLUSIONS:** The limitations associated with switching adjustment methods mean that different methods are appropriate in different scenarios. In some scenarios all methods may be prone to important bias. The data requirements of adjustment methods have important implications for people who design and analyse trials which allow treatment switching.

MO2

USE OF REAL-WORLD EVIDENCE (RWE) TO VALIDATE A TRIAL-BASED HEALTH ECONOMIC MODEL

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OBJECTIVES: Decision makers often rely on health economic models populated with clinical trial data to inform initial assessments about treatment selection, coverage, and reimbursement. To date, there have been few (if any) published model re-analyses using real-world evidence (RWE). The purpose of this study is to 1) assess real-world health and economic outcomes associated with oral anticoagulant vs. low molecular weight heparin (LMWH) as prophylaxis for venous thromboembolism (VTE) in patients undergoing total hip (THR) or knee (TKR) replacement, and 2) compare results of a health economic model populated with clinical trial data vs. RWE. **METHODS:** Patients who underwent THR or TKR between July 2011 and June 2012 were identified in a US commercial insurance claims database. Patients were required to be continuously enrolled 3 months pre-/post-index and were excluded if treated with multiple anti-coagulants within 10 days post-index. A propensity score matching technique was employed to reduce selection bias. Patient characteristics, inpatient-related VTE events and health care costs were determined. A health economic model previously parameterized with clinical trial data was repopulated and reanalyzed using inputs derived from the claims study. **RESULTS:** A total of 14,880 patients were identified (7,440 oral anticoagulant, 7,440 LMWH). In both groups, mean age was 59 and 53% were female. Compared with LMWH, oral anticoagulant use was associated with fewer symptomatic VTE events over 1-year. When repopulated with clinical inputs from claims data, the model projected similar VTE event differences as trial-based model (-0.023 vs. -0.015). Costs (per patient/year) in oral anticoagulant and LMWH groups were consistent across the trial-based model ($385 vs. $1,011), claims-based model ($437 vs. $1,290), and direct reported results from claims analysis ($506 vs. $1,125). **CONCLUSIONS:** Use of RWE is a practical and objective way to validate a trial-based health economic model. Future work should consider study design issues and practical use of results.

MO3

MULTI-STATE STATISTICAL MODELLING TO QUANTIFY AN INDIVIDUAL-BASED MICRO SIMULATION MODEL FOR RADIOTHERAPY TREATMENT IN LUNG CANCER PATIENTS

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OBJECTIVES: We developed an individual-based micro-simulation model for radiotherapy treatment in non small-cell lung cancer (NSCLC). The aim was to explore the suitability of multi-state statistical modelling in heath economics, as a tool to parameterize a simulation model that tracks clinical events over time, taking patient and tumour features into account. **METHODS:** The model contains the four clinical states 'A: alive without local recurrence (LR) or metastasis (M)', 'LR', 'M', and 'Death'. Transition rates were estimated using multi-state statistical modelling, a technique that allows the simultaneous estimation of hazards for multiple transitions, taking covariates as well as the occurrence and timing of previous events into account. Each of the hazards from A to either LR, M and Death were adjusted for the presence of the other competing risks. Individual patients were simulated by repeatedly sampling a patient profile, consisting of patient and tumour characteristics. Subsequently, for each patient a pathway through the model was simulated. The internal validity of the model was verified by comparing intermediate simulation outcomes and overall survival under two different radiotherapy strategies to the original data used for estimation. Finally, the model was externally validated by comparing model outcomes to Dutch cancer registry data. **RESULTS:** Model simulations for the two radiotherapy strategies demonstrated internal validity, with predicted probabilities for the occurrence of LRs, Ms, deaths, and the occurrence of toxicities within 3 years that fell within the 95% confidence intervals of the data. The same was observed for the prediction of overall survival. Comparison of the model predictions to the Dutch cancer registry data showed a moderate fit. **CONCLUSIONS:** Multi-state statistical modelling is a useful technique for obtaining the transition rates that are required for the quantification of a micro-simulation model. In future, our model will be used to evaluate the cost-effectiveness of individualized treatment strategies.

MO4

BAYESIAN CALIBRATION METHOD TO ESTIMATE TRANSITION PROBABILITIES FOR A MARKOV MODEL BASED ON A CONTINUOUS OUTCOME MEASURE: APPLICATION IN PARKINSON'S DISEASE

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OBJECTIVES: Estimating transition probabilities for Markov models is challenging when the effectiveness of the studied intervention is measured using a continuous score, and only aggregate data by treatment are available. We developed a Bayesian calibration method to estimate transition probabilities and applied it in Parkinson's disease (PD). **METHODS:** A previously published Markov model with health states corresponding to Hoehn and Yahr (H&Y) stages was adapted. Patient-level datasets were simulated to replicate results of clinical trials for different drugs, using the UPDRS scale to assess severity, and transition probabilities were estimated from simulated data to provide a reference case. Two calibrations methods were tested for obtaining transition probabilities without patient-level data. Firstly, the Solver tool of Excel was used, with the mean change in UPDRS score and associated variance as targets. Secondly, a Bayesian calibration was implemented in OpenBUGS to estimate the posterior distribution of transition probabilities, assuming the change in UPDRS score has a normal distribution, with observed mean and variance. All other model input parameters were taken from the original model. **RESULTS:** With simulated patient-level data, the incremental cost (IC) was estimated at €-7,015 (95% credibility interval: €-23,953; €5,977) and incremental QALYs (IQ) at 0.455 (0.112; 0.950). With calibration using the Solver tool, there was an infinity of solutions resulting in IC ranging from €-10,141 to €-8,206 and IQ ranging from 0.422 to 0.473. With calibration using OpenBugs, the IC was estimated at €-6,852 (€-24,244; €6,448) and the IQ at -0.448 (0.108; 0.959). **CONCLUSIONS:** Incremental costs and QALYs obtained using the Bayesian calibration and analysis of patient-level data were similarly distributed. Mean results obtained using the Solver tool were comparable, but no statistical distribution around results could be provided. This example suggests that the Bayesian calibration is a valid method to derive transition probabilities from continuous outcome measures.

PATIENT PREFERENCE STUDIES

PP1
A METHODOLOGY FOR PREDICTING THE IMPACT OF COPAYMENTS ON THE UTILIZATION OF HEALTH TECHNOLOGIES

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OBJECTIVES: Copays (or copayments) for health-technologies, such as pharmaceutical products, are used by governments and insurers to prevent moral hazard, reduce unnecessary utilization of resources, and contribute to the cost of health care. Nevertheless they may also reduce access to necessary care, and the financial protection associated with health insurance. In addition, from the perspective of the manufacturer, the introduction of copays may determine unexpected and abrupt falls in demand. The methodology here presented uses data extracted from surveys on product utilization and patient income, prior and after the introduction of copays in various countries and regions, to predict the potential impact of copays on the demand for a pharmaceutical product in a given country or region. **METHODS:** This approach uses multi-level multivariate regressions and a micro-economic model of demand (which assumes maximization of utility and preference independence) to anticipate changes in utilization (and therefore in demand) as a function of the amount of copay charges. Data from a computer simulation were used to test the method. **RESULTS:** A non-linear relationship between copay and drug-consumption, determined by the combined effect of the amount charged and of the average population income was identified, predicting changes in aggregate demand and in income-specific demand. For instance: if we consider two countries both adopting a 1 Euro co-pay charge on a (not easily substitutable) product and whose average income differs by 20%, we expect the demand to be almost 3% lower in the country with the lower income than in the country with the higher income. **CONCLUSIONS:** Under general market assumptions, it is possible to build models that estimate the potential impact of copay charges. These models can be used to help design health policies and market strategies.

PP2
MULTINATIONAL CONSISTENCY OF A DISCRETE CHOICE MODEL IN QUANTIFYING HEALTH STATES FOR THE EXTENDED 5-LEVEL EQ-5D

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OBJECTIVES: To investigate the feasibility of choice experiments for EQ-5D-5L states using computer-based data collection, and to examine the consistency of the estimated parameters values derived after modeling the stated preference data across countries in a multinational study. **METHODS:** Similar choice experiments were executed in Canada, England, The Netherlands, and United States (US). Interactive software was developed to standardize the format of the choice tasks across countries, except for England where face-to-face interviewers were used. The choice task required respondents to choose between two sub-optimal health states. A Bayesian design was used to generate 200 pairs of states that were randomly grouped into 20 blocks. Each respondent completed one block consisting of 10 pairs. A main-effect alternative-specific multinomial probit regression model was used to estimate regression coefficients and to derive values for each health state that capture the relative differences in levels between states. **RESULTS:** In total there were 1775 respondents, at least 400 respondents from each country, who completed 17750 paired comparisons, resulting into 35500 assessed health states. The mean time to perform one choice task was between 29.2 (US) and 45.2 (England) seconds. All regression coefficients were statistically significant, except level 2 for Usual Activities in The Netherlands (p=0.51). Three regression coefficients with illogical ordering were observed (The Netherlands: level 3 Pain/Discomfort, England: Level 3 Usual Activities & Pain/Discomfort). Predictions for the complete set of 3125 EQ-5D-5L states were similar for the four countries. Intra class correlation coefficients between the countries were high: from 0.89 (England vs. US) through 0.99 (Canada vs. US). **CONCLUSIONS:** This proof of concept study indicates that computer-based choice tasks for the EQ-5D-5L in the general population are feasible and parameter of the choice tasks estimates are generally consistent and logical, and the estimated values are largely consistent between the 4 countries.

PP3
CAN THE USE OF SOCIAL MEDIA AND MOBILE APPS IMPROVE PATIENT KNOWLEDGE OF DISEASE AND HEALTH OUTCOMES? A SYSTEMATIC REVIEW

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OBJECTIVES: The use of interactive social media (SM) based on Web 2.0 technology, e.g. Twitter, Facebook, MySpace; and mobile apps, is increasing but its role in improving patient knowledge of their disease and its management is unclear. We conducted a systematic review to assess the evidence for health benefits from SM. **METHODS:** We searched MEDLINE and EMBASE for relevant articles published in the last five years that used words synonymous with SM; patient, carer, or parents' preferences, opinions or views; pharmacological interventions; and disease. We included comparative studies or systematic reviews on the use of any SM by patients, that measured differences in knowledge about disease, uptake of pharmacological interventions, or clinical outcomes from better management of disease. Articles were excluded if they reported only the use of SM by health care professionals, or if they were case studies, narrative reviews or expressed expert opinions. **RESULTS:** We identified 3,232 unique abstracts, 24 of which reported the use of interactive, internet-delivered programs (n=13), Facebook (n=4), and mobile apps (n=3) , for improving health outcomes of patients with cancer, or inflammatory, mental health, musculoskeletal, neurologic, ophthalmologic, or sexual health-related disorders. Patients receiving SM-based interventions showed improved knowledge of their disease, and better clinical outcomes compared with controls. Two additional studies reported on the use of SM aimed at increasing knowledge, and self-efficacy in parents of children with cystic fibrosis. Overall, the studies showed that SM-based interventions improved knowledge of disease and clinical outcomes compared with control groups. **CONCLUSIONS:** Surprisingly little research has been conducted on the value of SM to aid and support patients. What evidence exists suggests that SM tools offer health benefits. fFrther work is needed to confirm these effects and to assess how best the tools might increase patients' knowledge about disease, treatment adherence and clinical outcomes.

PP4
THE IMPORTANCE OF PATIENT REPORTED OUTCOMES IN REIMBURSEMENT OF ORPHAN PRODUCTS IN EUROPE

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OBJECTIVES: To determine the importance of patient reported outcomes (PROs) in the reimbursement of orphan drugs in Europe and identify any HTA authority preferences for particular PRO measures. **METHODS:** All 31 products assigned an orphan designation by the European Medicines Agency (EMA), between January 2009 and May 2013, were evaluated against the following criteria: approval for marketing, submission for reimbursement/price negotiation to NICE, SMC, G-BA, and HAS, presence or absence of PROs, approval or rejection of reimbursement application. Where available, HTA guidance documents resulting from the applications were reviewed in detail to determine the impact of PRO measures on the reimbursement decision. **RESULTS:** Of the 31 products assigned an orphan designation, 26 were granted marketing authorisation by the EMA. Eleven products were submitted to NICE for reimbursement in England of which 7 submissions contained PROs and 6 were approved. In Scotland, 11 products were submitted for reimbursement to the SMC and of the 7 submissions containing PRO data, 3 were recommended for reimbursement. One submission is still pending. In Germany, 7 products were submitted to the G-BA of which 5 contained PROs and were allowed to enter into price negotiations. The French HTA authority, HAS, evaluated 20 submissions of which 9 contained PROs and 19 were approved. **CONCLUSIONS:** The results of our assessment of EMA approved orphan drugs indicates that a great deal of variation exists across Europe with respect to the evaluation of orphan drugs for reimbursement or price negotiation. In some countries, reimbursement is largely independent of evidence of reported patient benefit while in others, where evidence of economic value is critical for success, robust PRO data are essential.

RESEARCH PODIUM PRESENTATIONS – SESSION II
RESEARCH ON METHODS – CLINICAL STUDIES

CL1
A COMPARISON OF METHODOLOGIES FOR ESTIMATING SURVIVAL IN PATIENTS TREATED WITH SECOND-GENERATION TYROSINE-KINASE INHIBITORS (TKIS) FOR CHRONIC MYELOID LEUKAEMIA (CML)

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OBJECTIVES: NICE have previously recommended nilotinib, but not dasatinib, as a first-line (TA251) and second-line (TA241) treatment in chronic phase (CP) CML. Within these appraisals, different methods were used to estimate overall survival (OS). Bosutinib, a potent dual Src/Abl TKI, is undergoing a NICE appraisal in second-line or later CML (ID495). The objective is to review the OS methods used and assess their impact on cost-effectiveness and recommendations in CML appraisals. **METHODS:** We identify the methodologies used for estimating OS in TA241 and TA251 and investigate the impact of using these to estimate OS for the TKIs, including bosutinib, in relapsed/refractory CML. Finally, we consider the implications of the various methodologies on the cost-effectiveness results and recommendations in previous and future NICE assessments of TKIs for CML. **RESULTS:** The base-case in TA241 used a surrogate relationship between response (MCyR) and OS

to derive OS estimates for nilotinib and dasatinib of 13.0 and 13.4 years respectively (second-line CP). Using the same approach for bosutinib gives an OS of 12.8 years (third-line CP). The base-case in TA251 used a cumulative approach, where OS is equal to the duration of treatments in the pathway. If this method is applied to the TKIs in second-line CML (TA241), OS is reduced to approximately 9.4 and 10.1 years for nilotinib and dasatinib respectively (second-line CP). Similarly, bosutinib OS (third-line CP) is also reduced using this method and a substantial increase in the ICER is seen. **CONCLUSIONS:** There are methodological inconsistencies in NICE's assessments of TKIs for CML. Applying the OS methodology from TA251 to TA241 may have led to nilotinib not being recommended for routine use in the NHS. The impact of new methodologies on previous appraisal results and recommendations should be considered when assessing the validity of a new approach.

CL2
ADDRESSING HETEROGENEITY IN BASELINE RISK OF COPD EXACERBATIONS USING META-REGRESSION

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OBJECTIVES: To evaluate differences across randomized controlled trials (RCTs) concerning interventions for moderate to severe chronic obstructive pulmonary disease (COPD) in terms of baseline exacerbation rates and the association with treatment effects by means of a network meta-analysis (NMA). This NMA is performed based on RCTs evaluating the long-acting bronchodilators indacaterol 75/150/300µg OD, salmeterol 50µg BID, formoterol 12µg BID, tiotropium bromide 18µg/5µg OD, and glycopyrronium bromide 50µg OD. **METHODS:** The rate of moderate or severe exacerbations was extracted from RCTs identified with a systematic literature review. A Bayesian NMA was used to synthesize the treatment effects of the different trials. The association between treatment effects and baseline exacerbation rate with placebo was assessed with a meta-regression model assuming a constant treatment-by-baseline risk interaction term. **RESULTS:** Twenty-four RCTs were included that differed mainly in terms of smoking status, COPD severity, use of inhaled corticosteroids, exacerbation definition, and exacerbation history. Across the RCTs the rate of exacerbations per patient year for patients in the placebo arm ranged from 0.40 to 1.91. Baseline risk was negatively associated with the rate ratios reflecting treatment effects across the RCTs. The coefficient for baseline risk was -0.35 (95% credible intervals: -0.49, -0.18). **CONCLUSIONS:** Based on a NMA of RCTs regarding the efficacy of long-acting bronchodilators in terms of the rate of exacerbations per patient year, baseline risk of exacerbations acts as a significant treatment effect modifier and should be accounted for in the model.

CL3
VALIDATION OF SURROGATE ENDPOINTS IN ADVANCED SOLID TUMOURS: SYSTEMATIC REVIEW OF STATISTICAL METHODS, RESULTS, AND IMPLICATIONS FOR POLICY MAKERS

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OBJECTIVES: Licensing and reimbursement of anticancer drugs should rely on evidence from patient-relevant endpoints such as overall survival (OS). Nevertheless, evidence from surrogate endpoints may also be useful, as it may expedite the regulatory approval and coverage decisions of new therapies. It is therefore essential that candidate surrogate endpoints be properly validated. However, there is no consensus on statistical methods for such validation and on how the evidence thus derived should be applied by policy makers. **METHODS:** We review meta-analyses of therapeutic interventions against advanced solid tumours published until December 2012 that quantified the statistical association between progression-free survival (PFS) or time-to-progression (TTP) and OS. We assessed the suitability of the two surrogates using three current surrogate validation frameworks: Bucher's framework, the German Institute of Quality and Efficiency in Health Care's (IQWiG) framework and the Biomarker-Surrogacy Evaluation Schema (BSES3). **RESULTS:** Thirty-one meta-analyses were included which employed a variety of statistical methods to assess surrogate validity. The strength of the association between PFS or TTP and OS was generally low. The level of evidence (observation-level vs. treatment-level) available supporting an association between PFS or TTP and OS varied considerably by cancer type, by evaluation tools and was not always consistent even within one specific cancer type. **CONCLUSIONS:** Not in all solid tumours the treatment-level association between PFS or TTP and OS has been investigated. According to the IQWiG's framework, only PFS achieved acceptable evidence of surrogacy in metastatic colorectal and ovarian cancer treated with cytotoxic agents, whereas in no indication did the two candidate endpoints achieve good evidence of surrogacy according to BSES3. Our study emphasises the challenges of surrogate-endpoint validation and the importance of building consensus on appropriate statistical techniques to examine surrogacy and on the development of evaluation frameworks for policy makers.

CL4
FRAMEWORK FOR EVIDENCE ASSESSMENT BASED ON GRADE AND APPLICATION TO HPV VACCINATION IN MALES IN THE EUROPEAN HEALTH CARE CONTEXT

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OBJECTIVES: To develop and apply an extended framework for evidence assessment based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach using the example of male human papilloma virus (HPV) vaccination Europe. **METHODS:** A pan-European multidisciplinary expert group was established to develop an extended GRADE framework that includes explicit assessment of cost-effectiveness, medical needs, and patient aspects, ethical and social issues. Using an expert panel process, we assessed the feasibility of using this framework by applying it to male HPV vaccination in Europe. Studies were assessed using the specific framework tools; results and feasibility were discussed; and consensus was achieved through a modified Delphi method. **RESULTS:** We identified three advisory committees (ACIP/USA; NACI/Canada; STIKO/Germany) using GRADE for vaccines assessment. Institutions handled data beyond vaccine efficacy and safety differently and did not formally grade economic evidence. We adopted the grading methodology of ACIP for the key factor 'Benefits and Harms' and developed modules for grading evidence type and quality of economic evaluations ('Economic Evaluation') and for systematically assessing epidemiology, disease burden and unmet medical needs, as well as ethical, social and patient aspects ('Values and Preferences'). The feasibility test demonstrated that all framework components were feasible in the case of HPV vaccination. Overall evidence type for cost-effectiveness was low with uncertainty in results. Cost-effectiveness was best, when all HPV-related diseases and outcomes were included and when assuming low coverage in females and lower vaccine prices. **CONCLUSIONS:** The GRADE approach is applicable in assessing vaccinations and was successfully applied to HPV vaccination in males. The assessment of benefits and harms can be extended by explicit assessment of the evidence on cost-effectiveness and other key factors including unmet medical needs, and ethical, social and patient aspects. This extended framework can better inform policy- and decison makers.

CARDIOVASCULAR DISEASE OUTCOMES RESEARCH STUDIES

CV1
CHALLENGES IN MODELLING THE COST EFFECTIVENESS OF INTERVENTIONS IN CARDIOVASCULAR DISEASE

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OBJECTIVES: Modelling is essential in performing economic evaluations for various reasons. For example, modelling is necessary if extrapolation of short-term or intermediate results to long-term outcomes is required and numerous strategies need to be evaluated without direct evidence. However, modelling inherently poses challenges that need to be dealt with since models always represent a simplification of reality. The aim of this study is to identify and analyse the challenges in modelling the cost-effectiveness of cardiovascular disease (CVD) interventions. **METHODS:** A questionnaire was sent to 40 corresponding authors (systematically selected) of recent model-based economic evaluations of CVD interventions published in high-impact cardiovascular, health economics and general medical journals. Respondents were asked to provide their own challenges and also rank the importance of challenges identified using a pilot version of the questionnaire distributed to 7 experienced researchers. Furthermore, we analysed the discussion sections of the papers to identify unmentioned challenges. Solutions, if available, were based on input from the respondents and the recommendations of the ISPOR-SMDM task force. **RESULTS:** The systematic literature search identified 1720 potentially relevant articles. The limit of 40 authors was reached after screening 294 titles and abstracts. Beside the challenge of lack of data, preliminary results show that it was difficult to obtain a sufficiently valid, precise and accurate cost-effectiveness estimate due, for example, to interrelating clinical outcomes or extrapolating from surrogate outcomes. Both challenges often exist in CEAs evaluating CVD prevention strategies. **CONCLUSIONS:** The preliminary results of this study showed examples of CVD modelling challenges encountered during studies published in high-impact journals. Modelling guidelines do not provide sufficient assistance in resolving all challenges but it is probably unrealistic to expect this. Some of the reported challenges are specific to the type of intervention and disease, but most challenges are present in all types of interventions and diseases.

CV2
APPLICATION OF BEHAVIOURAL ECONOMICS TO THE UNDERSTANDING OF ADHERENCE: DOES AN INDIVIDUAL'S TIME PREFERENCE INFLUENCE ADHERENCE TO MEDICATIONS?

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OBJECTIVES: There is general support that individual time preference affects health-related behaviours. People with a high, positive time preference value their immediate health higher than future health, even if presented with extreme scenarios of intertemporal choice. We hypothesised that adherence to medication requires trade-offs between immediate and delayed health benefits. Patients with lower time preference rates may be more adherent to medication as they place a higher value on the future benefits of adherence. **METHODS:** Hypertensive adult patients across Europe were invited to complete a web-based survey that had been translated and piloted. Patients' time preference was assessed (4-items) to calculate individual discount rates (%) in both short term (3-years) and medium term (6-years). Medication adherence was measured using the Morisky questionnaire (primary analysis) and the Medication Adherence Report Scale (MARS, secondary analysis). Sample size calculation, based on 5% one-sided confidence, assuming 30% non-adherence with Morisky measure indicated n=323 per country. Missing data were imputed using multiple imputation in STATA. The significance of the association with adherence was assessed using the Wald test statistic. **RESULTS:** 969 patients completed the questionnaire across England, Wales and Hungary, 79% of possible responses were observed. Short and medium term time preference rates in England, Wales and Hungary were in the expected directions, but the relationship was not statistically significant. Based on Morisky adherence - Wales (short): adherent 8.7%, non-adherent 9.4% (p=0.541); (medium): adherent 4.7%, non-adherent 5.0% (p=0.611). England (short): adherent 7.8%, non-adherent 9.5% (p=0.163); (medium): adherent 3.7%, non-adherent 4.5% (p=0.095). Hungary (short): adherent 19.0%, non-adherent 18.2% (p=0.504); (medium): adherent 8.9%, non-adherent 8.6%

(p=0.596). **CONCLUSIONS:** Time preference rates were aligned with those in the published literature but the association between time preference and adherence was non-significant in both primary and secondary analyses at an individual country level.

CV3
PATTERNS OF GENERIC AND PROPRIETARY PRESCRIBING OF STATINS OVER TIME IN ENGLAND
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OBJECTIVES: Given economic pressure on UK National Health Service resources, it has been recommended that general practitioners prescribe more low-cost, generic drugs as opposed to high-cost, proprietary drugs when a substitution can be made without compromising patient care. One of the Better Care Better Value (BCBV) indicators of good prescribing practice proposed by the NHS Institute for Innovation and Improvement is an increase in the prescription of low-cost drugs for lipid modification. The objective of this analysis was to evaluate patterns of generic and proprietary prescribing of statins from 2007–2012 inclusive. **METHODS:** Prescription Cost Analysis databases from data.gov.uk were reviewed between 2007–2012. Data on the number of prescription items dispensed each year in the community in England for simvastatin and atorvastatin (as commonly-prescribed examples) were extracted, along with each drug's preparation class: drugs prescribed and available generically, or drugs prescribed and dispensed by proprietary brand name. For both simvastatin and atorvastatin, the proportions of prescription items in the different preparation classes were compared each year. **RESULTS:** Proprietary simvastatin prescription items as a proportion of all simvastatin prescription items decreased each year, from 2.87% in 2007 (843,000 proprietary items) to 1.76% in 2012 (752,000 items), representing a proportional decrease of 39% in the 6-year period assessed. Proprietary atorvastatin prescription items as a proportion of all atorvastatin prescription items were close to 100% between 2007–2011 (approximately 11 million proprietary items each year), but fell to 30.55% in 2012 (3.9 million items), coinciding with the expiry of atorvastatin's patent in May 2012. **CONCLUSIONS:** In England, prescribing of high-cost proprietary items for these two examples of lipid-modifying drugs has decreased since 2007, suggesting that the BCBV prescribing indicator for statins is being met. Such reductions, particularly as seen with atorvastatin in 2012, are likely to have a significant budget impact.

CV4
IMPACT OF SHORT PERIODS WITH IMPROVED OR WORSENED INR CONTROL ON LIFE EXPECTANCY AND QALYS IN PATIENTS WITH ATRIAL FIBRILLATION
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OBJECTIVES: Warfarin-treated patients with poor international normalized ratio (INR) control, measured with time in therapeutic range (TTR) or the standard deviation of transformed INR (SDT_{INR}), have an increased risk for clinical events. To what extent only a short period with an altered INR control may influence outcomes remains unknown. This study assessed the impact of transient periods of improved or worsened INR control on life expectancy and quality-adjusted life years (QALYs) among warfarin-treated patients with atrial fibrillation (AF) using both metrics. **METHODS:** Warfarin-treated patients with AF, registered in the patient record system Journalia during years 1985-2000, were included. Information on all-cause mortality was collected from the Cause of Death Register. Scenarios where patients were assumed to have a transiently altered INR control during 30 days were modeled statistically using hazard functions, and the impact on remaining life expectancy and QALYs was assessed. **RESULTS:** When using SDT_{INR}, a 70-year old man within the 2.5th worst INR control percentile was estimated to gain 10.8 days of life or 0.0168 QALYs from a 30-day improvement in INR control to that of an average 70-year old man. Correspondingly, 15.5 days of life or 0.0196 QALYs would be lost if a 70-year old man within the 2.5th best INR control percentile would have an average INR control during 30 days. The magnitudes were smaller when TTR was used to determine INR control. **CONCLUSIONS:** Even short periods of altered INR control is expected to have impact on life expectancy and QALYs among patients with AF.

MEDICAL DEVICE & DIAGNOSTIC RESEARCH

MD1
COMPARING VIRTUAL COLONOGRAPHY WITH CONVENTIONAL COLONOSCOPY FOR COLORECTAL CANCER SCREENING: WHAT ARE THE DRIVERS OF COST-EFFECTIVENESS?
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OBJECTIVES: The majority of recent cost-effectiveness reviews concluded that computerized tomographic colonography (CTC) is not a cost-effective Colorectal Cancer (CRC) screening strategy yet. The objective of this review is to examine cost-effectiveness of CTC versus optical colonoscopy (COL) for CRC screening and identify the main drivers influencing cost-effectiveness due to the emergence of new research. **METHODS:** A systematic review was conducted for cost-effectiveness studies comparing CTC and COL as a screening tool and providing outcomes in life-years saved, published between January 2006 and November 2012. The following databases were searched: PubMed, Science Direct, Cochrane Library and the York Centre for Reviews and Dissemination databases. The search methodology was in line with PRISMA guidelines, including the use of the PICOS review system. **RESULTS:** Nine studies were included in the review. There was considerable heterogeneity in modelling complexity and methodology. Different model assumptions and inputs had large effects on resulting cost-effectiveness. The most important assumptions that influenced the cost-effectiveness of CTC and COL were related to CTC threshold-based reporting of polyps, CTC cost, CTC sensitivity for large polyps, natural history of adenoma transition to cancer and importantly, adherence. CTC was found to be cost-effective in three studies, assuming the most favourable scenario. **CONCLUSIONS:** CTC has the potential to be a cost-effective CRC screening strategy when compared to COL. There is a strong need for a differential consideration of patient adherence and compliance to CTC and COL. Recent research shows that laxative-free CTC screening has the potential to become a viable alternative screening method for CRC as it can improve patient uptake of screening. This project is supported by the German Federal Ministry of Education and Research (BMBF) as part of the National Cluster of Excellence, Medical Technologies – Medical Valley EMN' (Project grant No. 13EX1013B).

MD2
MARKET ACCESS OF IMPLANTABLE MEDICAL DEVICES: EVIDENTIARY REQUIREMENTS ACROSS GLOBAL MARKETS
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OBJECTIVES: With tightening health system budgets, medical devices (MDs) are being increasingly scrutinized for their impact on overall health care cost. The evidence bar for implantable MDs is particular high since most implantable devices are not reimbursed separately by payers, but via direct bundled payments to the provider. To characterize that trend, the objectives of this study were to: 1) Identify specific evidence criteria that maximally impact the payer decision, 2) Note differences in HTAs across global markets, and finally 3) Outline differences in evidence requirements between drugs and devices. **METHODS:** A multimarket review of implantable MD HTAs and reimbursement decisions published from 2008-2013 was conducted. Identified by HTA Watch, HTAs included those from Australia, Belgium, Canada, France, Germany, Italy, the UK and the US. They spanned a variety of indications, including cardiovascular, orthopedic, neurological, trauma, among others. HTAs and reimbursement decisions were characterized for clinical and economic evidence requirements and apparent correlations and/or impacts on ultimate agency recommendation. **RESULTS:** Evidence criteria evaluated by HTA agencies and payers primarily included: 1) Availability of supportive randomized controlled trials (RCTs), 2) Safety, 3) Efficacy/long-term outcomes, 4) Cost/cost-offsets/budget impact, and 5) Quality of-life improvement. In contrast to drug HTAs, clinician training and learning curve effects were often evaluated. Importantly, agencies recognized the challenge in demonstrating statistically- and clinically-significant evidence of improvement in outcomes. As such, many MDs were recommended on a restricted basis to specific patient subpopulations or on a coverage based on continued evidence development. While requirements considered most critical were largely uniform across global markets, regional nuances impacted the ability to obtain favorable reimbursement of implantable devices. **CONCLUSIONS:** Similar to drugs, MDs face rising hurdles in terms of demonstrating value, both clinical and economic. Optimal global market access for implantable MDs hinges on monitoring evolving evidentiary requirements and on carefully planning to collect evidence early in the developmental cycle.

MD3
DECISON MAKING UNDER UNCERTAINTY: COVERAGE WITH EVIDENCE DEVELOPMENT IN THE CONTEXT OF MEDICAL DEVICES
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OBJECTIVES: Coverage with evidence development (CED) is increasingly being used to provide provisional coverage for promising, but unproven, interventions, while additional data are generated. This study aimed to explore the application of CED in the context of devices. **METHODS:** First, a literature review was conducted on international CED schemes and the CED approach more generally. In total, 50 articles were gathered and reviewed. Second, semi-structured telephone interviews were conducted with different expert groups (payers/HTA bodies, industry, and academics/policy analysts) to better understand the use of CED in different jurisdictions; identify and explore device CED case studies; and, gather expert opinion on the challenges associated with the CED approach and potential strategies to improve current policy and practice. A total of 25 experts were invited to participate, of which 20 (80%) agreed and were interviewed. **RESULTS:** Canada, the UK, and US have the most experience with CED applied to devices; Germany and The Netherlands have both recently introduced new CED policies for devices and procedures. Devices that have undergone CED in these jurisdictions include ICDs, stents, TAVI, laparoscopic surgery, and spinal cord stimulators. While there are distinct differences in the national approaches to CED, common challenges were identified: 1) establishing a clear framework for initiating, overseeing, and stopping CED studies, 2) identifying and applying appropriate study methods, 3) funding CED studies, 4) incentivizing studies, and 5) applying new evidence to inform coverage decisions. **CONCLUSIONS:** Devices are viable candidates for CED, given some of their unique characteristics and often uncertain evidence base at the time of coverage determination. However, improvements are needed, including enhanced clarity and predictability of CED selection criteria and processes, greater stakeholder collaboration, new models to fund studies and collect data, better incentives for physicians to engage in studies, and strengthened requirements for use of new evidence in coverage policies.

MD4
QUALITY CRITERIA FOR THE DEVELOPMENT OF IMPLANT REGISTRIES
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OBJECTIVES: During the last few years, there has been a steady increase in the number of implant registries, mainly in the field of arthroplasty. The benefit of a registry depends on its content and quality. However, there are no further data requirements, legal and financial issues or requirements for the organizational

procedure specified for implant registries in general. Therefore, the aim of this work is to identify quality criteria for the design and development of implant registries and to develop a minimal data set. **METHODS:** The systematic literature search was performed in different databases (Pubmed, Medline, the Cochrane Library, Scopus, Embase as well as the CRD York database) and different journals. **RESULTS:** Ten articles were identified that describe a general implant registry design and structure as well as 45 articles about the creation of specific registries. Most recommendations for the organization of implant registries could be found in the field of arthroplasty. To generalize the results, it can be said, that all registries have to deliver a minimal data set including prostheses, patient and surgical procedure details. The geographical area, length and periodicity of data collection, number of patients enrolled, the composition of the team as well as information about security and confidentiality of data should be reported. **CONCLUSIONS:** Well-structured registries are a cornerstone of the regulatory process of medical devices and a major tool for decison makers and managers. However, only a small number of papers that describe specific requirements for the construction of an implant registry could be identified. With the establishment of clear guidelines, the outcomes of the implant registries can be fundamentally improved. This project is supported by the German Federal Ministry of Education and Research (BMBF) as part of the National Cluster of Excellence, Medical Technologies – Medical Valley EMN' (Project grant No. 13EX1013B).

PRICING STUDIES

PR1

PRICE DIFFERENCES TRIGGERED BY THE AVAILABILITY OF BIOSIMILARS IN DEVELOPED COUNTRIES

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OBJECTIVES: The goal of this study is to analyse price differences triggered by the availability of biosimilars in developed pharmaceutical markets. **METHODS:** 1) Market availability of biosimilars in the following markets was studied: Australia, Canada, France, Germany, Italy, Spain, UK, Japan and the United States. Biosimilars were selected based on their availability in these markets, and 2) Ex-factory price differences at launch between biosimilars and their originator counterparts were analysed. **RESULTS:** Price differences between biosimilars and their originator counterpart were on average 25%. One exception aside, biosimilars always trigger double digit price differences. Given the limited availability of biosimilars, it is too soon to say if results will be consistent over time. Nevertheless, the general trend shows that large price differences are observed in Canada and the US (at least 35%) and lower trends in Australia (around 16%). In the top 5 European pharmaceutical markets, price differences range between 17% and 30%. In Japan, price differences are also high, 29% on average. It should also be highlighted that the market entry of biosimilars does not always trigger the price of their originator to drop; in rare occasions only are their prices brought into line. **CONCLUSIONS:** Owing to the fact that biologic drugs are commonly expensive and with double digit price differences between biosimilars and their originator counterpart, the market entry of biosimilars should enable governments to generate significant savings. Nevertheless, a limited number of biosimilars are at the moment approved and in addition to the fact that no legislation is in place in the US, there is no sign of improvement in the other countries studied. As a consequence, savings will only be achieved if governments incentivise the development of biosimilars as well as their use.

PR2

PHARMACEUTICAL POLICIES, REGULATION AND EFFICIENCY

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OBJECTIVES: In the context of ever increasing demand and expenditure for health services it is important to identify policies which may maximise efficiency. Often, pharmaceuticals (approximately 20% of total health care expenditure) are a primary target for achieving efficiencies. This study aims to study the efficiency of pharmaceutical control policies. **METHODS:** Data on pharmaceutical policies and markets across 65 countries were collected from the published literature, with emphasis on the following domains: pricing, reimbursement, dispensing, expenditure and demand control. In each domain, policies were classified and through a multiple-country expert survey were graded for the degree of regulation. Countries were clustered according to their policy mix. Principal component analysis (PCA) served to group policies into three components: pricing policies, reimbursement policies and demand and cost control policies. Regression analysis with pharmaceutical expenditure as % of GDP as dependent variable was used to analyse the efficiency of policies. Independent variables were life expectancy, dependency ratios, mortality rates, GDP per capita and health system type. **RESULTS:** Spearman correlation coefficients indicated that there was no statistically significant association between total pharmaceutical expenditure as % of GDP and regulation in the coverage, pricing, reimbursement, dispensing policy and system type. A statistically significant positive correlation between regulation and indirect price and cost controls (0.334, p=0.028) and demand controls (0.333, p=0.019) implies that more regulation in these domains is associated with higher expenditure. Following the PCA, regulation in demand control policies was associated with higher expenditure (0.342, p=0.025) and the same applies for the aggregate of the components (0.314, p=0.040). In regression analysis the coefficients (p-value) were pricing:-0.003(0.950), demand control:0.062(p=0.067), reimbursement: -0.057(0.439), mortality: 0.001(0.414), Life Expectancy: 0.062(0.474), elderly ratio: 0.689(0.774), GDP-per-capita: -1.788(0.017). **CONCLUSIONS:** A variety of policies were developed recently to control pharmaceuticals. More regulation does not appear to increase efficiency or decrease expenditure.

PR3

VARIABILITY IN HYBRID DRUG AVAILABILITY AND PRICING IN EUROPE

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OBJECTIVES: Medicinal products where active substance, strength, form, or administration route have been modified differ from generic drugs as bioequivalence cannot be demonstrated. In Europe, these 'hybrid' products have a clear registration pathway (Directive 2001/83/EC) requiring investment in pre-clinical and clinical trials. However; beyond the regulatory pathway, pricing and market access remains a national matter and few countries have specific methods to evaluate hybrids; both innovative- and generic-like prices may result. This study evaluated hybrid price differences and consequences for availability of hybrids across Europe. **METHODS:** Using IMS MIDAS data and the HMA database of registered drugs, we screened 5,000 products to identify 40 hybrid products which were significantly differentiated from the reference product, launched between 2008-2012 and analysed their prices and availability based on sales achieved, versus the reference product within and across 10 European markets. **RESULTS:** Hybrid prices vary widely, but most frequently, generic rules are applied, limiting the interest of companies to make hybrids available across European markets. There is wide variation in availability of hybrids across markets, suggesting a decision not to launch in markets where prices are particularly unfavourable. Countries applying fixed generic pricing rules appear to have fewer hybrids. Yet where they are launched, hybrids are not classified as generics, so uptake is inhibited by non-substitution rules and prescribing quotas. **CONCLUSIONS:** The lack of clear evaluation criteria and pricing variability within and across countries are barriers to the availability of hybrid products to patients in Europe. To the degree that such products better meet patient needs versus generic medicines, these barriers reduce patient welfare and prescriber choice. In a context where patient-oriented outcomes are increasingly seen as important, hybrid drugs have a role to play given their ability to improve administration, compliance, convenience and in some cases improve safety and efficacy. Consequently, clear rules for hybrid evaluation, pricing and access are desirable as they would improve patient care and reduce uncertainty for hybrid manufacturers.

PR4

OVERVIEW OF COVERAGE WITH EVIDENCE DEVELOPMENT IN SWEDEN

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OBJECTIVES: Coverage with evidence development (CED) in Sweden has become common over the last decade. It is considered as a tool to address uncertainty. The objective of this research is to assess from 2005 to 2012 CED in Sweden. **METHODS:** We downloaded available CED from pricing authority (TLV) database, and extracted detailed information in an ad hoc grid developed for that purpose. The following information was extracted: date of product approval, name, indication, date of CED installation, end of CED, type of evidence to be generated, limitation of initial file supporting the need of additional evidences. **RESULTS:** A total of 28 cases were retrieved covering 9 main disease areas. Eleven were for orphan drugs and 10 for Central nervous system (CNS) disorders including depression anxiety, epilepsy, pain, ADHD, schizophrenia, restless syndrome and Parkinson disease. Other were classified as follow, 5 for cardiovascular disorders, 3 oncology, 2 diabetes, 2 respiratory disorders and 5 others. The main drivers to request CED were weak cost-effectiveness model (14 cases) driven by uncertainty about utility, patients benefit, transition probabilities, model structure etc. The second reason was low relevance of clinical evidence for clinical practice (8 cases), followed by long term efficacy extrapolation (5 cases) and others mainly related to comparative effectiveness, daily dosage, safety, target population, etc. (11 cases). For each CED more than one driver could be identified. Requirements were mostly real world evidence generation. **CONCLUSIONS:** CED in Sweden is likely to be driven more by uncertainty than drug prices due to low involvement of oncology, inflammation and other disease area where biologics are prescribed. Orphan drugs represent a leading target for CED as often little information is available at time of launch. Most CED are not finalised to assess the actual CED impact on long term coverage.

RESEARCH ON METHODS – PRO/QOL STUDIES

QL1

MAPPING THE CCQ ONTO EQ-5D SCORES (IM)POSSIBLE?

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OBJECTIVES: Studies assessing the effectiveness of new Chronic Obstructive Pulmonary Disease (COPD) treatments commonly use disease-specific health-related quality-of-life (HR-QoL) instruments such as the Clinical COPD Questionnaire (CCQ). However, for the economic evaluations, utility data is necessary. This study aims to develop a model to predict mean utility values for a group of COPD patients using CCQ data. **METHODS:** We combined the data from two trials (RECODE and GO-AHEAD) including over 5000 observations with a broad range of disease severity. Data was randomly split into an estimation and validation sample. The overlap between the CCQ and EQ-5D was assessed using principal component and correlation matrix analysis. Different types of models were created with increasing complexity. We analysed the effect of using different observations of the same patients as unique observations and performed a sensitivity analysis using different EQ-5D value sets to estimate EQ-5D utilities. The external validity was tested with the dataset of the MARCH trial. **RESULTS:** The principal component analyses showed a poor correlation of the dimension pain/discomfort with any of the CCQ items and the CCQ items cough and produce phlegm did not load onto any EQ-5D dimension. The model using ordinary least square with the individual CCQ items as dummy variables, controlled for sex, resulted in the best predicted performance. The mean

absolute error was on average 0.15 but was considerably high (>0.34) if the observed EQ-5D value was below 0.5. Sensitivity analysis revealed that different EQ-5D value sets resulted in different algorithms but similar predicting ability. **CONCLUSIONS:** Our study showed that there are conceptual differences between the CCQ and EQ-5D and mapping should be considered as second-best option compared to directly collected EQ-5D data. Furthermore, the mapping performance seems to depend on the severity of the study population.

QL2

MEASURING PATIENT-RELEVANT TREATMENT BENEFIT IN DERMATOLOGY – DEVELOPMENT AND VALIDATION OF THE SHORT QUESTIONNAIRE "PATIENT BENEFIT INDEX 2.0"

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OBJECTIVES: Evidence on patient-relevant treatment benefit is the main criterion for reimbursement decisions in many European countries. Usually, an increase of quality of life (QoL) during treatment is used as benefit indicator. The Patient Benefit Index (PBI) method, in contrast, evaluates benefit retrospectively: Before treatment, patients rate importance of treatment goals; after treatment, they rate goal achievement. This prevents any bias due to response shift which has repeatedly been found in pre-post QoL assessment. Here, we developed a short PBI version ("PBI 2.0") applicable to different skin diseases. **METHODS:** Treatment goal items for the PBI 2.0 were developed based on nine validated disease-specific PBI versions. Items were tested for content, completeness, and comprehensiveness in qualitative interviews with n=16 patients with atopic dermatitis, leg ulcers, psoriasis, and vitiligo. Items were revised on basis of patient feedback. The PBI 2.0 was tested for convergent validity, completeness, and congruence with disease-specific PBI versions in a cross-sectional study on n=379 patients with the above-mentioned diagnoses. **RESULTS:** The 74 disease-specific items could be condensed to 15 pilot items. Based on the qualitative interviews, we could reduce to 12 items. The majority of patients rated the PBI 2.0 to be comprehensible (93-98%, depending on diagnosis group), readable (94-100%), easy to answer throughout (78-90%), and complete (65-88%). Treatment goals mentioned as missing mostly concerned goals unrelated to benefit of medical treatment (e.g. information on the disease). The percentage of missing values ranged from 0.0% to 2.9%. PBI 2.0 preference-weighted global scores correlated significantly with QoL as measured with Dermatology Life Quality Index and EQ-5D (r=0.19 to 0.58). Convergent validity of the PBI 2.0 and the respective – about twice as long – disease-specific versions were equal, except for the vitiligo version. **CONCLUSIONS:** The PBI 2.0 is a qualitatively and quantitatively validated short questionnaire on patient-relevant treatment benefit in dermatology.

QL3

THE MEASUREMENT OF HEALTH-RELATED QUALITY OF LIFE: GERMAN FINDINGS FROM THE MULTI-INSTRUMENT COMPARISON (MIC) STUDY

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OBJECTIVES: Different multi-attribute utility (MAU) instruments are known to produce different values for "utility" and measure different constructs, despite the common label "utility". To date, the Multi-Instrument Comparison (MIC) project has been the largest comparative study of health and well-being instruments undertaken worldwide. Here we report the first results from the German branch of the study. **METHODS:** A total of 1269 German respondents (either healthy or suffering from defined chronic disorders, i.e., asthma, arthritis, cancer, depression, diabetes, hearing loss, heart disease) were recruited and participated in the study, completing various MAU instruments, including the EQ-5D, SF-6D, HUI3, 15D, QWB, AQoL(-4D and-8D). Cross-validation tests drew heavily on correlation. Preliminary findings, based upon Pearson correlation coefficients (indicating the extent to which changes in one variable correspond with changes in another), showed low correlations between measures of utility and measures of subjective well-being. While preferences might differ from subjective well-being, their correlation might be higher. Hence, a better measure should be intraclass correlation (ICC). **RESULTS:** Intraclass correlations between MAU instruments ranged from to 0.8 (HUI3 vs. AQoL-8D) to 0.4 (AQoL-4D vs. 15D). Linear regression results, reflecting the comparative performance of the various MAU instruments with regard to changes in measured utilities (as applied in standard cost utility analysis), and detailed results including pairwise comparisons of instruments, especially as to sensitivity to changes in a given dimension, will be presented. **CONCLUSIONS:** A major conclusion of the present study is that, despite some similarity in the mean scores, the instruments tested are dissimilar with regard to virtually all other criteria used to compare them. In effect, each instrument appears to measure a different construct of "health". Implications for the presumably "generic" measurement of "utility" may be far reaching and will be discussed.

QL4

PSYCHOMETRIC VALIDATION OF PERCEIVED DEFICITS QUESTIONNAIRE – DEPRESSION (PDQ-D) IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD)

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OBJECTIVES: The Perceived Deficits Questionnaire (PDQ) provides a self-report measure of cognitive dysfunction. The current work aims at assessing the psychometric properties of the PDQ adapted for MDD (PDQ-D). **METHODS:** A non-interventional, online panel survey with baseline assessment and 6-week follow-up of US and UK residents (aged ≥18 years) with and without MDD [diagnosed with depression by a physician and current Patient Health Questionnaire-9 (PHQ-9) score ≥10]. In addition to PDQ-D, the following instruments were included: Medical Outcomes Study Cognitive Functioning-Revised [MOS COG-R]; PHQ-9, Patient Global Impression of Severity [PGIS] and Change [PGIC]; SF-36 Health Survey [SF-36], Lam Employment Absence and Productivity Scale [LEAPS], Sheehan Disability Scale [SDS] and Work Productivity and Activity Impairment: Specific Health Problem [WPAI:SHP]. **RESULTS:** The study population consisted of 855 subjects at baseline (418 US and 437 UK), with MDD patients representing 49% of the sample in each country; 169 and 153 MDD patients were invited for the follow-up in the US and UK, respectively. Internal consistency was high for the total scale and for the four proposed subscales (Attention, Retrospective memory, Prospective memory, and Planning), with Cronbach's alpha ranging from 0.81 to 0.96. Convergent validity was supported by strong correlations with other measures of cognitive functioning (0.8 Pearson's coefficient) and moderate correlations with several construct measures known to be associated with cognitive functioning, including health-related quality of life, productivity at work, and other functional impairment (Pearson's coefficients ranging from 0.3 to 0.6), and by substantial differences in scores in subgroups known to differ in cognitive functioning impairment. The PDQ-D was also responsive to changes in depression symptom severity. Confirmatory factor analyses supported the scoring of a global scale for perceived cognitive functioning. **CONCLUSIONS:** The PDQ-D is a reliable, valid and responsive instrument for assessing MDD patients' perception of deficits related to cognitive functioning.

RESEARCH POSTER PRESENTATIONS – SESSION I
DISEASE-SPECIFIC STUDIES

INDIVIDUAL'S HEALTH – Clinical Outcomes Studies

PIH1

MOTHERS' OWN MILK FOR THE FEEDING OF PRETERM INFANTS: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: To conduct a systematic review to examine the incremental benefits of mothers' own milk (MM), with or without fortification, compared with donor milk (DM) and/or preterm formula (PF) for the nutritional support of preterm infants both in the neonatal intensive care unit (NICU) and following hospital discharge. **METHODS:** English-language studies published post-1990 were identified from electronic databases (Medline, EMBASE and Cochrane Library) and conference proceedings. Eligible studies enrolled infants with mean gestational age less than 35 weeks with no restriction on geographical location. **RESULTS:** Thirty-three unique studies met eligibility criteria: United States (n=12), Canada (n=2), Australia (n=2), Mexico (n=1), Israel (n=2), Europe (n=13) or multinational (n=1). There was a paucity of both RCT data (n=7) and studies which reported exclusive use of MM feeding (n=3). In addition, there was considerable heterogeneity between studies with regard to study design, duration of follow up and amounts of MM ingested, and a robust meta-analysis was therefore not feasible. However, a significant beneficial effect for MM over DM and/or PF for the incidence of sepsis, necrotizing enterocolitis (NEC) and longer-term neurodevelopment was reported in a number of individual studies. With regard to anthropomorphic outcomes of body weight, length and head circumference, there was no clear consensus on the effect of feeding regimen. Sixteen studies reported the relationship between the dose of MM received and outcomes; increased MM dosages in the feeding regimen were associated with significantly lower rates of sepsis, NEC, and hospital readmissions, reduced NICU costs, and improved neurodevelopment. **CONCLUSIONS:** Exclusive or high-dose MM with or without fortification is associated with short- and long-term beneficial effects in preterm infants. These results confirm MM to be the optimal nutrition for preterm infants and stress the importance of developing comprehensive strategies to overcome the challenges of providing MM and improving breastfeeding rates in preterm infants in the NICU.

PIH2

UTERINE-SPARING SURGICAL TREATMENT MODALITIES IN WOMEN WITH UTERINE FIBROIDS: A SYSTEMATIC REVIEW AND INDIRECT TREATMENT COMPARISON

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OBJECTIVES: To evaluate the safety and effectiveness of conservative surgical treatments for uterine fibroids in women who wish to preserve their uterus. **METHODS:** A systematic literature search of electronic databases (MEDLINE, EMBASE, CENTRAL) and grey literature up to October 2012 identified 5 RCTs (436 patients): 2 comparing uterine artery embolization (UAE) with myomectomy (MYO) and 3 comparing UAE with laparoscopic uterine artery occlusion (LUAO). Primary outcome measures included patients' satisfaction, re-intervention and ovarian failure rate. Secondary outcomes were clinical failure, hysterectomy and complication rates, hospitalization and recovery times, pregnancy rate, pregnancy complications and live-birth rate. Standard and network meta-analysis were performed on relevant outcomes. **RESULTS:** Of the three most popular uterine-sparing surgical treatments for fibroids, network meta-analysis showed that MYO and UAE resulted in higher rates of patient satisfaction and lower rates of clinical failure than LUAO in the first year after treatment [OR 2.56, 95%CrI 0.56-11.75, P(better)=11% and 2.7, 95%CrI 1.1- 7.14, P(better)=1%; 0.29, 95%CrI 0.06- 1.46, P(better)=7% and 0.37, 95%CrI 0.13- 0.93, P(better)=2% respectively]. Moreover, MYO resulted in lower re-intervention and hysterectomy rates than UAE and LUAO [0.08, 95%CrI 0.02- 0.27, P(better)<1%, 0.08, 95%CrI 0.01- 0.37 P(better)<1%); 0.16, 95%CrI 0.01-0.85 P(better)=2%, 0.15 95%CrI 0- 8.74 P(better)=16% respectively] even though the later techniques had an advantage over MYO due to shorter hospitalization and quicker recovery. There was no evidence of convincing difference between the three techniques in the number of women experiencing ovarian failure, minor or major complications. However, MYO may lead to better conception outcomes in

comparison to UAE (pregnancies: 3.44, 95%CI 1.18- 10.03; live-births: 3.02, 95%CI 1.00- 9.09). **CONCLUSIONS:** LUAO is less effective than UAE and MYO in the treatment of symptomatic fibroids for women who want to preserve their uterus. The choice between UAE and MYO should be based on individuals' short and long-term expectations.

PIH3

META-ANALYSIS OF BCG VACCINE EFFICACY FOR INFANTS IN IRELAND

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OBJECTIVES: BCG vaccination policy is greatly debated. An important issue for countries using the vaccine is to try and estimate any influence it has on the tuberculosis (TB) incidence in their population. The aim of this study is to estimate the effectiveness of the BCG vaccine in infants in Ireland. **METHODS:** We searched PubMed and Embase for studies assessing a relative reduction in TB events after vaccination in infants. Studies meeting relevant inclusion and exclusion criteria were sought. Observational data from Ireland was combined with raw data from studies identified in the literature in a random-effects meta-analysis model to estimate the relative risk (RR) of vaccine efficacy against pulmonary TB, extra-pulmonary TB (EPTB), TB meningitis and TB deaths. **RESULTS:** Two meta-analyses were found. The first meta-analysis reviewed identified 5 randomised control trials and 11 case control studies against pulmonary TB (Trials 0.26 95% CI 0.17, 0.38; Cases 0.48 95% CI 0.37, 0.62) and TB deaths (Trials 0.35 95% CI 0.14, 0.88). The second meta-analysis identified a further 7 case-control studies and evaluated BCG efficacy against EPTB (0.23 95%CI 0.13, 0.42] and TB meningitis (0.27 95%CI 0.21, 0.33). Estimates from observational data from Ireland for pulmonary TB were (0.14, 95%CI 0.09, 0.20), EPTB (0.11, 95%CI 0.05, 0.21), TB meningitis (0.17, 95%CI 0.04, 0.75) and TB deaths (0.13, 95%CI 0.00, 6.37). Pooled RR estimates from Irish data and international estimates show a significant reduction in TB cases: Pulmonary TB: 0.26 (95% CI: 0.13, 0.54), EPTB: 0.16 (95%CI: 0.08, 0.34), TB meningitis: 0.27 (95%CI: 0.21, 0.34) and TB deaths: 0.33 (95%CI: 0.14, 0.81). **CONCLUSIONS:** This meta-analysis of local observational data with international trial data indicates that vaccination of infants with the BCG vaccine reduces the risk of pulmonary TB, EPTB, TB meningitis and TB deaths.

PIH4

CO-ADMINISTRATION OF ANTIPSYCHOTICS AND ANTI-DEMENTIA DRUGS IN AUSTRIA

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OBJECTIVES: The use of antipsychotics for people with dementia is regarded as problematic, causing cerebrovascular side effects and increasing mortality. In some countries, health-policy makers have already addressed a need for action to reduce the prescription of antipsychotics in dementia. The main goal of the analysis is to determine the extent of co-medication of antipsychotics for patients with medically-treated dementia in Austria, stratified by age and sex. **METHODS:** Provided in a pseudonymised manner, the data comprise all filled prescriptions of cholinesterase inhibitors and memantine in the years 2011 and 2012 at the expense of the 13 major Austrian health insurance funds, covering more than 97% of the Austrian population. Additionally, antipsychotic medication of the involved patient pseudonyms is included, as well as age, sex and – where occurred – date of death. For the analysis, the overlapping time frame is relevant, i.e. when both substance groups were consumed. Descriptive statistics are used to capture the extent and variability of a co-medication of these two substance groups. **RESULTS:** Starting with 72,549 patients included in the data (66% female), 31,605 (43.6%) were concurrently being prescribed antipsychotics to their anti-dementia drugs. The median for the overlapping time frame is 294 days, for anti-dementia prescriptions it is eleven and for antipsychotics it is seven. Age is a factor for increasing antipsychotic medication. Considering demography, there are no remarkable differences between men and women. **CONCLUSIONS:** Our data demonstrate that the use of antipsychotics in dementia is notably common in Austria, with a high prevalence as well as a tendency to long-term use. The results reflect the prescription reality and can be used as a solid basis for discussions, possible actions and evaluations about antipsychotics in dementia in the Austrian health system.

PIH6

ASSESSING PRODUCT SAFETY VIA PATIENT BASED ACTIVE SURVEILLANCE (AS): A STUDY IN 30.000 WOMEN USING HORMONE REPLACEMENT THERAPY (HRT)

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OBJECTIVES: The novel progestin drospirenone (DRSP) has antimineralocorticoid properties with potentially beneficial as well as unfavorable effects on cardiovascular outcomes compared to other progestins. A patient based AS study was set up to compare incidence rates of serious adverse events – in particular cardiovascular outcomes - in users of oral continuous combined preparations. **METHODS:** Prospective, controlled cohort study (2002-2011) with three arms: women using 1) DRSP/estradiol; 2) other oral continuous-combined HRT (occHRT); and 3) all other oral HRTs. The study population included women aged 40 or older in seven European countries starting or switching to an oral HRT at time of inclusion in the study. Outcomes were collected from the patients and validated by the treating physicians. A multifaceted 4-level follow-up procedure was to ensure low loss to follow-up rates. The analysis is based on Cox regression models comparing the cohorts. **RESULTS:** A total of 30,597 users of oral HRT preparations – reflecting more than 101,000 WY of observation – were recruited by 1,052 centers. Incidence rates of DRSP/estradiol and low-dose occHRT for venous thromboembolic events were 17.5 (95% CI: 11.2-26.0) and 18.2 (95% CI: 11.9-26.6) per 10,000 WY, respectively. The respective incidence rates for arterial thromboembolism were 10.9 (95% CI: 6.1-18.0) and 29.8 (95% CI: 24.1-36.4) per 10,000 WY with a hazard ratio adjusted for age, BMI, hypertension, region, family history of fatal ATE, diabetes, user status of 0.5 (95%CI: 0.3-0.8) for DRSP/estradiol vs. other occHRT. **CONCLUSIONS:** Results indicate a good safety profile with respect to cardiovascular risk for DRSP/estradiol. Serious cardiovascular events occur less frequently in DRSP/estradiol users compared to users of other continuous-combined HRT. This specificAS approach proved to be a successful approach with high long term follow-up success and high validity of safety results.

INDIVIDUAL'S HEALTH – Cost Studies

PIH7

BUDGET IMPACT OF HPV16/18 GENOTYPING TESTS FOR THE MANAGEMENT OF NON-CONCORDANT COTESTING CERVICAL CANCER SCREENING RESULTS: A UNITED STATES PAYER PERSPECTIVE

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OBJECTIVES: To assess the impact of managing women with high-risk HPV positive and Pap negative results (hrHPV+/Pap-) attending cervical cancer (CxCa) screening with a Pap and HPV test (co-testing). The strategies tested reflect different options available if a hrHPV test versus a hrHPV including 16/18 genotyping (3-in-1 test) is used upon initial screen. **METHODS:** A budget-impact model was developed, from a US payer perspective. Data from the ATHENA (Addressing THE Need for Advanced HPV Diagnostics) trial and published literature were used to populate the model. The scenarios tested include repeat co-testing in 12 months, reflex genotyping HPV16/18, or routine co-testing with genotyping results already available from a 3-in-1 test for triage to colposcopy. The model examined the annual cost of testing and treatment for cervical intraepithelial neoplasia grade 2 or worse (≥CIN2) and the cost of patients loss-to-follow-up. For a hypothetical population of women between ages 30 to 69, it assumes 48.5% were co-tested within the CxCa screening program every 3 years. Of those, 6.7% of women receive hrHPV+/Pap-results. Test performance was modeled as equivalent for both genotyping scenarios. **RESULTS:** In the hrHPV+/Pap- population, the cost of ≥CIN2 cases detected and treated for each testing strategy and the rate of progression to invasive CxCa per 10,000 hrHPV+/Pap- results was $10,530/9.2 (repeat co-testing at 12 months), $8,500/2.6 (reflex HPV16/18) and $7,278/2.6 (routine co-testing with 3-in-1 test). Using HPV16/18 genotyping to manage discordant co-testing results increased ≥CIN2 cases detected and prevented disease progression. Compared to other HPV tests that require reflex genotyping, screening with a 3-in-1 test reduced the cost of follow-up by 17% annually. **CONCLUSIONS:** Genotyping for HPV 16/18 improved the detection of ≥CIN2 cases over repeat co-testing in 12 months; moreover, compared to other HPV testing strategies, the 3-in-1 test reduced costs and may be a prudent screening alternative.

PIH8

ECONOMIC IMPACT OF THE USE OF AN ABSORBABLE ADHESION BARRIER IN PREVENTING ADHESIONS FOLLOWING OPEN GYNECOLOGIC SURGERIES

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OBJECTIVES: Abdominal adhesions are common after gynecologic surgeries, often resulting in complications such as bowel obstruction and chronic pain, which may lead to increased length of stay and more frequent readmissions. GYNECARE INTERCEED® Absorbable Adhesion Barrier is associated with fewer adhesion-related outcomes compared to surgeries without an adhesion-barrier. This analysis assesses the budget impact of GYNECARE INTERCEED® for reducing the incidence of postoperative adhesions in open surgical gynecologic procedures. **METHODS:** A model was constructed to evaluate the budget impact to hospitals of adopting GYNECARE INTERCEED® for women undergoing open surgical gynecologic procedures. C-section surgery, hysterectomy, myomectomy, ovarian surgery, tubal surgery, and endometriosis surgery were modeled with and without the use of GYNECARE INTERCEED®. Incremental GYNECARE INTERCEED® material costs, medical costs arising from complications, and adhesion-related readmissions were considered. GYNECARE INTERCEED® use was assumed in 50% of all procedures. Budget impact was reported over a 3-year period from a US hospital perspective (US$2013). **RESULTS:** Assuming 100 gynecologic surgeries of each type and an average of one GYNECARE INTERCEED® sheet per surgery, a net savings of $439,975 with GYNECARE INTERCEED® over 3 years is estimated. GYNECARE INTERCEED® use resulted in 80 fewer patient cases developing adhesions. Although the use of GYNECARE INTERCEED® added $91,500 in material costs, this was completely offset by the reduction in complication costs ($230,766 savings) and fewer adhesion-related readmissions ($300,709 savings). By preventing adhesion-related complications, GYNECARE INTERCEED® prevented over 206 additional hospital days for patients. **CONCLUSIONS:** This analysis represents the first economic assessment of GYNECARE INTERCEED® use in open gynecologic surgeries that incorporates the cost of the adhesion barrier, complications, and readmissions. Adoption of GYNECARE INTERCEED® absorbable adhesion barrier for appropriate gynecologic surgeries would likely result in significant savings for hospitals which would largely be driven by clinical patient benefits in terms of fewer complications and adhesion-related readmissions.

PIH9

BUDGET IMPACT OF DIENOGEST IN TREATING ENDOMETRIOSIS ASSOCIATED PELVIC PAIN IN BRAZIL: A PUBLIC PERSPECTIVE ANALYSIS

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OBJECTIVES: Evaluate the budget impact to the public health care system in Brazil after introducing dienogest (2 mg) as a treatment option in detriment of GnRH analogues (GnRHa) for patients with endometriosis-associated pelvic pain (EAPP). **METHODS:** The analysis was conducted from the public perspective over a five-year time horizon. The budget impact model (BIM) specifically considered

women with EAPP. A recently cost-minimization (CM) model developed for EAPP provided the estimates of average treatment cost in Brazil based on local guidelines. This CM model compared different treatment pathways for women with EAPP and used a 50% improvement in pelvic pain as a definition of a treatment response. A patient flow was developed based on epidemiological and demographical data. Based on market uptake assumptions, results from the CM model and the patient flow, the BIM estimated the incremental budget impact after adopting dienogest. The model assumed that during the first year, 6.76% of EAPP patients receive dienogest in detriment of GnRHa. After five years, it was assumed that dienogest would capture 30% of the GnRHa market in EAPP. **RESULTS:** Based on the patient flow developed, approximately 0.52% of the population were estimated to be diagnosed with EAPP and receiving treatment with GnRHa. In the year after introduction of dienogest, the overall budget used to treat EAPP was estimated to decrease by up to 2.98% with the budget saving estimated to increase to around 12.98% by Year 5. **CONCLUSIONS:** This analysis portends that the budgetary impact of adding dienogest to the public health care system in Brazil, in detriment of the GnRHa, result in a budgetary cost saving alternative.

PIH10

HOW MUCH DOES BENIGN PROSTATIC HYPERPLASIA COST? A BUDGET IMPACT ANALYSIS ON ITALIAN PATIENTS TREATED WITH 5A-REDUCTASE INHIBITORS

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OBJECTIVES: Second-line pharmacological therapy for benign prostatic hyperplasia (BPH) includes 5α-reductase inhibitors (5ARIs, dutasteride and finasteride). Aim of this study was the evaluation of the budget impact related to the variation in dutasteride and finasteride prescribing trends. **METHODS:** Target population is the number of Italian BPH-patients, age ≥ 40 years, treated with dutasteride or finasteride. The BPH-patients management was modeled on a dynamic cohort for 4-years. Epidemiological input data were elaborated from a observational study on pharmaceutical prescription data of Italian BPH-patients; hospitalization rates were taken from a cohort study investigating BPH-related surgical and not surgical hospitalizations. Costs were calculated as average of Italian DRGs weighted for BPH-related procedure frequency. Current Italian prescription shares of dutasteride and finasteride were compared with a 20% shift of prescriptions from dutasteride to finasteride (Scenario A) and a 20% shift of prescription from finasteride to dutasteride (Scenario B). **RESULTS:** According to current prescribing trends, 372,078 hospitalizations for BPH are expected in 4 years. Mean annual cost for BPH-patients management results in 355 million €. Hospitalization cost is the main driver (228 milion €/year) while pharmacological therapy accounts for 35% of the total cost (126 million Euro/year). Scenario A: additional 11.485 hospitalizations related with BPH occur in 4 years; these lead to an increase in NHS cost only slightly offset by the savings in drugs acquisition cost: -0,08% savings on NHS budget (-0,28 milion €/year) Scenario B: the cost of drugs increases of 5% (+6 million €/year) and prevents 9,920 hospitalizations in 4 years; the net budget impact of scenario B is +0,08% increase in cost (+0,27 milion €/year). **CONCLUSIONS:** The shift of prescription from dutasteride to finasteride leads to modest savings on NHS Budget while the shift from finasteride to dutasteride offsets the majority of increase in drug budget improving the outcome in patients.

PIH12

COSTS OF ALTERNATIVE METHODS OF CHILD DELIVERY IN SERBIA

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OBJECTIVES: Different types of labour need different resources. Therefore, different costs could be expected. Objectives of this study were to determine if significant differences in costs of different type of labour and methods of delivery exist and to determine factors related to estimated costs. The costs of spontaneous labour with vaginal delivery (SVD), induced labour with vaginal delivery (IVD), and planned C-section (CS) without labour were estimated. **METHODS:** Retrospective, population-based study was conducted for the period January – December, 2010. Health Insurance Fund of Republic of Serbia (HIFRS) database was used as a data source. Direct medical costs of mother/newborn pair were estimated. Costs were observed from the perspective of HIFRS and expressed in European Monetary Unit (EUR). **RESULTS:** A total of 99 women were selected for the study sample; average age was 30.55±5.42 years. The majority of women (46.5%) had SVD, 28.3% had IVD and 25.2% had CS. Women with CS were longer hospitalized compared to women with SVD and IVD (8.52±4.74 vs. 4.59±2.89 and 5.04±3.01 days, respectively, p<0.05). Newborns after CS were longer hospitalized compared to newborns after SVD and IVD (5.76±2.20 vs. 4.0±2.07 (p<0.05) and 5.14±3.39 (p>0.05)). Majority of women (88.0%) and children (80.0%) after CS were hospitalized at semi-intensive and/or intensive care unites. The average costs of delivery, regardless of the method, were 417.02±284.14 EUR. The costs of C-section were higher compare to SVD (640.18±240.04 vs. 243.27±131.70 EUR, p<0.05) and IVD (640.18±240.04 vs. 497.10±327.91 EUR, p>0.05). **CONCLUSIONS:** The highest costs of labour in Serbia were costs of planned CS. Longer maternal/newborns hospital stay and more frequent hospitalization at semi-intensive and/or intensive care unites after CS were leading factors of estimated high costs. Considering high costs of CS, it is necessary to review such clinical practice for the purpose of optimizing the use of resources.

PIH13

COST BURDEN OF ROTAVIRUS GASTRO-ENTERITIS REQUIRING HOSPITALIZATIONS IN THE CZECH REPUBLIC AND IN SLOVAKIA

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OBJECTIVES: Rotavirus (RV) is the most frequent cause of severe gastroenteritis frequently requiring hospitalization. RV is responsible for > 1/2 of all hospital stays for acute gastroenteritis. The objective was to estimate the burden of community acquired rotavirus gastro-enteritis requiring hospitalization (CRVGE) in children ≤ 5 years old in Czech Republic (CR) and Slovakia (SK). **METHODS:** Multi-center, retrospective patient chart review was conducted in both pediatric and infection disease settings in CR (n=109) and SK (n=115). Resource use analysis including length of hospital stay and tests performed were evaluated. Patients requiring rehydration, complications and comorbidities were considered. Direct cost from payer's perspective were retrieved from official DRG lists (CR) and fixed hospitalization cost rates per case (SK). Micro-costing was done in parallel based on the resource use data. **RESULTS:** Mean length of hospital stay in CR and SK was 3.9 (SD 1.9) and 4.1 days (SD 1.7) respectively. Prevalent diagnostic tests used were latex agglutination 44.0% (CR) and immunochromatography 92% (SK). Rehydration was required in 84.4% (CR) and 97% (SK) of cases. Comorbidities were reported in 24.8% (CR) and 27% (SK); complications in 10.1% (CR) and 7.8% (SK). The national list-based reimbursement per hospitalized CRVGE is € 370-645 (CR) and € 561 (SK). The calculated average total costs, including treatment prior to, and after admission, were € 462 (CR) and € 583 (SK). The major cost item was the hospital stay with €391 (CR) and €540 (SK). Costs for tests and drugs during hospitalization were €30 (CR) and €25 (SK). The costs of pre and post-hospitalization care were €20 (CR) and €13 (SK). **CONCLUSIONS:** Although the length of hospitalization in both countries is similar costs seem to be substantially lower in CR, possibly as a result of recently launched DRG system. Common complications and comorbidities account for 30% of average hospital costs.

PIH14

USE OF ANTENATAL CORTICOSTEROIDS LOWERS HOSPITALIZATION COSTS RELATED TO PREMATURITY

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OBJECTIVES: According to WHO the use of antenatal corticosteroids (CEA) in pregnant women at risk of preterm birth <34 weeks can prevent thousands of preterm neonates (PN) deaths. The impact of the use of CEA in hospital costs in developing countries is not known. Our objective was to compare morbidity and hospital costs of PN whose mothers received or not CEA. **METHODS:** Analysis of PN medical records with gestational age 26-32 weeks born from Jan/2006-Dez/2009 in a tertiary, public and university hospital. We excluded infants with malformations. Maternal characteristics, hospital neonatal morbidity, use and doses of CEA and all used resources (tests, medications and procedures) were collected. Costs were estimated in Brazilian Reais, from the hospital perspective. **RESULTS:** Of 211 PN, 170 received at least one dose of CEA to 6 hours before delivery (G1) and 41 did not (G2). The groups had similar characteristics but G1 had more male infants (p <0.05) and cesarean sections (p <0,00). Morbidity: G2 needed more advanced resuscitation (16.5% vs 34%, p = 0.01), experienced more intraventricular hemorrhage III / IV (7.6% vs. 22%, p <0.00) and retinopathy of prematurity (12.4% vs. 24.4%, p = 0.05). Resource use: G1 consumed less mechanical ventilation days (5.3 vs 10.6, p = 0.04) and oxygen days (10.7 vs 17, p = 0.02); the number of NICU and Intermediate Care Nursery days were respectively (19.6 vs 27.5, p = 0.07) and (24 vs 29.5 days, p = 0.14); there was no difference concerning use of CPAP (p = 0.07) and surfactant (p = 0.06). The average cost of hospitalization per patient was BRL 18,409 in G1 and BRL 24,090 in G2 (p = 0.03). **CONCLUSIONS:** The CEA is a simple measure, which helps to reduce PN morbidity and utilization of health care resources, reducing hospital costs.

PIH15

EXAMINING THE BURDEN OF ILLNESS OF THE UNITED STATES VETERAN PATIENTS DIAGNOSED WITH ALZHEIMER'S DISEASE

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OBJECTIVES: To examine the burden of illness of patients diagnosed with Alzheimer's disease (AD) in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration (VHA) Medical SAS datasets from October 1, 2008 through September 30, 2012. Patients diagnosed with AD were identified using International Classification of Disease 9th Revision Clinical Modification (ICD-9-CM) diagnosis code 331.0. The first diagnosis date was designated as the index date. A comparator group was created as well by identifying patients without an AD diagnosis but with the same age, region, gender, index year, and matching Charlson Comorbidity Index (CCI). The index date for the comparator group was randomly chosen to reduce the selection bias. A 1-year continuous health plan enrollment was required before and after the index date for both groups. One-to-one propensity score matching was used to compare the health care costs and utilizations during the follow-up period between the disease and comparator groups. **RESULTS:** A total of 68,856 patients were included in the AD and comparison cohorts. After 1:1 matching, a total of 24,542 of patients were matched from each group, and the baseline characteristics were proportionate. The AD cohort had higher percentages of inpatient (18.46% vs. 2.06%, p<0.01), emergency room (15.80% vs. 4.31%, p<0.01), physician office (98.17% vs. 58.18%, p<0.01), outpatient (98.30% vs. 58.92, p<0.01), and pharmacy visits (84.89% vs. 61.78%, p<0.01). AD patients also incurred higher inpatient ($7,416 vs. $636, p<0.01), emergency room ($150 vs. $41, p<0.01), physician office ($2,752 vs. $1,155, p<0.01), outpatient visits ($3,086 vs. $1,300) and pharmacy costs ($774 vs. $350, p<0.01) compared to patients without AD. **CONCLUSIONS:** In this study, AD was associated with higher health care resource utilization and a significantly higher economic burden.

PIH17

A COST OF A CHILDBIRTH WITH IN VITRO FERTILIZATION IN POLAND

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OBJECTIVES: To predict the cost of a delivery following assisted reproductive technologies (ART) in Poland. Moreover, the cumulated *in vitro* fertilization (IVF) effectiveness ratio was calculated and the costs of drugs for each of the three stimulation protocols used in IVF (long with GnRH agonist, short with GnRH antagonist and short with GnRH agonist) were estimated. **METHODS:** In order to calculate the IVF effectiveness, a pooled analysis of the results from European IVF monitoring reports concerning Poland from 2008 to 2010 was performed. Costs of the clinical and biotechnological parts of IVF were based on the Ministry of Health calculation. Drugs' costs were estimated considering both dosages based on the Summaries of Products Characteristics and the retail prices. Costs were calculated based on identified costs in both the patient and payer perspectives. **RESULTS:** The overall birth rate per cycle was 21,70%. The probability of a delivery was 1,5 higher during fresh cycle than in frozen embryo transfer. A total of 24,09% of embryo transfers resulted in delivery. The cost of drugs used during ovarian stimulation protocol was estimated on 6 055 PLN. The average cost per cycle was 13 565 PLN. Drugs account for 45% of this value. The average cost per birth was 42 848 PLN. **CONCLUSIONS:** *In vitro* fertilization is an expensive procedure for a patient in Poland. It is due to a limited effectiveness, usually requiring several repeats of the whole cycle of IVF with no drugs reimbursement. The ovarian stimulation is the most expensive part of the procedure. Thus, reimbursement of medication should also be established.

PIH18

COST-EFFECTIVENESS OF MATERNAL TOXOPLASMA SCREENING IN AUSTRIA: A DECISION-ANALYTIC MODEL

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OBJECTIVES: Toxoplasma infection during pregnancy presents a serious hazard to the fetus including lifelong disabilities of connatal infected children. This foodborne illness is a common burden worldwide. Prevention strategies of the health care providers are diverse. In Austria, the maternal toxoplasma screening has been implemented four decades ago. The aim of this study was to determine cost-effectiveness of the maternal toxoplasma screening. **METHODS:** We developed a two arm decision-analytic model. One arm of the model assessed the costs and consequences of no prevention, while the other one evaluated the screening. The study population included pregnant women and offspring screened and treated for toxoplasma infection. The average number of births was 76,547 and 50,000 pregnant women were susceptible to infection. The analysis focused on lifetime consequences of the connatal infection. This encompassed direct costs (screening, cost of illness, maternal and pediatric treatment), indirect costs (changed job situation of parents, human-capital of dead individuals, blindness and special schools), quality-adjusted-life-years (QALYs) and reduced expectation of life. Costs were presented per child and for the Austrian birth cohort. Costs from published sources were used (2012 Euro) from the societal perspective. QALYs, life-years (LYs) and costs were projected over a life-time horizon and discounted at 3% p.a. **RESULTS:** Maternal toxoplasma screening reduced transmission risk by 40% and one quarter of affected children showed symptoms. We found five-times higher lifetime costs per child without prevention compared to screening. Also direct costs were lower in the latter group; screening costs did not offset costs of sequelae. A split in direct and indirect costs components demonstrated that proportion of direct costs without prevention amounted to 20% and 95% with screening. Screening resulted in QALYs gained and LYs saved. **CONCLUSIONS:** Funding the maternal toxoplasma screening saves money and is cost-effective for the society and the Austrian health care system.

PIH19

COST-EFFECTIVENESS OF UNIVERSAL PAEDIATRIC ROTAVIRUS VACCINATION WITH RIX4414 IN GREECE

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OBJECTIVES: Rotavirus gastroenteritis is a major health burden in young children worldwide. This study investigates the cost-effectiveness of universal paediatric rotavirus vaccination with RIX4414, a two-dose human rotavirus vaccine, in Greece. **METHODS:** A Markov cohort model with a cycle time of one month was constructed in Microsoft Excel. The birth cohort of 114,766 infants, based on 2010 official registry was entered into the model and followed over average life expectancy with acute rotavirus events measured up to five years of age. Probabilities, utility scores and costs for hospitalisations, hospital-acquired rotavirus infection, medical consultations, emergency visits and deaths due to rotavirus were taken from published sources and national databases. Costs and benefits were reported at 2012 euros, discounted at 3% and 1.5% respectively per year and compared between a vaccinated and unvaccinated cohort from a Social Sick-Fund perspective. **RESULTS:** Vaccination with RIX4414 incurred an incremental cost of €16,569 per QALY at a price of €48/dose. The estimated number of rotavirus-related diarrhoea events per year up to the age of five is 45,906. Total direct medical cost of rotavirus disease without vaccination is around €8,980,000 per year in Greece. Vaccination (40% coverage) reduces the number of gastro-enteritis events by 27% to 33,492 and the number of rotavirus-related medical visits from 17,214 per year to less than 11,000. Total cost of rotavirus disease, including the costs of vaccination, in the vaccinated cohort is estimated at €10,087,614 per year, with a cost reduction on direct medical costs of €3,343,781. This cost reduction reflects the high financial disease burden related to the medical visits including paediatricians, emergency and hospital visits. **CONCLUSIONS:** Paediatric vaccination against rotavirus with RIX4414 versus no vaccination in Greece improves health outcomes, reduces direct medical costs and is cost-effective from a social sick fund perspective.

PIH20

CLINICAL AND COST-EFFECTIVENESS OF A PROCALCITONIN TEST AS A PROMPT INDICATOR OF PRODOMOL MENINGOCOCCAL DISEASE IN FEBRILE CHILDREN: COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: To establish if the procalcitonin (PCT) test's diagnostic performance is more clinically and cost-effective than C reactive protein (CRP) and White Cell Count (WCC) tests for suspicion of prodomal stage Meningococcal disease (MD) in children presenting at emergency department (ED) with a fever without source. **METHODS:** A decision analytic model was designed to reflect realistic clinical pathways for a child presenting with non-specific fever to ED. Test accuracy was evaluated using data from independent studies carried out in developed countries identified through a systematic literature search. Studies were combined to determine the optimal cut-off value for the PCT, CRP and WCC tests, each as an indicator of MD. Summary Receiver Operator Curve (SROC) analysis was used to determine the inter-study and overall diagnostic performance of each test from the areas under the curve (AUC), with 95% confidence intervals (CIs). Components of each clinical pathway were costed in UK sterling using the National Schedule of Reference Costs 2010-2011. Hospital stays were costed using the appropriate Health Resource Group code. **RESULTS:** Seven studies involving 881 children with non-specific fever provided data for inclusion. The PCT test was more accurate (sensitivity=89%, 95%CI=75-96; specificity=71%, 95%CI=37-91) for early MD compared to CRP (sensitivity=84%, 95%CI=74-90; specificity=60%, 95%CI=44-74) and WCC (sensitivity=50%, 95%CI=39-60; specificity=68%, 95%CI=54-79). PCT had the best PLR (3.0, 95%CI=1.8-7.8) to be viable as a rule-in test for MD and a borderline NLR as a rule-out test, making it a better option to either CRP (2.1, 95%CI=1.4-3.1) or WCC (1.5, 95%CI=1.0-2.3). Outcomes from the decision analytic model indicated that the PCT test was the most cost-effective (£2547 per patient treated), followed by the combined CRP and WCC test (£3069 per patient treated). **CONCLUSIONS:** The improved sensitivity and specificity of the PCT test provides a more cost-effective test than the currently recommended CRP and WCC tests.

PIH21

COST-EFFECTIVENESS ANALYSIS IN THE TREATMENT OF HEAVY MENSTRUAL BLEEDING IN SPAIN

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OBJECTIVES: To evaluate the cost-effectiveness of first-line treatment of heavy menstrual Bleeding (HMB) from the perspective of the Spanish National Healthcare System. **METHODS:** A cost-effectiveness analysis was performed using a Markov model to simulate the evolution of a cohort of women in reproductive age, with HMB and who wish to preserve their fertility status, in a time horizon of 5 years. The treatment strategies were levonorgestrel intrauterine system (LNG-IUS), estradiol valerate/dienogest (E2V/DNG), combined oral contraceptives (COC) and oral progestins (PROG). Clinical data was modelled indirectly combining literature and expert opinion. Outcomes were symptom-free months (SFM), quality-adjusted life months (QALM) and costs expressed in € in 2012. A probabilistic sensitivity analysis was conducted to examine the robustness of the results. **RESULTS:** The mean treatment cost of HMB at 6 month was 205€ for LNG-IUS, 318€ for E2V/DNG, 412€ COC and 766€ PROG. In the analysis over 5 years, LNG-IUS produced savings of 578€ compared to E2V/DNG, 991€ compared to COC and 1,821€ compared to PROG. Regarding the effectiveness, LNG-IUS provided 51.30 SFM, while E2V/DNG, COC and PROG provided 50.64, 49.09 and 47.77 SFM, respectively. Moreover, 77%, 65%, 56% and 46% of the patients treated with LNG-IUS, E2V/DNG, COC and PROG, respectively, continued treatment without surgery during the 5 year period. Considering QALM as outcome, LNG-IUS and E2V/DNG were the options that yielded more gains in QALM (49.71 for LNG-IUS, 48.09 for E2V/DNG, 46.59 for COC and 44.66 for PROG). LNG-IUS was the most effective and less costly, therefore dominant option. In the oral treatments comparison, E2V/DNG was dominant, providing savings and gains in terms of SFM and QALM. The probabilistic sensitivity analysis on the key parameters confirmed the robustness of the base case. **CONCLUSIONS:** LNG-IUS is a cost-saving option for the treatment of HMB in Spain. Among oral treatments, E2V/DNG is also a dominant strategy.

PIH22

SYSTEMATIC LITERATURE REVIEW AND COST-EFFECTIVENESS ANALYSIS OF FETAL FIBRONECTIN TEST FOR PREDICTING PRETERM IN BRAZIL

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OBJECTIVES: Brazil is among the countries with the highest incidence of preterm births. Incorporation of diagnostic tests to predict a preterm birth could improve the efficiency of the clinical practice reducing hospital expenses related to maternal hospitalization. The aim of this study was to compare the cost-effectiveness of fibronectin testing (FN) vs cervical length (CL) measurement in women with symptomatic preterm labor. **METHODS:** Systematic review of the literature of the diagnostic tests and development of a decision analytic model using the accuracy of the diagnostic tests to predict preterm birth and project the results in terms of effectiveness and cost. The analysis was performed for a hypothetical cohort of 10,000 patients, for each test, with symptomatic preterm labor between 24 and 34 weeks of gestation. The primary perspective of the study was of the Brazilian Health system (SUS). Data sources were the medical literature, SUS official published prices for medicines and DATASUS (SUS database). Costs are in 2012 Brazilian Reais. **RESULTS:** A total of 14 studies were included. There was a wide variation concerning the accuracy of the tests among the studies, particularly with respect to gestational age at

testing/delivering and definition of the CL test threshold. The values obtained were LR+ 3,98/LR- 0,33 (FN) and LR+ 2,22/LR- 0,54 (CL). For the whole hypothetical cohort the total costs of the FN and CL were 2,3 billion and 890 million, respectively. The difference of avoided hospitalizations between the tests was 244 for FN. ICER was BRL 5,834,35. **CONCLUSIONS:** Both diagnostic tests are important alternatives for the detection of premature birth in Brazil. Studies of prediction of preterm delivery using CL have important limitations beyond the fact that CL measure is an operator/machine dependent procedure. In women with symptomatic preterm labor FN is a cost-effective test strategy for prediction of preterm births.

PIH23

COST-EFFECTIVENESS OF VACCINATION AGAINST HERPES ZOSTER AND POSTHERPETIC NEURALGIA: A CRITICAL REVIEW

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OBJECTIVES: To systematically review cost-effectiveness studies of vaccination against herpes zoster (HZ) and post-herpetic neuralgia (PHN). **METHODS:** We searched MEDLINE and EMBASE databases for eligible studies until June 2013. We extracted information regarding model structure, model input parameters, and study results. We compared the results across studies by projecting the health and economic impacts of vaccinating 1 million adults over their lifetimes. **RESULTS:** We identified 14 cost-effectiveness studies performed in North America and Europe. Results ranged from approximately US$10,000 to US$100,000 per quality-adjusted life years gained, though most studies in Europe concluded that zoster vaccination is likely to be cost-effective. All studies used similar model structure. Differences in results among studies are largely due to differing assumptions regarding duration of vaccine protection and a loss in quality of life associated with HZ and to a larger extent, PHN. In addition, studies found that vaccine efficacy against PHN, age at vaccination, and vaccine cost strongly influenced the results in sensitivity analysis. **CONCLUSIONS:** Our review generally supports the economic value of this preventive intervention, particularly in Europe, which will become increasingly important as population ages. Future research addressing key model parameters and cost-effectiveness studies in other parts of the world are needed.

PIH24

AN ECONOMIC EVALUATION ALONGSIDE A CLINICAL TRIAL (EEACT) IN PELVIC FLOOR MEDICINE

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OBJECTIVES: To determine the cost-effectiveness of using an online questionnaire (ePAQ-PF) in combination with a telephone consultation compared to standard care. **METHODS:** All women, aged ≥ 18 years and referred to urogynaecology services in Sheffield were eligible. Women completed ePAQ-PF online and then received a telephone consultation (intervention), or face-to-face consultation (standard care). Costs for ePAQ-PF completion and consultation were derived in a microcosting study. Resource use data were collected at 6-months follow-up. The SF-12 was administered at baseline and follow-up. SF-6D estimates were used to calculate quality-adjusted life-years (QALYs). Patient experience was measured by the Patient Experience Questionnaire and Client Satisfaction Questionnaire. **RESULTS:** A total of 195 women were randomised. Consultation costs for the intervention group (£31.75) were lower than for the control (£72.17). The intervention group incurred greater direct costs and personal expenditure during follow-up. However lower costs associated with productivity loss for the intervention group resulted in lower indirect costs per-patient. Mean total costs per-patient were £38.04 greater in the intervention group (£1,139.86) than the control (£1101.82). SF-6D scores reduced slightly during follow-up for the intervention group, and increased slightly for the control, resulting in QALY loss for the intervention group, and QALY gains for the control. Statistically significant gains in patient experience were identified for the intervention group, although in strict cost-utility terms the intervention was dominated by the control. Incremental costs and QALYs resulted in a negative incremental cost-effectiveness ratio (ICER). **CONCLUSIONS:** Although the intervention was not cost-effective compared to the controls, there was a significant difference in an important aspect of the care process, which was not captured by the ICER. This highlights the importance of decision makers accounting for intervention effects that fall outside the conventional conceptualization of the QALY. Methods could be developed that allow non-health effects, such as process utility, to be incorporated into the QALY.

PIH25

PHARMACOECONOMIC ANALYSIS OF PROGESTOGEN PREPARATIONS FOR THREATENED ABORTION TREATMENT IN UKRAINE

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OBJECTIVES: Comparative evaluation the cost effectiveness of threatened abortion treatment by two regimens: oxyprogesteronicaproas and dydrogesterone in Ukraine. **METHODS:** Pharmacoeconomic analysis was based on the results of comparative randomized trial (Belousov Yu. B., Karpov O.I., Ailamazian E.K., 2008). Two regimens for threatened abortion treatment: oxyprogesteronicaproas and dydrogesterone were evaluated. Treatment with dydrogesterone (20 mg per day or 2 tablets per day) was carried out during 8 weeks before closure forming placenta (56 days). Oxyprogesteronicaproas (250 mg per day) was used from 14 to 20 weeks of gestation (42 days). For determining the cost of therapy only the cost of drugs and auxiliary materials (syringes, alcohol) for both schemes were taken into account. The prices of drugs were taken from the information system "Drugs" of Company "Morion" (February, 2013, Ukraine). The currency ratio of UAH to dollar (USA) on 01.02.13 was 8,12:1. As an indicator of efficacy the number of saved pregnancy after treatment was used. **RESULTS:** The effectiveness of oxyprogesteronicaproas therapy was 88.6%, and dydrogesterone - 96.3%, the cost of treatment was $ 78.63 and $ 77.96 respectively. Cost-effectiveness ratio was $ 88.7 for oxyprogesteronicaproas and $ 80.9 for dydrogesterone. **CONCLUSIONS:** Cost-effectiveness analysis shown, that the use of dydrogesterone is more effective and less costly for threatened abortion treatment in Ukraine. The results of pharmacoeconomic analysis will optimize the government, insurance companies and patients cost.

PIH26

COST-EFFECTIVENESS OF INFANT PNEUMOCOCCAL VACCINATION IN THE NETHERLANDS

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OBJECTIVES: The Dutch National Immunization Program offers the 10-valent pneumococcal conjugate vaccine (PCV10). Also licensed for use in the infant population is the 13-valent PCV (PCV13). To update cost-effectiveness (CE) estimates of PCV13 over PCV10, using current epidemiological and economic data. **METHODS:** We modeled vaccinating a birth cohort with either PCV10 or PCV13 (3+1 dose schedule), and calculated costs and effects linked to resulting disease. We modeled invasive pneumococcal disease (IPD), non-invasive pneumonia and acute otitis media, and considered death and lifetime impairments after IPD. We calculated direct effects in the vaccinated cohort and indirect effects –herd immunity for the vaccine-type (VT) serotypes and replacement for the non-VT serotypes– in the rest of the population. Since no price is available, we use a price difference of €11 per dose and vary this price difference in sensitivity analyses. Epidemiological and economic data are taken as current as possible. A set of scenarios explore different assumptions, including different sets of epidemiological data, assumptions on vaccine efficacy and indirect effects. **RESULTS:** Taking only direct effects into account PCV13 cannot be considered cost-effective, unless the price difference is much lower than €11 per dose. In three scenarios, PCV10 dominates PCV13; in the other scenarios the ICER is between €89000 and €153000 per QALY gained. If indirect effects are also taken into account, the ICER of PCV13 compared to PCV10 is below € 20,000 per QALY for all scenarios. Scenarios do not have a large impact on the policy decision, unless we assume extra efficacy of PCV10 against non-typeable Haemophilus influenzae. **CONCLUSIONS:** Replacing PCV10 with PCV13 is not likely to be cost-effective in preventing invasive pneumococcal disease in young children. Taking potential benefits in elderly into account, PCV13 is likely cost-effective. The CE of PCV13 was highly sensitive for indirect effects our analysis.

PIH27

COST-MINIMIZATION ANALYSIS OF DIENOGEST VERSUS GONADOTROPHIN-RELEASING HORMONE ANALOGUES OR DYDROGESTERONE FOR ENDOMETRIOSIS TREATMENT IN RUSSIA

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OBJECTIVES: To perform pharmacoeconomic evaluation of dienogest vs gonadotrophin-releasing hormone analogues (GnRHa) or dydrogesterone for endometriosis in Russia. **METHODS:** Literature search did not reveale clinically significant differences in efficacy between dienogest 2 mg and GnRHa in terms of pain reduction associated with endometriosis. There was no difference in efficacy with dydrogesterone 60 mg once daily and placebo. Cost-minimization analysis was used to assess and compare drug costs of dienogest 2 mg daily, GnRHa - most often used in Russia including triptorelin, leuprorelin, buserelin (with obligatory application of add-back therapy for all three GnRHa) and dydrogesterone. Costs were calculated for a period of 6 months. **RESULTS:** Costs of endometriosis treatment per patient per 6 months were 1102€ for triptorelin, 1118€ for leuprorelin, 340€ for buserelin, 369€ for dydrogesterone and 295€ for dienogest. Dydrogesterone is less effective and more costly alternative in comparison with buserelin and dienogest. Among alternatives with the same efficacy dienogest is the most efficient option leading to savings from 74€ to 823€ per patient in 6 months. **CONCLUSIONS:** Using dienogest for treatment of endometriosis in Russia is as effective as using GnRHa but can lead to considerable cost savings because add-back therapy is not required.

PIH28

COST MINIMIZATION ANALYSIS OF THE DIENOGEST USE IN PATIENTS WITH ENDOMETRIS UNDER BRAZILIAN PUBLIC AND PRIVATE PERSPECTIVE

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OBJECTIVES: To provide the results from a cost-minimization (CM) model that compares the use of dienogest with the use of GnRH antagonist (GnRHa) leuprorelin acetate, both for 6 months, in women with endometriosis-associated pelvic pain (EAPP) in Brazil. **METHODS:** A(CM) model was developed in the form of a decision tree to mimic treatment sequence in Brazil. The analysis was conducted under the private and public payer perspectives, only direct costs were included, procedures and drug costs were obtain from Brazilian official databases of public and private health care system fees. This CM model compared different treatment pathways for women with EAPP and used a 50% improvement in pelvic pain as a definition of a treatment responder to elicit treatment duration. Treatment response assessment was at 12 week period. Two basic treatment pathways were defined: a two treatment sequence (2TS) and tree treatment sequence (3TS). The 2TS consists of: GnRHa/dienogest followed by surgery. The 3TS consists of: GnRHa/dienogest, dienogest/GnRH as second treatment and surgery as final option. Subsequent treatments were only for patients that did not respond to previous treatment. Discount was not applied as costs occurred within 1 year period. **RESULTS:** The CM model shows that for both treatment pathways and perspectives dienogest is a cost-saving alternative. Under private payer perspective for 2TS and 3TS: BRL 1020.42 VS BRL 2328.94 and BRL 1461.22 VS BRL 2377.52 for dienogest and GnRHa respectively. Under public payer perspective for 2TS and 3TS: BRL 882.74 VS BRL 768.13 and BRL 942.18 VS BRL 856.77 for dienogest and GnRHa respectively. Efficacy for 2TS and 3TS are: 91.58%

and 97.87% respectively. **CONCLUSIONS:** This analysis portends dienogest as a cost-saving alternative for the treatment of EAPP compared to GnRHa in Brazil from the public and private payer perspective.

PIH29

INVESTIGATING THE IMPACT OF MENTAL HEALTH STATUS ON HEALTH AND SOCIAL CARE COSTS OF OLDER PEOPLE AFTER ACUTE HOSPITAL ADMISSION

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OBJECTIVES: In England, nearly two-thirds of older people in acute hospital care suffer from co-morbid physical and mental health conditions. This study investigated the health and social care costs for a group of older (70+) people identified with a mental health condition after hospital admission. **METHODS:** The Better Mental Health (BMH) study recruited 247 patients at hospital admission in Nottingham, England. Electronic administrative records were sought for six months post-admission from health (services: general practices, hospitals, ambulance transport, intermediate and mental health care) and social care. The cohort was characterised by one or more aspects of mental health: cognitive impairment, depression, delirium, and neuropsychiatric health. Differences in mean cost between groups were assessed using t-tests; association between mental health and service-level cost was investigated using GLM regression. **RESULTS:** Health and social care costs were derived for all 247 participants, except primary care, derived for 122 (subset) participants due to GP recruitment. In the subset, mean (95% CI, median, range) total cost was £9842 (8573-11256, 7717, 715-48795). Mean cost (95% CI) for mental health care was significantly ($p<0.05$) higher for patients: with depression than without (£194 (106-322) Vs. £55 (17-111)); bottom-50% on the neuropsychiatric health scale (£202 (124-298) Vs. £55 (16-118)). Patients with delirium, compared to without, had significantly lower costs for GP consultations (£316 (196-492) Vs. £552 (429-701)) and hospital outpatient visits (£333 (253-444) Vs. £497 (400-621)). The GLM did not identify a significant association between aspects of mental health and service-level costs. **CONCLUSIONS:** This study suggests a person's mental health affects consumption of some, but not all, services evaluated. In general, these patients are costly, high resource-users, of health and social care services; however, this consumption pattern cannot be attributed to one particular aspect of mental health. Future work should investigate the impact of physical *and* mental health comorbidities on resource-use.

INDIVIDUAL'S HEALTH – Patient-Reported Outcomes & Patient Preference Studies

PIH30

MEDICATION ADHERENCE AND ADVERSE HEALTH OUTCOMES IN COMMUNITY DWELLING OLDER PATIENTS

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OBJECTIVES: To determine the association between medication adherence and adverse drug events (ADEs), health related quality of life (HRQOL) and hospitalisation in older community dwelling patients. **METHODS:** A retrospective cohort study of 855 patients aged ≥70 years from 15 general practices in Ireland in 2010. Medication adherence was measured by: (i) the Medication Possession Ratio (MPR) using national pharmacy claims dispensing data; and (ii) self-report using the Morisky Medication Adherence Scale. ADEs and hospitalisation were measured by patient medical record and self-report for the previous 6 months. ADEs were reviewed by two independent clinicians. HRQOL was measured using EQ-5D. Multilevel Poisson and linear regression were used to examine how the number of ADEs, utility and hospitalisation varied by adherence after adjusting for patient and practice level covariates; socioeconomic status, deprivation, co-morbidity, number of drugs, functional disabilities, social support and health insurance. **RESULTS:** A total of 592 (69%) patients were adherent based on dispensed pharmacy claims data (MPR ≥80%) and 553 (63%) self-reported adherence to their medication. The median MPR for self-reported adherent patients was 0.88 (IQR: 0.78, 0.95) compared to 0.86 (IQR: 0.71, 0.93) for non-adherent patients ($p<0.01$). Non-adherence (MPR<80%) was not significantly associated with any ADEs but self-reported non-adherent patients had an increased risk of any ADEs (IRR 1.18; 95% CI 1.05, 0, 1.33 $p<0.01$). Non-adherent patients had a significantly lower mean HRQOL utility (MPR coefficient, -0.11, SE 0.03, $p<0.001$; self-report coefficient, -0.06, SE 0.01, $p<0.001$) and an almost two-fold increased risk in the expected rate of any hospitalisation (MPR IRR, 1.75; 95% CI, 1.42, 2.15, $p<0.001$; self-report IRR, 1.53; 95% CI, 1.16, 2.01, $p<0.01$) compared to adherent patients. **CONCLUSIONS:** Non-adherence was significantly associated with adverse health outcomes. Developing methods to assist older adults in accurate and safe management of their medications may increase their quality of life.

PIH31

VALIDATION OF ACCEPT, A NEW GENERIC MEASURE TO ASSESS HOW PATIENTS WITH CHRONIC DISEASES BALANCE BETWEEN THE ADVANTAGES AND DISADVANTAGES OF FOLLOWING THE RECOMMENDED TREATMENT REGIMEN IN REAL-LIFE

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OBJECTIVES: To reduce, score, and validate the Accept questionnaire. **METHODS:** Accept is a 32-items PRO questionnaire measuring the concept of Acceptance. It was developed based on grounded theory and qualitative research. Each treatment characteristic was assessed on a response scale opposing "easy to accept" to "not easy to accept". We conducted an observational prospective study on 182 subjects engaged in long-term treatment regimen. Adult patients where consecutively recruited by a network of pharmacists when prescribed with a drug indicated in various chronic diseases (including asthma, diabetes, various cardio-vascular diseases, retroviral infections, osteoporosis). Patients were asked to complete Accept and MMAS-4 questionnaires at Month 1, 3 and 6 after having given their informed consent. The structure was explored through PCA, and confirmed with multi-trait analysis. Internal consistency reliability of dimensions was assessed through Cronbach's alpha. Scale-scale correlations were calculated. **RESULTS:** After reduction, Accept was made of 25 items organised in 1 overall Acceptance score and 6 domain-specific scores (efficacy, tolerance, convenience, constraints, treatment duration, multiple medication). Cronbach's alpha was 0,85 for overall Acceptance score, which met convergent and divergent validity criteria (both 100%). The domain-specific scores showed satisfactory to good results (Cronbach's alpha ranging from 0,67 - 0,87, convegrent validity ranging from 63% to 100%, and divergent validity ranging from 33% - 100%). Scale-scale correlations ranged from 0.02 to 0.58, confirming the multi-dimensional nature of the questionnaire. The good properties of Accept were stable over time. **CONCLUSIONS:** Accept is a brief, comprehensive, generic questionnaire focused on Acceptance. Initial validation in a population of patients with a wide range of long-term treatment showed promising results and confirmed the position of Acceptance. Further, disease-specific, large prospective study are needed to assess the ability of Accept to predict persistence to treatment.

PIH32

DETERMINANTS OF NON-ADHERENCE TO MEDICATIONS AMONG CHRONIC PATIENTS IN MACCABI HEALTH CARE SERVICES

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OBJECTIVES: Implementation of co-payments may reduce the use of essential medications, worsen patients' outcomes, and increase overall health care costs. The aim of this study was to examine to what extent non-adherence of chronic patients to medication stems from financial reasons and what determinants are associated with non-adherence. **METHODS:** A telephone survey was conducted among a representative sample of Maccabi Healthcare Services chronic patients aged ≥55 yrs (n=522). Respondents were defined as non-adherent if they reported they had stopped taking prescribed medications in the previous year and/or not purchasing prescribed medications due to its cost. Additional information collected included: age, gender, income, receiving explanation from a physician regarding the therapy, and out-of-pocket expenditure for prescribed medications. **RESULTS:** Mean age of the study population was 69.9±9.0 yrs (53% were male). Sixteen percent of respondents were defined as non-adherent, in 60% of them it was due to medication's cost. No significant differences were found between adherent and non-adherent respondents with regard to: age, gender, family status, country of birth, supplementary insurance coverage, or education. In a multivariable logistic regression model, non-adherence was associated with: lack of physician explanation about prescribed medications (OR=2.88, 95%CI: 1.46-5.68, P=0.002); higher out-of-pocket expenditure on medications (OR=1.93, 95%CI: 1.04-3.61, P=0.04), and lower household income (OR=0.81, 95%CI: 0.69-0.96, P=0.01). **CONCLUSIONS:** Information provided by physicians is associated with adherence of chronic patients to prescribed medications. Low income and high out-of-pocket expenditure for prescribed medication are associated with non-adherence. Since adherence is strongly affected even by a relatively low and flat co-payment as applied in Maccabi Healthcare Services, health policy makers may consider adoption of value-based co-payments that are differentiated by treatment value rather than by its cost, and targeted mainly at chronic patients. This approach may lead to improved adherence and outcomes with the potential of reducing long-term costs.

PIH33

COST-EFFECTIVENESS OF MEDICATION ADHERENCE ENHANCING INTERVENTIONS: A SYSTEMATIC REVIEW

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OBJECTIVES: In light of the presumed costs of non-adherence to medication and the pressure to reduce unnecessary health care expenditures in the current economic climate, a review that assesses evidence of cost-effectiveness of adherence enhancing interventions would be timely. The objective of this paper is to examine the cost-effectiveness of adherence enhancing interventions and the quality of the studies reviewed. **METHODS:** MEDLINE, PsycInfo, EconLit and the Centre for Reviews and Dissemination databases were searched for randomised controlled trials that performed full economic evaluations of adherence enhancing interventions. Information was collected on study characteristics, cost-effectiveness of treatment alternatives, quality of economic evaluations, and risk of bias. **RESULTS:** Fourteen studies were included, of which the overall quality was found to be moderate. Five used a societal perspective, eight a provider perspective, and a single study used a patient perspective. Ten studies examined interventions that were both more costly and more effective than usual care, and four were less costly and more effective. Comprehensive evidence from the societal perspective yielded disappointing results for potential cost-effectiveness of adherence interventions. Studies from other perspectives provided weak to moderately promising evidence that adherence interventions can be cost-effective. **CONCLUSIONS:** Few randomised controlled trials examined the cost-effectiveness of adherence interventions. There was limited evidence of potential cost-effectiveness of adherence programmes. Most interventions did not report whether their intervention was effective in the first place, and many suffered from methodological limitations. To demonstrate that adherence interventions offer societal benefits, we recommend that the most promising interventions are subjected to a rigorous cost-effectiveness evaluation.

PIH34

A SYSTEMATIC REVIEW OF PATIENT PREFERENCES FOR SUBCUTANEOUS MEDICATIONS

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OBJECTIVES: Of the many routes of drug administration, some are more acceptable to patients than others; for example when a choice is presented, patients will usually prefer an oral over an injectable medication, all else being equal. Patient preference may be expressed in terms of health and non-health-related measures, which include: health technology-related attributes (including ergonomics, ease of use, convenience), behaviour (e.g. needle phobia and patients' perceptions of treatment), and adverse reactions attributable to the route of administration. Preferences may result in process-related (dis)utility, and be revealed as (non)adherence. This review aims to examine ambulatory patients' preferences for subcutaneously administered, self-injectable medications, compared with other routes of administration for the same medicines. **METHODS:** Ten electronic databases were searched for publications published between 2002 and 2012 using terms pertaining to methods of administration, preferences and adherence. Eligibility for inclusion was determined through reference to specific criteria by two independent reviewers. **RESULTS:** Of the 1,146 papers screened, 70 met the inclusion criteria. Studies focused mainly on methods of administration for insulin and treatments of paediatric growth disorders and multiple sclerosis. Pen devices were significantly preferred to needle & syringes administration in 11 out of 12 studies – particularly with respect to ergonomics, convenience and portability; however, preferences between autoinjectors and pen devices were less pronounced. Oral administration was preferred to subcutaneous administration in 6 studies (but did not reach statistical significance), as was inhaler therapy (favoured significantly in 3 out of 4 studies). **CONCLUSIONS:** The review identified a number of studies which revealed important differences in patient preference between methods and routes of drug delivery. Further evidence is required to support the notion that preference translates to better adherence.

PIH35

THE EFFECT OF MEDICAL DEVICES WITH DOSE-MEMORY AND REMINDER FUNCTIONS ON PATIENTS' TREATMENT ADHERENCE, CONFIDENCE AND DISEASE SELF-MANAGEMENT

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OBJECTIVES: Adherence to treatment is an important issue in the management of chronic diseases and an indicator of patients' ability to self-manage their condition. Some medical devices have been designed to help support patients' self-management and adherence by including dose-memory and reminder functions. This literature review explored the role and impact of these devices on patients' adherence to treatment, confidence and disease self-management. **METHODS:** A search of Medline, Embase and PsycInfo was performed to identify articles published in English from 2003-2013, which studied the effect of devices with memory and/or reminder functions on treatment adherence, confidence and self-management. The main attributes of the abstracts selected for inclusion and full-text review, were summarized. **RESULTS:** The database searches yielded 940 abstracts. Of the 47 meeting the inclusion criteria, 32 were retained. The articles explored the impact of memory and/or reminder devices on treatment adherence, device usability and users' (patients, health care professionals (HCPs) and caregivers) relationship and attitudes towards the devices. Devices with memory and/or reminder functions were found to improve self-reported and electronically-monitored treatment adherence in prophylactic medication use (e.g. contraceptives) and a range of chronic diseases including HIV, diabetes and asthma. Memory functions were considered valuable in disease management by patients and HCPs. Of particular value was that memory and/or reminder functions provided dose-history information, enhanced patients' confidence with, and ability to manage their medication and condition, and helped reduce forgotten or incorrect medication dosing. **CONCLUSIONS:** The incorporation of memory functions alone and in combination with reminder features in medical devices can improve patient's adherence, confidence and self-management. This can lead to improvements in disease control and clinical outcomes, thereby offering clinical and economic value. This review highlights the importance of conducting further qualitative and quantitative research in this area to fully understand the value of these types of devices to patients and HCPs.

PIH36

COMPARISON OF ELDERLY ADULTS BY NUMBER OF RX MEDICATIONS USED: RESULTS FROM THE NATIONAL HEALTH AND WELLNESS SURVEY ACROSS 5EU COUNTRIES

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OBJECTIVES: Compliance with medications among elderly patients is particularly important, as the consequences may be quite serious. Results suggest that use of three or more medications may put a considerable burden on elderly patients and may affect their compliance. This analysis profiles elderly patients across 5EU by the number of medications currently used and their compliance related behaviors. Combination products were considered as one prescription medication. **METHODS:** Results were taken from the 2011 5EU National Health and Wellness Survey, a nationally representative, self-administered survey. Respondents were adults age 18 and over from France, Germany, Italy, Spain and UK. This analysis focuses on adults age >= 65. Physical and mental quality of life was measured using the SF12v2 scale. Activity impairment was measured using the Work Productivity and Activity Impairment scale. **RESULTS:** Out of the total sample of age >=65 (n=10,612), ~37% of elderly adults across 5EU currently use four or more prescription (Rx) medications to treat their conditions, 44% use 1-3 Rx medications, and 18% use no Rx medications. Activity impairment is greater among those using 4+ medications (38.6 vs. 22.7 vs. 16.0). Emergency room visits and hospitalizations are also higher. This group appears to be more proactive in engaging in cost-saving behaviors to alleviate some of the treatment costs in the past 6 months (30% vs 24% vs 15%) (e.g., asking for generic alternatives (19% vs 16% vs 8%), ever changing prescription to another drug (61% vs 51% vs 45%) and switching to a generic version of a prescribed drug (35% vs 27% vs 18%). **CONCLUSIONS:** Considerably higher health care costs and greater activity impairment can be seen among elderly patients using more prescription medications. Given the financial burden of using multiple medications, and the lower incomes of these patients, cost-saving methods are more frequently utilized by these patients.

PIH37

PRELIMINARY ITALIAN ARCHIVE OF EQ-5D DATA ON INDIVIDUALS FROM THE GENERAL POPULATION AND WITH DIFFERENT DISEASE CONDITIONS

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OBJECTIVES: In the last 15 years our research activity collected several HRQoL data, through the EQ-5D-3L and other generic (SF-36) or condition-specific questionnaires. The objective was to assess and compare HRQoL among different population subgroups. **METHODS:** We reviewed all the HRQoL studies conducted by our research group between 1998 and 2012. We identified several conditions to be compared in terms of VAS score and utility index: these were assessed using the Italian social tariffs and then adjusted for age and sex. **RESULTS:** The archive included QoL data from 7,754 subjects (51.5% male), grouped in 29 different subgroups: type 1 and 2 diabetes mellitus, moderate to severe haemophilia, major depression, atopic dermatitis, severe and chronic hand eczema, psoriatic arthritis, schizophrenia/schizophrenic disorder, β-thalassemia major, gastroesophageal reflux, abdominal aortic aneurysm, systemic sclerosis, chronic hepatitis B, chronic hepatitis C, hepatitis from other causes, cirrhosis, hepatocellular carcinoma, liver transplant, general Italian population aged from 18 to 75 years. Overall, the subjects were aged from 14 to 96 years (mean(+SD)=55.7(+17.1), median=57.7). The adjusted EQ-5D-VAS mean+SD ranged from a minimum of 33.9+14.1 in patients with a major depression episode, to a maximum of 82.5+12.9 in patients with atopic dermatitis 8 weeks after flare. The mean+SD VAS was 73.2+11.4 in the general population. The adjusted mean+SD utility index ranged from 0.60+0.17 in psoriatic arthritis before starting treatment with biological agents, to 0.931+0.09 among chronic hepatitis B patients. **CONCLUSIONS:** The many EQ-5D data collected in the last 15 years are merged now in a unique archive that can be used to assess and compare the burden of disease in terms of HRQoL in different subpopulations. This archive is to be considered preliminary and deemed to be integrated with additional data from ongoing or future projects, and perhaps with other analogous archives created in other contexts and Countires.

PIH38

LEVEL AND FACTORS IMPACTING THE PATIENT DISSATISFACTION IN THE PRIMARY CARE VISITS BASED ON THE CROSS-SECTION MEASUREMENT – A PROSPECTIVE FINNISH STUDY

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OBJECTIVES: A key dimension impacting clinical outcomes in health care evaluation is satisfaction (i.e. the level of meeting user's expectations for the service), which impact adherence and persistence. Yet, evidence regarding patient dissatisfaction is scarce. Thus, we asked what the level of dissatisfaction is after a health centre (HC) visit, and which factors impact the dissatisfaction? **METHODS:** A prospective survey to primary care patients visiting 3 Finnish HCs (Linnainmaa, Omapihlaja, Pirkkala) in Pirkanmaa district during 31.1–11.2.2011 was done. No inclusion/exclusion criteria were used. Comprehensive patient-, clinician- and HC-related data was collected. The patient's satisfaction was measured immediately after the visit in the form of handling problem during a visit (Likert range 0–10). This was inversed to assess the drawback related to the visit (0=full benefit; problem was solved; 10=no benefit; full drawback). An explorative statistical analysis was done including multivariate data mining in order to find the model with the best Akaike information criteria. The model aimed to demonstrate the independent factors impacting the drawback and control heterogeneity. **RESULTS:** A total of 90.1% of the full sample (n=647) answered to the drawback question. 40.3% of the patients had problem solved during the visit (i.e. reported 0) and just 6.9% of the patients experienced drawback exceeding 5. The factors increasing the drawback in the stepwise OLS regression model with the +1 ln-transformation for the drawback were longer waiting time, asthma/copd and male sex. The factors decreasing the drawback were patient's higher subjective health status, patient's higher subjective health status in comparison to others of same age/sex, some long-term conditions (rheumatoid disease, allergy, hip/knee joint erosion), clinician's longer experience, clinician in specialising education and certain HC. **CONCLUSIONS:** Some 60% of the patients experienced that their problem was not fully handled. Multiple factors impact the drawback which could be notified in the planning of HC services.

PIH40

MEASUREMENT OF SOCIETAL MEDICAL CARE PREFERENCES WITH THE SAME COST PER QALY: A DISCRETE CHOICE STUDY

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OBJECTIVES: The principal of QALY is sometimes referred to as "A QALY is a QALY is a QALY", which means all QALYs have the same value, while QALYs may not fully reflect public preferences. If the use of QALYs in decision making proves beneficial but insufficient, what other factors should be taken into consideration simultaneously? **METHODS:** We conducted a face-to-face survey using a discrete choice method to measure societal medical care preferences. The profiles of assumed patients consisted of the following four factors: (a) age (young or elderly patient); (b) objective of care (treatment or prevention); (c) severity of health state (severe or mild); and (d) past experience of receiving care (yes or no). These

factors were orthogonally combined to construct 16 patient profiles. All assumed medical care had the same ICER (cost per QALY). Respondents were randomly assigned to two of the 16 profiles and asked which one of the patients should preferentially receive treatment from a societal point of view, given a limited medical resource. Respondents were stratified by age and sex. **RESULTS:** A total of 1091 responses were collected from 50 sites across Japan. The most preferred factor was "younger patient (a)", followed by "treatment (b)" and "severe health state (c)", which had the same degree of preference. No statistical significance was found for "no past experience of care (d)". Public preference for medical care for elderly patients increased with increasing age. University-graduated people tended to prioritize care for patients who are younger and in severer conditions. **CONCLUSIONS:** Our survey revealed that public medical care preferences are influenced by factors such as age, even with the same cost per QALY. Based on an economic evaluation, age is an important factor for decision-making that reflects societal preferences.

PIH41

POTENTIALLY INAPPROPRIATE PRESCRIBING (PIP) AND ITS ASSOCIATION WITH INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADL) IMPAIRMENT IN OLDER PEOPLE

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OBJECTIVES: Older people are particularly vulnerable to adverse effects of prescribed drugs. PIP can be defined as the use of medicines with an unfavourable risk benefit ratio. There has been little research on the relationship between PIP and humanistic outcomes, such as functional impairment. This study aims to measure the prevalence of PIP in an older Irish population and to investigate its association with IADL impairment. **METHODS:** A retrospective cohort study of 2,051 community-dwelling participants in The Irish Longitudinal Study on Ageing (TILDA) aged ≥65 years with linked medication dispensing history from a national pharmacy claims database was carried out. Exposure to PIP in the 12 months prior to assessing functional impairment was determined using the Screening Tool for Older Persons' Prescriptions (STOPP), the Beers' criteria (2012) and Assessing Care of Vulnerable Elders (ACOVE) indicators relating to inappropriate medications. Logistic regression was used to determine the association between exposure to PIP and presence of any IADL impairment, adjusting for age, gender, socioeconomic status, number of repeat drug classes co-morbidity and medication adherence. **RESULTS:** The overall prevalence of PIP was 66.89% (n=1,372). Of these 514 (25.06%) had one instance of PIP, while 858 (41.83%) had two or more. Prevalence was highest using the STOPP criteria (57.29%), compared to prevalences of 37.64% (Beers' criteria) and 23.5% (ACOVE indicators. Participants with ≥2 PIP indicators were significantly more likely to have an IADL impairment (adjusted OR=1.91; 95%CI=1.15-3.18) compared to no PIP. Similar associations were found for the individual measures of PIP. Age, number of repeat drug classes and co-morbidity were also significantly associated with IADL impairment. **CONCLUSIONS:** PIP in the elderly is highly prevalent and exposure to PIP is independently associated with increased risk of having IADL impairment. This suggests the importance of considering appropriateness when prescribing medicines in order to minimise adverse outcomes.

PIH42

ADDING A REMINDER SHORT MESSAGE SERVICE (SMS) BEFORE AND TABLET COMPUTER DURING CLINIC IMPROVES ELECTRONIC PATIENT REPORTED OUTCOME MEASURES (EPROMS) COLLECTION

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OBJECTIVES: Patient Reported Outcome Measures (PROMs) monitor both symptom progression and treatment effectiveness, and play an increasing role in everyday clinical practice. Electronic PROMs (ePROMs) enable real-time reporting back to the patient and medical team, comparison with similar patient cohorts and long-term cost-effective outcome measurement. Concerns have, however, been expressed about electronic PROMs collection in the elderly. The primary objective of this three-phase pilot study was to measure uptake using a web-based ePROMs platform following the introduction of reminder short messaging service (SMS) before and Tablet Computer during clinic. **METHODS:** Eighty-seven consecutive new elective orthopaedic patients in a single surgeon's practice were recruited. Group 1 (n=27) received only a reminder letter, Group 2 (n=34) also received a reminder SMS message via mobile or home telephone and Group 3 (n=26) also had access to a Tablet Computer in clinic. **RESULTS:** Mean age in Group 1 was 55.1 (24-77) years, Group 2 was 60.5 (23-85) years and Group 3 was 54.2 (17-77) years (p>0.05). Overall 75% patients had Internet access and 33% of Group 1, 50% of Group 2 and 73% of Group 3 recorded an ePROMs score (p=0.03). In Group 2 and 3 26% of patients did not remember receiving a SMS message that was delivered. **CONCLUSIONS:** Collecting and using PROMs data in everyday clinical practice is challenging. This small pilot study shows that adding a reminder SMS before and access to a Tablet Computer during clinic improves ePROMs collection onto a clinical outcomes web-based system. Further process improvements, such as additional staff training and telephone call reminders, might further improve uptake and a more comprehensive study is planned.

PIH43

EIGHTY-NINE LOCAL ROCHE SPONSORED FRENCH STUDIES PERFORMED IN THE PAST 10 YEARS WERE EVALUATED TO DETERMINE HOW PATIENT REPORTED OUTCOMES WERE USED

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OBJECTIVES: Patient Reported Outcomes (PROs) are increasingly used in clinical studies as well as requested by health authorities (EMA, FDA). This descriptive analysis aims to explore how PRO were used in the French affiliate of Roche. **METHODS:** A total of 89 local studies performed between 2003 and 2013 were evaluated to determine how PROs were collected and evaluated. **RESULTS:** Forty (45%) out of 89 studies were clinical trials, 44 (49%) were non-interventional studies (NIS) and 5 were expanded access program studies. A total of 33 (37%) studies used at least one PRO; 13 (39%) were clinical trials and 20 (61%) were NIS. There were no PRO in the field of transplantation, 21% of the studies in oncology used PRO, 47% in virology, 60% in anemia and 72% in rheumatology. More than 3600 sites participated in the 33 studies using PRO: 17424 patients were included, 14237 patients (82%) answered at least one PRO and 12314 (86%) of the questionnaires received were considered to be analyzable for statistical analysis (non analyzable PROs were usually due to missing data). The median number of questionnaires per study was 2, (range 1-6). While most studies in virology and anemia used 1 or 2 questionnaires per study, rheumatology studies used at least 3 questionnaires per study. The median study duration was 12 months, (range 1-60). While 84% of PRO were collected at inclusion in the study, 73% of PROs were received after the 6 month visit, 65% at the 12 month visit and less than 50% after 12 months. Seven studies (21%) used PRO as a primary endpoint, and the percentage of patients who answered the questionnaire answered was higher (mean 91%) than when PRO was a secondary endpoint (mean 79%). **CONCLUSIONS:** Careful consideration should be given to number of questionnaires used per study as quality decreases as number of evaluations increases.

PIH44

CONFIRMATORY FACTOR ANALYSIS AND EVALUATION OF CLINICALLY IMPORTANT DIFFERENCES IN MENOPAUSE-SPECIFIC QUALITY OF LIFE ASSOCIATED WITH BAZEDOXIFENE/CONJUGATED ESTROGENS IN A VULVAR/VAGINAL ATROPHY POPULATION

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OBJECTIVES: To confirm the factor structure of the Menopause-Specific Quality of Life (MENQOL) questionnaire for a vulvar/vaginal atrophy (VVA) population by applying confirmatory factor analysis (CFA), and to determine whether improvements in health-related quality of life (HRQL) observed in a VVA population with bazedoxifene/conjugated estrogens (BZA/CE) relative to placebo can be deemed clinically relevant. **METHODS:** In a randomized control trial, postmenopausal women with ≥ 1 bothersome moderate-to-severe VVA symptom received BZA 20 mg/CE 0.45 or 0.625 mg, BZA 20mg or placebo for 12 weeks. HRQL and treatment satisfaction were evaluated using the MENQOL questionnaire and the Menopause Symptoms-Treatment Satisfaction Questionnaire (MS-TSQ), respectively. The structure of the MENQOL questionnaire was evaluated using a CFA. Clinically important differences (CID) for the MENQOL were determined using a regression model to estimate differences in domain and total scores corresponding to one category difference in MS-TSQ items, which were used as anchors. **RESULTS:** The postulated CFA model fit the MENQOL data (Bentler's Comparative Fit Index >0.9). Treatment with BZA 20 mg/CE 0.45 and 0.625 mg compared with placebo was associated with statistically significant improvements in MENQOL vasomotor and sexual functioning domains, and total score (p <0.001). BZA 20 mg/CE 0.625 mg was also associated with significant improvements in physical functioning (p=0.019). Change from baseline in MENQOL vasomotor functioning for BZA 20 mg/CE 0.625 mg over placebo was greater than the estimated CID, with BZA 20 mg/CE 0.45 mg approaching CID. Changes in total score for BZA 20 mg/CE 0.625 mg compared with placebo also approacöhed CID. Changes in MENQOL sexual functioning from baseline over placebo, while statistically significant and quite large, were less than the CID estimate. **CONCLUSIONS:** CFA modeling provides strong support for the existing factor structure of the MENQOL questionnaire. Improvements in HRQL seen with BZA/CE approached or exceeded CIDs for VMS functioning and total score.

PIH45

EXAMINATION OF PELVIC FLOOR MUSCLE FUNCTION AFTER PELVIC FLOOR MUSCLE TRAINING AND USING CUBE PESSARY

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OBJECTIVES: Follow up of pelvic floor muscle function after pelvic floor muscle training and using cube pessary, paying special attention to the changes in the strength of pelvic floor muscle and in the ability to relax. **METHODS:** To determine the degree of the changes in the strength of pelvic floor muscle and in the ability to relax, 35 patients had been contacted before provided with cube pessaries and pelvic floor muscle training. Thirty out of 35 subjects supported our study. Five subjects were excluded due to vaginitis, so finally 30 survey data were processed. Pelvic floor muscle function measurements were performed at the beginning when cube pessaries were given to the subjects and later after a 3-week period of usage. Patients were selected with the help of the non random sample method. Demographic data and gynecological history selection were based on our own general survey questionnaire, while FemiScan surface EMG was used to measure pelvic floor muscle strength and the ability to relax. Statistical analysis involved t-test or Mann-Whitney U-test, significance level was defined at p< 0.05. **RESULTS:** Although pelvic floor muscle strength showed positive changes, statistically significant changes were not detected in the surveyed group. In the analysis of survey data of the ability to relax pelvic floor muscle statistically significant difference (p=0,001) could be detected in the average results either at the beginning when cube pessaries were given to the subjects or after a 3-week period of usage. **CONCLUSIONS:** Cube pessary usage and pelvic floor muscle training may have a positive effect on pelvic floor muscle function.

PIH46
A PARENT-ADMINISTERED BUT CHILD-COMPLETED PATIENT-REPORTED OUTCOME (PRO) PROVIDES A MEASURE WITH CONTENT VALIDITY THAT IS VALID AND RELIABLE FOR USE IN CHILDREN AGED 6 TO 11 YEARS
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OBJECTIVES: Collecting data about symptoms and health-related quality of life impacts in children aged 6-11 is particularly challenging. Children themselves do not necessarily have the reading skills or the cognitive and recall capacity to self-report on their own, but equally parents are not always with their child or may not observe them closely enough and some symptoms are not observable. To overcome these challenges we developed a parent-administered child-report symptom measure in which the parents helped the child read and understand the PRO items. **METHODS:** Iterative rounds of qualitative concept elicitation and cognitive debriefing interviews with children (aged 6-11) and parents supported the development and refinement of daily diary instructions, items and response scales. The resulting items were included in an observational study of 185 children (aged 6-11) who completed the diary at home for seven days in order to support the development of scoring and psychometric validation. Feedback on the draft scales was obtained from both children and parents following the at-home completion phase, with the parent survey and debriefing focusing on how much help they had provided to the children in regards to reading, understanding, recalling and responding during the seven days. **RESULTS:** The diary questions were developed to be completed by the child, but instructions indicated that the parent could help the child read and understand them. Observation of parents helping the child and subsequent debriefing provided evidence that parental help aided the child in recalling accurately. However, the children did push back if they disagreed with their parent's suggested response, suggesting they were not unduly influenced. Subsequent psychometric validation confirmed that this approach and the refined items provided valid, reliable and responsive scores. **CONCLUSIONS:** This PRO development provides evidence that a parent-assisted child self-report symptom measure had strong content validity and was valid, reliable and responsive to changes over time.

PIH47
PATIENT SURVEY DATA RESULTS: PREFERENCES FOR REMINDERS IN PRO STUDIES
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OBJECTIVES: To identify effective reminder strategies, survey data focused on patient preferences for reminders in Patient Reported Outcomes (PRO) studies was investigated. This presentation will share these results to provide recommendations for patient reminder strategies to optimize patient compliance and data quality. **METHODS:** A survey was completed in 2013, involving patients who participated in at least one clinical study in the past two years that required patient diaries. The survey sought to establish patient preferences (modality/timing) for receiving diary reminders based on their experiences, including an evaluation on their personal technology behaviors. **RESULTS:** Responses were provided by 405 patients. The patients stated their reasons for non-compliance of their patient diaries: 51.4% reported "non-compliance due to forgetting"; 41.1% reported "being too busy"; 27.6% reported "a lack of diary access"; and 2.7% reported "other reasons". Patients also stated their modality preferences for reminders. The preferred choice was text messages (67.2%); followed by hand-held alerts (34.3%); phone calls (34.1%); calendar alerts (32.6%); and email (6.2%). Although the majority of patients indicated checking text messages and emails daily, significantly more patients checked text messages immediately when compared to email (52.9% vs. 15.1%) suggesting that text messages would be a more effective way to remind patients. The majority of patients wanted to be reminded of their diary assessments (97.3%), appointments (95.8%), and medication dosing (95.0%). **CONCLUSIONS:** As the top reason for non-compliance was "forgetting", this suggests that reminders can be helpful in improving compliance. Results show that patients prefer to be reminded, also suggesting that reminders can improve compliance. Technology behaviors suggest that text messages could be an effective way to remind patients. Patient preferences for reminders should be given careful consideration – since incorporating optimal reminder strategies can likely improve the patient experience, compliance and data quality.

PIH48
STRUCTURAL VALIDITY OF A 14-ITEM ABRIDGED VERSION OF THE MENOPAUSE CERVANTES HEALTH-RELATED-QUALITY-OF-LIFE SCALE
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OBJECTIVES: The Cervantes scale is a specific health-related-quality-of-life (HRQoL) questionnaire developed in Spanish women through and beyond menopause. The original scale contains 31-items and it is time-consuming in the routine medical practice. The aim of this work was to reduce the 31-item scale and to produce an abridged version with the same dimensional structure and similar psychometric properties. **METHODS:** A representative sample of 563 women [mean age 60 years old (SD=6.7, Min=46, Max=82)] extracted from the Ginerisk study was used. The Ginerisk was an epidemiological, cross-sectional study carried out in 4,157 Spanish post-menopausal women attending out-patient clinics of Gynecology throughout Spain in year 2011. Item analysis, internal consistency reliability, item-total and item-domain correlations and item correlation with the generic Spanish version of the MOS-SF12v2 questionnaire dimensions were initially studied. Dimensional Confirmatory Factor Analysis (CFA) and Full-model CFA were used to check structure stability. A 3-fold cross-validation method was used to obtain stable estimates, by means of multi-group analysis. **RESULTS:** The scale was reduced to a 14-items version: The Cervantes-SF, containing four main dimensions: Menopause and health, Mental health, Sexuality, and Couple Relationship, being the first dimension composed by 3 sub-dimensions: vasomotor symptoms, health, and Aging. Goodness-of-fit statistics were better than those of the extended version (chi-square/df=2.130, AGFI=0.859, PCFI=0.919, RMSEA=0.044). Internal consistency was good (Cronbach's alpha=0.830) but slightly lower than that of the original scale. Correlations between extended and reduced subscales was high and significant in all cases ($p<0.001$), ranging from r=0.857 for Aging to r=0.971 for Vasomotor symptoms. **CONCLUSIONS:** The Cervantes scale may be reduced to an abridged version of 14-item (Cervantes-SF) which maintains the original dimensional structure and psychometric properties. This version extends 45% of the original length, being faster to apply and making it specially suitable for routine medical practice.

PIH49
VALUE ATTRIBUTES OF GENERIC VERSUS BRANDED DRUGS IN SÃO PAULO, BRAZIL
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OBJECTIVES: To assess the patients' and their accompanying family members or carers' value attributes and perceptions about GD when compared to the corresponding brand name drugs (BD). **METHODS:** A total of 25 patients and 25 accompanying persons were consecutively selected and interviewed while visiting 6 commercial pharmacies located in different regions of São Paulo city. Also 25 patients and 25 accompanying persons were consecutively selected and interviewed while waiting for their regular outpatient visits at the university outpatient clinic. The questionnaire consisted of questions regarding socio-economic, demographic and educational items, quality of life (QoL), and the interviewee perception regarding the value attributes of GD when compared to BD. The study was approved by the local ethic committee. **RESULTS:** Respondents were predominantly women (57%) and the mean age was 54 years. Additionally, 55% relied exclusively in public health care system and 55% were regularly employed. Mean QoL as assessed by SF-6D was 0,74. Respondents overwhelmingly (99%) believed GD to be cheaper than BD. Some 36% and 63% also reported GD to be less and equally effective, respectively, as compared to BD. GD were perceived as either safe or less safe than BD in 46% and 46%, respectively. Some 74% of the sample agreed with the statement that they would prefer to take a BD if there was no price difference to the GD, and 85% admitted they regularly compare the prices of BD and GD before deciding which drug to buy. **CONCLUSIONS:** Multiple factors may contribute to the decision to buy a GD. Among these perceived effectiveness, safety and price appear to be the most important factors. Further studies are needed to better understand the decision-making process regarding GD use and its consequences for the health care system and families.

PIH50
ARE ISRAELI ADULTS WILLING TO PAY HIGHER HEALTH TAXES FOR A WIDER COVERAGE OF LIFE-EXTENDING MEDICATIONS?
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OBJECTIVES: The Israeli National List of Health Services (NLHS) offers a generous coverage for drugs and other technologies. However, not all approved drugs are covered under the basic health insurance and are frequently subject to out-of-pocket payments. We assessed the ex-ante willingness to pay (WTP) for a more generous public coverage for life-extending medications. **METHODS:** We conducted a telephone survey among a representative sample of the adult population in Israel (n=502). We asked participants to indicate whether they will be willing to pay an increased health tax assuring that all life-extending interventions will be covered and provided by their health insurance plans with no cost-sharing. We also collected information on respondent age, gender, income, education, self-rated health and coverage of supplementary/private health insurance. **RESULTS:** Mean age of the study population was 51.7±15.9 years. 63.5% indicated that they would be willing-to-pay an increased health tax for a generous public coverage of medications. Respondents willing-to-pay were younger (49.3±15.0 vs. 55.9±16.4 years; $p<0.001$), reported a higher self-rated health ($p=0.001$), and WTP increased with respondent's income ($p=0.005$), and were also covered by a commercial health insurance ($p=0.002$). Among all respondents (WTP set at zero for those unwilling to pay) the median extra monthly WTP was in the range of 0-$7. The independent predictors for WTP identified in the logistic regression analysis were: respondent age (OR=0.974; 95% CI 0.960-0.989); and being Jewish (OR=2.997; 95% CI 1.745-5.147). **CONCLUSIONS:** Additional sources of funding should be identified and allocated to allow a more generous coverage of life-extending medications. Respondents are willing-to-pay extra health taxes (up to 7.5% of the current average health tax) to assure that all life-extending interventions are included in the NLHS at no co-payment. While these potential extra funds are sufficient to cover a wide range of technologies it is unlikely that the health tax will be raised in Israel in the near future.

PIH51
WILLINGNESS TO PAY (WTP) FOR A BRAND NAME DRUG IN SÂO PAULO, BRAZIL
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OBJECTIVES: To assess WTP of patients and accompanying family members or carers for a brand name drug (BD) as compared to a GD for treating an acute and a chronic condition. **METHODS:** A total of 25 patients and 25 accompanying family members or carers were consecutively selected and interviewed while visiting 6 commercial pharmacies located in different regions of São Paulo city. Also another 25 patients and 25 accompanying family members or carers were consecutively selected and interviewed while waiting for their regular outpatient visits at the university outpatient clinic. A questionnaire with 2 hypothetical scenarios describing

an acute condition (acute tonsillitis in an 8 year old child) and a chronic condition (an adult with diabetes mellitus type 2) was developed. WTP for a BD as compared with a GD was assessed in both scenarios using the payment scale and the open-ended formats. The study was approved by the local ethical committee. **RESULTS:** Respondents were predominantly women (57%) and the mean age was 54 y.o. A family income of less than R$ 1.356,00 was reported by 16%. For the total study sample, the maximum WTP for a BD (over and above the mean retail price of a GD) for the acute and chronic case scenarios were on average R$ 27,54 and R$ 21,04 when measured by the payment scale and R$ 36,54 and R$ 24,77 when measured by the open-ended question, respectively. These values are 36% to 65% above the mean retail prices of the corresponding GD. **CONCLUSIONS:** Patients and accompanying persons were willing to pay considerably more for the BD when compared to GD. This may be driven by the perception of higher perceived effectiveness and safety of BD.

INDIVIDUAL'S HEALTH – Health Care Use & Policy Studies

PIH52
PROTECTIVE FACTORS FOR UNIVERSITY STUDENTS' HEALTH

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OBJECTIVES: To assess which of the studied factors were positively associated with the students' health and to investigate which of these factors stood out as the most important protective factors for their health. **METHODS:** Data were obtained from a cross-sectional study conducted during the academic 2011/2012th at the universities in Niš, Belgrade and Novi Sad, which surveyed a total of 2285 students of both sexes. This study examines variables such as physical, psychological and social health, protective factors and risk factors. Students were assessing their own health answering the questionnaire. **RESULTS:** Only 11.8% of the surveyed students have assessed their health as excellent, 72.5% as very good or good, and 15.7% as poor or very poor. Better health status was positively correlated with the quality of sleep, the existence of free time, physical and social activities, religiosity and built health values in all three universities. Kruskal-Wallis H test showed that better students are more satisfied with their life ($p < 0.001$), that better assess their health ($p < 0.01$) and less drink alcoholic beverages. Female students had more physical pain, were more frequently depressed than men, they were more easily tired, they were much more nervous and had more problems than men with sleep. Men assessed their health as better than female students. However, the satisfaction scale ($\chi 2$ homogeneity test; $p < 0.001$) were found females to be more satisfied with their lives than male students. **CONCLUSIONS:** General health is affected by various physical, psychological and social aspects of health. The results show that there are significant protective factors for better social, psychological and general health in students that may be affected. Therefore, health promotion decision makers should adopt contemporary strategies that will in the future put emphasis on the social and psychological components of students' health.

PIH53
SOCIETAL BURDEN OF HYSTERECTOMY IN REPRODUCTIVE-AGED WOMEN WITH UTERINE FIBROIDS

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OBJECTIVES: Uterine fibroids (UF) affect approximately 20% to 40% of reproductive-aged women. The mainstay of treatment of symptomatic UF is surgical. Myomectomy surgically removes UF while preserving the uterus. However, hysterectomy that is considered to be the definitive treatment of UF, causes infertility.The aim of our study was to analyze the prevalence of hysterectomy in Hungary among reproductive-aged women with UF to assess the societal burden due to lost fertility. **METHODS:** Database were analyzed. Surgical procedures for the treatment of UF (ICD-10: D25), in 20-45 years old women between 2007 and 2012 were analyzed based on the Hungarian National Health Insurance Fund database. Economic burden of lost fertility was assessed by the human capital approach. Present value of life for a newborn child was calculated by applying 2011 GDP per capita and 3.7% discount rate. **RESULTS:** Among 11,095 women with surgical procedure related to UF the prevalence of hysterectomy was 61.5% (n=6827). Most hysterectomised women (n=4781) were 40-45 years old; unexpectedly a significant number of 20-40 years old women with UF had hysterectomy (n=2046). Present value of a newborn child was 262,314 EUR in 2011. **CONCLUSIONS:** Our results indicate that immediate hysterectomy, even in women under 40 years, is still a frequently performed surgical procedure for the treatment of UF. The macroeconomic consequences of lost fertility due to hysterectomy in reproductive-aged women with UF are significant. Even only one additional child-birth due to avoided hysterectomy would result in significant societal and economic benefits. Further scientific evaluations are needed to define more accurately the long term macroeconomic impact of preserved fertility in women with UF.

PIH54
MANAGEMENT OF OBESE WOMEN DURING PREGNANCY ACROSS EUROPE ACCORDING TO CLINICAL PRACTICE GUIDELINES

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OBJECTIVES: To review, within the framework of the FP7 DALI (Vitamin D And Lifestyle Intervention for Gestational Diabetes Mellitus (GDM) Prevention) study, guidelines for the management of obese women during pregnancy across Europe to assess the specificity of the recommendations in this group at risk of adverse pregnancy outcomes. **METHODS:** To determine whether additional clinical tests, advice, planning, management or pregnancy follow-up were recommended for obese women during pregnancy,Clinical Practice Guidelines (CPGs) were collated from across the Endocrinology and Obstetrics National Societies websites of the 9 European countries participating in the FP7 DALI study (Austria, Belgium, Denmark, Ireland, Italy, The Netherlands, Poland, Spain, UK). This was complemented by a Medline search and a survey among the investigators of the DALI study. **RESULTS:** Fifteen CPG for 9 countries were retrieved. All but Spanish guidelines, which recommend O'Sullivan test, recommend OGTT 75g to detect GDM in obese women. Most of them include 24-28 weeks as the time for OGTT, but other schedules are also used, especially when risk factors other than obesity are present. Other common recommendations for obese women in European CPGs were diet advice (included in the guidelines of 6 different countries), special birth planning (5 countries), exercise and other lifestyle recommendations (4 countries) and vitamin D supplementation, multidisciplinary follow-up (including endocrinologist or diabetologist) and additional ultrasound scan (3 countries). **CONCLUSIONS:** Recommendations for obese women in the studied countries are heterogeneous and in many cases do not include actions beyond screening for GDM. Existing guidelines will be reviewed in the light of the findings from the interventions studied in the framework of the DALI study.

PIH55
LONG-TERM FISCAL IMPLICATIONS OF FUNDING ASSISTED REPRODUCTIVE THERAPIES: A GENERATIONAL ACCOUNTING MODEL FOR SPAIN

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OBJECTIVES: Infertility affects 14% of couples in reproductive age in Spain. Progressive population ageing leads the assessment of policies that favor birth-rates. The objective is estimating the lifetime economic benefits of publicly financing assisted reproductive therapies (ART) in Spain, by calculating the return on this investment. **METHODS:** Generational accounting model that simulates the flow of taxes paid by the individual minus those direct government transfers received (e.g. health care, education, pensions) over the lifecycle of a child. The cost of ART was calculated as the average cost of conceiving a child through currently available ART in Spain. The difference between discounted transfers and taxes minus the cost of ART equals the net present value (NPV) of a child conceived by ART. Year 2006 was set as the base case because of its macroeconomic stability. A 3.5% discount rate was applied. Sensitivity analysis tested robustness of results under different scenarios. **RESULTS:** An ART-conceived child would contribute €534,624 in net taxes to the government and would receive €479,952 in governmental transfers over her lifecycle. After discounting the cost of ART (9,000€) the NPV is estimated at €45,672. Each Euro invested in subsidizing ART reverts into fiscal benefits of €5. Sensitivity analysis shows that even in extreme macroeconomic scenarios, the long-run NPV of an ART-conceived child ranges between €11,233 and €62,470. The return on investment varies between €1.25 y €6.94 € for each Euro invested in ART. The break-even age at which the financial position begins to be favorable to the Spanish Treasury was set at 34-42 years. **CONCLUSIONS:** Generational accounting models allow estimating long-term fiscal implications of public funding of ART. Each Euro invested in subsidizing ART reverts into fiscal benefits of €5. Thus, investment in ART leads to substantial discounted future fiscal revenue for the Spanish Treasury, notwithstanding its beneficial psychological effect for infertile couples.

PIH56
WOULD A NEW THERAPY FOR CHILDREN BE REFUSED IN THE CONTEXT OF THE GERMAN AMNOG?

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OBJECTIVES: The new German law AMNOG was introduced in 2011. According to it all newly launched therapy options would need to be evaluated by the Institute for Quality and Efficiency in health care (IQWIG) and the joint federal committee (Gemeinsamer Bundesausschuss, GBA) before a final price negotiation will happen. Given the specific characteristics of pediatric patients it is uncertain if a new drug for those patients would successfully pass the AMNOG process. **METHODS:** The AMNOG evaluation criteria were applied to the specifics of pediatric drugs. A special focus was given to the benefit assessment method, clinical trial designs and the AMNOG process. **RESULTS:** Current HTA evaluation methods being applied to medical therapies, in general, need to be modified when applied to pediatric therapies. For example, traditional benefit evaluations that require randomized clinical trials are standard but cannot always be fulfilled in this patient population. In pediatric development programs one-arm studies are standard with surrogate endpoints in order to minimize the exposure of children to an experimental therapy. Additionally the naturally low sample size within pediatric indications linked to the different natural subgroups of children (babys, toddlers, etc.) make a formal additional benefit proof even harder. Hence from a benefit assessment perspective the clinical study design, sample size and choice of endpoint are most crucial but could hardly be executed in pediatric trials. With respect to the AMNOG process only pediatric trials in orphan disease could pass successfully given the exception rules for the additional benefit. **CONCLUSIONS:** If the German health care system is to secure the full benefits of potential new pediatric therapies, it will need to provide a similar process as it is granted for orphan drugs.

PIH57
HEALTH OUTCOMES OF FEMALE ANABOLIC-ANDROGENIC STEROID USERS

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OBJECTIVES: Anabolic-Androgenic Steroids (AAS) have been used for muscle mass development for over fifty years. The health outcomes of supraphysiologic doses of AAS have been debated, but most existing information pertains to men. This purpose of the study is to use the National Longitudinal Study of Adolescent Health (AddHealth) to elucidate health outcomes of AAS usage in women. **METHODS:** A cohort study of female AAS users were assessed in two time periods six years apart. Baseline descriptive statistics were used to describe age, income, race, drug use, education, and work performed for the sample. Follow up health outcomes include diabetes, heart disease, hyperlipidemia, anger, physician visit, use of medical care in the last year, Body Mass Index (BMI), blood pressure (BP), C-reactive protein, and HbA1C. Each dependent variable was tested in independent logistic regressions and in sensitivity tests using a MANOVA. **RESULTS:** The sample included 49 female respondents. Education was associated with a two-fold greater odds of AAS use comparing those who attended vocational school to those who attended college (OR=2.22, p=.03). Anger was associated with 88% greater risk of AAS use (OR=1.88, p=.04). HbA1c in the pre-diabetic range, while not statistically significant may be associated with AAS use (OR=1.85, p=.05). No other health outcomes were identified. **CONCLUSIONS:** This study contributes to the literature of female AAS use showing little in health care usage and long term health consequences. Anger is associated with male users but little research exists pertaining to this phenomenon in women. Elevated HbA1c is not commonly associated with AAS use, but due to the small sample size more research should assess AAS use among females.

PIH58

USER AND TREATMENT CHARACTERISTICS OF ORAL CONTRACEPTIVES IN THE EUROPEAN UNION

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OBJECTIVES: As a basis for future safety evaluations of oral contraceptive (OC) use in Europe, current user and treatment characteristics were assessed in four European health care databases. **METHODS:** A descriptive retrospective database study was performed over 2009-2010 in GP databases from The Netherlands (IPCI), UK (THIN) and Italy (HSD) and linked pharmacy dispensing and hospital admission data from The Netherlands (PHARMO). Study follow-up started at the first OC prescription in 2009-2010 (users), one year after database entry or at Jan 1, 2009. Health indicators at start of follow-up included BMI and previous diagnosis of, or use of drugs for selected chronic conditions. Also, previous diagnoses of deep vein thrombosis, pulmonary embolism, cerebrovascular disease, myocardial infarction, breast cancer and cervical cancer were assessed. Treatment characteristics of OC included history of use, type of OC (chemical substance) used during 2009-2010 and switches or discontinuations. **RESULTS:** Among 4.9 million women, 14% had OC prescribed in 2009-2010. In The Netherlands and UK, 12-16% and in Italy 6% had a record of OC use. The prevalence of OC recorded prescription at January 1, 2010 was 81 per 1000 women of all ages and 271 per 1000 women aged 15-24, a much lower figure than what is recorded by surveys, probably due to switches between use and non-use and to reimbursement and/or prescription policies that reduce recording in GP databases. Among the non-users in 2009-2010, up to 22% had a history of OC recorded use. Little differences in health indicators were found between users and non-users in the databases where the information was available. **CONCLUSIONS:** Trends in health among European women in general also apply to OC users. However, OC use is not registered very well in health care databases which limits the possibilities of pharmacovigilance. Distribution channels and reimbursement policies vary, as well as recording in the databases.

PIH59

MEDICATION TREATMENT AND HEALTH CARE UTILIZATION FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN GERMANY

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OBJECTIVES: To explore health care utilization and treatment patterns for attention-deficit/hyperactivity disorder (ADHD) in Germany, with particular emphasis on psychostimulant prescriptions. **METHODS:** The complete claims database of the organization of physicians registered with statutory health insurance (SHI) in Nordbaden/Germany was available for analysis, covering the total regional population enrolled in SHI (2.24 million lives). The dataset for years 2003 to 2009 was reorganized as to allow patient-centered evaluation. For calendar year 2009, 21,287 patients with ADHD (male, 15,108; female, 6,179; including 5,931 patients or 27.9% [male, 4,582; female, 1,349] with coexisting conduct disorder [F90.1 or a combination of F90 and F91 codes according to ICD-10]) were available for analysis. **RESULTS:** Preschool children (age 0-5 years) with ADHD were prescribed medication in very rare cases (1.6% in 2009) and after an average lead time of more than one year only. Most received some form of nonpharmacological therapy or were left untreated (42%). In contrast, 41% of children (age group 6-12 years, since 2003, continuously increasing from 32%) and 54% of adolescents (age group 13-17 years, rate remaining stable since 2006) were prescribed either stimulant (methylphenidate, MPH, or amphetamine) or nonstimulant (atomoxetine) drugs. Males and patients with concomitant conduct disorder were more likely to receive medication treatment. Modified-release MPH formulations were more widely used than immediate-release MPH. Overall use of medication increased steadily, from 32.2% of ADHD patients in 2003 to 39.9% in 2009, whereas its rate decreased over time in adult patients (declining from 38% in 2003 to 26% in 2009). – Upon individual review of all prescriptions of ADHD medication for members of the control group, no evidence was found supporting potentially inappropriate use of stimulant medication. **CONCLUSIONS:** Treatment patterns were highly age and gender specific. Except for preschoolers, therapeutic management of patients with ADHD relied heavily on drug treatment.

PIH60

TRENDS IN HOSPITAL ADMISSIONS AMONG MEN AND WOMEN ABOVE THE AGE OF 60 LIVING IN STOCKHOLM AND UPPSALA COUNTIES IN SWEDEN

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OBJECTIVES: To measure the change in the risk of first, second, and third hospitalization and the change in the proportion of hospitalization-free men and women above the age of 60 living in Stockholm and Uppsala counties in Sweden between 1972 and 2010. **METHODS:** Individuals were followed in national registers for hospitalizations and deaths from all causes between 1972 and 2010. Censoring occured at whichever of the following events appeared first; hospitalization (first, second, thrid), death, or December 31, 2010. Survival analysis was used to determine the proportion of hospitalization-free individuals. Discrete time logistic regression was used to obtain the the relative risk (RR) of first, second and third hospitalization. **RESULTS:** An increase in the proportion of hospitalization-free individuals over time was observed for both men and women; for example 87% more 82 year-old men, born in 1928, were free of hospitalizations since the age of 60 compared to those born in 1912. Between the years 1972 and 2010, the average annual decrease in the risk of first hospitalization after the age of 60 was 1% for both men (RR: 0.991, 95%CI: 0.991-0.992) and women. The average annual risk for hospitalization decreased for the second and thrid event as well; however the reduction was not significant. **CONCLUSIONS:** With the increase in the proportion of elderly in the population, the number of individuals with chronic diseases may increase, leading to higher demand for medical and social care. We have observed downward trends of the risk of first, second, and third hospitalization after the age of 60, which could be explained by a postponement of severe morbidity to higher ages. Focus on primary care and changes in inpatient care in Sweden may also partly exaplain the annual reduction in the risk of hospitalization.

PIH62

DO EMA AND FDA HAVE DIFFERENT OPINIONS/REQUIREMENTS IN TERMS OF PEDIATRIC STUDIES FOR SITAGLIPTIN (ALONE OR IN COMBINATION)?

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OBJECTIVES: Since the implementation of Pediatric Regulations/Legislations in the USA (Pediatric Research Equity Act - PREA) and in Europe (Pediatric Investigation Plans - PIPs), product development programs should include pediatric studies. The objective of this study is to review opinions (EMA) and requirements (FDA) given by both agencies in the case of sitagliptin (alone and combined) for the treatment of diabetes mellitus in children. **METHODS:** The EMA and FDA websites were explored to: 1) Identify the products marketed under the INN of sitagliptin (alone or in combination), and 2) Identify the associated PIPs or PREA requirements. The search was performed on January 18, 2013. **RESULTS:** Eight products were marketed in Europe [i.e., sitagliptin (Januvia, Ristaben, Tesavel, Xelvia) and sitagliptin + metformin (Janumet, Efficib, Ristfor, Velmetia)]. Four products were authorized in the USA [i.e., sitagliptin (Januvia); sitagliptin + metformin (Janumet, Janumet XR); sitagliptin + simvastatin (Juvisync)]. The FDA and the EMA provided the same opinion for sitagliptin alone, i.e., deferred pediatric study for patients aged 11 to 16. The FDA and the EMA disagreed on sitagliptin + metformin. The EMA granted a waiver for all subsets of the pediatric population on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments, while the FDA required a pediatric study under PREA for the treatment of type 2 diabetes in pediatric patients aged 11 to 16. As for sitagliptin + simvastatin, the FDA grants a waiver on the grounds that the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients. **CONCLUSIONS:** The FDA and the EMA have similar opinions except for the combination sitagliptin + metformin. One reason could be the higher prevalence of type 2 diabetes mellitus in children in the USA as compared to Europe.

INFECTION – Clinical Outcomes Studies

PIN1

THE GEOGRAPHIC CORRELATION BETWEEN LYME DISEASE INCIDENCE AND DEGENERATIVE NEUROLOGICAL DISEASE MORTALITY: AN ECOLOGICAL STUDY

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OBJECTIVES: The objective of the present study was to assess the geographic correlation between the incidence of Lyme disease (LD) and mortality due to certain degenerative neurologic diseases (DND) in the US. **METHODS:** For this ecological study, public data sources at the CDC were queried to quantify LD cases and DND deaths for the 5-year period 2002-2006. Alzheimer's disease, Parkinson's disease, and motor neuron disease were preselected as DND of interest. The separate datasets, for LD and DND, were combined by matching county and state names. Counties with at least 1 case of LD and at least 10 deaths due to DND were included in analyses. All analyses were performed in SAS. **RESULTS:** Of the 3141 counties of the US, 1372 reported at least 1 case of LD, 2742 reported at least 10 deaths due to DND, and 1339 met both conditions and were therefore included in analyses. The observed number of LD cases and DND deaths for a single county ranged from 1-6407 (mean: 78; median: 3) and 10-9207 (mean: 165; median: 55), respectively. The Spearman rank test indicated that there is a fair degree of correlation between LD incidence and DND mortality ($r=0.44$, $p<0.0001$). In sensitivity analyses, (1) excluding outliers, defined as observations $\geq 99^{th}$ percentile (LD>53; DND>1255), and (2) evaluating each disease separately, the correlation remained similar in magnitude and statistically significant (coefficient: 0.32-0.41; $p<0.0001$). **CONCLUSIONS:** There is a fair degree of correlation between LD incidence and DND mortality: US counties with a higher number of LD cases tend to have a higher number of

deaths due to DND. This study is limited by its ecological nature and more rigorous epidemiologic research is needed to elucidate the association between LD and DND.

PIN2

IMPACT OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) REGIMEN ON ADHERENCE AND RISK OF HOSPITALIZATION IN VETERANS WITH HIV/AIDS

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OBJECTIVES: High pill burden has been associated with poor adherence to HAART and adverse clinical outcomes. This study evaluated the impact of HAART as a single-tablet regimen (STR) and multiple-tablet regimen (MTR) on outcomes in HIV patients within the Veteran's Affairs (VA) system. **METHODS:** A retrospective, cohort study assessed patient VA dispensation data for HIV medications during the study enrollment period (7/1/2006 to 9/30/2011). Patients were assigned to the following cohorts: STR if they received a HAART regimen of a single tablet/day or MTR if they received a regimen of ≥2 tablets/day and no single tablet/day regimen during the enrollment period. Patients were followed from the index date (start of HAART regimen) until the earliest of treatment discontinuation, end of study period, or last date of health care-related activity (eg, VA benefits file or death). Hospitalization and adherence (medication possession ratio [MPR] ≥95%) were evaluated. Multivariate cohort differences in outcomes were controlled for using Cox-proportional hazard and logistic models; covariates were measured during a 6-month baseline period. **RESULTS:** In all, 15,602 patients (STR, n=6,191; MTR, n=9,411) met study criteria; average age of the study sample was 52 years. Both cohorts had similar CD4 counts (mean [SD]: 432.2 [282.8] vs 419.3 [280.9]; P=0.287) but significantly fewer patients receiving STR vs MTR had an undetectable viral load at baseline (42% vs 46%, P<0.001). During follow-up, significantly more STR patients were adherent compared to MTR patients (75% vs 55.7%, P<0.001). STR patients were also significantly less likely to experience hospitalization compared to MTR patients (26.8% vs 31.3%, P<0.001). After controlling for baseline covariates, STR patients had twice the odds of being adherent (OR: 1.98, P<0.001) and 31% lower hazard of experiencing hospitalization during follow-up (HR: 0.69, P<0.001). **CONCLUSIONS:** Treatment with STR compared to MTR improves adherence rates and decreases hospitalizations in patients with HIV/AIDS.

PIN3

A DECISION ANALYTIC MARKOV MODEL TO EVALUATE THE HEALTH OUTCOMES OF SOFOSBUVIR FOR PREVIOUSLY UNTREATED PATIENTS AND THOSE WITHOUT TREATMENT OPTIONS WITH CHRONIC HEPATITIS C VIRUS GENOTYPE 2 INFECTION

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OBJECTIVES: Sofosbuvir (SOF) is a nucleotide polymerase inhibitor with excellent clinical efficacy in combination with ribavirin (RBV) for 12 weeks for patients who are chronically infected with hepatitis C virus (HCV) genotype 2. A decision-analytic Markov model evaluated the health outcomes of SOF+RBV compared with current treatment options for patients who are previously untreated, had no response to prior interferon treatment, or are unable to take interferon. **METHODS:** The analysis modeled 3 cohorts of chronic HCV genotype 2 patients with an average age of 50 and 25% with cirrhosis at the start of treatment followed-up to 100 years of age from a US third-party payer perspective. SOF+RBV for 12 weeks was compared with 1) pegylated interferon (PegIFN)+RBV for 24 weeks in the treatment-naïve patients; 2) PegIFN+RBV for 48 weeks in the treatment-experienced; and 3) no treatment in those unable to take interferon. Sustained virologic response (SVR) and adverse event rates were based on phase III clinical trials. Transition probability, utility, and cost estimates (in 2013 US dollars) were based on a literature review, public sources, and consensus by a panel of 4 hepatologists. **RESULTS:** In the treatment-naïve cohort, the SOF+RBV regimen resulted in an 83% decrease in the cases of liver disease complications including hepatocellular carcinoma, decompensated cirrhosis, liver transplant, and HCV-related death compared with PegIFN+RBV. The reduction of the listed liver disease sequelae was 59% in the treatment-experienced vs. PegIFN+RBV and 93% in the interferon-unable cohort vs. no treatment. The number needed to treat (NNT) with SOF+RBV rather than PegIFN+RBV to achieve one additional SVR was 6 in the treatment-naïve and 4 in the treatment-experienced cohorts. **CONCLUSIONS:** SOF+RBV was projected to yield better health outcomes in genotype 2 patients compared to PegIFN+RBV, largely driven by superior efficacy, and the potential to cure those who are unable to take interferon-based therapies.

PIN4

THE RELATIVE EFFICACY AND SAFETY OF SIMEPREVIR AND TELAPREVIR IN TREATMENT-NAÏVE HEPATITIS C INFECTED PATIENTS IN A JAPANESE POPULATION – A BAYESIAN NETWORK META-ANALYSIS

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OBJECTIVES: Simeprevir (SMV) is an oral, once-daily potent protease inhibitor for the treatment of chronic Hepatitis C genotype-1 infection (cHCV). In phase IIb/III RCTs conducted in Japan, SMV, in combination with peginterferon-α and ribavirin (PegIFN/RBV), demonstrated potent efficacy in cHCV genotype 1-infected patients relative to PegIFN/RBV and was generally safe and well-tolerated. Telaprevir (TVR) in combination with PegIFN/RBV is licensed for the treatment of cHCV in Japan. In the absence of head-to-head comparisons of TVR and SMV, we undertook a network meta-analysis (NMA) to examine the relative efficacy and safety of SMV and TVR in combination with PegIFN/RBV in a Japanese population. **METHODS:** A systematic review identified RCTs in Japanese treatment-naive patients with the above treatments and with the following endpoints: Sustained Virological Response (SVR), discontinuation of all medications (overall/due to Adverse Events (AE)), and incidence of anemia, rash (all grades) and pruritus-common adverse events of cHCV treatment. A Bayesian NMA was performed for all endpoints, assuming fixed study effects. Unpublished SMV studies meeting the inclusion criteria were obtained. **RESULTS:** Three studies met the inclusion criteria: 2 phase III RCTs (SMV n=183; TVR n=189), and 1 SMV phase IIb RCT (n=92). Baseline characteristics were generally comparable for all studies. SMV shows a higher odds ratio (OR) of achieving SVR versus TVR (OR 1.68 (0.66-4.26)). SMV shows a lower OR of discontinuation: overall 0.35 (0.12-1.00) and due to AEs 0.87 (0.23-3.34) versus TVR. SMV shows a lower OR of experiencing anemia 0.20 (0.07-0.56) and rash 0.42 (0.17-0.99) but a higher OR of experiencing pruritus 1.26 (0.46-3.47) versus TVR. The main limitation of this study is the small number of trials included in the analysis. **CONCLUSIONS:** In this indirect comparison, SMV, in combination with PegIFN/RBV, showed a favourable risk-benefit profile compared to TVR with PegIFN/RBV in Japanese treatment-naïve Hepatitis C infected patients.

PIN5

PUBLIC HEALTH IMPACTS OF PROBIOTICS IN CONTROLLING UPPER RESPIRATORY TRACT INFECTIONS IN FRANCE

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OBJECTIVES: Two meta-analyses (York Health Economics Consortium [YHEC]; Cochrane) reported the beneficial effects of probiotics (live microorganisms which when administered in adequate amount confer a health benefit on the host). They demonstrated efficacy at reducing the duration and number of upper respiratory tract infections (URTI) and antibiotics use. The purchase of probiotics by consumers is likely to have positive externalities to the national health system and society. The aim of this analysis was to estimate the public health consequences of probiotics consumption, in France. **METHODS:** A 1/1,000 virtual age and gender standardized population was generated using a Markov model (TreeAge 2009). URTI risk factors were age, active/passive smoking, living in the community. Influenza like illness (ILI) and flu daily incidence rates came from Sentinelles, a practitioner network aimed at identifying flu outbreak. Epidemiologic data were used to differentiate cold, ILI and flu. One-day cycles were used over the 2011-2012 flu season. Probiotics effects came from two meta-analyses. Outcomes included numbers of URTIs days and episodes, antibiotics courses and sick leave days avoided with probiotics. **RESULTS:** According to YHEC data, probiotics reduced URTI episodes (average 7 days) by -0.77 days [-1.5;-0.04]. Extrapolating these results to the French population, probiotics would save 2.85 million URTI-days, the number of antibiotic courses would drop from 1,004,000 to 674,000 (difference about -330,000) and the number of sick leave days avoided in adults would be 653,000. According to Cochrane data, probiotics would reduce the probability to have an URTI episode by 0.58 [0.36;0.92] and antibiotic prescription by 0.67 [0.45;0.98]. The probiotic impact would become larger in terms of URTI-days avoided (-7.1 million), antibiotic courses (-509,000) and workdays lost (-1.2 million). **CONCLUSIONS:** The probiotics public health impact on URTI is significant at a national level even though this analysis was restricted to the 1% of patients visiting a practitioner.

PIN6

LONG-TERM OUTCOMES OF CHRONIC HEPATITIS C IN THE POPULATION OF NEWLY DIAGNOSED RUSSIAN PATIENTS

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OBJECTIVES: To predict the future incidence of chronic hepatitis C in Russia and assess potential impact of the available antiviral therapies (pegylated interferon a-2a/a-2b or standard interferon a-2b combined with ribavirin) on long-term morbidity and mortality rates in the population of newly diagnosed Russian patients with chronic hepatitis C. **METHODS:** Based on the national epidemiologic data and published natural history studies, the prognostic Markov model was developed. Depending on the results of antiviral therapy, patients' flows over 25-year time frame were simulated. End points of interests included: the incidence of compensated and decompensated cirrhosis, hepatocellular carcinoma and cumulative time that patients will spend in each state, the number of patients, who will require liver transplantation, and HCV-related mortality rates. **RESULTS:** During years 2013-2017 about 276,000 new cases of chronic hepatitis C will be diagnosed in Russia. After 25 years since being diagnosed 130, 189 and 227 of 1,000 patients received pegylated interferon a-2a, pegylated interferon a-2b and standard interferon a-2b, respectively, will develop compensated cirrhosis. The cumulative time that patients will spend in compensated cirrhosis state will be 848, 1,218 and 1,482 patient-years, respectively. During the established time frame, there will be expected 25, 36 and 43 cases of hepatocellular carcinoma and 35, 51 and 62 HCV-related deaths. 28, 40 and 49 patients, respectively, will require liver transplantation. **CONCLUSIONS:** The findings from the present study provide the opportunity to plan volumes of medical care that will be required to Russian patients with chronic hepatitis C during 25 years since disease was first diagnosed. The treatment with pegylated interferon alfa-2a is considered the most preferable strategy due to considerably lower long-term morbidity and mortality rates as compared to pegylated interferon a-2b and standard interferon a-2b treatment.

PIN7

EPIDEMIOLOGY, TREATMENT OUTCOMES AND COSTS OF TREATING HEPATITIS C IN ROUTINE CARE – RESULTS FROM A LARGE MULTICENTER TRIAL

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OBJECTIVES: Estimates assume that 400,000 to 500,000 people are chronically infected with Hepatitis C in Germany. About 27% of end-stage liver cirrhosis and 25% of hepatocellular carcinoma are associated with HCV. The economic relevance of hepatitis C results from high costs for antiviral treatment as well as accompanying and secondary diseases. The aim of the study was to gain information on epidemiological characteristics, treatment outcomes and costs. **METHODS:** Underlying data were collected in a non-interventional trial between 2008 and 2011. Inclusion criteria were a confirmed HCV diagnosis and need for antiviral treatment. Besides sociodemographic and clinical parameters, HCV related resource utilization was gathered for a subgroup of patients. Data presented are mean values. **RESULTS:** Data on 7,637 patients receiving antiviral treatment with peginterferon-α-2a and ribavirin were collected. This analysis relates on 3,708 patients without HIV coinfection and/or drug substitution treatment. Mean age was 43.7 years, 60.3% were male. Most patients had a genotype-1 (61.3%) or genotype-3 infection (28.5%). The majority of patients was treatment-naïve (86.5%), 7.3% were relapser and 5.6% non-responder. Main sources of infection were injection drug use (34.8%) and blood products (14.2%). Mean duration of infection was 13.6 years. In average 48.9% of treatment-naïve GT-1(4-6) and 63.0% of GT-2/3 patients achieved SVR. For prior relapse patients and non-responder SVR-rates were: GT-1(4-6): 35.4%; GT-2/3: 58.5 and GT-1(4-6): 23.3% GT-2/3: 37.9%, respectively. Costs for antiviral treatment amount for €20,889 in GT-1(4-6) patients and €13,610 in GT-2/3 patients. Costs for the management of adverse events or HCV-related diseases sum up for €11.70. Ambulatory care, diagnostics procedures and hospital care amount for a small proportion of total costs. **CONCLUSIONS:** This study provides an overview on epidemiologic characteristics, treatment outcomes and treating costs in routine care. Treatment of HCV is costly and mainly affected by length of antiviral therapy.

PIN8

ESTIMATION OF THE NUMBER OF CASES OF NOSOCOMIAL SKIN AND SOFT TISSUE INFECTION IN ADULTS CAUSED BY GRAM-POSITIVE BACTERIA IN PUBLIC HOSPITALS IN MEXICO

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OBJECTIVES: To estimate the number of cases of nosocomial skin and soft tissue infection (SSTIs) in adults caused by Gram-positive bacteria (GPB) in public hospitals in Mexico. **METHODS:** The total number of hospital discharges in patients ≥18 years were extracted from databases of the National Health Information System. A rate of 5.97 cases of nosocomial infection (NI) per 100 discharges (issued by Instituto Mexicano del Seguro Social between 2011 and 2012) was applied. Through a systematic literature review and critical reading of studies developed under the Mexican setting (using the Critical Appraisal Skills Programme guidelines), we assessed the type of infection and determined the proportions of: microbiological culture obtained and microbiological culture giving positive isolates. In the last stage, microorganisms were classified according to their Gram staining characteristics. **RESULTS:** In the year 2011 there were 5,517,139 discharges from public hospital, inferring 329,373 cases of NI rate (16.9% under 18 years and 83.1% in adults). We estimated that SSTIs represents 33.2% of NI (42,430 cases), of these, a microbiological culture was obtained only in 63.0% of the cases (26,731) and pathogen were isolated in 87.0% of microbiological cultures (23,256), among these, GPB was identified in 44.2%. According to our estimates a conservative number of cases of nosocomial SSTIs in adults caused by GPB in 2011 was 10,279 and the pathogens reported were *Staphylococcus aureus* (71.1%), *Enterococcus spp* (14.2%), and others (14.6%). **CONCLUSIONS:** Although we found high heterogeneity in NI reports which may decrease the quality of the estimates presented in this research, in our opinion these results could help clinicians in the choice of initial antibiotics in order to reduce the probability of failure due emergence of resistant organisms.

PIN9

EFFECT OF ANTIVIRAL TREATMENT RATES ON THE PREDICTED FUTURE BURDEN OF GENOTYPE-1 CHRONIC HEPATITIS C IN THE UNITED KINGDOM

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OBJECTIVES: Chronic hepatitis C (CHC) treatment aims to prevent end-stage liver disease (ESLD) through sustained viral response (SVR). Treatment rates differ significantly across Europe (<1-16%). New protease-inhibitor based therapy offers an opportunity for increased SVR rates versus pegylated-interferon/ribavirin (>70% vs. 50%). The analysis estimates the impact of various treatment rates on future ESLD sequelae associated with genotype-1 CHC in the UK. **METHODS:** A Markov model was applied to estimate disease progression of a cohort of genotype-1 CHC patients over a 20-year time horizon. Endpoints included the following ESLD states: decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), liver transplantation (LT) and liver-related death (LrD). Model structure, progression rates, CHC prevalence and disease severity at baseline were based on published economic evaluations. The number of ESLD cases averted by a 1-year increase in the current UK treatment rate (3%) to 12% and 16% was estimated for a 71.5% and 50.0% SVR rate. **RESULTS:** Applying a 3% treatment rate and 71.5%/50.0% SVR rate predicted 8590/8647 cumulative DCC and 3577/3595 HCC cases, 814/820 LTs and 7613/7659 LrDs. The number of ESLD cases averted by applying a 12% treatment rate was estimated to be 565/395 DCC and 180/126 HCC cases, 51/36 LTs and 453/317 LrDs. Increasing treatment rate to 16% showed a decrease of 816/571 DCC and 260/182 HCC cases, 74/52 LTs and 655/458 LrDs. The overall reduction in ESLD cases was estimated to be -6.1%/-4.2% and -8.8%/-6.1% in both scenarios respectively. **CONCLUSIONS:** A 1-year increase in treatment rate was predicted to reduce the burden of genotype-1 CHC in 20 years in the UK. Different treatment rates across Europe imply unequal opportunities for patients to prevent CHC sequelae. Identifying CHC patients and offering antiviral therapy to maximise SVR could prevent substantial further severe liver disease and mortality.

PIN10

RECENT TRENDS IN INCIDENCE AND DEMOGRAPHICS OF PEDIATRIC MENINGOCOCCAL DISEASE IN THE UNITED STATES

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OBJECTIVES: Approximately 1,000-1,200 people in the United States (US) develop meningococcal disease (MD) each year. MD is a life-threatening bacterial infection most common in infants (age <1 year), adolescents, and persons living in close quarters. We estimated annual incidence and demographic characteristics of MD in the US pediatric population from 2000 to 2009. **METHODS:** Data for pediatric (age ≤20 years) MD-related hospitalizations (discharges with ICD-9-CM 036.xx) from the 2000, 2003, 2006, and 2009 HCUP Kids' Inpatient Databases (KID) were retrospectively analyzed. Annual MD incidence per 100,000 pediatrics (adjusted to 2010 US population) was estimated using KID sampling weights and year-specific population denominators from US census data. **RESULTS:** Pediatric MD incidence steadily decreased from 1.9/100,000 in 2000 to 0.7/100,000 in 2009, a 63% decline. Incidence was highest, by far, in infants, which also decreased during 2000-2009 (7.6/100,000 to 3.8/100,000, a 50% decline). Among children aged 1-4 years, incidence fell from 2.7/100,000 to 0.8/100,000 during this period, a 70% decline. In children aged 5-10 years, we observed a 75% decline (1.2/100,000 to 0.3/100,000); similar incidence and trends were seen for age groups 11-18 and 19-20 years. Pediatric MD cases were predominantly male, with male representation increasing from 55% to 61% of cases during 2000-2009. The racial composition of pediatric MD shifted somewhat during this period, with representation declining among whites (from 56% to 45% of cases) and increasing among blacks (from 8% to 11% of cases). Geographic distribution remained fairly constant, with highest representation from the South (~30% of cases) and West (~30% of cases). **CONCLUSIONS:** Pediatric MD incidence declined during the 2000's, possibly due to the introduction of the meningococcal conjugate vaccine in 2005. However, MD incidence remained substantially higher in infants compared with other age groups and there appeared to be a demographic shift in cases away from females and whites.

PIN11

THE GLOBAL BURDEN, INCIDENCE, AND PREVALENCE OF CHRONIC HEPATITIS C

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OBJECTIVES: To identify and understand hepatitis C virus (HCV) prevalence and mortality rates, disease course, and the availability of data on patient and viral characteristics that may affect treatment and outcomes. **METHODS:** A targeted review was undertaken in MEDLINE, using a predefined search strategy, to identify studies describing HCV burden. Additional searches were performed on the ISPOR conference and key epidemiological websites. **RESULTS:** A total of 1,773 references were identified. Results indicated that global HCV prevalence increased from 2.3% to 2.8% between 1990 and 2005, with highest prevalence in East Asia (> 3.5%). HCV screening programmes and mandatory reporting are present in only a few countries, so prevalence is likely to be even greater. In 2010, there were estimated to be 499,000 deaths globally related to HCV, making HCV-related complications the 25th most common cause of death and a significant global health problem. The prevalence of HCV genotypes varies geographically. Genotype 1 is most prevalent in North and South America, Europe, and the Asia-Pacific region (~45%-80%). Genotype 3 is most prevalent in South Asia (Pakistan, India, and Thailand) (~52%-80%); genotype 4 is most prevalent in the Middle East (~60%-92%). There is a lack of data for the majority of African and some Middle Eastern countries. Genotype 1 is associated with increased insulin resistance, worse response to therapy, and higher risk of developing cirrhosis and hepatocellular carcinoma. Genotype 3 is associated with increased steatosis (up to 73% of patients vs. 51% in patients with other genotypes) and fibrosis. **CONCLUSIONS:** In light of upcoming treatment alternatives, detailed epidemiological studies will help ascertain more accurately the prevalence of each HCV genotype, so that the true burden of HCV can be understood and treatments targeted appropriately.

PIN12

BURDEN OF VARICELLA IN EASTERN EUROPE: A SYSTEMATIC REVIEW AND CRITICAL ANALYSIS

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OBJECTIVES: Varicella is a common and vaccine-preventable disease, but its impact on public health in Eastern Europe (EE) has received little attention. This study aimed to review the epidemiology and economic burden of varicella in EE. **METHODS:** A systematic literature review was conducted in PubMed and government websites to identify published data on epidemiology and economic burden of varicella in EE. Extracted study data included varicella incidence, complications, mortality, vaccination program availability and coverage rates, as well as health care resource utilization and medical costs associated with varicella. Critical analyses of study quality and data gaps were analyzed at the country level. **RESULTS:** Published varicella data were identified from fourteen countries including Bosnia Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Russia, Serbia, Slovakia, and Slovenia. Only Latvia has a universal varicella vaccination program, while the remaining countries either only recommend

varicella vaccination for high-risk individuals or have no recommendations. The annual incidence of varicella in EE ranged from 164 per 100,000 in Latvia to 481 per 100,000 in Poland. Hospitalization rates associated with varicella ranged from 1 per 1,000 cases in Estonia to 30 per 1,000 cases in Latvia. Frequent complications among hospitalized patients included respiratory, skin, hematologic, and neurologic complications. Mortality rates ranged from 0-20 per 100,000 cases in Poland, Serbia, and Slovenia. Varicella incidence peaked in winter in Poland and Slovenia. No data on direct and indirect costs of varicella in EE was available. Overall, Poland and Slovenia had the most data on burden of varicella while limited data existed for the remaining countries. **CONCLUSIONS:** Epidemiologic and economic burden of varicella in EE have not been extensively studied. Given limited varicella vaccination policy in this region, gaps in evidence need to be addressed to inform policy makers about the public health impact on varicella.

PIN13

PREVELANCE OF HYDETED DISEASE IN SUGICALY OPERATED PATIENT IN SOME LIBYAN GENERAL HOSPITAL

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OBJECTIVES: Determine the prevalence of HD in cases referred to surgical wards in four hospitals in east part of Libya during period from 2004 to 2009. **METHODS:** Data was collected from four hospitals; Tripoli medical centre, central Hospital, Alzawia hospital and Gharian general hospital. Hospital data of, patients diagnosed as HD were collected from surgical departments. **RESULTS:** Out of 94,142 files were reviewed from four Hospitals there were 401(0.42%) confirmed cases of Hydatid disease. Among these medical records there were 233(58.1%) from Tripoli Medical Centre, 144(35.9%) from Centre Tripoli Hospital, 16(4%) from Al Zawiyah Hospital and 8(2%) from Gharyan Hospital. The gender distributions were 41.4% males and 58.6% females. Young adult ages between 15-30 were most commonly infected (35%). Liver and lungs was most common site of infection (81.1% and 13.5% of cases, respectively) Spleen was (2.0%). Cysts were found in sites like Pancreas, Ovary and kidney were (3.4 %) **CONCLUSIONS:** Hydatid disease is a Health problem affecting young Libyan population. The mean age of the patients was (2-40) years and more common in women) housewives) and students, the most common site of HD found in liver followed by lungs. Further studies are required to find the etiologic factors of HD in different areas in Libya.

PIN14

PREDICTOR FACTORS FOR THE PRESENCE OF POST HERPETIC NEURALGIA AT 3 MONTHS IN HERPES ZOSTER PATIENTS AGED 50 AND OVER IN ITALY: RESULTS FROM A GP-BASED OBSERVATIONAL PROSPECTIVE MULTICENTER STUDY

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OBJECTIVES: To identify predictors for the presence of Post Herpetic Neuralgia (PHN) at 3 months in Herpes Zoster (HZ) patients aged 50 and over in Italy. **METHODS:** General Practitioners (GPs) from regions throughout Italy included immunocompetent patients over 50 years old with a new HZ diagnosis and followed them during 6 months with visits (V) at 0, 1, 3 and 6 months. Occurrence and level of pain using a 0 to 10 visual analogic scale (VAS), clinical symptoms, patients' quality of life (QoL) and their health care resources utilization were recorded. A multivariate regression model was run to assess the predictor factors for the presence of PHN at 3 months. Univariate analysis was first undertaken on each variable to identify possible associations with PHN (level of significance, 25%) to be considered in the multivariate regression model. **RESULTS:** From March 2009 to July 2010, 108 GPs included 413 patients (148 Males and 265 Females) with HZ aged 67.9 y± 10.7 years. Most of them (89.6%) had pain at V0 (VAS score:5.8/10) and 91.5% received systemic antivirals, 70% within 72 hours after rash onset. During the follow-up, 52 patients consulted at least one specialist (dermatologist, neurologist, ophthalmologist…) and no cases were hospitalized. At 3 month, 20.6% presented PHN (VAS score: 3.7/10), and still 9.2% at 6 months (VAS score: 3.7/10). By logistic regression analysis a VAS score over 3, the presence of more than 50 vesicles and the gender male were the main predictive factors at the initial visit that were significantly associated with the presence of PHN at 3 months. **CONCLUSIONS:** Even if most of patients with HZ received the standard of care, many experienced intense and long-lasting pain. This study identified specific factors at presentation that could help identify patients who will develop PHN.

PIN15

RISK FACTORS INFLUENCING THE VIRAL TRANSMISSION AND THE POTENTIAL DEVELOPMENT OF HPV-INDUCED PATHOLOGIES

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OBJECTIVES: The current study has been designed to investigate risk factors influencing the viral transmission and development of HPV infections within the Italian population. **METHODS:** A standardized and computer-guided questionnaire was administered to male and female patients with a HPV-induced pathology (e.g. atypical squamous cells of undetermined significance, cervical intraepithelial neoplasia, cervical cancer, anal-colorectal cancer, head-neck cancer and anogenital warts). Six clinical centres across Italy participated in this multicentre study. The patients' risk profile was assessed and compared to that of a control group of healthy subjects attending the same clinics. The effects of risk factors were evaluated using a backwards stepwise multivariate logistic regression model with covariate adjustment. The following predictors were included: level of education, occupation, age at first intercourse, number of sexual partners, smoking, previous sexually transmitted diseases, age at first pap smear, pap smear frequency, use of oral contraceptives and the number of pregnancies. **RESULTS:** Overall, 600 respondents were eligible for the analysis, consisting of 465 patients (44.0±16.3 years) and 135 controls (44.0±13.2 years). More than 5 sexual partners increased the risk of acquiring HPV infections up to 2.52-fold (95%CI: 1.34-4.74), while smoking or an early sexual debut (≤ 18 years) raised it by about a factor of 1.62. Higher levels of education were associated with a protective effect. The overall rate of individuals at high risk with more than 5 sexual partners and at least another additional factor corresponded to 26.3% (158 out of 600). The proportion of subjects with an average risk (respondents with less than 5 partners and at least another additional factor) amounted to 53.2% (319 out of 600). **CONCLUSIONS:** Analysis of risk factors can be used as part of the economic assessment of other effective HPV vaccination strategies, including an immunization programme for pre-adolescents of both sexes in Italy.

PIN16

A STUDY OF A. BAUMANNII IN A TERTIARY CARE HOSPITAL WITH CONSIDERATION TO RISK FACTORS OF INFECTION AND RESISTANCE PATTERN

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OBJECTIVES: To ascertain the epidemiological factors associated with Acinetobacter infections and the resistance pattern of this organism. **METHODS:** A cross sectional, observational, retrospective study was carried out, over a period of 6 months in a tertiary care hospital (Oct 2012 to Mar 2013). The data collected was analysed to understand the pattern with respect to patient demographics, prescription patterns, comorbidities as risk factors to infection, and resistance patterns. **RESULTS:** Based on this study it was observed that surgery was not a risk factor for Acinetobacter infections. Male patients had a greater risk of A. *baumannii* infections. Age distribution of infections was mainly in 41-60 years and 61-80 years. The bacteria were found to be resistant to almost all categories of drugs except colistin, and tigecycline. The mean length of stay of a patient of A.*baumanni* infection was found to be 23.51±27.97 days. Tigecycline and cefixime were the most prescribed antibiotics (97.9%) in the present study. Cefoperazone-sulbactam was found to have an antibiotic action against the bacterium. **CONCLUSIONS:** This study concluded that male patients were at a greater risk of A.*baumannii* infections. However surgery could not be considered as a risk factor for the same. Length of stay of patients was on average 23.51±27.97 days. This study showed tigecycline and cefixime were the most prominently used antibiotic. The strain in this study was resistant to almost all cephalosporins except Cefoperazone-Sulbactam which had activity in 57.14% of the samples tested.

INFECTION – Cost Studies

PIN17

BUDGET IMPACT ANALISIS OF SWITCHING FROM DPT AND MONOVALENT VACCINES TO DTAP–IPV-HIB COMBINED VACCINE INTO RUSSIAN IMMUNIZATION SCHEDULE

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OBJECTIVES: The current Russian immunization program for children from 0 to 20 months is carried mainly by DPT and monovalent vaccines. In addition, vaccination against Hib infection so far is only available for children at risk (approx. 20%). Introduction of DTaP-IPV-Hib combined vaccine could reduce the number of injections received by the child and increase coverage against Hib infection from 20% to 97%. The objective of this evaluation is to calculate the incremental of switching from current monovaccines and DTP-based routine immunization schedule using a pentavalent combined vaccine DTaP-IPV-Hib through a different schemes. **METHODS:** A budget impact analysis of the switching to the different schemes DTaP-IPV/Hib vaccine is performed on the suggested Markov model. The three alternatives (against current immunization program) are compared: a 3+1DTaP-IPV-Hib immunization (Scheme P), a mixed DTwP / DTaP-IPV-Hib immunization (Scheme mix) and a potential scenario - the current scheme, but with expanded (97%) Hib coverage- Scheme 1.The cohort of infants born in 2011 year is followed over their lifetime. Direct and indirect medical costs are measured from the perspective of the public payer. For reference, accepted exchange rate is 1€ = 41 rub. **RESULTS:** The budget impact analysis has shown that the switching from the current vaccination schedule for one of the alternative require additional funds in the amount of 705 101 317 rub. (17197593 €) for Scheme mix, 708 100 310 rub.(17270739€) for Scheme 1 and 1818409 406 rub.(44351449 €) for Scheme P. **CONCLUSIONS:** According to the budget impact analysis, the lowest additional cost of introduction one of alternative scheme would require Scheme mix. Thus, this scheme will be preferred for the Russian health care system.

PIN18

BUDGET IMPACT OF THE INTRODUCTION OF ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR, THE FIRST INTEGRASE INHIBITOR-BASED SINGLE TABLET ANTIRETROVIRAL REGIMEN FOR HIV TREATMENT, TO THIRD PARTY PAYERS IN THE UNITED STATES

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OBJECTIVES: Single tablet regimens like elvitegravir/cobicistat/emtricitabine/tenofovir (EVG/COBI/FTC/TDF) for the treatment of HIV infection are associated with

improved medication adherence, better virologic suppression, lower hospitalization rates, and lower health care costs. The objective of this study was to estimate the budget impact to a US health care plan of the use of EVG/COBI/FTC/TDF in adults with HIV who are treatment-naïve or currently on treatment with no resistance to the components of EVG/COBI/FTC/TDF. **METHODS:** The model estimates total direct health care costs associated with HIV management before and after the introduction of EVG/COBI/FTC/TDF. HIV epidemiology, hospitalization rates, and adverse event incidence and their associated costs were calculated using results of published studies or publically available sources. Regimen utilization was obtained from recent chart audit analysis and EVG/COBI/FTC/TDF market share was projected to come from protease inhibitor (PI)-based regimens in relative proportion to each regimen's market share. The budget impact was calculated annually and cumulatively over a 3-year period without discounting, following standard methodology for budget impact analyses. **RESULTS:** For a hypothetical health care plan with 1 million members, the model estimated 450 HIV-positive members currently on treatment and 72 HIV-positive members initiating HIV therapy each year. Over a 3-year period, the introduction of EVG/COBI/FTC/TDF was expected to result in greater use of single tablet regimens and lower use of more expensive PI-based regimens, yielding lower pharmacy costs ($226,194, 0.5% lower), fewer hospitalizations (1.1% fewer), and lower hospitalization costs ($31,288, 1.1% lower) versus scenario without EVG/COBI/FTC/TDF. Total cost savings over 3 years were estimated at $240,375 (0.4% lower), equivalent to a reduction in per-member-per-month (PMPM) costs from $1.61 to $1.60. PMPM results were insensitive to changes in parameters. **CONCLUSIONS:** The introduction of EVG/COBI/FTC/TDF is expected to result in fewer hospitalizations with a negligible impact on pharmacy and total costs over a 3-year period for a US health care plan.

PIN19

BUDGET IMPACTS OF PROBIOTICS IN CONTROLLING UPPER RESPIRATORY TRACT INFECTIONS IN FRANCE

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OBJECTIVES: Two meta-analyses associated with a public health model demonstrated that probiotics (live microorganisms which when administered in adequate amount confer a health benefit on the host) have an important public health impact: they reduce upper respiratory tract infection (URTI) episodes with less antibiotics and sick leave prescriptions, in France. This analysis reports the budget impact for the National Health System (NHS) and the Nation. **METHODS:** The public health impact model (1/1,000 virtual age-gender standardized population generated with a Markov model: 1-day cycles, 2011-2012 winter period, URTI incidence from a General Practitioner [GP] network) was used. Economic perspectives were society, NHS and family. The analysis was limited to patients having visited a GP. Resource utilization came from the GP network. Unit costs were applied: Ameli.fr for drugs, Classification Commune des Actes Médicaux for GP visits, gross domestic product (GDP)/capita or allowances for sick leaves. Outcomes included direct medical and indirect costs. Results were reported according to each meta-analysis, Cochrane and York Health Economics Consortium (YHEC). **RESULTS:** The economic impact of probiotics was about €95 million saved from the Society perspective according to YHEC (Family: -€21.7 million; NHS: -€15.4 million) and €229.1 million according to Cochrane (Family: -€130.4 million; NHS: -€34.6 million). Absenteeism was the main driver for the society perspective representing 98% (YHEC) or 78% (Cochrane) of the savings. For the NHS, the main driver was sick leave (94%, YHEC-based) or GP visit (67%, Cochrane-based): avoiding URTI episodes (Cochrane) generates more visit savings than reducing disease duration (YHEC). More savings were observed in children, active smokers and people with more human contacts compared to the general population. **CONCLUSIONS:** Probiotics savings are substantial, whether they reduce URTI episodes frequency or duration. Noteworthy, 2011-12 winter URTI incidence rate was low and this analysis focused on the 1% URTI accessing the NHS.

PIN20

ANTIBACTERIAL TREATMENT OF METICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS COMPLICATED SKIN AND SOFT TISSUE INFECTIONS: A BUDGET IMPACT ANALYSIS IN THE GREEK HOSPITAL SETTING

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OBJECTIVES: Meticillin-resistant staphylococcus aureus (MRSA) is an important cause of antimicrobial-resistant health care-associated infections worldwide. Its prevalence remains high in the Greek hospital setting. Complicated skin and soft tissue infections (cSSTIs) due to MRSA are associated with prolonged hospitalization, additional costs of care and significant morbidity. The purpose of this study was to conduct a budget impact analysis relative to different management scenarios for MRSA-cSSTIs from a hospital perspective. **METHODS:** Equal efficacy for the pharmacotherapies under evaluation was assumed and resource use was elicited via an expert panel. The model was based on a decision tree for the management of hospitalized patients with MRSA-cSSTIs, simulating costs and outcomes for the duration of hospitalization according to the therapeutic scenario, including empiric and first-line therapies. Inpatient costs consisted of hospitalization, diagnostic, medical and antibiotic costs. Economic results (Euros 2013) reflect the hospital setting. **RESULTS:** Total per patient cost according to first-line agent was €2,458, €2,730, €2,850, €3,495 and €3,098 and mean length of stay (LOS) was 9.2, 12.5, 10.3, 13.0 and 14.0 days for linezolid, vancomycin, daptomycin, tigecyline, teicoplanin respectively. An estimated 10,287 MRSA-cSSTI patients are treated annually in Greek hospitals. Thus, by increasing the use of linezolid by 11% over a three-year period, for the management of MRSA-cSSTIs, this could result in savings of €331,602 for the hospital budget (current:€29,081,597, projected:€28,749,994). By reducing the LOS for linezolid patients from 9.2 days (current LOS in Greece as per expert panel) to 7.6 days to match data from a large phase IV study in MRSA-cSSTIs (Itani 2010), potential savings amount to €808,673. **CONCLUSIONS:** The analysis corroborates literature findings with regards to the early switch/early discharge potential and outcomes due to oral antibacterial switching in cSSTIs. Increased use of linezolid in the treatment of MRSA-cSSTIs could result in substantial savings for the Greek hospital budget.

PIN21

COST REDUCTION ASSOCIATED WITH USE OF SUBGLOTTIC ASPIRATION TO REDUCE VENTILATOR-ASSOCIATED PNEUMONIA IN TURKEY

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OBJECTIVES: Ventilator-associated pneumonia(VAP) is a serious complication risk for patients who require invasive mechanical ventilation(IMV). VAP is associated with longer intensive care unit and hospital stays, which may increase health care expenditures. VAP may occur in 8% of IMV patients. Subglottic aspiration (SA) may decrease VAP by up to 45% in IMV patients. The goal of this analysis is to calculate the potential cost reduction associated with SA use for VAP reduction in IMV patients in Turkey. **METHODS:** A literature analysis was conducted in PubMed(2000-present) to determine the published cost of VAP in Turkey. Published costs were used for the conversion to Turkish Lira(TL). An annual inflation rate of 3% was applied to the cost data to project the estimated cost in 2013. The exchange rate for USD to TL was estimated at 1.8. A weighted average of the number of patients in each study was used to calculate the cost of treatment. The cost of SA to the Social Security Institution (SGK) was calculated as 33.94 TL, which includes the cost of the SA tube(TaperGuard EVAC; 25 TL) and the SA service reimbursement amount from the SGK of 8.94 TL. 8% and 45% were taken as the VAP rate and reduction with SA rate in IMV patients, respectively. The number of patients requiring IMV in a hospital was estimated at 1000 per year. **RESULTS:** The average inpatient costs of IMV patients with and without VAP were calculated to be 13.556 TL and 3.971 TL, respectively. The total VAP cost, based on 80 VAP cases in 1,000 IMV cases without SA, was calculated as 1.085.297 TL. A hospital using SA for all IMV cases is estimated to have VAP costs equal to 488.384 TL and SA costs of 33.940 TL for a total cost of 522.324 TL. Cost reduction from SA use was calculated as 562.973 TL. **CONCLUSIONS:** VAP increases health expenditures by 9.595 TL per patient. A hospital with 1,000 IMV patients per year that uses SA in all IMV patients may realize an estimated cost reduction of 562.973 TL associated with use of SA in IMV patients.

PIN22

BUDGET IMPACT OF AN INDIVIDUALIZED APPROACH IN THE TREATMENT OF HBEAG-NEGATIVE CHB PATIENTS EXPLOITING THE WEEK-12 PEGINTERFERON ALFA-2A STOPPING RULE IN ITALY

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OBJECTIVES: Treatment options for chronic hepatitis B (CHB) are the direct inhibition of viral replication by continuous administration of nucleosides analogues (NUCs) or a finite 48-weeks course of peg-interferon (PEG). PEG can induce the off-therapy immune control of CHB leading to HBsAg loss/anti-HBs seroconversion but at a low success rate. On the other hand life-long treatment with NUCs is expensive. Exploiting the early identification of PEG-non-responders by combined HBV-DNA and HBsAg quantification at week-12 (stopping-rule), a new sequential therapeutic strategy may benefit both patients and payers. We measured the impact on the Italian National Health Service budget using the PEG-week-12-stopping-rule in the treatment of HBeAg-negative CHB. **METHODS:** A Markov model was developed over a 5 year horizon in the states: CHB, virologic response, relapse, HBsAg clearance, compensated and decompensated cirrhosis, hepatocarcinoma, liver transplant, post-liver transplant and death. The target population (treatment naïve CHB patients) was determined based on Italian national population forecasts and epidemiological data. The current mix of treatment with NUCs (entecavir, tenofovir, adefovir, lamivudine and telbivudine) and PEG (with no stopping rule) was compared with a mix based on a hypothetical uptake of PEG (with the stopping rule). The percentage of uptake from NUCs started at 25%, increasing over time. **RESULTS:** The estimated impact on the Italian NHS budget, over 5 years of treatment, resulted in a saving of approximately €74 million, 95% of which accounted for drug cost. The beneficial impact of the stopping-rule became clear from the second year, when a break-even point was reached. **CONCLUSIONS:** The large estimated savings in drug costs following the uptake of PEG + stopping-rule in the treatment of CHB HBeAg negative patients, together with previously published cost-effectiveness results, demonstrate a potentially advantageous profile of such a strategy, that could allow for more efficient use of health care resources.

PIN23

EXAMINING THE RELATIONSHIP BETWEEN COUNTRY-LEVEL FACTORS AND VACCINE WASTAGE: A DATA DRIVEN MODEL OF SESSION SIZES IN BANGLADESH, MOZAMBIQUE, INDIA (UTTAR PRADESH), AND UGANDA

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OBJECTIVES: Vaccination is a cost-effective intervention; however limited infrastructure in developing countries can pose significant challenges in efficient vaccine delivery. Countries prefer multidose presentations due to lower acquisition and cold chain costs, but open vial vaccine wastage is a major part of program cost. The aim of this study was to examine country-level factors that impact open vial wastage. **METHODS:** A demographics-based budget impact model with a 10 year time horizon was developed in Excel v14 using Palisade's @Risk v6.0 software. The model estimated daily vaccine utilization and wastage rates for Pentavalent, Pneumococcal, HPV and IPV using Lee's (2010) model, calibrated to arrival distributions based on field data session sizes from Bangladesh, Mozambique, India (Uttar Pradesh), and Uganda. The statistical distribution was determined using maximum likelihood, stratified by urban/rural for each clinic type. The model ran 1000 iterations, with each drawing independently from the statistical distributions of session sizes by clinic type. **RESULTS:** The negative binomial family offered the best fit to session size by Akaike Information Criterion. The leading

determinant of wasted doses was the number of children arriving. Depending on whether the clinic setting was urban/ rural, or outreach/fixed center, median session sizes varied between 5-13 children. Vaccine wastage added significant cost due to variations in session size even when modeled using a low multidose vial strategy. For instance, open vial waste from pneumococcal delivered in 5-dose presentation contributed $20MM in waste to Ugandan 10-year program costs. Results for each country and the impact session size distributions will be presented. **CONCLUSIONS:** Our analysis of field data confirmed significant session size variation within/across country immunization settings. Given challenges in mandating session sizes, pressures on vaccine budgets and high value of vaccine delivery, policy makers must consider new solutions to reduce the impact of waste on total program costs.

PIN24

BUDGET IMPACT ANALYSIS OF CEFTAROLINE VERSUS LINEZOLID OR VANCOMYCIN ON THE TOP OF STANDARD THERAPY IN THE TREATMENT OF COMPLICATED SKIN AND SOFT TISSUES INFECTIONS IN RUSSIAN FEDERATION

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OBJECTIVES: To estimate the budget impact of the inclusion of ceftaroline compared to linezolid or vancomycin on the top of complicated skin and soft tissues infections treatment scheme with antimicrobials according to Russian health care system. **METHODS:** The budget impact analysis was conducted. Direct expenses associated with complicated skin and soft tissues infections and resulting follow-up costs were calculated using general tariff agreement of Russian obligatory insurance system and official national statistics. For reference, accepted exchange rate was 1 EUR = 40 RUB. **RESULTS:** Ceftaroline inclusion into the standard complicated skin and soft tissues infections therapy provided cost saving benefits compared with inclusion of linezolid or vancomycin in the complicated skin and soft tissues infections standard therapy scheme. Total health care costs of complicated skin and soft tissues infections therapy were approximately 77 997 RUB (1 950 EUR) per patient in ceftaroline group (therapy duration – 9 days), 78 816 RUB (1 970 EUR) per patient in vancomycin group (therapy duration – 10 days) and 117 893 RUB (2 947 EUR) per patient in linezolid group (therapy duration – 12 days). Treatment of complicated skin and soft tissues infections using standard therapy with ceftaroline inclusion compared to one with vancomycin or linezolid leads to cost savings of 819 RUB (20 EUR) or 39 896 RUB (997 EUR) per patient, respectively. **CONCLUSIONS:** The results of budget impact analysis illustrate that including ceftaroline into the standard therapy of complicated skin and soft tissues infections in comparison with vancomycin or linezolid has potential to reduce Russian health care system total costs for complicated skin and soft tissues infections treatment.

PIN25

ESTIMATING THE COST IMPACT OF SWITCHING FROM A VIAL TO A PRE-FILLED SYRINGE MODE OF ADMINISTRATION FOR THE DTAA-IPV-HIB '5-IN-1' VACCINE IN INFANTS

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OBJECTIVES: To estimate the cost impact to the NHS of switching from vial and syringe (V&S) to pre-filled syringe (PFS) administration of the '5-in-1' vaccine for diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b. **METHODS:** A model was developed to estimate the cost impact of the switch in children less than 2 years old. Vaccines supplied were assumed to reach three destinations: administered (an estimate of 785,320 primary courses); opened and not administered (assumed to account for 7% of V&S and 0% of PFS supplied); or not opened by the expiry date (assumed to account for 0% of supply). All vaccines accrued acquisition and storage costs. PFS has bulkier packaging, leading to higher storage costs. Administered vaccines incurred costs for staff time, consumables (only required for V&S) and potential needlestick injuries (assumed not to occur with PFS). As prices paid for vaccines by the NHS are not disclosed, the cost of a single dose was assumed equal for PFS and V&S. Appointment times were obtained from a survey of 200 nurses, which estimated that PFS saved on average 4 minutes 47 seconds relative to V&S across three doses. All unit costs were sourced from the literature. **RESULTS:** The introduction of PFS was estimated to save £7.91 per 3-dose primary course and £6,214,562 per year for the NHS. Reductions in wastage and staff time contributed the greatest savings. Varying the wastage rate from 1-10% resulted in total cost savings of £3-8million; investigation into better estimates of vial wastage would strengthen the results. All other sensitivity analyses had a minimal impact on results. **CONCLUSIONS:** The switch to PFS administration is estimated to have generated substantial cost-savings to the NHS. PFS has the potential to improve the efficiency of immunisation programmes by simplifying vaccine delivery and reducing the risk of handling errors.

PIN26

PHARMACOECONOMIC ANALYSIS OF DIFFERENT ANTIVIRAL THERAPIES IN THE TREATMENT OF RUSSIAN PATIENTS WITH CHRONIC HEPATITIS C

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OBJECTIVES: To assess the cost-effectiveness of pegylated interferons alfa-2a and alfa-2b combined with ribavirin in the treatment of Russian patients with chronic hepatitis C and identify potential budget impact considering the indicator of rational drug use (IRDU). **METHODS:** The pharmacoeconomic model was developed based on the data from randomized controlled trial MIST (M. Rumi et al., 2010). The cost-effectiveness ratios (CERs) for different patient subgroups were expressed as costs of medicines per one patient with sustained virologic response. 24- and 48-week time frames were used for patients with genotypes 2/3 and 1/4, respectively. To assess quantitatively the impact of pharmaceutical form and recommended dose regimens, the IRDU was used. One-way sensitivity analyses (SAs) were performed to investigate the robustness of the cost-effectiveness estimates. **RESULTS:** Treatment with pegylated interferon alfa-2a was associated with lower total costs. The estimated budget savings varied from 20,907.97 RUB to 104,366.07 RUB per one patient. CERs for pegylated interferon alfa-2a were less than that for pegylated interferon alfa-2b in all patient subgroups. The lowest CER was observed for patients with genotype 2 received pegylated interferon alfa-2a (240,789.70 RUB per one patient with SVR) and the highest CER – for cirrhotic patients with genotype 1 received pegylated interferon alfa-2b (1,879,694.72 RUB per one patient with SVR). The analysis of the IRDU showed, that inefficient budget expenses associated with pegylated interferon alfa-2b treatment may reach 58,770.84 RUB per one patient infected with HCV-genotypes 1/4. SAs demonstrated that results were robust to changes in the drug costs. **CONCLUSIONS:** The present study has demonstrated that administration of pegylated interferon alfa-2a has the better pharmacoeconomic profile in the treatment of Russian patients with chronic hepatitis C.

PIN27

THE COST OF STOPPING (FUTILITY) RULES TELAPREVIR AND BOCEPREVIR IN THE TREATMENT OF GENOTYPE 1 HEPATITIS C PATIENTS IN BRAZIL

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OBJECTIVES: To estimate the cost of treatment discontinuation due to label stopping (futility) rules of telaprevir (TVR) and boceprevir (BOC) triple therapy in Brazilian public (SUS) and private health care system (SS). **METHODS:** Treatment costs considered drug acquisition costs from a public and private payer perspective in Brazil. Stopping rules (SR) were defined according to the label of each drug. For TVR the SR were defined at week4 (SR WK4) and at week 12 (SR WK12) as viral load (VL) > 1.000 IU/ML. For BOC, SR were defined at week 12 (SR WK12) as VL >100 UI/mL and at week 24 (SR WK24) as detectable VL. Patients eligible for the SR were gathered for naïve and experienced patients from the respective phase 3 trials. As data for SR WK24 was not published for BOC in naïve patients it was assumed to be the same as SR WK12 and a deterministic sensitivity analysis was carried out. **RESULTS:** Under the SUS perspective, the average cost of naïve patients interrupting treatment with TVR was R$ 670 compared to an average cost of R$ 3.396 per interrupted treatment with BOC, and for treatment experienced patients, TVR had an average cost of R$ 352 compared to an average cost of R$ 3.041 for BOC per patient meeting the SR. Under the SS perspective, TVR had an average cost of R$ 1.433 per interrupted naïve treatment and R$ 753 per interrupted treatment in experienced patients and BOC had an average treatment cost of R$ 8.305 per naïve patient interrupting treatment and R$ 4.753 per interrupted treatment in experienced patients. **CONCLUSIONS:** BOC had higher costs associated with treatment futility when compared to TVR, especially in treatment experienced patients, in both the public and private health care systems in Brazil.

PIN28

COMPARATIVE EFFECTIVENESS OF TRIPLE THERAPY VERSUS DUAL THERAPY FOR CHRONIC HEPATITIS C VIRUS INFECTION IN KAZAKHSTAN

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OBJECTIVES: Currently, 23 thousand people (registered) are suffering from Hepatitis C in Germany (more 60% genotype 1). TThe licensing of direct-acting antivirals heralds a new era in the treatment of hepatitis C virus (HCV) genotype 1. Clinical studies showed a significant increase in sustained virological response rates from 38-46% to 63-79%. This study was to evaluate the cost-effectiveness of newly introduced triple therapy with Telaprevir (TVR+PR) compared to dual therapy (PR) for the treatment of genotype 1 hepatitis C virus (HCV) infection in previously untreated patients. **METHODS:** A systematic literature review identified relevant studies. A Bayesian mixed treatment comparison model was fitted for each patient population. Previously published economic Markov model comparing triple therapy (TVR + PR) and dual therapy (PR) has been adjusted for the Kazakhstan context of health care (payer perspective). Clinical outcomes and dose were taken from the phase ADVANCE-3 trial. Other parameters of the model - including utilities - were adapted from Kazakhstan or if not available from the international literature after an extensive search of the literature. Drug costs were taken from the list of drugs Kazakhstan. All costs were inflated to 2012 goda.Skidka of 3% and the horizon of life were considered. **RESULTS:** Base-case analysis shows that the triple treatment (TVR + PR) than dual therapy (PR) leads to increased costs, and the best results. The results were robust when analyzing multiple sensitivity. The discount rate seemed to have a great impact. **CONCLUSIONS:** Telaprevir triple therapy for previously treated patients with HCV-genotype 1, more efficient than the dual therapy, but it leads to increased costs (in particular, the cost of medications).

PIN29

PHARMACOECONOMIC EVALUATION OF THE FIXED-DOSE COMBINATION OF ABACAVIR/LAMIVUDINE IN THE ANTIRETROVIRAL THERAPY OF NAÏVE HIV INFECTED PATIENTS IN RUSSIA

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OBJECTIVES: To estimate the costs of once-daily fixed dose combination (FDC) abacavir/lamivudine (ABC/3TC) compared with twice-daily combination of its individual components (ABC+3TC) and twice-daily FDC zidovudine/lamivudine (ZDV/3TC) in efavirenz (EFV)-based regimens for treatment-naïve adults with HIV infection in Russia. **METHODS:** An Excel based model was developed to estimate the costs over 48- and 96-week time horizon for three compared regimens. Probabilities of switching to alternative and 2[d] line therapy due to low adherence and side effects were estimated for each regimen based on literature search. Costs of antiretroviral

drugs in the 1st and 2d line of therapy and routine follow-up costs were calculated based on prices of state procurements in the framework of national project of HIV prevention and the tariffs of the Russian health care system in 2012. One-way sensitivity analysis was performed. **RESULTS:** ABC/3TC+EFV is not associated with more costs vs ABC + 3TC + EFV regimen and even saves approximately 3390.60 rub (€80.30) per patient over 96 weeks of treatment. The sensitivity analysis showed that ABC/3TC FDC remains to be cost saving compared with ABC+3TC as long as the its package price is less than 6564.17 rub (€155.46) while keeping other model parameters unchanged. Still ABC/3TC+EFV is 28% more expensive than ZDV/3TC+EFV, though more effective and safe treatment option: the difference in costs vs ABC/3TC+EFV is 45267.05 rub. (€1,072.05) per patient over 96 weeks. **CONCLUSIONS:** FDC ABC/3TC may be considered as a more efficient and convenient treatment option than its monocomponents combination for first-line antiretroviral therapy of HIV patients in Russia. FDC ABC/3TC is more expensive versus ZDV/3TC, but the difference in costs seems appropriate for more safe and convenient alternative.

PIN30

THE IMPACT OF CHLAMYDIA AND GONORRHOEA POINT OF CARE NUCLEIC ACID AMPLIFICATION TESTS ON CLINICAL PATHWAYS AND COSTS IN GENITO-URINARY MEDICINE CLINICS IN THE UNITED KINGDOM

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OBJECTIVES: To explore new patient pathways using a chlamydia/gonorrhoea point of care nucleic acid amplification test (POC NAAT), and estimate and compare the costs of the new pathways with the current pathways using standard laboratory-based NAAT testing in the UK. **METHODS:** Consensus building activities were conducted with four sexual health clinics in the UK. They were selected through purposeful sampling to reflect a wide range of service delivery. Current pathways in which a chlamydia/gonorrhoea test was used were mapped out, and then new pathways using a POC NAAT were constructed. The consensus pathways were then costed using a patient pathway model built in Excel, and the cost of the current and POC NAAT pathways compared. **RESULTS:** Pathways using a POC NAAT for asymptomatic and symptomatic patients and chlamydia/gonorrhoea only tests were shorter and less expensive than most of the current pathways (average savings of £4-8 for symptomatic and asymptomatic screening pathways if the POC NAAT costs £18/test). Patients that are tested using the POC NAAT can be treated on the same day, thus saving costs compared to patients who are treated at a subsequent appointment. **CONCLUSIONS:** A POC NAAT could be introduced to services and reduce current costs, and may mean more appropriate and quicker care for positive patients.

PIN31

COST ANALYSIS OF VACCINATION FOR CHILDREN IN UKRAINE

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OBJECTIVES: In Ukraine immunization by age conducts against 10 infectious diseases: tuberculosis, hepatitis B (HBV), diphtheria, pertussis, tetanus, polio, Haemophilus influenzae, measles, rubella, mumps .The Law of Ukraine from 21.10.2009 N 1658-VI approved the Program of immunization and protection against infectious diseases during 2009-2015.During the years 2011-2012 the media incorrectly submitted data on the results of vaccination and many parents refused vaccination and as a result there were about 12,000 cases of measles and rubella, it's 80 times more than in previous years. On State program of vaccination in 2010 was allocated 237 mln UAH (1 USD=7.99 UAH), in 2011 - 237 mln, in 2012 - 302 mln UAH. **METHODS:** We conducted a cost per 1,000 children aged 0 to 1 years. Direct costs were calculated for vaccine Pentaxim (Sanofi Pasteur) which combined vaccine against hepatitis B (ukrainian producer "Biolik") and was compared the costs for vaccine Infanrix hexa (GSK). We included the vaccine costs, the loss during storage, and the costs of medical personnel for vaccination. We used the prices from the ukrainian electronic pricing database "MORION" on 01.06.2012. Analysis of evidence-based data has shown that Pentaxim is equal clinical efficacy of Infanrix hexa, but increases the rate of vaccination coverage against hepatitis B. **RESULTS:** The costs for Pentaxim and HiB vaccine were 633 240 UAH and costs of medical personnel (pediatrics, nurses) were 36763 UAH. The costs using vaccine Infanrix hexa were 803880 UAH, the costs of medical personnel – 18 381 UAH, respectively. **CONCLUSIONS:** In 2012, 385 116 children vaccinated by Infanrix hexa and general costs were 118 307 590 UAH vs 363 000 children by Pentaxim were 95 830 447 UAH. The results shown the need additional 22477143 UAH, which is justified to increase vaccination coverage against hepatitis B by 6%.

PIN32

ASSESSING THE ECONOMIC BURDEN AND HEALTH CARE UTILIZATIONS OF VETERAN PATIENTS DIAGNOSED WITH THE HEPATITIS C VIRUS IN THE UNITED STATES

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OBJECTIVES: To examine the economic burden and health care utilizations of the hepatitis C virus (HCV) in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration Medical SAS datasets 01OCT2008-30SEP2012). Patients diagnosed with HCV (International Classification of Disease 9th Revision Clinical Modification [ICD-9-CM] codes 070.41, 070.44, 070.51, 070.54, v02.62) were identified, and the first diagnosis date served as the index date. A comparator group was created by identifying patients without HCV but with the same age, region, gender and index year, and matching them by baseline Charlson Comorbidity Index. The index date for the comparator group was randomly chosen to reduce selection bias. A 1-year continuous health plan enrollment period pre- and post-index date was required for both groups. One-to-one propensity score matching (PSM) was used to compare health care costs and utilizations during the follow-up period between the HCV and comparison groups, adjusting for baseline demographic and clinical characteristics. **RESULTS:** Eligible patients (N=270,752) were identified for the HCV and comparison cohorts. After applying 1:1 PSM matching, a total of 107,953 patients were matched from each group and baseline characteristics were well-balanced. HCV patients were more likely to be hospitalized (15.90% vs. 3.19%, p<0.01) and report more emergency room (20.36% vs. 8.17%, p<0.01), physician office (99.18% vs. 61.06%, p<0.01), outpatient (99.25% vs. 61.84%, p<0.01) and pharmacy visits (91.11% vs. 63.13%, p<0.01) which resulted in higher health care costs for inpatient ($5,284 vs. $911, p<0.01), emergency room ($237 vs.$76, p<0.01), outpatient ($4,673 vs. $1,760, p<0.01), physician office ($4,247 vs. $1,560, p<0.01), pharmacy ($889 vs. $460, p<0.01) and total costs ($10,846 vs. $3,131, p<0.01) for HCV patients relative to the comparison group. **CONCLUSIONS:** Patients diagnosed with HCV were more likely to report higher health care utilization and were associated with a higher economic burden compared to the matched controls.

PIN33

VACCINE TIMELINESS: A COST ANALYSIS OF THE IMPLICATIONS OF DELAYED VACCINATION

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OBJECTIVES: : Pertussis (whooping cough) is a highly contagious bacterial disease. Infants in the first few months of life are particularly vulnerable with the highest reported rate of pertussis, risk of severe disease and deaths. Although, vaccination coverage rates have reached record-high levels in the United States (US), vaccine timeliness remains an issue. **METHODS:** Using data from the 2010 National Immunization Survey (NIS), we estimated the vaccination timeliness for DTaP vaccines in US infants. A previously published static model accounted for the reduction of incidence of pertussis by vaccination according to a strict adherence to the ACIP vaccination schedule. The annual numbers of pertussis cases prevented in infants and the associated costs avoided from a health care system perspective were estimated. **RESULTS:** From the NIS dataset, the mean age at DTaP vaccination was 76.3, 147.4 and 223.9 days, which means that on average each vaccination was in average delayed by 16.3, 27.4 and 43.9 days (with delays accumulating over time), respectively. The model predicted 3052 pertussis cases annually in infants <1 year of age in the US. Applying a strict adherence to the vaccination schedule, approximately 313 cases of pertussis, 112 hospitalisations and 1 death could be avoided each year. This translates into savings of 57 QALYs and $1.3 million of costs to the health care system. **CONCLUSIONS:** Although previous publications have presented the number of cases avoided by timely vaccination, to our knowledge this is the first one to present the associated costs. Administering vaccines on time not only avoids cases but may also have a significant impact on quality of life and costs. These costs avoided may be redirected to developing tools and/or infrastructure to improve the vaccine timeliness of infants in future. Further research is needed to better understand the role of vaccination timeliness and completion.

PIN34

STUDY OF ANTIBIOTIC CONSUMPTION PATTERN IN HOSPITAL ACQUIRED PNEUMONIA

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OBJECTIVES: To analyse the antibiotic consumption pattern in hospital acquired pneumonia (HAP) patients in a tertiary care teaching hospital **METHODS:** A prospective observational study, carried out in a tertiary care teaching hospital from January 2011 to December 2012. HAP patients who fulfill the inclusion criteria were identified and enrolled into the study after taking informed consent. Patients were followed from the day of diagnosis of HAP, till the day of discharge or death. Patient data like demography (age, sex), antimicrobial agents used (dose, duration of treatment), length of hospital stay and clinical outcome were recorded in a predesigned data collection form. The cost of antimicrobial therapy was recorded from the day of admission till the day of discharge. Antibiotic consumption was calculated using defined daily dose (DDD) methodology. **RESULTS:** Total 310 patients were included in the study. Among study population 229 (73.9%) patients were male and mean age was 55.9±18.4 (mean±SD). Out of 310 patients 218 were improved, 37 were worsened or discharged against medical advice and 55 were expired. Mean length of hospitalization was 9.45±6.75 (mean±SD) days. Total 27 antimicrobial agents were used for the treatment pneumonia among these patients. Among these antimicrobial agents, consumption (DDD/100 bed days) was highest for piperacillin-tazobactum (parenteral, 0.12) followed by ceftriaxone (parenteral, 0.10), azithromycin (oral, 0.10) and trimethoprim-sulphamethoxazole (oral, 0.08). The percentage of treatment success was highest among patients treated with piperacillin-tazobactum+macrolide combination (10%) followed by cephalosopin+macrolide combination (8%). However the cost of treatment was high for piperacillin-tazobactum+macrolide regimen **CONCLUSIONS:** This study provides estimate of quantities of different antimicrobial agents used in the treatment of hospital acquired pneumonia. Piperacillin-tazobactum (parenteral) is highest consumed among 27 antimicrobial agents. Since percentage of treatment success is almost similar for piperacillin-tazobactum+macrolide combination (10%) and cephalosopin+macrolide combination (8%), use of cephalosopin+macrolide combination should be encouraged in susceptible patients considering the lesser cost.

PIN35

COUNTING THE COST OF MENINGOCOCCAL DISEASE IN FRANCE

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OBJECTIVES: Invasive meningococcal disease (IMD) is life-threatening and can result in severe sequelae. In France, no data has been published on the costs of severe IMD cases. This study aimed to estimate lifelong management costs associated with severe cases of IMD in France. **METHODS:** Two scenarios were developed: a 6-year old child with *purpura fulminans* resulting in amputation of both legs below the knee and a 3-year old with meningitis and severe neurological sequelae. Additional scenarios included other typical sequelae of IMD: chronic renal insufficiency (CRI), profound deafness, epilepsy. Scenarios were validated by national experts of IMD. Health, disability, educational and other resources were obtained from experts and families of patients with similar sequelae. Unit costs (2013) were obtained from the literature, the National Health Insurance (NHI) and companies' websites. Time horizon was based on life expectancies of patients (77 and 55-years respectively). A 4% discount rate decreasing to 2% after 30-years was applied. Costs are presented from NHI, public funded organisations and patient or his/her private health insurance perspectives. **RESULTS:** *Purpura fulminans*with amputations is associated with a lifelong discounted cost of €768,874. Adding CRI doubles the amount (€1,480,545). Meningitis with severe neurological sequelae results in a lifelong discounted cost of €1,924,475. Adding profound deafness and epilepsy slightly increases the total cost (€2,267,251). The first year is the most expensive in both scenarios (€166,890 and €160,647 respectively). The main cost drivers are respectively for each scenario prostheses and child/adult stay in institutions. Overall, NHI covers 1/2 of total cost, public funded organisations 1/3 and patient/private health insurance for the remainder. **CONCLUSIONS:** This study fills a gap in the body of knowledge on IMD sequalae care and costs in France. The potentially high economic burden of IMD, in addition to its physical, psychological and social burden, reinforces the need for prevention.

PIN36

HOW MUCH DENGUE COSTS TO BRAZIL? A RETROSPECTIVE ADMINISTRATIVE CLAIMS ANALYSIS FROM THE PUBLIC PAYER PERSPECTIVE

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OBJECTIVES: In the 21st century, Brazil became the country with the most reported cases of dengue fever. This study aims to describe hospital costs for managing dengue in the Brazilian Public Healthcare System (BPHS). **METHODS:** BPHS Hospital Information Database (SIH/SUS) was used to collect data for the period of 2008-2011. Individual claims coded as "Classic Dengue (CD) Treatment" or "Dengue Hemorrhagic Fever (DHF) Treatment" in the SIH/SUS (regardless ICD-10 codes) were identified in this system and compiled by geographic region, disease type and year. **RESULTS:** A total of 304,548 individual dengue claims were obtained for the 2008-2011 period. They represented an overall cost of 97,642,495BRL for all 4 years (ranging from 17,843,318BRL in 2009 to 31,235,501BRL in 2010). The 4-year national average cost per inpatient admission was 321BRL (295BRL [2008] - 333 BRL [2010]), with mean length of stay (LOS) of 3.3 days and in-hospital mortality rate of 0.46%. The northeast region represented 43.1% of overall expenditures, while the south accounted for only 1.6%. The hemorrhagic syndrome was responsible for 10%, 7% and 10% of overall cost, individual dengue claims and total hospitalization days, respectively. Mean cost per inpatient admission for DHF was 50.6% higher than CD's (468BRL vs. 316 BRL), mean LOS was 55.2% higher (5.0 vs. 3.2 days) and in- hospital mortality rate was 997.8% higher than the one from CD (3.0% vs. 0.27%). Stratifying by region, 9.6%, 36.6%, 34.7%, 1.7% and 17.4% of DHF costs were respectively localized on the North, Northeast, Southeast, South and Midwest. **CONCLUSIONS:** The analysis of SIH/SUS administrative information provided insightful information about dengue costs. Although DHF represented only 7% of individual claims, its mean cost per inpatient admission and in-hospital mortality rate was considerably higher than CD's, persisting as an object of concern for health authorities.

PIN37

BURDEN OF HERPES ZOSTER AND POST-HERPETIC NEURALGIA IN SWEDEN

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OBJECTIVES: Herpes zoster (HZ) and post-herpetic neuralgia (PHN), one of its more severe and frequent complication, are very painful and debilitating conditions. The societal economic burden of HZ in Sweden is not well described today. The objective of this study is to describe the burden of HZ and PHN in Sweden in the year 2011. **METHODS:** Data for inpatient care, outpatient primary care, the prescriptions of drugs, sick leave and the number or diagnostic tests were collected from national databases. The incidence of the HZ was estimated based on the number of prescriptions of antiviral drugs, on which a correcting factor has been applied. **RESULTS:** Almost 30,000 patients were diagnosed with HZ, with two third occurring in patients older than 50 years. The societal cost to treat these patients, including the cost to treat those patients who later developed PHN, added up to nearly 227 MSEK (21M€) which corresponds to 7,600 SEK per patient (876€). The main contributors to the total cost for the treatment of HZ patients were primary care (43%); sick leave (28%); hospitalization (10%) and specialist care (7%). Medication was a relatively small contributor with 8.5 MSEK (4%) to the overall costs for patients at all ages. **CONCLUSIONS:** The current study demonstrates that the burden of HZ is significant in Sweden, especially in people aged 50 years and older. This economic burden is expected to increase in the coming years since the population older than 50 years represents a growing proportion of the population. Thus, the society and the health care payers potentially have a lot to gain by introducing a vaccination program to patients aged 50 years and older, to reduce the burden and increase their quality-of-life.

PIN38

HOSPITAL ADMISSIONS RELATED TO TUBERCULOSIS IN BRAZIL: EPIDEMIOLOGICAL AND ECONOMIC PROFILE, FROM THE PUBLIC HEALTH CARE PERSPECTIVE

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OBJECTIVES: Among infectious diseases, tuberculosis is the second leading cause of mortality worldwide. Since 2000, Brazil is one of twenty two countries classified as "high burden countries" by World Health Organization. This study aims to report epidemiological and economic profile of tuberculosis related hospitalizations in Brazil. **METHODS:** Retrospective analysis of Brazilian public hospital admissions for tuberculosis was developed according to ICD-10 classification (A15-A19) as reported in Brazilian Hospital Information System (SIH/SUS) database, from January 2008 to December 2011. Epidemiological data were extracted from public reporting system. Costs represent federal reimbursement values for hospitalizations (medical procedures, exams, drugs and fees) estimated in 2013 Brazilian Real (BRL). **RESULTS:** Reported tuberculosis cases and prevalence rates per 100,000 inhabitants for 2008, 2009, 2010, and 2011 were: 85,329 (45.0); 88,800 (46.4); 86,654 (44.8); and 89,759 (46.0), respectively. Hospitalizations in the same period were 18,216, 15,338, 16,153, and 19,048, leading to a hospitalization rates of 21.35%, 17.27%, 18.64%, and 21.22% with mean length of stay varying from 15 to 17 days. Mortality rates showed stability, varying from 2.95% to 3.49% for overall tuberculosis related deaths, and 6.19% to 8.14% for in-hospital mortality. About 40% of all deaths were related to hospitalized patients. From 2008 to 2011, hospitalizations costs were 19,546,160BRL, 21,791,027BRL, 23,889,130BRL and 29,410,353BRL, respectively, with an increase in cost per patient over the years (1,073BRL in 2008 to 1,544BRL in 2011). Total cost for the period represents 3.5% of all hospitalizations costs related to infectious diseases (ICD-10 chapter I). Geographic distribution indicated southeast region accounting for 45% of cases, 38% of hospital admissions, and 47% of costs. **CONCLUSIONS:** Tuberculosis is a major public health issue, with great impact on patients' health and growing hospitalization related costs for the Brazilian health care system. Southern region concentrates most cases and costs, probably due to the presence of important treatment and diagnoses centers.

PIN39

USE OF ANTIBIOTICS AND PRESCRIPTION MEDICATION IN INFLUENZA DISEASE IN THE UNITED KINGDOM

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OBJECTIVES: Determine the use of antibiotics and prescription medication in primary care in the management of influenza, stratified by age, risk and complications. **METHODS:** A cross-sectional observational study was carried out using data derived from GPRD, (January 2001 - March 2009). Subjects included were: all those with general practitioner (GP) coded episodes of care for acute respiratory events related to infection (influenza and Influenza-like-illness). Analysis was stratified by age and 'at-risk' status recommended for influenza vaccination in the UK. Primary prescription information was collected for the following categories: antipyretics/analgesics, antibiotics, amantadine, aminoglycosides, nasal decongestants, antisecretory drugs and mucosal protectants, and antihistamines. UK 2011 NHS reference costs were used. **RESULTS:** A total of 53% of all patients had at least one medical prescription with 30% of patients receiving antibiotics. Proportionally more patients with complicated influenza had prescriptions (83%) compared to patients with uncomplicated influenza (50%), and most cases were unvaccinated. Across all age groups complicated influenza had a greater number of prescriptions compared to those with uncomplicated cases (3.0 vs. 2.5). 67% and 27% of complicated and uncomplicated influenza cases received antibiotics. Antipyretics and analgesics were prescribed to 7% of patients, with antisecretory drugs and mucosal protectants prescribed to 6% of patients. Antibiotics, analgesics and antisecretory drugs (including mucosal protectants), were the three most commonly prescribed classes of drugs, and represent 41%, 31% and 12% of all prescriptions respectively. The annual cost is expected to be around £13,956,177 per annum with 40% of this cost attributable to antibiotics. **CONCLUSIONS:** In-hospital and over-the-counter medication use is not collected in this database, therefore this is not a comprehensive assessment of the full extent of pharmaceutical management of influenza. The extensive use of antibiotics prescribed by GPs is of concern, especially in uncomplicated influenza episodes at a time of increasing resistance. Current clinical practice therefore needs urgent review.

PIN40

EVALUATING ECONOMIC BURDEN OF TICK-BORNE ENCEPHALITIS. EVIDENCE FROM RUSSIA

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About 3500 people have suffered tick-borne encephalitis (TBE) in 2011 in Russia, and approximately 16% of them had focal form with a high case-fatality and disability rate. However, no research has investigated its social costs. **OBJECTIVES:** to evaluate the socio-economic burden of TBE in Russia. **METHODS:** We proposed a probability-tree model accounting for 4 clinical outcomes of the disease: full recovery, progression to chronic disease, disability, and death; probabilities were taken from Russian clinical and epidemiological studies. Each outcome was associated with particular costs that included direct current and deferred medical and social costs. Tariffs of the Russian health care system were used to calculate all medical costs; indirect costs were estimated using the average monetary daily productivity and mean disability allowance. All future costs were discounted to the basis year (2011). The model estimated the one-year average socio-economic burden of the disease which could be aggregated into the gross burden by incorporating data on annual TBE incidence in previous years. Additionally we evaluated disability adjusted life years (DALYs) attributable to TBE using standard WHO methodology. **RESULTS:** We found that economic TBE burden in Russia in 2011 was about $49.5 million, 78% of which was deferred costs, caused by death and disability. We

estimate total 4177 DALYs caused by TBE in 2011. **CONCLUSIONS:** TBE burden is quite large in Russia, thus economic evaluation of preventive measures is essential in order to choose the most cost-effective options.

PIN41

HEALTH CARE COSTS ASSOCIATED WITH CHRONIC HEPATITIS C INFECTION IN EUROPE

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OBJECTIVES: Chronic hepatitis C virus (HCV) infection is estimated to effect approximately 15 million persons in Europe. It is a prevalent cause of progressive liver disease including cirrhosis and hepatocellular carcinoma (HCC) and nearly 90,000 deaths that occur annually in the European region are related to HCV infection. The objective of this study was to evaluate the direct health care costs of HCV infection in countries of the European Union. **METHODS:** ENTREZ PUBMED was searched systematically for studies published between 2008 and 2013 that evaluated the health care costs of persons with HCV infection in countries of the European Union. Of the 110 studies identified only 3 contained overall health care costs. Cost data was extracted, inflation adjusted to 2013 costs and averaged. **RESULTS:** Based on the included studies, the average annual health care cost for a person with chronic HCV infection is €2,756 with mild disease, €6,258 with cirrhosis, and €11,437 with HCC. An HCV-related liver transplantation is estimated to have an average cost of €68,497. The reported annual health care costs of patients with chronic HCV infection vary widely, with annual costs ranging between €340 and €6,773 among those categorized as having chronic infection and/or mild disease and between €34,834 and €124,594 among those who have had a liver transplantation. **CONCLUSIONS:** The majority of recent studies have investigated antiviral drug treatment costs; few have examined the overall health care costs associated with chronic HCV infection in Europe. Based upon the data available, chronic HCV infection is associated with a substantial health care burden even among those categorized as having mild disease. Further research is needed to better understand the costs of HCV infection to enable more relevant screening and treatment strategies, especially among those at high risk for developing severe liver disease.

PIN42

PERTUSSIS IN BRAZILIAN CHILDREN: MORTALITY, LENGTH OF STAY, AND COSTS IN HOSPITALIZED PATIENTS

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OBJECTIVES: Bordetella pertussisinfection is highly contagious and can progress to severe conditions, especially among young children and elderly. This study aims to describe hospitalization patterns and costs for pertussis in children in public hospitals in Brazil, from 2008 to 2011. **METHODS:** A retrospective analysis of Brazil public hospital admissions for pertussis was developed according to ICD-10 classification (A37: Pertussis) in children (aged ≤9 years), as reported in Brazilian Hospital Information System (SIH/DATASUS) database from January 2008 to December 2011. Costs represents federal reimbursement values for hospitalizations (includes medical procedures, exams, medications and taxes), presented in 2013 Brazilian Real (BRL). **RESULTS:** A total of 3055 hospital admissions for pertussis during the four-year period were identified. There was a downward trend in the first three years of the analysis, while the opposite occurred in the fourth year, with 2011 having the highest number of cases (907, 655, 394 and 1,099 for 2008, 2009, 2010, and 2011, respectively). Infants were the most affected, with those less than one year of age accounting for 91% (n = 2,779) of all pertussis admissions in the age group analyzed. In-hospital mortality rate was 13.9% for all cause in the period. Mean length of stay was 7.56 days. Total cost for the period was 3,754,877 BRL, which represents 94.9% of pertussis hospitalization costs for all ages (3,958,133 BRL). Mean cost per patient was 1,229 BRL. **CONCLUSIONS:** The costs with pertussis hospitalizations in children can be substantial in Brazil, from the public health care perspective. Despite the existence of a National Immunization Program, the number of cases in children remains high. It is therefore important that decision makers reassess the prevention and treatment patterns of this disease.

PIN43

COST OF INFLUENZA IN GERMANY

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OBJECTIVES: To evaluate cost of children and adults diagnosed with seasonal influenza in Germany, filling a data gap of more than a decade. **METHODS:** This cost-of-illness study was conducted from payer and societal perspective based on a retrospective database analysis by using a longitudinal electronic medical records database (IMS® Disease Analyzer). Patients with influenza episodes (ICD-10 diagnosis J09-11) being observable 12 months before index date and 1 month afterwards were included. The selection window was May 2010 to April 2012 to cover two influenza seasons. Published unit costs and tariffs for Germany in 2012 were used. **RESULTS:** A total of 23,068 influenza episodes (19,446 patients) managed by primary care practitioners (PCP) and 7,295 episodes (5,988 patients) managed by pediatricians were eligible for analysis. Mean age of patients with at least one episode was 43 years (SD 20) in the PCP panel and 7 years (SD 4) in the pediatrician panel. Total average mean cost (SD) from societal perspective in adult patients was €471 (576) and in children €99 (140)/episode. In about 11% of the adult patients the total cost exceeds €1,000/episode. This is primarily due to the higher percentage of patients with complications (63%) compared to the entire PCP study cohort (38%). Workdays lost were the main cost driver (82%) in adult patients; more than 40% of patients missed between 2 and 6 days of work/episode. In children, the main cost driver was physician visits (66%). Complications increase the cost by three fold in children and two fold in adults (average mean cost (SD) for children: €137 (144) vs. €49 (33) and adults: €622 (670) vs. €377 (485)). **CONCLUSIONS:** Results based on a large and representative patient sample demonstrate that the cost of seasonal influenza episodes is substantial, especially when complications occur. Costs in children may be higher of what is actually reported.

PIN44

THE COST OF CLOSTRIDIUM DIFFICILE INFECTION IN HUNGARY

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OBJECTIVES: Clostridium difficile is the leading cause of antibiotic associated infectious nosocomial diarrhoea. *C. difficile* infection is a high-priority problem of public health in each country. The available literature of *C. difficile* infection's disease burden is limited. The authors aimed to identify the most important cost elements and quantify the cost of *C. difficile* infection in Hungary. **METHODS:** A retrospective chart review and experts interviews were done in a sample of 151 patients with *C. difficile* infection in 2011 in two Hungarian hospitals. In the chart review data on demographic, disease severity, therapy, the standard precautions and the infection related contact precautions were collected. Cost analysis was done from the service provider's perspective. **RESULTS:** In department of medicine the annual average cost of *C. difficile* infection was €800 per patient, the annual total cost of a recurrent patient was €1810, the annual additional cost of contact precautions was €330 per patient, the annual average cost of an episode was €570, the additional cost of contact precautions was €235 per episode. In intensive care unit the annual average cost of *C. difficile* infection was €1810 per patient, the annual total cost of a recurrent patient was €3680, the annual additional cost of contact precautions was €470 per patient, the annual average cost of an episode was €1070, the additional cost of contact precautions was €330 per episode. The most notable cost elements in intensive care unit were the hygienic costs and nurse wages, in department of medicine were the hygenic costs. **CONCLUSIONS:** The importance of C. difficile infection in public health and the associated disease burden are significant. The costs differed based on the length of isolation, and the type of the provider department. The available data in Hungary are limited, further studies in epidemiology and health economics are required.

PIN45

DYNAMIC MODELING TO ESTIMATE THE ECONOMIC IMPACT OF INCREASING INFLUENZA VACCINATION IN THE UNITED STATES

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OBJECTIVES: This analysis was conducted to demonstrate potential downstream health care cost savings as a result of increasing vaccination rates for influenza in the United States. **METHODS:** An age-structured susceptible-exposed-infectious-recovered (SEIR) compartmental model was constructed to model the course of influenza infection over the course of 1 year in the United States. A realistic age structure was incorporated using mixing rates between age groups from the European POLYMOD survey. The SEIR model was adapted to include another compartment for vaccination. A series of difference equations was used to model transitions to and from each compartment. Time-dependent vaccination rates were obtained using monthly estimates of vaccination rates obtained from the Centers for Disease Control and Prevention (CDC). Cost and health care utilization data were obtained from the existing literature, and included outpatient visits, hospitalization, and antiviral drug treatment. Costs were reported in 2013 U.S. dollars. Microsoft Excel 2011 was used to conduct the analysis. **RESULTS:** Under a base case vaccination rate of 40 percent, an estimated 11 percent of individuals in the United States were projected to have symptoms of influenza infection. Health care costs attributable to influenza infection were estimated to be $13.6 billion. Increasing vaccination rates to 50 percent decreased the percentage of symptomatic individuals to approximately 7 percent, resulting in downstream health care costs of $9.5 billion. Further increasing vaccination rates to 60 percent is projected to further reduce downstream health care costs to approximately $5.0 billion. **CONCLUSIONS:** This exploratory analysis demonstrates that significant health care cost savings can be realized by increasing vaccination rates for influenza in the population.

PIN46

THE ASSOCIATION BETWEEN ADHERENCE TO ANTIRETROVIRAL THERAPY AND ECONOMIC OUTCOMES AMONG COMMERCIALLY INSURED AND MEDICAID HIV PATIENTS IN THE UNITED STATES

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OBJECTIVES: Achieving optimal outcomes in the treatment of HIV requires high, sustained levels of medication adherence to antiretroviral therapy (ART). Across many conditions, suboptimal adherence has been shown to lead to poorer outcomes among patients. This study assessed the extent to which patients diagnosed with HIV are adherent with ART treatment guidelines and to illustrate associations between ART adherence and economic outcomes. **METHODS:** Commercially insured and Medicaid patients in the US from MarketScan claims databases with ≥2 claims containing an HIV/AIDS diagnosis code between June 1, 2006 and December 31, 2011 who received an ART prescription between June 1, 2007 and December 31, 2010 were selected for initial inclusion. For each patient, the first ART prescription received during that time defined the index date. Patients were ≥18 years old on their index date and had ≥12 months of continuous health plan enrollment with drug benefits before and after their index date. Adherence was measured by patients' proportion of days covered (PDC) with a complete ART regimen during the 12-month post-index date period; patients with PDC ≥80% were considered adherent. Multivariable models (i.e., generalized linear; Poisson) assessed the relationship between ART adherence and economic outcomes (i.e., costs; number of health care encounters), controlling for demographic and clinical characteristics. **RESULTS:** A total of14,590 commercially insured patients met all inclusion criteria, and 59% were adherent; 5,744 Medicaid patients met all

inclusion criteria, and 42% were adherent. After adjusting for confounders, ART adherence was associated with 29% and 31% reductions in non-pharmacy costs (p<0.0001)), 67% and 80% increases in total pharmacy costs (p<0.0001), 43% and 49% reductions in hospitalizations (p<0.0001), and 41% and 26% reductions in emergency department visits (p<0.0001), among commercially insured and Medicaid patients, respectively. **CONCLUSIONS:** This study suggests that ART adherence among commercially insured and Medicaid HIV patients in the US may be suboptimal, and that adherence is associated with improved economic outcomes among these patients.

PIN47

A SYSTEMATIC REVIEW OF ECONOMIC EVIDENCE IN HEPATITIS C: AN OVERVIEW OF COST, UTILITY AND COST-EFFECTIVENESS DATA

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OBJECTIVES: To perform a systematic literature review of economic evidence for genotype 1 hepatitis C virus (HCV) treatments. **METHODS:** Searches were performed in MEDLINE, MEDLINE In-Process, EconLit, Embase, BIOSIS, and the Cochrane Library, to identify economic evaluations, cost/resource studies, and utility studies in patients with genotype 1 HCV. Searches were limited to articles published since 2000. Additional searches were performed on the ISPOR conference and key Health Technology Assessment (HTA) websites. **RESULTS:** The review identified 53 economic evaluations, 17 HTA documents, 57 cost/resource use studies, and 19 utility studies. The majority of economic evaluations were in interferon-containing regimens and were performed using lifetime horizon Markov models. Incremental cost-effectiveness ratios ranged from $4,570.31 to $157,404.13, depending on patient severity, the treatment used and the duration of treatment. Boceprevir and telaprevir triple therapies were shown to be cost-effective compared with peginterferon and ribavirin alone. In the cost studies, total all-cause, annual costs for patients with HCV ranged from $3,236 to $85,081, depending on the patients' disease status and whether they were currently receiving treatment. Indirect costs for HCV patients were reported less frequently, but they ranged from $1,424 to $10,316 per patient per year. Utilities for patients with HCV ranged from 0.24 for patients experiencing severe adverse events to 0.89 for patients in sustained virological response. Recent economic models tended to use utility data taken from previous models or HTA submissions. **CONCLUSIONS:** Numerous recent cost-effectiveness studies are available for HCV; however, many of the economic evaluations are based on previous models. There is a particular scarcity of updated country-specific utility data. As more treatment options become available, and more robust models are developed, enhanced utility and cost studies may be needed.

PIN48

RECENT TRENDS IN HOSPITAL COSTS, LENGTH OF STAY, AND MORTALITY ASSOCIATED WITH PEDIATRIC MENINGOCOCCAL DISEASE IN THE UNITED STATES

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OBJECTIVES: Meningococcal disease (MD) is a rare, life-threatening infection most common in infants (age <1 year), adolescents, and persons living in close quarters. In this study, we documented trends in hospital costs, length of stay (LOS), and mortality associated with pediatric MD cases in the United States (US) from 2000 to 2009. **METHODS:** Data for pediatric (age ≤20 years) MD-related hospitalizations (discharges with ICD-9-CM 036.xx) from the 2000, 2003, 2006, and 2009 HCUP Kids' Inpatient Databases (KID) were retrospectively analyzed. Charges were converted to costs using a 0.5 cost-to-charge ratio. Weighted, nationally representative estimates of costs per admission (in 2012 US dollars), LOS, and case fatality rates were descriptively analyzed for each year. **RESULTS:** By year, total (weighted) numbers of pediatric MD-related hospitalizations in the US were: 2000 (N=1,680), 2003 (N=1,089), 2006 (N=745), 2009 (N=581). Mean [SD] LOS for these hospitalizations was 8.4 [12.9] days in 2000, which decreased modestly to 7.7 [9.6] and 7.9 [8.3] days in 2003 and 2006, respectively, before a substantial increase to 9.3 [13.9] days in 2009. Mean [SD] cost per admission fluctuated accordingly, increasing from $25,739 [$60,929] in 2000 to $33,530 [$62,499] in 2009. Case fatality rates, however, remained relatively unchanged during the period, declining slightly from 4.7% in 2000 to 4.3% in 2009, although a noticeable spike occurred in 2003 when 5.8% of cases died. **CONCLUSIONS:** MD in the US pediatric population is associated with high costs resulting from hospital stays that typical exceed 1 week. Our estimated case fatality rate (~5%), while high, is lower than the 10-15% fatality rate estimated by the US Centers for Disease Control, which includes estimates from all age groups combined (pediatrics and adults). In light of these findings, recent efforts to raise awareness of MD as a serious public health concern should be continued.

PIN49

HEALTH CARE COSTS OF HIV IN THE CZECH REPUBLIC. A SINGLE CENTER ANALYSIS

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OBJECTIVES: To assess direct medical costs of HIV patients, based on CD4+ lymphocyte count and duration since diagnosis in the Czech setting. **METHODS:** We analyzed retrospectively costs of HIV patients in a single center. The analyzed sample included patients with a disease history of 12 month and longer, who regularly visited the center. Resource use, derived from the hospital information system, included services delivered at the HIV center and other hospital wards. The retrospective period covered up to 36 months; average annual costs were calculated. Resource use was analyzed separately for (a) groups of CD4+ count (<200; 200-499; ≥500); (b) time since diagnosis (<5 years; 5-10 years; >10 years). For comparison, two-sided Student's t-test was used; to achieve normal distribution, values were transformed to common logarithms. Costs are stated in € (1€=25.5CZK). **RESULTS:** A total 100 patients (about 10-15% of all HIV treated in the Czech Republic) were included. The mean age was 41.9 years (range 23-71), time since diagnosis 5.8 years (range 1-26), and period of assessment 30.5 months. Average total annual costs were highest for CD4+ <200 (22,905€; p<0.05) vs. CD4+ 200-499 (17,801€) and CD4+ >500 (17,043€). HIV medication accounted for the majority of costs in all three subgroups (range 62% in CD4+ <200 to 88% in CD4+ >500). Patients with a disease duration of >10 years had highest annual costs of 22,841€ (p<0.05) compared to 15,783€ (duration 5-10 years) and 16,777€ (<5 years). HIV-medication accounted for the majority of costs here as well (from 70% to 88%; NS). In this analysis 17 % of costs in patients with disease duration of >10 years were due to hospitalization vs. 5 % in both other groups (NS). **CONCLUSIONS:** Similarly to published literature, we found highest costs in patients with low CD4+ lymphocytes and longer disease duration.

PIN50

THE BURDEN OF CLOSTRIDIUM DIFFICILE IN SPAIN: A RETROSPECTIVE MATCHED-COHORT STUDY

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OBJECTIVES: Clostridium difficileinfection (CDI) is the leading cause of infectious diarrhoea in hospitalised patients. The majority of published burden of CDI studies refer to US or northern European populations. Knowledge of the burden of CDI on health care resource utilisation in Spain is limited. The aim of the study was to provide recent data on the burden of CDI in terms of hospital resources and costs and in particular attributable length of stay. **METHODS:** A retrospective study was carried at a leading teaching hospital in Madrid. Data refer to sequential cases of CDI during the year 2011. Data were extracted from patient records using a predefined structured protocol. Hospital onset CDI cases were matched at a ratio of two non-infected patients for each case to adjust for confounding variables. **RESULTS:** A total of 44 CDI cases were identified of whom 25 were health care-associated and hospital-onset. The mean duration of diarrhoea (days) was 10.12+7.98. Using median regression, the attributable length of stay (LOS) due to CDI was 9.98+2.21 days. The average number of isolation days was 9.21+8.27. The majority of patients were treated with oral metronidazole. The first episode cure rate was 83.7%, 30-day and overall mortality were 18.6 and 25.6% respectively, attributable mortality was 4.65%. A total of 9.3% of patients experienced a recurrence occurring within 2-8 weeks within hospital stay. The cost attributable to an individual case of CDI would be 4,331 euros, of which over 90% is associated with hospital LOS. **CONCLUSIONS:** Our results highlight the significant burden of CDI in a large Spanish hospital. These costs will only continue to rise as the incidence of CDI continues to increase. A major breakthrough in cost reduction of CDI would be an intervention or procedure that shortens hospital length of stay and/or reduces episode recurrence.

PIN51

COST AND LENGTH OF STAY ASSOCIATED WITH VANCOMYCIN-INDUCED NEPHROTOXICITY

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OBJECTIVES: Decreased susceptibility to vancomycin has led to recommendations for increased serum concentration targets for some infections, which has been shown to increase the risk of nephrotoxicity (NT). The objective of this study was to determine if vancomycin-induced nephrotoxicity has a significant impact on cost from the hospital perspective or on length of stay. **METHODS:** A cost of illness study from the hospital perspective. We conducted a secondary analysis of a cohort of 398 randomly selected inpatients receiving vancomycin in a tertiary care hospital in Rochester, New York, USA. Total and variable costs were generated by hospital accountants using micro-costing methods. NT was defined as 0.5 or 50% or greater increase in serum creatinine from baseline. Generalized linear models with log link and gamma distribution and semi-log regression were used to model total and variable costs and length of stay, respectively. Cost estimates are reported in 2009 USD. **RESULTS:** Forty-nine (12%) of patients had NT. The unadjusted median variable costs for patients with NT were higher than for patients without NT ($47,511 vs. $22,355, p<.0001). On multivariable analysis, variable costs were 18% greater for patients with NT compared to patients without, but this difference was not statistically significant. The median length of stay for patients with NT was two-fold greater than for patients without NT (22 vs. 11 days, unadjusted, p<.0001). After accounting for severity of illness and other factors, NT patients stayed on average 46% longer than non-nephrotoxic patients. **CONCLUSIONS:** Patients with NT have significantly increased length of stay relative to patients without NT. Further research is needed to confirm whether increased length of stay has a meaningful impact on costs. As vancomycin susceptibility continues to decrease, higher doses of vancomycin may lead to an increased incidence of NT and an increase in resource utilization among these patients.

PIN52

COST ASSOCIATED WITH ADVERSE EVENTS AND HEALTH CARE RESOURCES UTILIZATION IN HEPATITIS C VIRUS INFECTION IN QUEBEC, CANADA

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OBJECTIVES: The purpose of this study was to estimate the health care resource utilization, more specifically resource utilization for management of the most common adverse events (AE) associated with current treatment of hepatitis C virus (HCV) infection, in a real life setting. **METHODS:** A retrospective study of the Quebec provincial drug reimbursement program (RAMQ) was conducted using a random sample of patients who filed at least one script for an HCV medication (pegylated-interferon and ribavirin (Peg-Riba) +/-boceprevir or telaprevir) between January 2007 and December 2012. Data on medical (excluding nurse visits) and pharmaceutical services were extracted from the RAMQ database. We report health care resources used during HCV treatment including outpatient physician's visits and procedures, emergency

visits, hospitalization days and costs associated with adverse events, which included medical services and medications. **RESULTS:** The study included 1,081 patients who used at least one HCV medication (mean age of 46.4 years [SD=10.7], 64.8% men). Peg-Riba only, Peg-Riba+boceprevir and Peg-Riba+telaprevir was used by 1,029 (95.2%), 50 (4.6%) and 18 (1.7%) patients respectively. Fifty-seven patients (5.3%) required a subsequent HCV treatment during the study period. The mean duration of treatments was 30.4 weeks (SD=16.1). During HCV treatment, the average number of health care resources per patient was 13.2 physician's visits and procedures, 1.0 hospitalization day and 0.9 emergency visit. While receiving HCV treatment, 191 (17.7%) of patients required erythropoietin, 353 (32.7%) received rash treatments and 541 (50.0%) were treated for depression. Estimated costs associated with management of these three AE were CDN$10,834, CDN$78 and CDN$268 per patient respectively. **CONCLUSIONS:** HCV treatment is associated with significant health care resource utilization. A high proportion of patients experienced AE for which management was associated with substantial additional costs, especially the anemia treatment. Thus, the cost of AE should be considered in future treatment options.

PIN53

THE COSTS OF MANAGING GENITAL WARTS IN THE UK BY DEVOLVED NATION: ENGLAND, SCOTLAND, WALES AND NORTHERN IRELAND

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OBJECTIVES: Genital warts (GW), 90% of which are caused by human papillomavirus (HPV) types 6 and 11, are a significant problem in the UK. The cost of managing GW in 2010 was previously estimated at £52.4 million. The objective of this study was to estimate the cost of GW management up to 2012, and to determine the cost by UK jurisdiction. **METHODS:** Population statistics were obtained from the Office of National Statistics for the UK, England and Wales; the General Register Office and 2011 census data for Scotland; and the Northern Ireland (NI) Statistics and Research Agency. Numbers of GW cases in genito-urinary medicine (GUM) clinics were obtained from the Health Protection Agency for the UK and England; the Information Services Division for Scotland; the Communicable Disease Surveillance Centre for Wales; and the Public Health Agency for NI. The number of cases treated in primary care was estimated from The Health Improvement Network database. Population statistics and GW cases were extrapolated by jurisdiction to 2012. The number of visits and therapy required for GW management were estimated by GUM experts for standard and hard-to-treat patients. Costs were obtained from the most recent National Health Service (NHS) Payment by Results tariffs, Personal Social Services Research Unit and British National Formulary. **RESULTS:** The model estimated 220,779 GW cases in the UK, costing £58.42 million annually (£265 per patient). For England, 157,693 cases were estimated costing £41.72 million; for Scotland 7,461 cases costing £1.90 million; for Wales 7,091 cases costing £1.87 million; and for NI 3,619 cases costing £0.95 million. **CONCLUSIONS:** The full NHS costs for the management of GW have never before been estimated separately for each jurisdiction. The results of the model reveal a significant economic burden which is important to quantify when understanding the value of quadrivalent HPV vaccination.

PIN54

IMPACT OF TREATMENT FAILURE ON THE TOTAL COST OF TRIPLE THERAPY INCLUDING BOCEPREVIR OR TELAPREVIR BASED ON THE FRENCH EARLY ACCESS PROGRAM (ANRS CO20-CUPIC) STUDY

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OBJECTIVES: The ANRS CO20-CUPIC study was designed to evaluate triple therapy (TT) efficacy and safety in HCV-cirrhosis treatment-experienced patients in the French Early Access Programme. A 60-week interim analysis has been reported confirming better clinical outcomes than double therapy in a real clinical setting. However, independently of the protease inhibitor (PI) used, boceprevir (BOC) or telaprevir (TLV), treatment failure (TF) was reported in up to 60% of the patients. Little is known about these patients' treatment cost: that of successfully treated patients can be generally calculated from the full course of PI treatment, but the cost of those who failed highly depends on TF timing. Our objective is to estimate the average PI cost/patient who failed treatment based on CUPIC study reported data. **METHODS:** Using reported data on ITT virological response and TF, BOC and TLV on-treatment rates over time were estimated. Based on this curve, the average PI treatment duration and average PI cost/patient who failed treatment were calculated. When not enough information about time to treatment discontinuation was available, the same conservative approach was applied for both drugs, considering the midpoint of the treatment interval. Sensitivity analyses on the time to TF were performed to confirm the robustness of the results. **RESULTS:** A total of 472 patients (72%) were included in the 60-week interim analysis. Independently of the IP used, about 60% the patients who start treatment did not achieve viral cure and their estimated average PI treatment duration was 26 wks in BOC patients and 11 wks in TLV patients. The average PI cost/patient who failed treatment with TLV (23.012€) was 26% higher than that of treatment with BOC (18.253€). The sensitivity analysis confirmed the robustness of the base case estimation. **CONCLUSIONS:** In a scenario of comparable efficacy between both PIs, the resources wasted on TF acquire a great importance in selecting the least costly of the two alternatives. Based on CUPIC study reported data, the average PI cost/patient who failed treatment was significantly higher in TLV patients than in BOC patients.

PIN55

PREDICTORS OF COSTS OF ANTIRETROVIRALS FOR HIV INFECTION IN ITALY: A MULTICENTRIC RETROSPECTION IN 2012

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OBJECTIVES: Most industrialized countries strive to guarantee long term sustainability for HIV antiretroviral treatment . By assessing the most relevant current predictors of costs of antiretrovirals(HAART) might represent the first step to understand spending drivers and to plan cost reduction strategies. **METHODS:** A retrospective sample of HIV outpatients followed at 5 Italian Hospitals in 2012 was collected. Demographic features, current HIV viral load, current and Nadir CD4 T-celI counts, time from HIV diagnosis, AIDS-defining events, HAART line and HCV coinfection were taken into consideration. Individual ARV regimen-costs were based on local pharmacy datasets from December, 2011, and log-transformed in the final multivariate models. Univariate analyses were performed to identify potential predictors and stepwise multivariate regressions were used to identify independent predictors of higher individual costs, using Stata 10.1 package. **RESULTS:** We included 2044 patients, 69.0% males, mean age 47.2±10.0 years; 33.4% HCV-coinfected, mean time from HIV diagnosis 13.3±7.9 years, mean nadir CD4 T cell counts 239±169.3 cell/mm3; mean current CD4T-cell counts 590±302.6 cell/mm3, 30.8% AIDS classified. Patients on HAART were 1,902 (93.0%),among treated patients, 19.0% presented an HIV-viremia>50 c/mL. Mean annual individual HAART-costs were € 9,376±3,501 (782-29,852). At univariate analysis, a significant association was found between costs and age time from HIV diagnosis, previous AIDS diagnosis, HCV-coinfection current and Nadir CD4T-cell counts, HAART-line, HIV-viremia and site of care. In the final regression model, HAART costs showed independent and direct correlation with HAART lines (p<0.001), detectable viremia (p<0.001) and time from HIV diagnosis (p=0.009); inverse correlation with Nadir CD4 T-cell counts (p=0.01). Being treated at 2 of 5 centre was another predictor of higher costs.(P<0.001). **CONCLUSIONS:** Higher HAART-costs were strongly associated with previous treatment failures and detectable HIV-viremia; a more compromised immune status at clinical presentation and a longer duration of HIV infection showed independent contribution, focusing on timely diagnosis of HIV infection.

PIN56

ECONOMIC IMPLICATIONS OF ALTERNATIVE TREATMENTS AND CARE LOCATIONS FOR ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTIONS WITH SUSPECTED MRSA

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OBJECTIVES: Develop model simulating economic implications of alternative treatment strategies for acute bacterial skin and skin structure infections (ABSSSIs) with suspected Methicillin-Resistant *Staphylococcus aureus* (MRSA) that considers antibiotic switches, course duration, route of administration and location of care (LOC). **METHODS:** Discrete event simulation (DES) tracks patient pathways through various LOC (ED, inpatient, outpatient) during ABSSSI treatment for suspected MRSA. Model assumes 60% of patients hospitalized. Multiple pathways are allowed: patients responding can move to outpatient to finish treatment, switch treatment at discharge or receive 2nd line treatment if not responding. Patients accrue resource use, time in LOC and costs. Hospital days obtained from analysis of Premier Hospital Database. Three cohorts created; all assigned to receive vancomycin (VAN) 1st line therapy. Upon discharge, one cohort continued on VAN, one switched to oral linezolid (LIN), one to daptomycin (DAP) to complete treatment. Costs are from the Medicare perspective in 2012 USD. **RESULTS:** Hospital plus outpatient days range from 11.1 (VAN) to 14.5 (LIN); costs ranged from $6,983 (LIN) to $8,122 (VAN) with suspected MRSA. By comparison, reatment duration ranged from 9.97 (VAN) to 13.02 (LIN) and total costs ranged from $6,889 (LIN) to $9,354 (VAN) when MRSA is not always suspected. Despite longer LIN treatment, costs are lower because of avoided infusion costs. Outpatient costs account for 22% (LIN) to 33% (VAN) of total costs. Sensitivity analysis examined impact on cost when treatment duration varied per drug labeling. Total costs varied from $6,756 to $7,158 when duration of LIN ranges from 8 days to 12 days. **CONCLUSIONS:** Treatment choice and LOC have major impact on ABSSSI resource use and costs. Suspected MRSA increases treatment duration and cost. Economic implications for payers and providers should be evaluated using models that capture these elements in view of long-acting lipoglycopeptide IV antibiotics in development that avoid repeated infusions and may allow for less inpatient treatment.

PIN57

WHEN TREATMENT IS MITIGATED BY ADVERSE EVENTS: THE ECONOMIC IMPACT OF TREATMENT-ASSOCIATED ADVERSE EVENTS IN CIRRHOTIC NON-RESPONDERS TREATED WITH BOCEPREVIR OR TELAPREVIR AND PEGINTERFERON ALPHA/RIBAVIRIN

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OBJECTIVES: Adverse events (AEs) and premature treatment discontinuation of protease inhibitor (PI) therapy in the treatment of chronic hepatitis C (CHC) may mitigate the benefits of improved sustained virologic response. We use data from a recent study to estimate the economic impact of PI therapy in the cirrhotic non-responder population. **METHODS:** In the Compassionate Use of Protease Inhibitors in viral C cirrhosis (CUPIC) study, patients with compensated cirrhosis and genotype 1 CHC were treated with boceprevir (n=205) or telaprevir (n=292) in combination with peginterferon alpha and ribavirin. The investigators reported safety and tolerability in an interim 16-week analysis. Using CUPIC data and micro-costing technique, we estimate the costs of treatment-related hematologic and rash AEs by severity (Grades 2-4) and the cost of drug wastage using PI discontinuation rates due to serious AEs (SAEs) (7.3% boceprevir; 14.7% telaprevir). We surveyed 3 hepatologists to ascertain treatment patterns related to AEs and combined these estimates with cost data to compute mean costs per treatment group from the US payer perspective during the first 16 weeks of therapy. **RESULTS:** The AE-related costs were $1,980 and $2,161 for telaprevir and boceprevir treated patients, respectively, for the first 28 days of treatment. Medication-related costs of premature discontinuation due to SAEs were estimated at $8,463 for telaprevir and $1,575 for

boceprevir. Total costs of AE and discontinuation were $10,443 and $3,736 for telaprevir and boceprevir treated groups, respectively. The results were not sensitive to variation in treatment practices and costs. **CONCLUSIONS:** The costs of treatment of cirrhotic non-responders during the first 16 weeks were estimated to increase by 18% over triple therapy costs due to AEs. These data indicate that the total cost per cure may be substantially higher than the drug costs and underscore the importance of evaluating total cost of HCV treatment when selecting new agents.

PIN58

DIRECT MEDICAL COSTS AND HEALTH CARE RESOURCE UTILIZATION ASSOCIATED WITH SELECTED ANTIBIOTIC TREATMENT PATHWAYS IN ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTIONS IN THE UNITED STATES

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OBJECTIVES: Current guidelines for the treatment of acute bacterial skin and skin structure infections (ABSSSI) recommend several treatment pathways based on the infection types and severity. The objective of this study is to establish the health care resource utilization (HRU) and costs associated with the most common patient treatment pathways in US. **METHODS:** The medical and pharmacy administrative claims of adult ABSSSI patients with continuous commercial or Medicare Advantage enrollment with Part D prescription drug coverage between 01 January 2009 and 31 December 2011 were extracted from a large national health plan affiliated with OptumInsight. The four most common treatment pathways were identified based on the evidences of antibiotics over the entire ABSSSI treatment course. All four pathways start with vancomycin IV use during a hospital stay. At discharge, patients followed one of four pathways: 1) continue IV vancomycin as an Outpatient Parenteral Antibiotic Therapy (OPAT); 2) switch to oral linezolid; 3) switch to daptomycin; or 4) switch to any oral antibiotic other than linezolid, clindamycin, or TMP-SMX. Health care resource utilization and costs were determined for each pathway. **RESULTS:** A total of 1418 patients met all of inclusion/exclusion criteria. The majority of patients either continued Vancomycin IV (46.5%) or switched to oral linezolid (41.4%) at discharge. Only about 12% of patients were switched to Daptomycin or other non-MRSA active oral antibiotics. The average ABSSSI-related total health care cost was $16,571 for the entire ABSSSI treatment. Total costs were comprised of $12,519 (75.5%) for inpatient cost, $201 (1.2%) for emergency department (ED) visits, $879 (5.3%) for outpatient treatment/office visits, and $1,015(6.1%) for pharmacy claims cost. The costs overall and in various locations of care varied by pathway. **CONCLUSIONS:** Inpatient treatment remains the largest component of total ABSSSI treatment cost. Utilization of linezolid and daptomycin increased the pharmacy or OPAT costs.

PIN59

COMPARISON OF THE HEALTH CARE COSTS AND UTILIZATIONS BETWEEN PATIENTS DIAGNOSED WITH THE HEPATITIS B VIRUS VERSUS THOSE WITHOUT

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OBJECTIVES: To examine the economic burden and health care utilizations of patients diagnosed with the hepatitis B virus (HBV) in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration (VHA) Medical SAS datasets from October 1, 2008 to September 30, 2012. Patients diagnosed with HBV were identified using International Classification of Disease 9th Revision Clinical Modification (ICD-9-CM 070.22, 070.23, 070.32, 070.33, V02,61) diagnosis codes. The first diagnosis date was defined as the index date. A group of patients of the same age, region, gender and index year but without HBV infection were identified and matched by baseline Charlson Comorbidity Index (CCI) as the comparison group. A 1-year continuous health plan enrollment was required before and after the index date for both groups. Study outcomes, including health care costs and utilizations, were compared between the HBV and comparator groups using 1:1 propensity score matching. **RESULTS:** A total of 9,718 patients were identified for the HBV and comparison cohorts. After applying a 1:1 matching, a total of 3,093 patients were matched from each cohort, and the baseline characteristics were proportionate. Patients diagnosed with HBV infection were more likely to report higher health care utilizations, including inpatient (28.74% vs. 3.3%, $p<0.01$), emergency room (25.67% vs. 8.3%, $p<0.01$), physician office (98.60% vs. 62.75%) and pharmacy visits (88.23% vs. 63.65%, $p<0.01$). The risk-adjusted health care costs were also higher for patients infected with HBV due to increased inpatient ($10,481 vs. $804, $p<0.01$), emergency room ($382 vs. $80, $p<0.01$), physician office ($4,635 vs. $1,678, $p<0.01$), and pharmacy visits ($1,166 vs. $398, $p<0.01$) resulting in higher total costs ($16,909 vs. $3,045, $p<0.01$) relative to the comparator cohort. **CONCLUSIONS:** During a period of 12 months, VHA patients diagnosed with HBV reported higher health care utilization and costs than their matched controls.

PIN60

A COMPARATIVE STUDY ON THE COST OF ANTIBIOTICS FOR THE YEARS 2011-2012 IN THREE GENERAL HOSPITALS OF GREECE

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OBJECTIVES: Since Greece came under the regime of IMF and signed the memorandum, several curtailments had to be made to various areas of the public sector. Drug treatment seems to be quite expensive. As part of the strict economic rules, Greek hospitals were obliged to reduce their health care costs. The pharmacy of each hospital incurred considerable weight of this attempt. One of its implemented actions was the drugs' price negotiation with the pharmaceutical companies. **METHODS:** In order to measure the effectiveness of this action, we performed a comparative study of the antibiotics used in 3 hospitals, PAGNI, Evaggelismos and Tzaneio. PAGNI and Evaggelismos are among the 5 biggest hospitals of Greece (pharmaceutical budget around 40M€) while Tzaneio is a small general hospital (PB 6M€). We chose 24 active ingredients (95 different antibiotics) that represent about 1/3 of total hospital antibiotics and 80% of the total antibiotics' budget. We studied their consumption for the years 2011 and 2012 and calculated the costs based on the official drug pricelist and their price after the negotiation. **RESULTS:** From 2011 to 2012 the discounts gained from each hospital were increased. Price negotiation does not apply in prototype drugs that their companies are only obliged to offer a 5% rebate. Unfortunately, these medications are more expensive, represent 36% of the studied antibiotics' cost and their consumption was increased by 20%. But, the discounts for all the studied off-patent drugs and their generics were from 12.8% till 89.9%. Thus, the total cost saving for them was 33.2% at PAGNI, 26.0% at Evaggelismos and 43.1% at Tzaneio. The total benefit for the pharmaceutical expenditure was 3% for both PAGNI and Evaggelismos, and 6% for Tzaneio. **CONCLUSIONS:** Price negotiation is an effective mean of decreasing the cost of off-patent and generic drugs but newer and expensive drugs get doctors' preference, undermining the Pharmacy's cost-saving effort.

PIN61

WHAT ARE THE CLINICAL AND ECONOMIC COSTS AND BENEFITS OF IMPLEMENTING POINT OF CARE TESTS FOR CHLAMYDIA TRACHOMATIS AND NEISSERIA GONORRHOEA IN GENITO-URINARY MEDICINE CLINICS IN THE UNITED KINGDOM?

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OBJECTIVES: To estimate the costs and benefits of patient pathways incorporating a point of care nucleic acid amplification test (POC NAAT) for chlamydia and gonorrhoea in genito-urinary medicine (GUM) clinics in the UK compared with standard off-site laboratory testing. **METHODS:** We simulated 1.2 million men and women GUM clinic attendees based on GUMCAD reports from the UK (2011). A Markov model with Monte Carlo simulation in Microsoft Excel was developed to compare existing standard pathways of testing and treatment for chlamydia and gonorrhoea with a POC NAAT. We conducted sensitivity analyses to evaluate the robustness of the model findings. The primary outcome was the incremental cost-effectiveness ratio (ICER = £/QALY). Secondary outcomes included the number of inappropriate treatments, complications and transmissions averted and change in time from test to treatment. **RESULTS:** The total cost of using the POCT in our cohort was £103.3 million compared with £113.9 million for standard care. The ICER was -£4,182/QALY, making the new pathways cost saving. Nearly 100,000 inappropriate treatments might be avoided by using a POC NAAT. Patients receive diagnosis and treatment on the same day as testing, which may also prevent 162 cases of pelvic inflammatory disease and 17,561 transmissions. **CONCLUSIONS:** Replacing standard laboratory tests for chlamydia and gonorrhoea with a POCT could be cost saving and patients would benefit from more accurate diagnosis and less unnecessary treatment. Overtreatment currently accounts for about a tenth of the reported treatments for chlamydia and gonorrhoea and POC NAATs would effectively eliminate the need for presumptive treatment.

PIN62

COST-EFFECTIVENESS OF CHILDHOOD ROTAVIRUS VACCINATION IN GERMANY

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OBJECTIVES: Rotavirus (RV) causes highly contagious gastroenteritis especially in children under five years of age. Since 2006, two RV-vaccines are available in Europe (Rotarix® and RotaTeq®). We evaluated the cost-effectiveness of these vaccines for the German health care setting, inter alia to support an informed decision-making concerning a potential vaccination-recommendation. **METHODS:** A Markov Model was developed to evaluate the cost-effectiveness from the statutory health insurance (SHI) (direct costs) and from the societal perspective (SHI plus indirect costs). Health outcomes considered were RV-cases prevented, RV-associated hospitalizations avoided, and quality-adjusted life-years (QALY) gained. RV-incidences were derived from the national mandatory disease reporting system. RV-vaccine efficacy was calculated as pooled estimates based on data from randomized controlled trials. Costs (reference year 2010) were derived from official price catalogues. An annual discount rate of 3% for effects and costs was applied. The first five life-years were considered as model's time horizon. **RESULTS:** The base-case analysis (SHI-perspective) resulted in an incremental cost-effectiveness and cost-utility ratio (ICER) for Rotarix® of € 184 per RV-case prevented, € 2,457 per RV-associated hospitalization avoided, and € 116,973 per QALY gained. For RotaTeq®, the results were slightly higher (€ 234, € 2,622, and € 142,732, respectively). In sensitivity analyses parameter variation showed effects on the ICERs without changing the overall trend. A threshold analysis suggests that cost-saving scenarios are possible with vaccine prices reduced by ~62-66%. When applying base-case scenario results to the 2012 birth-cohort with 80% vaccination coverage, an estimated 206,000-242,000 RV-cases and 18,000 RV-associated hospitalizations can be prevented in this birth-cohort over 5 years for an incremental cost of 44.5-48.2 million Euros. **CONCLUSIONS:** Routine RV-vaccination is expected to prevent a considerable number of RV-cases and RV-associated hospitalizations in Germany. Though, the amount of QALYs gained is low. With current vaccine prices, RV-vaccination is not a cost-saving preventive measure.

PIN63

COST-EFFECTIVENESS ANALYSIS OF 3 CANDINS AND FLUCONAZOLE IN THE TREATMENT OF CONFIRMED INVASIVE CANDIDIASIS IN ADULT NON-NEUTROPAENIC PATIENTS IN SPAIN

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OBJECTIVES: To estimate the cost-effectiveness (CE) of the 3 echinocandins (Anidulafungin, Caspofungin and Micafungin) and generic Fluconazole in the treatment of adult non-neutropaenic patients with invasive candidiasis (IC) in a Spanish Intensive Care Unit (ICU) setting. **METHODS:** A 4 arm decision tree model was developed with the 3 echinocandins and generic Fluconazole as first line treatment. In case of treatment failure, a 2nd line treatment was administered (Liposomal Amphotericin-B following the echinocandins and either one of the 3 echinocandins for Fluconazole arm). After 2nd line failure, treatment was discontinued. Total treatment length was 14 days. Efficacy and safety (adverse events/lack of efficacy) parameters where obtained from a mixed-treatment-comparison and a meta-analysis respectively. Efficacy was considered as first line success (Anidulafungin 75.32%; Micafungin 71.65%; Caspofungin 70.62%; and Fluconazole 56.7%). Length of the first and the second line were elicited using experts' opinion through Delphi methodology. Daily drug acquisition costs were considered only. The CE was expressed as an incremental cost-effectiveness ratio (ICER). Univariate sensitivity analyses were also applied and included, length of treatment in 1st or 2nd line and finally drug dosages calculated as per SmPC recommendations according to different patient characteristics. **RESULTS:** Total costs of IC treatment for Anidulafungin, Micafungin, Caspofungin and Fluconazole were €5,552; €5,985; €6,350; €1,654 respectively. Anidulafungin was dominant compared to Micafungin and Caspofungin. Anidulafungin and Micafungin were cost-effective (€20,934; 29.576€ respectively) compared to Fluconazole (CE threshold of €30,000). Sensitivity analyses revealed that ICER was sensitive to increases in the length of the 1st and 2nd line treatments, although Anidulafungin was cost-effective in all scenarios. **CONCLUSIONS:** Based on the model's assumptions, Anidulafungin is cost-saving compared to Micafungin and Caspofungin and cost-effective vs. Fluconazole in the treatment of patients with confirmed invasive candidiasis from a Spanish Hospital ICU perspective.

PIN64

COST-EFFECTIVENESS OF LINEZOLID VERSUS VANCOMYCIN IN THE TREATMENT OF VENTILATOR ASSOCIATED PNEUMONIA IN JAMAICA

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OBJECTIVES: The ventilator associated pneumonia (VAP) refers to the pneumonia that appears after 48-72 hours of endotracheal intubation and is the most common nosocomial infections in patients receiving mechanical ventilation. Late-onset VAP is responsible for prolonged ICU stay and higher mortality rates (24 to 50% and can even increase to 76%), which explains the importance of using more effective antibiotics depending on the severity of each case. The aim of this study is to assess the cost-effectiveness (CE) of linezolid against vancomycin in the treatment of VAP, from the public health care perspective. **METHODS:** A cohort of patients with VAP was simulated using a decision-tree model to compare costs and effectiveness of linezolid (600 mg/12 hours) and vancomycin (1 g/12 hours). Effectiveness measures were: microbiological success rates, mortality rates, and ICU and ward LOS. The model used a 12-week time horizon and only direct medical costs were considered (inpatient costs, medication expenses, adverse events costs). Effectiveness and epidemiologic data were retrieved from published literature. Local costs (2013 US$) were gathered from the official databases of Jamaican Health System. Monte Carlo probabilistic sensitivity analysis (PSA) was constructed. **RESULTS:** Linezolid resulted as the most effective and less expensive option for VAP adult patients. Clinical success rate was higher with linezolid (64.4%) against vancomicyn (56.1%). Mean expected ICU LOS was 14 days for linezolid and 17 days for vancomycin, ward LOS was 14 and 24 days with linezolid and vancomycin, respectively. Mortality rate was found lower in the linezolid arm (10.13%) in comparison to vancomycin (15.74%). Overall costs per patient were $36721.65 with linezolid and $40776.82 with vancomycin. In the CE incremental analysis, linezolid appeared as the cost-saving option. PSA outcomes support the robustness of these findings. **CONCLUSIONS:** Linezolid resulted as the cost-saving therapy for treating VAP adult patients in Jamaica.

PIN65

COST EFFECTIVENESS ANALYSIS OF BOCEPREVIR (BOC) ADDED TO PEGIFN/ RIBAVIRIN (P/R) VERSUS PEGIFN/RIBAVIRIN (CURRENT STANDARD OF CARE) FOR THE TREATMENT OF PATIENTS WITH GENOTYPE 1 CHRONIC HEPATITIS C IN GREECE

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OBJECTIVES: Boceprevir plus P/R has demonstrated a superior clinical profile, compared to P/R alone, in the treatment of genotype 1 chronic hepatitis C (G1-CHC) patients. The objective of this study was to evaluate the cost-effectiveness of BOC/P/R therapy for treatment naïve and treatment experienced G1-CHC patients in Greece. **METHODS:** A Markov-model simulating the quality-adjusted life years and corresponding costs of G1-CHC treatment provided the basis of the analyses. The BOC/P/R regimens recommended in the label for treatment naïve and treatment experienced patients were compared to P/R to calculate incremental costs and outcomes. The inputs for the model were derived from post-hoc subset analyses of SPRINT-2 and RESPOND-2 data. Resource use for patient monitoring and treatment of events was elicited via expert panel. Lifetime horizon with 3% discount rate was used and the perspective of analysis was third-party payers. **RESULTS:** BOC-based therapy was projected to reduce liver complications (decompensated cirrhosis, hepatocellular carcinoma, liver transplant and liver–related death) by 44% and 49-53% in treatment naïve and experienced patients, respectively, leading to corresponding gains of 0.87 and 1.25 QALYs per patient. Taking into account medication costs, treatment and management of events, the ICER for BOC-based therapy versus P/R were estimated at 10,003€/QALY and 10,852€/QALY for treatment naïve and experienced patients, respectively. Extensive sensitivity analyses indicated that results were robust. **CONCLUSIONS:** Based on the results of this analysis, the addition of Boceprevir to P/R for treatment of G1 CHC patients can be a cost-effective treatment option in the Greek health care setting.

PIN66

COST PER CURE OF TELAPREVIR AND BOCEPREVIR IN TREATMENT-NAÏVE GENOTYPE 1 HEPATITIS C PATIENTS WITH F2 FIBROSIS IN BRAZIL

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OBJECTIVES: Compare the cost per cure of telaprevir of peginterferon and ribavirin (TVR+PR) compared to boceprevir plus peginterferon and ribavirin (BOC+PR) in the treatment of METAVIR scale F2 patients with previously untreated chronic hepatitis C genotype 1 in the Brazilian public (SUS) and private (SS) health care system. **METHODS:** Treatment costs considered drug acquisition costs of TVR+PR and BOC+PR from a public and private payer perspective in Brazil. The cost/cure was defined as the cost/sustained virological response (SVR) according to the phase 3 trials of TVR and BOC. The SVR rate for TVR+PR was defined as 79% and 49% for PR in patients with F2 fibrosis. Based on the SPRINT-2 trial, the SVR-rate for F2 patients treated with BOC+PR was assumed 57%, average between F0/F1 and F3/F4 patients, compared to 38% for PR. Treatment duration, based on the extended rapid virological response (eRVR), was taken from the respective trials of BOC (eRVR = 44%) and TVR (eRVR = 58%). Deterministic sensitivity analysis was carried out for the eRVR rate. **RESULTS:** In the SUS, TVR+PR had an average treatment cost of R$ 40.093 per F2 fibrosis patient compared to R$ 36.185 with BOC+PR. Considering the SVR rate and the sensitivity analysis, TVR+PR had a cost/SVR of R$ 50.751 (R$ 49.797-R$ 51.705) compared to R$ 63.481 (R$ 61.771-R$ 65.191) with BOC+PR. In the private health care system, TVR+PR had a treatment cost of R$ R$ 88.508 per F2 fibrosis patient compared to R$ 82.518 with BOC+PR. Considering the cost/SVR and sensitivity analysis, TVR+PR had a cost/SVR of R$ 112.036 (R$ 108.253-R$ 115.819) compared to BOC+PR with a cost/SVR of R$ 144.768 (R$ 140.631-R$ 148.905) per F2 patient in the SS. **CONCLUSIONS:** Compared to BOC+PR, TVR+PR was a more cost-effective treatment of F2 fibrosis patients in both public and private health care systems.

PIN67

COST-EFFECTIVENESS OF PEGINTERFERON ALFA AND RIBAVIRIN FOR THE TREATMENT OF CHILDREN AND YOUNG PEOPLE WITH CHRONIC HEPATITIS C FROM THE PERSPECTIVE OF THE NHS IN ENGLAND AND WALES

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OBJECTIVES: To evaluate the cost-effectiveness of peginterferon (PEG INF) alfa and ribavirin for the treatment of children and young people ages 3 to 17 years with Chronic Hepatitis C (CHC), from the perspective of the NHS in England and Wales. This analysis was submitted to NICE as part of a submission dossier for the multiple technology appraisal of PEG INF alfa and ribavirin for the respective population. **METHODS:** A Markov model was developed based on previous economic evaluations for treatment of adults with CHC with PEG INF alfa and ribavirin. The model evaluated the cost-effectiveness of PEG INF alfa-2a or alfa-2b and ribavirin, and supportive care, for the treatment of people aged 5 to 17 years. An additional analysis was conducted on 3 and 4 year olds comparing supportive care to PEG INF alfa-2b and ribavirin in line with license. The cost-effectiveness was evaluated using the incremental cost-effectiveness ratio (ICER) from the perspective of the NHS over a lifetime horizon. The results were assessed overall and by age and genotype subgroups. **RESULTS:** The results reported that both combinations of PEG INF alfa and ribavirin dominated supportive care for all patients. Driven by small variation in the comparative efficacy and costs, the comparison between PEG INF alfa-2a and alfa-2b, in combination with ribavirin, showed that PEG INF alfa-2b dominated PEG INF alfa-2a overall and in the following subgroups: 5 to 8 years, 14 to17 years and genotypes 2/3. The ICER for the 9 to13 years subgroup was £4,697. PEG INF alfa-2a dominated PEG INF alfa-2b for the other genotype subgroup **CONCLUSIONS:** The results of the economic evaluation demonstrated that treatment with either combination of PEG INF alfa and ribavirin is a cost-effective treatment option for children and young people aged 3 to 17 years with CHC.

PIN68

COST-EFFECTIVENESS OF 13-VALENT VERSUS 10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE USE IN THE CZECH NATIONAL IMMUNIZATION PROGRAM

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OBJECTIVES: Streptococcus pneumoniae is presumed to be the major etiology agent responsible for a significant amount of meningitis, bacteremia and sepsis (invasive pneumococcal disease; IPD) as well as Community Acquired Pneumonia (CAP) and Acute Otitis Media (AOM). The Czech Republic (CR), as well as many other European countries have only a limited local evidence on the underlying epidemiology. The objective was to estimate the expected outcomes, costs, cost-effectiveness of the pediatric national immunization program (NIP) with 13-valent pneumococcal conjugated vaccine (PCV13) and 10-valent pneumococcal conjugated vaccine (PCV10) as a comparator among specific populations of children and adults in preventing and reducing the incidence of IPD, CAP and AOM in CR. **METHODS:** A Markov decision-analytic model was developed to examine impacts of infant vaccination with PCV13 versus PCV10. PCV13 direct effectiveness was extrapolated from PCV7 efficacy data from clinical trials, using assumptions regarding serotype prevalence and PCV13 protection against additional serotypes, while indirect (herd) effect was extrapolated from US surveillance data following universal PCV7 use. The local epidemiology and cost data were used to achieve maximum national specificity. **RESULTS:** Model predicts incremental EUR 64.5 million for the PCV13 NIP from the payer's perspective in the 10-year horizon, as compared to PCV10. This would lead to an reduction in IPD, all cause inpatient and outpatient CAP and AOM by approximately 921, 22 900, 56 796 and 40 598 cases, respectively, thus savings EUR 35.4 million. This gives a total cost of EUR 29.0 million in the 10 years. The incremental cost per LYG or QALY gained is estimated as EUR 929 or EUR 1 164, respectively, from the payer's perspective as compared to PCV10. **CONCLUSIONS:** Comparing the national GDP per capita with the WHO

recommendation on health care spending per QALY gained, PCV13 NIP in Czech Republic can be considered cost-effective.

PIN69

ECONOMIC EVALUATION OF FIDAXOMICIN FOR THE TREATMENT OF CLOSTRIDIUM DIFFICILE INFECTIONS (CDI) ALSO KNOWN AS C. DIFFICILE-ASSOCIATED DIARRHOEA (CDAD) IN IRELAND

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OBJECTIVES: Fidaxomicin is the first in a new class of macrocylic antibiotics, indicated in adults for the treatment of Clostridium difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD). The study objective was to perform a cost-utility analysis of fidaxomicin for the treatment of CDI compared to oral metronidazole (used to treat initial non-severe CDI and first non-severe recurrence) and oral vancomycin (used to treat severe CDI and any non-severe recurrence beyond the first one). **METHODS:** A Markov model was used to determine the cost-utility of fidaxomicin in the treatment of all adult CDI patients (base case), patients with severe CDI, and patients with initial CDI recurrences, respectively. The cycle length was 10 days. The patient enters the model in the CDI health state and is treated either with fidaxomicin, oral metronidazole or vancomycin for 10 days. The time horizon was one-year. Deterministic and probabilistic sensitivity analyses were performed. Health state utilities were derived from the literature. The perspective was that of the Irish Health Service Executive (HSE). **RESULTS:** In the base case, fidaxomicin was dominant compared to current standard of care, resulting in cost savings of €2,904 and an incremental QALY gain of 0.031. The main drivers of cost-effectiveness were the reduction in rate of recurrence in patients treated with fidaxomicin and the cost of hospitalisation. Fidaxomicin was also found to be dominant for all patient subgroups. The ICERs were highly sensitive to recurrence rates. The probability of the cost-effectiveness of fidaxomicin in all CDI patients at a willingness to pay threshold of €45,000 per QALY gained was estimated to be approx. 82%. **CONCLUSIONS:** Fidaxomicin was dominant compared to current standard of care with an approx. 82% probability of being cost-effective in all CDI patients at a willingness to pay threshold of €45,000 per QALY gained.

PIN70

A UK CASE STUDY OF SOCIETAL AND HERD-EFFECT IMPACT OF UNIVERSAL MASS INFLUENZA VACCINATION IN THE UNITED KINGDOM

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OBJECTIVES: To demonstrate the impact of influenza vaccination in currently non-recommended populations in the UK. To understand critical elements of influenza infection (herd-effect and productivity losses) and management of disease. Management includes direct medical, non-medical and indirect resources. **METHODS:** A multicohort, static, one-year Markov-model was constructed. Universal influenza mass vaccination of healthy individuals ≥6 months to ≤64 years was applied, using either trivalent (TIV) or quadrivalent (QIV) influenza vaccines. Current vaccination coverage rates for high risk persons were utilized as a proxy. Vaccine efficacy data were derived from Cochrane Databases (TIV) and meta-analyses (QIV). The impact of herd-effect was evaluated by two different estimates from published literature, providing a range of results. A societal perspective was adopted and 2010 was the cost reference year. **RESULTS:** Using the average influenza-B circulation and vaccine matching data of 2000 to 2010, between 71,000-82,000 additional cases will be prevented with QIV versus TIV in one influenza season. QIV is anticipated to prevent more medical visits, complications, and hospitalisations (15,000-17,000); (8,000-9,300) and (889-1,044), respectively. QIV programme costs are higher due to acquisition costs compared to TIV, however influenza treatment and management costs are lower due to fewer cases/complications for direct medical, non-medical and indirect categories (absenteeism/presenteeism), (savings: £4,800,000-£5,700,000); (savings: £215,000-£253,000); (savings: £22,400,000-£26,400,000), respectively. In addition, future productivity losses caused by premature mortality are also minimized with maximal effect with QIV rather than TIV (savings: £5,100,000-£6,700,000). **CONCLUSIONS:** Herd-effect is a well understood and appreciated benefit of vaccinating children and mass vaccination within a population. This model suggests that there are vast benefits in universal mass vaccination of healthy persons in the UK with QIV instead of TIV, due to greater health-related benefits and lower treatment-related costs. However, vaccine acquisition costs need to be considered.

PIN71

THE ECONOMIC ASSESSMENT OF AN ENVIRONMENTAL INTERVENTION: DISCRETE DEPLOYMENT OF COPPER FOR INFECTION CONTROL IN ICUS

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OBJECTIVES: Health Economics evaluations are typically applied to medications or surgery costs, but this unique study has investigated the economic benefits of discrete deployment of antimicrobial copper alloy touch surfaces in ICUs. Copper/copper alloy surfaces have been shown to act as an adjunct to standard infection control practices in diverse clinical settings, continuously reducing contamination by over 90%. A study by Salgado in 2013 investigated the use of copper surfaces in ICUs and reported a 58% reduction in hospital acquired infections. This study investigates the cost-effectiveness of this intervention. **METHODS:** Following an extensive literature review and use of expert opinion a number of factors have been considered in this evaluation. These are the component costs of the items used in the ICU, the cost of and extra day in bed due to an infection, baseline infection rates and risk reduction of copper items. The model is based on a single room configuration in an intensive care unit with 20 beds in the UK using 6 critical items - bed rails, overbed tray table, chair, call button, data device and IV pole. The model has been created to show the economic impact of an environmental intervention. **RESULTS:** The model predicts the cost of replacing key, frequently-touched surfaces in a 20-bed UK ICU with copper equivalents will be recouped in less than two months. Over 5 years there were 325 fewer infections in the copper arm at a cost per QALY of £262.84. **CONCLUSIONS:** The investigation allowed the derivation of a spreadsheet-based model that uses the best current published information and shows the rapid ROI of a copper intervention. It also calculates the impact on bed days and quality-adjusted life years (QALY). The model is simple, transparent to those with knowledge of spreadsheets, and allows adaptation to specific local settings.

PIN72

COST-EFFECTIVENESS OF A 13-VALENT CONJUGATE PNEUMOCOCCAL VACCINATION PROGRAM IN COPD PATIENTS AGED ≥50 YEARS IN SPAIN: PRELIMINARY RESULTS

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OBJECTIVES: Patients with chronic obstructive pulmonary disease (COPD) are at risk of pneumococcal infection. A 13-valent pneumococcal-conjugate vaccine (PCV13) has recently been approved for adult protection against *S. pneumoniae*. This study estimated the clinical and economic consequences of vaccinating COPD patients aged ≥50 years with PCV13 compared to current vaccination recommendations using a 23-valent pneumococcal-polysaccharide vaccine, from the Spanish Healthcare System perspective. **METHODS:** A microsimulation model with a Markov process accounting for risks and costs for invasive pneumococcal disease (IPD) and all-cause nonbacteremic pneumonia (NBP) was developed. Prevalence, mortality rates, vaccination and serotype coverage, and vaccination and disease-related costs (€2013) were based on published data. Vaccines effectiveness was modified by a waning effect over time. Herd-immunity and revaccination were not considered. Outcomes and costs (both discounted at 3%/year) were simulated 100 times with, 1.6 million COPD patients per simulation. Outcomes were pneumococcal cases averted and incremental cost–effectiveness ratio (ICER) in terms of cost per life-year gained (LYG). Sensitivity analyses were performed modifying the time horizon, discount rate and vaccination coverage. **RESULTS:** Over a 5-year period, the use of PCV13 vs current vaccination strategy in adult COPD subjects would prevent 529 IPD cases, 6,329 inpatient-NBP cases, and 697 outpatient-NBP cases. Additionally, 231 IPD and 148 inpatient-NBP related deaths would be averted. The ICER was €24,557/LYG for PCV13 vs current vaccination strategy. In sensitivity analyses, ICER ranged from €26,986/LYG (when changing discount rate from 3% to 5%) to €7,661/LYG (when changing vaccination coverage from 80% to 66%). Using a lifetime horizon 1,271 IPD cases, 10,294 inpatient-NBP cases, and 2,072 outpatient-NBP cases would be prevented, with an ICER of €5,030/LYG. **CONCLUSIONS:** At a willingness-to-pay of €30,000/LYG, PCV13 vaccination in COPD patients aged ≥50 years in Spain is a cost-effective strategy compared to current vaccination recommendations under both 5-year and lifetime time horizons.

PIN73

LINEZOLID FOR THE TREATMENT OF PATIENTS WITH CONFIRMED MRSA NOSOCOMIAL PNEUMONIA IN NANJING, CHINA: A COST EFFECTIVE ALTERNATIVE TO VANCOMYCIN

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OBJECTIVES: Vancomycin has been the treatment of choice for several years while linezolid is a relatively new alternative in China. Although clinical superiority of linezolid was demonstrated in a recent head-to-head clinical study, economic evaluation comparing the two treatments provides additional useful decision making information. This study aimed to compare the cost-effectiveness of linezolid versus vancomycin in treating confirmed MRSA NP from a payer's perspective in Nanjing. **METHODS:** A cost-effectiveness model primarily driven by the head-to-head clinical data (Wunderink, CID: 2012), was adapted with local published data and expert opinion on resource use and unit costs. The model structure and assumptions were verified to reflect local clinical practice. Both linezolid and vancomycin arms were assumed to have same life expectancy in full health upon discharge. The base case analysis considered 10-day treatment duration for both treatments. Scenario analyses were conducted by varying treatment duration, per day total costs in ICU and general ward, drug acquisition costs, and including costs for managing key adverse events. All costs were reported in 2012 Chinese RMB. **RESULTS:** A higher treatment success rate by 2.7% was predicted for linezolid. Both treatment arms were estimated to have very similar average total costs in the region of RMB 78,800 with the key cost drivers being drug acquisition costs and ICU per day total cost. The ICER for linezolid was RMB 163 for each additional successfully treated patient. Dominance of linezolid attributed to greater treatment success but lower total cost was observed in most of the scenario analyses. The highest ICER was RMB 31,663 in the scenario where the acquisition cost of vancomycin reduced by 20%. **CONCLUSIONS:** Given the estimated low ICERs with dominance in most of the scenario analyses, linezolid can be considered a cost effective option compared to vancomycin in managing confirmed MRSA NP in Nanjing.

PIN74

A COST-EFFECTIVENESS ANALYSIS OF LINEZOLID VERSUS VANCOMYCIN FOR VENTILATOR-ASSOCIATED PNEUMONIA PATIENTS IN COSTA RICA

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OBJECTIVES: Ventilator-associated pneumonia (VAP) is the most common nosocomial infection in the intensive care unit (ICU). It's associated with significant morbidity, increasing the ICU and hospital length of stay (LOS), and raising overall costs. Literature suggests that costs could be reduced using the most efficient empiric

therapy. The aim of this study was to assess the cost-effectiveness (CE) of Linezolid against generic Vancomycin as an empiric therapy for VAP patients, from the health care payer's perspective. **METHODS:** A decision-tree model was used to compare costs and effectiveness of Linezolid (600 mg/12 hours) and Vancomycin (1g / 12 hours) (comparator) for a cohort of patients with VAP. Effectiveness measures were: microbiological success rates, mortality rates, ICU and ward LOS and overall costs. Effectiveness and epidemiologic data were collected from published literature. Local costs (2012 US$) were obtained from Costa Rica's Health System official databases. The model used a 12-week time horizon and only direct medical costs were considered (hospital LOS, medication costs, hematologic, gastrointestinal and skin adverse events and lab exams). Monte Carlo probabilistic sensitivity analysis (PSA) was constructed. **RESULTS:** Results showed Linezolid as more effective and less expensive option for VAP. Clinical success rate was higher with Linezolid (64.4%) against Vancomicyn, (56.1%). Mortality was lower with linezolid (10.13% vs 15.74%). Average ICU (and ward) LOS was 18 (9) days with Linezolid and 22 (10) days with Vancomycin. Overall medical costs per patient were $87782.52 with Linezolid and $92771.51 with Vancomycin. CE analyses showed Linezolid is the dominant strategy. **CONCLUSIONS:** This is the first CE study for VAP developed in Costa Rica. Linezolid resulted as the cost-saving option for treating VAP patients in the Costa Rican clinical environment.

PIN75

COST-EFFECTIVENESS OF TELAPREVIR PLUS PEGINTERFERON/RIBAVIRIN (TVR+PR) VERSUS PEGINTERFERON/RIBAVIRIN (PR) IN TREATMENT-NAÏVE GENOTYPE 1 CHRONIC HEPATITIS C PATIENTS WITH F2 FIBROSIS IN BRAZIL

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OBJECTIVES: To compare the cost-effectiveness of telaprevir associated with peginterferon and ribavirin (TVR+PR) compared to peginterferon and ribavirin (PR) alone in the treatment of patients with METAVIR scale F2) fibrosis and with previously untreated chronic hepatitis C genotype 1. **METHODS:** Markov model, Curtis et al 2012, was adapted to a Brazilian public payer perspective. The model estimated chronic hepatitis C disease progression based on transition probabilities for a cohort of patients with F2 fibrosis. Clinical outcomes and drug dosage were taken from the phase-3 trial (Marcellin et al), with the SVR-rate for TVR+PR as 79% and 49% for PR in patients with F2 fibrosis. Drug costs of TVR and PR were gathered from the ministry of health website, www.comprasnet.gov.br. Costs associated with each disease state were gathered from a study by Barros et al. A discount rate of 3.5 % and a lifetime horizon were assumed. **RESULTS:** TVR+PR therapy resulted in higher costs (R$ BRL57,164 vs BRL27,971) and better outcomes (278 cirrhosis avoided per 1,000 patients) compared to PR alone. Treatment with TVR+PR resulted in 19.94 life years gained compared to PR alone with 19.19. TVR+PR was estimated to give a quality adjusted life year (QALY) expectancy of 13.83, 1.16 higher than with PR (12.67 QALYs), resulted in an incremental cost-effectiveness ratio (ICER) of R$23,734 per QALY gained. Compared to PR alone, the treatment with TVR+PR avoided about 11 deaths and 17 liver transplants per 1,000 treated patients. Treatment with TVR+PR resulted in an incremental cost of R$1,595 per liver transplant avoided and R$2,613 per death avoided compared to PR alone. **CONCLUSIONS:** Treating F2 fibrosis patients with TVR+PR was cost-effective compared with PR alone with an ICER below to the WHO recommended threshold. The benefits of TVR+PR treatment were clear with the low incremental cost per death or liver transplant avoided.

PIN76

COST-EFFECTIVENESS OF ANTI-RABIES PROPHYLAXIS AFTER EXPOSURE TO UNOBSERVABLE DOGS IN ERADICATION CONTEXT: THE FRENCH CASE

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OBJECTIVES: WHO recommends Post-Exposure Prophylaxis (PEP) in countries like France, where rabies cases observed are linked to bats or imported. This study aims to assess effectiveness and cost-effectiveness of anti-rabies PEP algorithms in this low rabies risk countries. **METHODS:** A model-based analysis simulated PEP administration incorporating risk of rabies according to exposure categories (CII: minor scratches; CIII: transdermal bite(s)), PEP strategy, and risk of death on car crash in trips to anti-rabies centers. Strategies compared were: A) No PEP for CII and CIII; B) vaccine for CIII only; C) vaccine for CII and CIII; D) vaccine+immunoglobulins for CIII only; E)vaccine for CII and vaccine+immunoglobulins for C III. We simulated the trajectory of 2,807 patients exposed to unobservable dogs in Metropolitan France, in 2011. Model parameters were estimated from French and international literature. The probability that the dog to which the patient was exposed is rabid was $4x10^{-9}$ and the average risk of death on car crash in trips to anti-rabies centers was $7x10^{-7}$. Total vaccine, immunoglobulins and consultation costs for Zagreb regimens (4 vaccine injections) were €160, €700 and €70, respectively. **RESULTS:** Strategy E led to the lowest number of rabies cases ($4.36x10^{-8}$), the highest costs (€2,493,000), but also to $1.74x10^{-3}$ lethal car crashes. Strategy A had the highest number of rabies cases ($5.71x10^{-6}$), but no risk of lethal crash and no costs; therefore it was the most effective and the least costly strategy. In the sensitivity analysis when the probability that the dog is rabid was>$1.4x10^{-6}$, strategy D becomes more effective than strategy A; and when>$1.4x10^{-4}$, strategy B becomes cost-effective (i.e. cost-effectiveness ratio vs. A>3x French GPD=€30,000). **CONCLUSIONS:** In 2011, in France, anti-rabies PEP appears to be less effective and more expensive than No PEP. These model-based results could be used by decision makers to establish national guidelines.

PIN77

AN ECONOMIC MODEL TO COMPARE LINEZOLID AND VANCOMYCIN FOR THE TREATMENT OF CONFIRMED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS NOSOCOMIAL PNEUMONIA IN GERMANY

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OBJECTIVES: To evaluate economic impact of linezolid (LZD) versus vancomycin (VAN) for treatment of confirmed methicillin-resistant *Staphylococcus aureus*(MRSA) nosocomial pneumonia (NP) in German health care system. **METHODS:** A 4 week decision model was developed capturing 1st and 2nd line therapy. Published literature (primarily Wunderink 2012, reported 54.8% clinical efficacy for LZD vs. 44.9% for VAN in modified Intent-to-Treat population at End of Study for treatment of MRSA NP) and expert opinion provided clinical and resource use data, such as efficacy, mortality, adverse events (AEs), treatment duration, and length of hospital/ICU stay. German cost data was obtained from published literature. Base-case analysis used 10-day treatment duration. In event of treatment failure/severe AEs on 1st-line therapy, drug was switched after 7 days. Costs were reported in 2012 Euros. **RESULTS:** LZD was associated with minimally lower costs (€16,119 vs. €16,144), and greater overall treatment success compared to VAN, resulting in LZD 'dominating' VAN. About 80% of treatment costs were related to hospital stay, primarily ICU (72%). Drug therapy, physician visits, laboratory tests and AEs/treatment failure each account for ≤5% of total costs. Several scenarios were tested by varying treatment duration (7 or 14 days), and varying discontinuation/switch of therapy (at 5 or 10 days). In cases of shorter treatment duration (7 day) or delayed switch of therapy (at 10 day), linezolid continues to 'dominate'. However, with 14 day treatment duration or early switch (at 5 day) linezolid becomes more costly, but still has greater effectiveness resulting in a relatively low Incremental Cost Effectiveness Ratio (ICER) of €8,207 and €2,343 per successfully treated patient. **CONCLUSIONS:** LZD is a cost-effective alternative to VAN for treatment of MRSA-confirmed NP, owing primarily to its higher clinical response rate. Future analyses should use other country costs/resource use data to test result generalizability and assess empiric treatment phase.

PIN78

COST-EFFECTIVENESS OF BOCEPREVIR ADD-ON TREATMENT OF HEPATITIS C VIRUS GENOTYPE 1 PATIENTS IN DENMARK

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OBJECTIVES: Despite available treatment options chronic hepatitis C virus (HCV) infection remains a significant disease burden in Denmark, in particular among genotype 1 difficult-to-treat patients The aim of this study was to evaluate the cost effectiveness of boceprevir (BOC), a protease inhibitor, in combination with pegylated interferon *plus* ribavirin (PEG+R), compared to PEG+R alone, among treatment naïve and treatment experienced genotype 1 HCV patients. **METHODS:** A Markov model simulating antiviral therapy and disease progression was developed to estimate the lifetime health care costs and clinical outcomes of alternative treatment strategies. The model simulated the treatment regimens of dual therapy (PEG+R) and triple therapy (PEG+R+BOC), respectively, as recommended in the summary of product (SPC) and the Danish treatment guidelines. Data on clinical efficacy was taken from phase III clinical trials (SPRINT-2 and RESPOND-2). Costs were measured in 2012 Danish Kroner (DKK) and clinical outcomes in quality adjusted life years (QALYs). The incremental cost-effectiveness ratio (ICER) was estimated for treatment naïve and experienced patients. Deterministic and probabilistic sensitivity analyses (PSA) on clinical inputs, costs, health state utility values, and SVR rates were performed to assess the overall decision uncertainty. **RESULTS:** The ICER for PEG+R+BOC therapy versus standard of care with PEG+R was DKK 241.774 for treatment naïve HCV patients and DKK 98.371 for treatment experienced patients. PSA for treatment naïve patients showed a probability of cost-effectiveness of PEG+R+BOC therapy compared to PEG+R of more than 65 % at a willingness-to-pay threshold of DKK 300.000 (approx. £30.000). **CONCLUSIONS:** From a Danish health sector perspective, the model suggests PEG+R+BOC therapy is cost effective in HCV genotype 1 patients to prevent development of late manifestations in the liver, such as cirrhosis and hepatocellular carcinoma (HCC) irrespectively of treatment experience status.

PIN79

COST-EFFECTIVENESS COMPARISON OF GENOTYPE 1 HEPATITIS C VIRUS (HCV) TREATMENTS USING TELAPREVIR (TVR) IN PATIENTS WITH MILD FIBROSIS VERSUS PATIENTS WITH BRIDGING FIBROSIS AND CIRRHOSIS

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OBJECTIVES: To estimate, from a Spanish Healthcare System perspective, the cost-effectiveness of the usage of telaprevir (TVR) with peginterferon and ribavirin (PR) in patients with mild fibrosis (METAVIR F2) vs. patients with bridging fibrosis or cirrhosis (METAVIR scores F3 and F4, respectively). **METHODS:** A decision tree model was developed to assess cost-efficacy of TVR+PR according to the degree of fibrosis and previous response to treatment in patients with HCV Genotype 1. Treatment costs were estimated excluding futility rules but contemplating the potential to shorten treatment in treatment-naïve and relapsers that are either F2 or F3. The efficacy of triple therapy treatment by patient type is derived from the TVR phase III clinical trials. To estimate cost-effectiveness, the following values were calculated for each alternative: the cost per cured patient and the number of cured and not cured patients assuming a fixed budget. **RESULTS:** TVR+PR in F2 patients has a lower cost per cured patient than F3+F4 both in naïve patients (20% less) and in experienced patients (in relapsers: 5% less; in partial responders: 47% less; and in null responders: 39% less). This difference is statistically significant for naïve and partial responding patients. For a 1 million EUR investment in each patient type, resources allocated to F2 patients offers maximum cured patients (94 in F2 vs. 71 in F3+F4) and minimum non-cured patients (37 in F2 vs. 58 in F3+F4). This conclusion stands when different sensitivity analyses are conducted. **CONCLUSIONS:** The usage of TVR+PR in patients with mild fibrosis could be a more cost-effective alternative than in patients with bridging fibrosis or cirrhosis regardless of the patient's previous response to treatment. A long-term cost-effectiveness analysis is required in order to validate this data.

PIN80

COST-EFFECTIVENESS ANALYSIS OF STRIBILD COMPARED TO SIMILAR ANTIRETROVIRAL THERAPIES IN A SPECIALTY RETAIL PHARMACY

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OBJECTIVES: Approximately 1.1 million people in the U.S. are living with HIV, with 50,000 new infections per year. The FDA approved Stribild™, a once-daily HIV medication, in September of 2012. The primary objective of this study was to assess the cost and disease-related outcomes of Stribild versus guideline-recommended treatment options for HIV patients in a specialty retail pharmacy. A secondary objective was to assess compliance via Medication Possession Ratios (MPRs). **METHODS:** HIV patients who were prescribed one of five antiretroviral regimens in the period from January 1, 2010 to June 21, 2013 and who obtained their medications through Schnucks Specialty Pharmacy were selected via a retrospective chart review. By measuring the direct cost of the medications to the pharmacy and the disease-related outcomes, change in CD4 count and viral load suppression, the cost-effectiveness of Stribild versus its comparators was assessed. **RESULTS:** A total of 92 patients were included in this study: 50 Stribild patients and 42 patients on alternate regimens: 15 Atripla®; 6 Isentress®; 10 Prezista®; and 11 Reyataz®. Incremental Cost-Effectiveness Ratios (ICERs) were conducted between Stribild and the comparators for change in mean CD4 count and percent viral load suppression (<20 copies/ml) achieved. In terms of CD4 count, Stribild was most cost-effective when compared to Prezista and least cost-effective when compared to Isentress. Analyses of viral load suppression indicated that Stribild is more cost-effective than Prezista and Reyataz but less cost-effective than Atripla or Isentress. Mean MPR was greater than 95% for Stribild and three of its comparators (not including Atripla); however, 78 percent of Stribild patients achieved MPR ≥ 95% which demonstrates higher compliance than all comparators except the Isentress patients. **CONCLUSIONS:** The once-daily regimen Stribild appears effective at treating the HIV virus while maintaining compliance for most of its patients; its high cost remains a concern for formulary decision makers.

PIN81

COST-EFFECTIVENESS OF ANTIMICROBIALS AS TREATMENT FOR PATIENTS WITH COMPLICATED SKIN AND SOFT TISSUES INFECTIONS: A COMPARISON BETWEEN CEFTAROLINE, LINEZOLID AND VANCOMYCIN IN THE RUSSIAN HEALTH CARE

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OBJECTIVES: To estimate the cost-effectiveness of antimicrobials (ceftaroline, linezolid and vancomycin) as treatment for patients with complicated skin and soft tissues infections. **METHODS:** A literature-based cost-effectiveness analysis was developed to estimate the costs of complicated skin and soft tissues infections patients initiating therapy with ceftaroline, linezolid or vancomycin. Direct expenses associated with complicated skin and soft tissues infections and resulting follow-up costs were calculated using general tariff agreement of Russian obligatory insurance system and official national statistics. For reference, accepted exchange rate was 1 EUR = 40 RUB. **RESULTS:** Compared to ceftaroline, linezolid or vancomycin results in increases in drug therapy costs: 77 997 RUB (1 950 EUR) per patient in ceftaroline group (therapy duration – 9 days), 78 816 RUB (1 970 EUR) per patient in vancomycin group (therapy duration – 10 days) and 117 893 RUB (2 947 EUR) per patient in linezolid group (therapy duration – 12 days). The values of cost/clinical cure rate are estimated at 96 055 RUB (2 401 EUR) in ceftaroline group, 98 030 RUB (2 451 EUR) in vancomycin group, and 138 860 RUB (3 472 EUR) in linezolid group per patient. **CONCLUSIONS:** The results of cost-effectiveness illustrate that ceftaroline is dominant in Russian patients with complicated skin and soft tissues infections who are initiating antimicrobials therapy compared with linezolid or vancomycin.

PIN82

ANTIBACTERIAL TREATMENT OF METICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS COMPLICATED SKIN AND SOFT TISSUE INFECTIONS: A COST-EFFECTIVENESS ANALYSIS IN GREECE

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OBJECTIVES: Meticillin-resistant staphylococcus aureus (MRSA) is an important cause of antimicrobial-resistant health care-associated infections worldwide. Its prevalence remains high in the Greek hospital setting. Complicated skin and soft tissue infections (cSSTIs) due to MRSA are associated with prolonged hospitalization, additional costs of care and significant morbidity. The purpose of this study was to conduct a cost-effectiveness analysis of different treatment scenarios in the management of MRSA-cSSTIs, under a third-party payer perspective. **METHODS:** The model was based on a decision tree simulating costs and outcomes for a maximum of 28 days, consisting of empiric, first-line and second-line treatment, for patients with MRSA-cSSTIs. Inpatient and outpatient health care services were included in the analysis. Data on efficacy of the pharmacotherapies under evaluation were derived from a recent meta-analysis (Bassetti et al 2013) and resource use was elicited via an expert panel. Economic results, expressed in Euros (2013), reflect the Greek social insurance setting. **RESULTS:** Three different first→second line treatment scenarios (daptomycin→linezolid, linezolid→daptomycin, vancomycin→linezolid) were evaluated, as recommended by the expert panel. Total management costs per patient were €4,199, €3,809, and €3,900; quality adjusted life years (QALY) gained were 0.058, 0.059 and 0.057 respectively for the above scenarios. The scenario containing first-line linezolid proved to be a dominant therapeutic option vs. the other scenarios (less costly, higher QALYs), whereas first-line daptomycin scenario did not appear to be cost-effective vs. the respective vancomycin scenario (incremental cost-utility ratio €243,932) in the management of MRSA-cSSTIs. Second line oral linezolid was used as continuation treatment after failure/intolerance or switch from intravenous vancomycin and daptomycin. Second line intravenous daptomycin was assumed to be administered via an outpatient parenteral treatment service. **CONCLUSIONS:** Findings suggest that use of first-line linezolid in the management of MRSA-cSSTIs could result in savings for the third-party payer in Greece accompanied by enhanced quality of life results.

PIN83

MATHEMATICAL MODELS OF HEPATITIS B VACCINATION AND SCREENING PROGRAMMES IN THE UNITED KINGDOM: A SYSTEMATIC REVIEW

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OBJECTIVES: The United Kingdom (UK) has a targeted hepatitis B (HBV) vaccination programme for at-risk patient groups; however such a programme can be challenging to implement. The World Health Organisation (WHO) recommends universal HBV vaccination and this approach has been adopted by most developed countries. A systematic review was conducted to identify UK-based mathematical models for HBV to determine whether current evidence supports the use of a universal vaccination programme versus a targeted approach. **METHODS:** Embase, Medline, Econlit and The Cochrane Library were searched for studies reporting HBV mathematical models (economic or epidemiological) in the UK population. Hand searching of Health Protection Agency and National Institute for Health and Clinical Excellence guidance documents was also performed. Economic models (cost-effectiveness, cost-utility, cost-benefit, cost-consequence) were included if they assessed HBV vaccination or screening programmes. Epidemiological studies were included if they modelled HBV immunity and infection rates. Data were independently extracted and summarised into evidence tables by two reviewers and quality appraisal of included studies was performed. **RESULTS:** Electronic database searches identified a total of 649 citations resulting in 11 relevant publications. Hand searching yielded an additional two publications; a total of 13 included publications representing seven economic evaluations and six epidemiological modelling studies. Overall, there was considerable variation in model methodologies including methods of discounting used, static versus dynamic approaches and sources of model inputs. Only one epidemiological modelling study considered HBV transmission patterns across the UK. **CONCLUSIONS:** Current HBV vaccination policy in the UK is dependent on the demonstration of cost-effectiveness. However, this review highlights some of the limitations inherent in the models which have been used to support policy decisions. Alternative modelling approaches, as well as new data on key inputs, are desirable if the full value of a universal HBV vaccination programme in the UK is to be assessed.

PIN84

COST-EFFECTIVENESS OF ROUTINE INFANT VACCINATION STRATEGIES IN RUSSIA: AN ECONOMIC EVALUATION

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OBJECTIVES: Today vaccination for children from 0 to 20 months in the Russian Federation is carried mainly by DPT and monovalent vaccines. As a result, a child of this age receives 12 injections. Vaccination against Hib infection so far is only available for children at risk (approx. 20%). Introdution of DTaP-IPV-Hib combined vaccine could reduce the number of injections received by the child and increase the coverage against Hib infection from 20% to 97%. The objective of the present study is to assess the economic evaluation of DTaP-IPV-Hib vaccine introduction into immunization schedule and select the most cost-effective vaccination scheme against Hib infection. **METHODS:** A cost-effectiveness analysis of the DTaP-IPV-Hib vaccine is performed on suggested Markov model. The four vaccination schemes are intercompared : the current immunization program (Scheme0), a 3+1 immunization DTaP-IPV-Hib vaccine (Scheme P), a mixed DTwP /DTaP-IPV-Hib immunization (Scheme mix) and a potential scenario - the current scheme, but with expanded (97%) Hib coverage - Scheme 1. The cohort of infants born in 2011 year is followed over their lifetime. Direct and indirect medical costs are measured from the perspective of the public payer. Outcomes are measured in life years gained (LYG).Exchange rate is 1€ = 41 rub. **RESULTS:** According to the model, total costs of immunization Scheme are: 0 – 4216723519 rub. (102 846 915€), Scheme 1 –4924823829 rub.(120 117 654€), Scheme P -6035132925rub.(147 198 364€), Scheme mix - 4 921 824 835 rub (120 044 508€). The values of cost/LYG are estimated at 4243 198 rub .(103493€) for Scheme 0, 1 224 270rub.(29860€)for Scheme 1, 1500 283 rub. (36592€) for Scheme P, 1223 525rub.(29842€)– for Scheme mix. **CONCLUSIONS:** The introduction of DTaP-IPV-Hib combined vaccine would bring improvement into the Russian immunization program through a Scheme mix.

PIN85

DIFFERENT DISCOUNTING APPROACHES AND THEIR IMPACT IN ECONOMIC EVALUATION: A PRACTICAL EXAMPLE USING HEPATITIS B VACCINATION

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OBJECTIVES: To evaluate the impact of different discounting approaches on economic evaluation using an example of Hepatitis B model. Currently, constant discounting rates of 3.5% are applied for costs and outcomes in the UK. This study applied different approaches such as empirical, stepwise and time-shifted discounting in parallel to the constant discounting to identify their respective impact on the cost-effectiveness results with respect to the NICE threshold. **METHODS:** To compare costs and outcomes of a vaccination policy, a Markov model was built for the UK population birth cohort. Patients entered after contracting Hepatitis B and were followed until 80 years old. The health states included chronic carrier phase, immune, compensated and decompensated cirrhosis, hepatocellular carcinoma and death. The different discounting approaches were applied to the costs and health outcomes. The Incremental Cost-Effectiveness Ratios (ICERs) thus obtained were compared. **RESULTS:** The ICER obtained was higher than the NICE threshold of £20,000 to £30,000 per QALY gained

using the constant discounting approach. The empirical , hyperbolic and proportional discounting methods provided ICERs three times higher. The time-shifted and stepwise discounting led to favorable ICERs that were much below the NICE threshold. **CONCLUSIONS:** The use of different discounting approaches had a considerable effect on the cost-effectiveness results. For preventive programs and vaccines constant discounting approach was unfavorable since the health benefits are revealed decades later. Constant discounting could not justify the theory of social and individual time preference. The empirical discounting though discounted the outcomes at a much slower rate in the long term; the approach remained unfavorable owing to the heavy discounting in the short term. The time-shifted and stepwise discounting were feasible for the vaccines as they related to the moment of risk reduction and were persistent with the time-preference theory, respectively.

PIN86

COST-EFFECTIVENESS ANALYSIS OF EMPIRIC LIPOSOMAL AMPHOTERICIN B VERSUS VORICONAZOLE IN TURKEY

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OBJECTIVES: A pivotal clinical trial failed to demonstrate non-inferiority of voriconazole (VORI) vs. liposomal amphotericin B (LAMB) for empiric treatment of febrile neutropaenia (FN). This study investigated the cost-effectiveness of the two options from the Turkish health care system's perspective. **METHODS:** A decision-tree analysis was used to capture downstream consequences of each agent. Outcome measures included success, breakthrough fungal infection, persistent base-line fungal infection, persistent fever, premature discontinuation and death. Probability data were extracted from the published clinical trial. Resource consumption and alternative treatment after initial failure with either agent were estimated by an expert panel. Cost was based on 2012 data within Turkey. Deterministic and probabilistic sensitivity analyses were performed to determine the model's robustness. **RESULTS:** Compared to LAMB, VORI was the cost-effective alternative per patient treated and per patient survival (by TL2,523 (approx USD1,396) and TL2,520 (approx USD1,394), respectively). LAMB was preferred when considering the cost per successfully treated patient (TL5,362 difference in favor of LAMB, approx USD2,966). LAMB had a higher likelihood of success (30.57% vs. 26.02%) and lower probability of death than VORI (5.92% vs. 7.95%). Increasing the list cost or length of stay (LOS) of VORI by >32.4% or 1.2 days, respectively, changes the study outcomes. Decreasing list cost or LOS for LAMB by >15.8% or 1.0 days, respectively, resulted in LAMB becoming favorable. Monte Carlo simulation (MCS) of 10,000 subjects, with variability imputed upon the published outcome probabilities, LOS and hospitalization costs, resulted in a 69.4% chance of favoring VORI. **CONCLUSIONS:** VORI appears to be cost-effective when compared to LAMB in the empiric treatment of FN from the Turkish perspective. One-way sensitivity analyses did not change the conclusion with MCS indicating a 69.4% chance of favoring VORI. The outcome was highly sensitive to list cost and LOS.

PIN87

NON-HOMOGENEOUS COST-EFFECTIVENESS MODELING OF A NEW CHG-DRESSING FOR PREVENTING CATHETER-RELATED BLOODSTREAM INFECTIONS FOR PATIENTS IN INTENSIVE CARE UNITS

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OBJECTIVES: Catheter-related bloodstream infection (CRBSI) is a frequent (1-5/1000 catheter-days) and life-threatening complication in intensive care unit (ICU), preventable by systematic use of a new antimicrobial transparent dressing containing a chlorhexidine gluconate (CHG) hydrogel (60% risk reduction in a recent RCT). Our purpose is to evaluate the advantages of routine use of the new CHG-dressing to secure central lines of patients in ICU from the medico-economic viewpoint compared to non-antimicrobial (reference). Both medical and economic criteria are embedded into an analytic decision model to support the choice of the best dressing strategy. **METHODS:** A 30-day ICU-time non-homogeneous markovian model comprises eight states: five combining either occurrence or no-occurrence of: CRBSI, contact dermatitis, and the need of a new central line; one for changing alternative dressing in case of dermatitis and two absorbent states (death and discharge). The probabilities of events derive a multicentre RCT on 1,879 patients. Monte Carlo simulations of 1,000 patients are used for probabilistic sensitivity analysis and 95% confidence intervals (CI) calculations. The final health outcome is the number of CRBSI averted. Costs of ICU stay are updated from estimations of a French study from 2010. This economic evaluation takes into account ICU perspective in France. **RESULTS:** The CHG-dressing prevents 11.75 infections (95% CI: [-19.64; -3.85], number needed to treat=85) for 1,000 patients as estimated via probabilistic cost-effectiveness sensitivity analysis. The mean adjusted cost per patient is $€_{2013}$ 21,391 [95% CI: €20,339; €22,443] for the CHG-dressing group and $€_{2013}$ 20,882 [95% CI: €19,905; €21,859] for the reference dressing. **CONCLUSIONS:** The CHG-dressing, significantly more efficacious to prevent CRBSI when compared to the reference dressing, contributes to preserve patients' health capital at the same cost for the ICU. According to the base case scenario the CHG-dressing is more cost-effective than the reference dressing.

PIN88

COSTS EVALUATIONS OF READY-TO-USE PROPOFOL SYRINGES VERSUS SYRINGES DRAWN FROM VIALS IN CRITICALLY ILL

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OBJECTIVES: Primary nosocomial bloodstream infections (BSI) (5-15% of all infections) are associated with increased length of stay and additional hospital costs. Propofol infusions, commonly used for sedation in intensive care units (ICU), are formulated in lipid emulsion which promotes microbial growth. The present study aimed at identifying the probabilities and costs of contamination of syringes of propofol in critically ill patients, and subsequently determining the best strategy for administering propofol. **METHODS:** Costs of propofol-related infection and the different strategies of administration of propofol were computed according to the literature and microcosting method. The additional length of stay in ICU due to major infections related to propofol administration was estimated using the disability model, assuming a cost of CHF 2'118/intensive care unit day (local cost). The cost of each strategy was estimated based on all costs and on the probability of major infections related to propofol administration. **RESULTS:** According to the links found in the literature by genotyping bacteria (syringe-patient), we assumed that a patient has a mean 22.6% risk of developing an infection by a contaminated preparation of propofol. Thus, the ready-to-use syringe and syringes drawn from vials have an infection probability of 0.0014 [0.0009 – 0.0038] and 0.0118 [0.0056 – 0.0181] respectively. Probability of infection and the extended length of stay were the cost-drivers of this analysis. Ready-to-use syringes of propofol saved money, decreasing the cost by at least CHF 251 per sedation. Ready-to-use syringes remained a cost saving strategy when the propofol related infection rate probability according to the literature was as high as 0.38%. **CONCLUSIONS:** Ready-to-use syringes of propofol save money by preventing major infections related to its administration.

PIN89

COST EFFECTIVENESS OF PREPEX DEVICE AND DORSAL–SLIT TECHNIQUE FOR SCALING-UP ADULT SAFE MEDICAL MALE CIRCUMCISION IN HIV PREVENTION IN RURAL CENTRAL UGANDA

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OBJECTIVES: Averting 20% of new HIV infections, the country has to achieve 80% national circumcision coverage. Given the inadequacy of human resource at circumcision centers in Uganda, we conducted a study to assess the cost-effectiveness of PrePex device (none surgical) and Dorsal-slit technique (surgical) for scaling-up adult safe medical male circumcision. **METHODS:** In a four weeks cost effectiveness course project during November 2012, we modeled the costs and effects of male circumcision of the 2 commonest strategies (Dorsal-slit technique as standard and PrePex device) used in Uganda. Effectiveness was defined as days of complete healing measured by costs from start of procedure to complete healing. This was the time until end of each procedure when all scores for drainage from incision, epithelialization, granulation of tissue, and edema were zero. We estimated costs and effects from previous studies in developing countries. Direct and indirect costs were included in a cost effectiveness analysis with limited government perspective. Costs for demand creation (training, patient counseling, and promotion campaigns) were excluded. One-way sensitivity analysis was done by varying costs and days of complete healing as main model parameters. Analyses were done using TreeAge Pro-2011 software. **RESULTS:** PrePex (none surgical) utilized $52.13 over the days to complete healing (31 days) compared to dorsal-slit (surgical) utilizing $67.8 over the days to complete healing (23 days). PrePex was less costly ($52) and with lowest adverse-events (0.98) compared to dorsal-slit technique 0.96 adverse-events costing $65.9. PrePex device was mostly not sensitive to changes in costs and days to complete healing. **CONCLUSIONS:** PrePex device was cost-saving and cost effective.

PIN90

COST-EFFECTIVENESS OF CASPOFUNGIN VERSUS VORICONAZOLE FOR EMPIRIC THERAPY IN TURKEY

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OBJECTIVES: Two major clinical trials examined the efficacy of caspofungin (CAS) and voriconazole (VORI) for empiric therapy of febrile neutropaenia (FN). We investigated the cost-effectiveness of empiric CAS vs. VORI in FN from the Turkish perspective. **METHODS:** The downstream consequences of CAS or VORI were captured through decision tree analysis. Outcome measures included success, breakthrough fungal infection, persistent base-line fungal infection, persistent fever, premature discontinuation and death. Probability data were extracted from the major studies. An expert panel estimated health care resource consumption and alternative treatment after initial failure with either agent. Cost was based on 2012 data using Turkish Lira (TL). Deterministic and probabilistic sensitivity analyses were performed. **RESULTS:** Compared to VORI, CAS was dominant by TL2,533, TL29,256 and TL2,536 per patient treated, successfully treated and patient survival, respectively (approx. USD1,414, 16,328 and 1,415). CAS had a higher likelihood of success and lower mortality than VOR (34.17% vs. 26.02% and 7.37% vs. 7.95%, respectively). Increasing the list cost or length of stay (LOS) for CAS by >35% or 1.3 days, respectively, changes the study outcomes. A decrease of list cost or LOS for VOR by >32% or 1.2 days resulted in it being favorable. Removing fever resolution as part of the composite outcome afforded a contracted difference (CAS preferred by TL298 and 299 per patient treated and surviving with VORI preferred by TL488 per patient successfully treated). Monte Carlo simulation of 10,000 subjects, with variability imputed on the outcome probabilities taken from the literature, LOS and hospitalisation costs, resulted in a 78.8% chance of favoring CAS. **CONCLUSIONS:** There is a high likelihood of CAS being cost-effective compared to VORI in the treatment of FN in Turkey. Sensitivity analyses highlighted a robust advantage towards CAS. The model is moderately sensitive to changes in LOS or cost of each agent.

PIN91

ECONOMIC ANALYSIS OF PROTEASE INHIBITORS IN FIRST-LINE HAART IN ADULT PATIENTS WITH HIV

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OBJECTIVES: To conduct pharmacoeconomic analysis of ritonavir-boosted atazanavir (ATV/r) vs ritonavir-boosted lopinavir (LPV/r) and ritonavir-boosted darunavir (DRV/r) in combination with nucleoside reverse transcriptase inhibitors (NRTIs) in treatment-naïve adult patients with HIV-infection from Russian health care system point of view. **METHODS:** Cost-effectiveness analysis (CEA) with calculation of incremental cost-effectiveness ratio (ICER) was used for comparison of ATV/r with LPV/r. Cost-minimization analysis (CMA) with calculation of cost minimization difference (CMD) was used for comparison of ATV/r with DRV/r. Direct comparison of clinical efficacy and safety of ATV/r vs LPV/r was based on the results of randomized controlled trial (RCT) CASTLE. Indirect comparison of clinical efficacy and safety of ATV/r with DRV/r was performed on the basis of results of RCTs CASTLE and ARTEMIS. Virological response after 96 weeks of treatment and protease inhibitors (PIs)-induced diarrhea were considered as clinical efficacy and safety outcomes, respectively. Direct medical costs were calculated for the hypothetical cohort of 100 patients treated for 96 weeks. **RESULTS:** ATV/r + NRTIs had statistically significant higher rate of virological response after 96 weeks of treatment than LPV/r + NRTIs (risk ratio (RR) = 1.090 [95% CI 1.002; 1.186], p<0.05) with statistically significant lower risk of PI-induced diarrhea (RR = 0.202 [95% CI 0.107; 0.381], p<0.0001). There were no statistically significant difference between combinations ATV/r + NRTIs and DRV/r + NRTIs in terms of rate of virological response and risk of PI-induced diarrhea (RR = 0.981 [95% CI 0.869; 1.107], p=0.77 and 0.543 [95% CI 0.227; 1.296], p=0.17, respectively). ICER for ATV/r vs LPV/r was 4063.58 EUR per one additional patient with virological response. CMD for ATV/r vs DRV/r was 5485.38 EUR per patient. **CONCLUSIONS:** ATV/r is more preferable than LPV/r and DRV/r for administration in combination with NRTIs in treatment-naïve adult patients with HIV infection.

PIN92

TOO EARLY OR TOO LATE? IMPACT OF DIFFERENT HERPES ZOSTER VACCINE'S WANING RATES ON AGE-SPECIFIC INCREMENTAL COST-EFFECTIVENESS RATIO

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OBJECTIVES: Herpes Zoster (HZ) is a painful skin rash that occurs most frequently among the elderly. A vaccine has recently been licensed in Europe to prevent HZ in individuals aged ≥50 years. As of today, the actual annual waning-rate (WR) of vaccine-induced-immunity (VI) is unknown. To investigate the impact of different WRs on the incremental-cost-effectiveness-ratio (ICER) at different ages at vaccination, we performed a health economic analysis for the German statutory-health-insurance setting. **METHODS:** Based on a Markov-model, we compared a HZ-vaccination-strategy to a scenario without vaccination in Germany targeting different cohorts to identify the most efficient age at vaccination (50, 60, or 70 years). A societal-perspective (SP) was considered, country- and age-specific demographic, epidemiological, and cost-of-illness input-data were utilized. We assumed a vaccine-price of 140.48 Euro/dose and 10 year stable VI. Thereafter an exponential waning of VI based on several annual relative WR (0, 2.5, 5, 7.5, 10 and 50%) was assumed. All monetary amounts were in Euro 2010. The cycle-length was a quarter; we considered a lifelong time-horizon. The discount-rate was 3% for outcomes and costs. Results were presented as costs/quality-adjusted life-year (QALY) gained ICERs. **RESULTS:** With annual WR <5% ICERs increase with age at vaccination from 50 (0% WR: 16,567€/QALY gained) to 70 years (0% WR: 37,285€/QALY gained). When WR is ≥5% the vaccination-age-specific ICERs become U-shaped with the minimum ICERs at 60 years (5% WR: 25,474€/QALY gained). With high annual WR (50%) the ICERs at vaccination-age 70 (50,847€/QALY) are lower than ICERs at 50 years (56,871€/QALY). **CONCLUSIONS:** The annual WR has a high impact on vaccination-age-specific ICERs. To obtain lowest ICERs, HZ-vaccine should be given early in life (e.g. 50 years) if WR is low. When annual WR is >4%, the most efficient age at vaccination is 60 years. Evidence on the actual WR after HZ-vaccination has yet to be established.

PIN93

COST-EFFECTIVENESS OF UNIVERSAL VACCINATION AGAINST VARICELLA IN THE NETHERLANDS

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OBJECTIVES: The Netherlands has no varicella vaccination in its National Immunization Program (NIP). Although varicella is regarded as a mild disease, implementation of varicella vaccination in the immunization schedule of several countries has shown to be cost-effective. Dutch children are infected with varicella zoster virus at younger age and make less use of the health care system as compared to other European countries. Therefore, a specific cost-effectiveness study of varicella vaccination for The Netherlands is needed. We aimed to estimate the incremental cost-effectiveness ratio (ICER) of universal vaccination of children against varicella in the Dutch NIP as compared with no such vaccination. **METHODS:** A static cohort model was developed to assess the cost-effectiveness of varicella childhood vaccination in the first 30 years. Several vaccination strategies were explored by varying the age of the booster vaccination. Dutch sources of varicella incidence and health care use were combined with vaccine efficacy data from other countries. This study was performed from the societal perspective as well as from the payer's perspective. Results were expressed in euros (€) per quality-adjusted life year (QALY) gained. **RESULTS:** Vaccinating a birth-cohort of 180,000 children could avert 105,091 varicella cases and save 301.1 QALYs and €13.7 million of direct and indirect costs. The optimal vaccinating-strategy from cost-effectiveness point of view was vaccinating at 14 months and 4 years. This scenario resulted in an ICER of €2844/QALY gained from the societal perspective and €40,582/QALY gained from the health care payer's perspective, when a vaccine price of €45 was used. Results were sensitive to vaccine price, waning rate of the second vaccination and indirect costs. **CONCLUSIONS:** Introduction of varicella vaccination in the Dutch NIP would be cost-effective from the societal perspective when a threshold of €20.000/QALY gained was used, which corresponds to the minimum threshold mentioned for the Dutch context.

PIN94

QUADRIVALENT VERSUS TRIVALENT INFLUENZA VACCINE: IS IT GOOD VALUE FOR MONEY?

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OBJECTIVES: To assess the cost-effectiveness of quadrivalent influenza vaccine (QIV) compared to trivalent vaccine (TIV) in the Italian population aged 65 years or more or at high-risk for influenza. **METHODS:** A static and multi-cohort Markov model was modified to simulate the disease process of influenza (type A and B) over a lifetime horizon using annual cycles. Several cohorts based on the Italian population (nine different age-groups and two level of risks: high and low) entered the model and could be vaccinated with QIV or TIV. Vaccine coverage rate, epidemiological and demographic estimates were taken from local statistics, surveillance data and Italian published studies, while circulation of type A versus B virus and type of lineage was taken from Euroflu estimates (from 2003-2004 to 2012-2013). Vaccine efficacy against influenza A and B were taken from 2 meta-analyses of clinical trials. Costs and resource use were based on local tariffs and published estimates (price year 2013). Quality of life scores were obtained from a Spanish study, using the EQ-5D questionnaire. The perspective of the National Health Service (NHS) was used and a 3% discount rate was applied to costs and benefits, according to Italian guidelines. To deal with the issue of uncertainty both deterministic and probabilistic sensitivity analyses were conducted. **RESULTS:** In the basecase, the incremental cost per QALY and per LY saved for QIV versus TIV were €10,940 and €9,452, respectively. The most sensitive parameters were vaccine efficacy and probability of circulation of virus A versus B, but the probabilistic analysis showed that at a threshold of €50,000 per QALY, there was about 90% probability for QIV to be cost-effective. **CONCLUSIONS:** This study suggests that the introduction of QIV at the same level of price of the most recent adjuvated vaccines is likely to be a cost-effective strategy from the perspective of the Italian NHS.

PIN95

VARICELLA VACCINE AS POST-EXPOSURE PROPHYLAXIS – A COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: Chickenpox, or varicella, is a highly communicative infectious disease affecting mainly young children. Varicella is self-limiting in the majority of cases, yet serious complications, including secondary bacterial infections of skin and soft tissues, pneumonia and encephalitis, can occur and result in hospitalization. Varicella vaccine is an effective post-exposure prophylaxis (PEP) of chickenpox. This study aimed to analyze cost-effectiveness of PEP using varicella vaccine for pediatric patients from the perspective of public health care provider in Hong Kong. **METHODS:** A decision tree was designed to compare cost and clinical outcomes of PEP with varicella vaccine versus no PEP in pediatric patients (aged 1-18 years old) susceptible to chickenpox with household exposure. Two tiers of outcomes were simulated: 1) Total direct medical cost, and 2) the quality-adjusted life year (QALY) loss associated with chickenpox. Model inputs were retrieved from local epidemiology and medical literature. Sensitivity analysis was performed on all parameters to test the robustness of model results. **RESULTS:** Base-case analysis showed PEP with varicella vaccine to be less costly (expected cost USD320 vs. USD731) with lower QALY loss (0.00423 QALYs vs. 0.01122 QALYs), comparing to no PEP. Sensitivity analysis showed that PEP with varicella vaccine was less costly if PEP effectiveness was >6.2% or chickenpox infection rate without PEP was >8.6%. In 10,000 Monte Carlo simulations, PEP with vaccine was cost-effective in over 99% of the time with mean cost saving of USD611per patient (95% CI USD602-620; P<0.001) and lower mean QALY loss of 0.00809 QALYs (95% CI 0.00802-0.00816 QALYs; P<0.001). **CONCLUSIONS:** Using varicella vaccine as PEP seems to be a cost-saving strategy to avert QALY loss in susceptible pediatric patients exposed to chickenpox in Hong Kong.

PIN96

LONG-TERM OUTCOMES OF SOFOSBUVIR (SOF) FOR THE TREATMENT OF CHRONIC HEPATITIS C INFECTED (CHC) PATIENTS

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OBJECTIVES: Sofosbuvir is a uridine analogue polymerase inhibitor. Pan-genotypic efficacy and safety have been demonstrated in four phase III clinical trials of SOF administered with ribavirin (RBV) or with a combination of pegylated interferon alfa and RBV (PR). This analysis evaluated the long-term outcomes of SOF/RBV in treatment-naïve (TN) genotype (GT) 1/4/5/6 and TN, treatment-experienced (TE), interferon ineligible (TNI) GT 2 and 3 patients **METHODS:** A Markov-model followed a cohort of 10,000 patients for a lifetime, with 50% initiating treatment at the compensated cirrhotic stage. In GT 1, 4/5/6 TN patients, SOF/PR for 12 weeks was compared to, telaprevir (TVR) or PR, respectively. SOF/RBV for 12 or 16 weeks for GT 2 and 3, respectively, was compared to no treatment for TNI and TE, and PR for 24 or 48 weeks (PR24/PR48) for TN and TE respectively. SVR 12 weeks have been reported as 90% for TN GT 1 and 97% for GT 4/5/6 patients; 78% for patients with no treatment option (TNI and TE); 97% and 56% for GT 2 and 3 TN; for GT 2 and 3 TE, 86% and 30% with 12-week and, 94% and 62% with 16-week regimens, respectively. **RESULTS:** SOF was shown to be highly effective in preventing advanced liver disease (ALD) and mortality due to HCV across all GTs. This was particularly favorable for patients with no current treatment option (TNI and TE) where up to 7,000 ALD cases can be avoided and more than 200 lives saved. The model demonstrated that in GT 1 and 4/5/6 TN patients, SOF/PR prevented around 5,000 and 900 more ALD cases than PR and TVR treatment arms, respectively. **CONCLUSIONS:** SOF, including within interferon-free regimens, was shown to be highly effective in preventing progression to ALD and reducing HCV-related mortality, particularly in patients with no current treatment option.

PIN97

ECONOMIC EVALUATIONS OF VARICELLA AND HERPES ZOSTER VACCINATION PROGRAMMES: A SYSTEMATIC REVIEW

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OBJECTIVES: This systematic review aimed to assess the cost-effectiveness of routine varicella and herpes zoster vaccination in high-income countries. **METHODS:** A PubMed search was performed for identifying English- and German-language publications on economic analysis of varicella and herpes zoster (HZ) vaccination programmes published before May 2013. A study was included if it was a full economic evaluation of a routine childhood or adolescent varicella vaccination programme and/or a HZ vaccination scheme targeting the elderly and if the study reported results for a high-income country as specified by the World Bank. To improve comparability between studies and across countries, all cost estimates were inflated to 2010 values applying country-specific consumer price indices and converted to Euros with the German level of purchasing power using purchasing power parities obtained from the Organisation for Economic Co-operation and Development. **RESULTS:** After the study selection process, 37 model-based studies remained to be included in the review. Routine childhood or adolescent varicella vaccination was cost-effective or cost-saving from a payer perspective and always cost-saving from a societal perspective when ignoring a potential impact on HZ due to exogenous boosting. The inclusion of the impact on HZ led to net QALY losses or incremental cost-effectiveness ratios exceeding commonly accepted thresholds. Additional HZ vaccination could partially mitigate this effect. Results of the studies only focusing on the evaluation of HZ vaccination ranged from EUR 1,200 to 291,240 per QALY in one study assessing multiple scenarios and from EUR 5,572 to 140,125 per QALY across all other studies. **CONCLUSIONS:** While cost-effectiveness of HZ vaccination was strongly dependent on the age of vaccination, cost-effectiveness of varicella vaccination was primarily dependent on the in- or exclusion of the potential impact on HZ. As a consequence, clarification on the role of exogenous boosting is crucial for decision-making regarding varicella vaccination.

PIN98

PREVENTION OF GRAM-POSITIVE INFECTIONS IN PERITONEAL DIALYSIS PATIENTS – A COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: Gram-positive bacteria cause clinically severe peritonitis and exit-site infection (ESI) in patients on peritoneal dialysis (PD). Incident PD patients are most prone to developing ESI and peritonitis within the first year of dialysis. We investigated the potential costs, quality of life, and clinical outcomes of incident PD patients with or without regular application of mupirocin on exit-site from the perspective of health care provider in Hong Kong. **METHODS:** We designed a decision tree to simulate potential outcomes of incident PD patients with and without regular application of mupirocin over a period of one year. Outcome measures included total direct medical cost per patient, quality-adjusted life-years (QALYs) gained and gram-positive bacterial infection-related mortality rate. Model inputs were derived from literature. Sensitivity analyses evaluated the impact of uncertainty in all model variables. **RESULTS:** In base-case analysis, the mupirocin group showed higher expected QALYs (0.6496 vs. 0.6456), lower infection-related mortality rate (0.18% vs. 1.64%) and lower total cost per patient (USD258 vs. USD1,661) comparing with the control group. Rate of gram-positive bacterial peritonitis without mupirocin and the risk of gram-positive bacterial peritonitis with mupirocin were identified to be potential influential factors. In 10,000 Monte Carlo simulations, mupirocin group was significantly ($p<0.001$) less costly, gained higher QALYs with lower mortality rate 99.9% of the time. **CONCLUSIONS:** Daily application of mupirocin at catheter exit-site during the first 12 months of PD seems to be cost-saving and effective in reducing mortality of PD-related gram-positive infections as well as improving health-related quality of life from the perspective of health care provider in Hong Kong.

PIN99

COST-EFFECTIVENESS ANALYSIS (CEA) OF LINEZOLID VERSUS VANCOMYCIN IN THE TREATMENT OF NOSOCOMIAL PNEUMONIA CAUSED BY METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA-NP) BASED ON A PHASE IV CLINICAL TRIAL: RESULTS FROM FOUR MAJOR CITIES IN CHINA

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OBJECTIVES: To assess the cost-effectiveness of linezolid versus vancomycin in the treatment of NP in four major cities (Beijing, Guangzhou, Nanjing, and Xi'an) in China. **METHODS:** We conducted cost-effectiveness analyses from Chinese payers' perspective piggybacked to a phase IV, randomized, double-blind, multicenter study (Wunderink et al, CID 2012) in MRSA-NP patients (microbiologic confirmed intent-to-treat cohort). Efficacy was measured by treatment success (defined as Cure+Improvement) at the end of study (i.e., 7-30 days after the end of treatment). Direct medical costs from four cities in China (¥, 2012) were calculated from the health care resource use data collected from the trial, including study medication, hospitalization, mechanical ventilation, and continuous renal replacement therapy. Nonparametric bootstrapping method was used to calculate confidence intervals (CI) for costs, efficacy, and incremental cost-effectiveness ratios (ICER). **RESULTS:** Data from 391 patients (186 linezolid, 205 vancomycin) were analyzed. More linezolid patients achieved treatment success vs. vancomycin patients [mean (95% CI)]: 55% (48.3%-61.9%) vs. 45% (38%-52.3%). The total treatment costs of linezolid vs. vancomycin were: ¥79,551(¥72,421-¥86,680) vs. ¥77,587(¥70,656-¥84,519) for Beijing, ¥90,995(¥82,598-¥99,393) vs. ¥89,448(¥81,295-¥97,601) for Guangzhou, ¥82,383(¥74,956-¥89,810) vs. ¥80,799(¥73,545-¥88,054) for Nanjing, and ¥59,413(¥54,366-¥64,460) vs. ¥57,804(¥52,613-¥62,996) for Xi'an. The ICER of linezolid over vancomycin were ¥19,719(-¥143,553-¥320,980), ¥15,532(-¥185,411-¥349,693), ¥15,904(-¥161,935-¥314,987), and ¥16,145(-¥100,738-¥234,412) per additional treatment success for Beijing, Guangzhou, Nanjing, and Xi'an, respectively. Out of 10,000 bootstrap simulations, majority cases had greater efficacies and higher costs for linezolid (in quadrant I of the E-EC plane: Beijing(64%), Guangzhou(59%), Nanjing(61%), Xi'an(66%)), more than one third had greater efficacies and lower costs for linezolid (linezolid dominated vancomycin: Beijing(33%), Guangzhou(38%), Nanjing(37%), Xi'an(32%)); only <2% had greater efficacies and lower costs for vancomycin in all cities (vancomycin dominated linezolid). **CONCLUSIONS:** In this clinical trial population, linezolid appears to be cost-effective from Chinese payers' perspective when compared to vancomycin in treating patients with nosocomial pneumonia caused by MRSA.

PIN100

ECONOMIC EVALUATION OF FLUOROQUINOLONE-BASED REGIMENS FOR THE TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN A MULTI-FIELD HOSPITAL IN RUSSIA

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OBJECTIVES: Respiratory fluoroquinolones are considered to be an important treatment option in hospitalized adults with community-acquired pneumonia (CAP). We aimed to compare cost-effectiveness of sequential intravenous to oral therapy of CAP with moxifloxacin and levofloxacin ± beta-lactam in a multi-field Russian hospital. **METHODS:** Standard search of prospective randomized clinical trials (RCT) was performed for the period since 1st Jan 1995 till 31st Dec 2012. RCTs quality was assessed by Jadad scale. Three RCTs with direct comparison of moxifloxacin vs. levofloxacin±ceftriaxone in adults with CAP required initial intravenous antimicrobial therapy [Torres A. 2008, File T.M. Jr. 2001, Anzueto A. 2006] were included in the analysis. As similar efficacy and safety was shown between comparators a cost-minimisation model was applied. Original drugs' costs were extracted from hospital receipt notes of three multi-field hospitals and wholesale prices database (www.pharmindex.ru). Cost of therapy was calculated to respective treatment regiments in selected trials: moxifloxacin 400 mg QD vs. levofloxacin 500 mg QD/BID±ceftriaxone 2 g QD for 11 days. Uncertainty was explored in a series of one- and two-way sensitivity analysis. **RESULTS:** The respective total drug therapy costs per patient were as follows: €249 for moxifloxacin vs. €161/€321 for levofloxacin QD/BID and €419/€579 for levofloxacin QD/BID+ceftriaxone. In levofloxacin monotherapy regimens the results were sensitive for IV therapy duration and oral/IV levofloxacin cost. In both levofloxacin+ceftriaxone regimens the results were insensitive to all variables of interest. **CONCLUSIONS:** Moxifloxacin is more cost effective strategy then levofloxacin+ceftriaxone for the treatment of hospitalized adults with CAP. The higher cost-effectiveness for moxifloxacin vs. levofloxacin monotherapy depends on IV therapy duration, levofloxacin regimen and oral/IV levofloxacin cost.

PIN101

ECONOMIC EVALUATION OF CEFTOBIPROLE COMPARED TO A COMBINATION OF LINEZOLID WITH CEFTAZIDIME IN THE MANAGEMENT OF HOSPITALISED PNEUNOMIA IN SCOTLAND

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OBJECTIVES: Ceftobiprole is a new i.v. anti-infective, which has bactericidal activity against difficult to treat Gram-positive (including multidrug-resistant pneumococci and methicillin-resistant Staphylococcus aureus; MRSA) and Gram-negative (including Pseudomonas aeruginosa) bacteria, which are important aetiological agents of nosocomial pneumonia (NP) and hospitalised community-acquired pneumonia (CAP). The objective of this analysis was to estimate the economic value of ceftobiprole (TID) compared to linezolid (BID)/ceftazidime (TID) in the treatment of hospitalised pneumonia patients in Scotland, when coverage of MRSA and Gram-negative pathogens, including P. aeruginosa,is required. **METHODS:** A cost-minimisation analysis, including only direct medical (drug) costs, was considered appropriate since the ceftobiprole phase 3 trials in NP and CAP demonstrated that ceftobiprole is non-inferior to a combination therapy consisting of linezolid and ceftazidime (NP) or ceftriaxone with or without linezolid (CAP). The base case model included drug acquisition, treatment duration, and administration costs. In additional scenario analyses, the cost-minimisation analysis included ICU and total hospitalisation costs as well. The resource use data were derived from the NP trial. **RESULTS:** Treatment with ceftobiprole resulted in a cost-saving of £258 per treated patient compared to linezolid/ceftazidime therapy. While no change in the drug budget is estimated, cost-savings are expected due to less administration time. Scenario analyses evaluated the reduction in length of ICU stay and overall hospital stay that will potentially lead to further cost savings for NHS Scotland (-£2,182 and -£904 per treated patient, respectively). **CONCLUSIONS:** This economic evaluation shows that ceftobiprole is at least a cost-neutral alternative to a combination of linezolid with ceftazidime and provides an effective and safe alternative for hospitalised pneumonia patients in Scotland.

PIN102

COST-MINIMIZATION ANALYSIS OF MARAVIROC VERSUS DARUNAVIR RALTEGRAVIR AND ENFUVIRTIDE FOR CCR5-TROPIC TREATMENT-EXPERIENCED PATIENTS WITH HIV INFECTION IN RUSSIA

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OBJECTIVES: New antiretroviral drugs have a major impact on future treatment options for treatment-experienced HIV-patients with antiretroviral resistance. The

goal of this study was to perform economic evaluation of maraviroc compared with other new antiretroviral agents, such as raltegravir, darunavir and enfuvirtide for treatment-experience patients with HIV infection in Russia. **METHODS:** Indirect comparison was performed to assess the relative clinical efficacy and safety of compared drugs, all in combination with optimized background therapy (OBT). A mathematical model was created in Microsoft Excel software to estimate the direct medical costs of: compared drugs, an average OBT regimen and routine outpatient follow-up (including visits to specialists and diagnostic tests). Drug and medical services cost calculations were based on registered prices from the list of vital and essential drugs and financial standards of regional program of national guarantees for the provision of free medical care to Russian citizens in Moscow in 2012, respectively. The obtained results were tested in sensitivity analysis. **RESULTS:** According to indirect comparison results, there were no statistically significant differences between maraviroc, raltegravir, darunavir and enfuvirtide neither by the undetectable HIV RNA level nor CD4(+) cell-count changes. The rate of adverse events was comparable (except enfuvirtide that has more injection-site reactions). Maraviroc-containing regimen compared with raltegravir-, darunavir- and enfuvirtide-containing regimen is associated with reduced costs and saves an average 177 764.16 rub (€4 209.94), 59 929.92 rub (€1 419.30) and 462 295.92 rub (€10 948.42) per 48 weeks of therapy, and 340 714.64 rub (€8 069.05) and 114 865.68 rub (€2 720.33) and 886 067.18 rub (€20 984.47) per 96 weeks of therapy per patient, respectively. Results were robust in one-way sensitivity analyses. **CONCLUSIONS:** The analysis showed that maraviroc compared with darunavir, raltegravir and enfuvirtide is a cost-saving treatment option for CCR5 tropic treatment-experienced patients in Russia.

PIN103

BOCEPREVIR USE IN FRANCE: A MARKOV MODEL OF DISEASE PROGRESSION AND COST-EFFECTIVENESS FOR CHRONIC HEPATITIS C (VIRUS G1)

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OBJECTIVES: The addition of boceprevir (BOC) to peginterferon–ribavirin (PR) resulted in significantly higher rates of sustained virologic response in naive or pretreated patients with the chronic hepatitis C virus (HCV) genotype 1 infection, as compared with PR alone. The objective is to project the long-term clinical benefits and estimate the cost-effectiveness of the treatment strategies recommended in the BOC label compared with PR alone. **METHODS:** A Markov model was created to estimate the expected costs and quality adjusted life-years (QALYs) associated with the BOC tritherapy and PR. The model simulates the treatment regimens and the natural history of the chronic HCV to project the lifetime cumulative incidence of advanced liver-related diseases (decompensated cirrhosis (DC), hepatocellular carcinoma (HCC)) and liver transplant. Series of 30 cohorts representing all combinations of pre-specified patient characteristics progress through the model. The baseline characteristics used to define the cohorts are: naive/pretreated, age, gender, baseline fibrosis score and race cohort for the treatment naive population only. Separate analyses were run for naive and pretreated patients. The distribution of baseline fibrosis score for each analysis was based on the subjects enrolled in the clinical trials; the average age and distribution of race cohort were based on French observational study (F. Roudot Thoraval, ADEQUATION, AFEF 2009). The comparator was PR (48 weeks). **RESULTS:** The model predicted relative reductions in patients treated with BOC vs PR alone: 33% and 32% in DC/HCC in naive patients and also 46% and 53% in DC/HCC in pretreated patients. The ICER of BOC-based therapy compared with PR were 15,681€/QALY for naive patients and 10,563€/QALY for pretreated patients. **CONCLUSIONS:** Compared with PR, boceprevir-based treatment is projected to substantially reduce the burden of liver complications associated with the chronic hepatitis C virus genotype 1 and is highly cost-effective if a threshold of 50,000€/QALY is assumed.

PIN104

COST-UTILITY ANALYSIS OF POSACONAZOLE VERSUS FLUCONAZOLE FOR PREVENTION OF INVASIVE FUNGAL INFECTIONS IN PATIENTS WITH GRAFT-VERSUS-HOST DISEASE IN SWEDEN

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OBJECTIVES: In allogeneic transplant (allo-SCT) recipients with graft-versus-host disease (GVHD) the risk of contracting an invasive fungal infection (IFI) is high and antifungal prophylaxis to prevent IFIs is routinely given. Fluconazole, has been standard antifungal prophylaxis in GVHD-patients in Sweden. Recently many Swedish centers have switched from fluconazole, which lacks efficacy against Aspergillus, to posaconazole, for the prevention of IFIs in GVHD-patients receiving moderate to high doses of glucocorticoids. Although, the superior efficacy of posaconazole vs. fluconazole in preventing IFIs have been demonstrated in this clinical setting, the cost-effectiveness of posaconazole vs. fluconazole for GVHD-patients in Sweden has not been established. The aim of this analysis is to estimate the cost-effectiveness of posacoanzole vs. fluconazole prophylaxis in allo-SCT recipients with severe GVHD receiving immunosuppressive therapy in Sweden. **METHODS:** A decision-analytic model was used to determine life-time outcomes of patients with GVHD at high risk of contracting IFIs. The model outcomes were quality adjusted life years (QALYs), costs associated with IFI-prophylaxis and treatment of IFIs and the incremental cost-utility ratio. The efficacy data were gathered from a clinical trial comparing posaconazole with fluconazole prophylaxis in patients with GVHD. The resource use for treatment of IFIs was gathered by expert opinion. Utility, mortality and unit costs were gathered from the literature. To assess the uncertainty of the modeled outcomes a probabilistic sensitivity analysis (PSA) was developed. **RESULTS:** The incremental cost-utility ratio of posaconazole vs. fluconazole for the prevention of IFI in GVHD-patients in Sweden was 541,628 SEK/QALY. The PSA showed a 56.4% probability for a cost per QALY less than 600,000 SEK. **CONCLUSIONS:** Given a willingness-to-pay threshold of 600,000 SEK/QALY, posaconazole is likely to be cost-effective for preventing IFIs in GVHD-patients compared to fluconazole.

PIN105

ECONOMIC EVALUATION OF UNIVERSAL ANTENATAL HIV SCREENING COMPARED WITH CURRENT "AT RISK" POLICY IN ISRAEL

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Israeli ministry of health guidelines for antenatal screening recommend HIV testing only in women belonging to high risk groups. This policy resulted in the last 10 years in an annual average of two infected children from unidentified Israeli women. **OBJECTIVES:** To evaluate an alternative strategy of universal screening using a cost utility analysis. **METHODS:** A budget impact analysis was first conducted to evaluate the cost of introducing universal screening using a payer perspective. Following, a cost-utility analysis (CUA) was carried out to evaluate long term effects of such strategy, compared with current policy. The model was comprised of two steps: a decision tree simulating the period from pregnancy to delivery and a successive Markov model simulating life expectancy of the newborn. Screening test sensitivity and specificity were regarded as 99.94% and 99.5% respectively. Probabilities for having HIV for the low and high-risk populations were based on experts' opinion. They were then adjusted to allow model calibration to reflect real-life finding as presented above. The cost of the screening test was US$ 5.5. Other costs included physician visits, viral load and blood tests, CD4 counts, and medications. QALY weights were 0.83 for HIV and 0.7 for AIDS. **RESULTS:** Probabilities for having HIV for the low and high-risk populations were 0.0215% and 1% respectively. The incremental cost of the universal screening over current policy for an annual cohort of 166,000 Israeli pregnant women was US$1 million, reflecting a cost of $500,000 per a case of an HIV+ baby avoided. For this cohort, an incremental 18 QALYS were projected over a 90 year time horizon with an incremental cost-effectiveness ratio of US$ -30,000. **CONCLUSIONS:** Universal Antenatal HIV screening should be implemented in Israel. The current policy of screening identified high-risk women is both less effective and more costly.

PIN106

HEALTH ECONOMICS ASSESSMENT OF RILPIVIRINE VERSUS COMPARATORS AS FIRST-LINE ANTIRETROVIRAL THERAPIES IN HIV-1 PATIENTS WITH A VIRAL LOAD (VL) ≤100,000 COPIES/ML IN FRANCE

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OBJECTIVES: In France, rilpivirine is reimbursed for HIV-1-infected treatment-naïve patients with VL≤100,000 copies/mL for whom the use of efavirenz is not appropriate. This analysis aims to compare costs and outcomes of rilpivirine vs. other third antiretroviral (ARVs) agent recommended in France (in addition to two NRTIS). **METHODS:** A cohort-based Markov model with four therapy lines and six health states based on CD4+ cell-count ranges was developed based on 1-year cycle and a 5-year time horizon. First-line efficacy data at 48 and 96 weeks was first assumed to be similar across treatments, and subsequently set to statistically significantly different (SSD) values from phase-III trial analyses of patients with VL≤100,000 copies/mL. Costs of first-line treatments were obtained from the French National Formulary. Costs associated with subsequent treatments and CD4+ health states were derived from a French cost-effectiveness analysis. Other clinical inputs, HIV-related mortality rates and utility were derived from international publications. Outcomes and costs were discounted at 4%. Robustness of results was assessed using sensitivity analyses (e.g. using efficacy values no SSD). **RESULTS:** All phase-III trials (i.e. ECHO/THRIVE, STARTMRK, CASTLE, ARTEMIS, KLEAN, GEMINI, 2NN) demonstrated a non-inferior antiviral efficacy between arms. In patients with VL≤100,000 copies/mL, response rates were available for rilpivirine (1-year: 90,2%; 2-year: 84,0%), ritonavir-boosted (/r) darunavir (1-year: 79,5%; 2-year: 76,1%), lopinavir/r (1-year: 84,5%; 2-year: 75,2%), atazanavir/r (1-year: 82%; 2-year: 75%), fosamprenavir/r (1-year: 67%) and raltegravir (1-year: 93%). CD4+ cell count changes per mm^3 were available for atazanavir/r (1-year: +179; 2-year: +243), lopinavir/r (1-year: +194; 2-year: +267), rilpivirine (1-year: +185) and raltegravir (1-year: +180). Rilpivirine was the less expensive option in the cost-minimisation analyses and dominated all treatments in the cost-effectiveness analyses when considering SSD efficacy values. **CONCLUSIONS:** The analysis provided health economic results for HIV-1-infected treatment-naïve patients with VL≤100,000 copies/mL favoring rilpivirine over all other ARVs analysed.

PIN107

COST-EFFECTIVENESS OF TELAPREVIR COMBINATION THERAPY COMPARED TO PEGINTERFERON WITH RIBAVIRIN ALONE FOR NAIVE AND TREATMENT EXPERIENCED PATIENTS WITH GENOTYPE 1 CHRONIC HEPATITIS C IN POLAND

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OBJECTIVES: To assess the cost-effectiveness of telaprevir (TVR) added to peginterferon and ribavirin (PR) therapy in treatment naive (TN) and experienced (TE) genotype 1 chronic HCV patients in Poland. **METHODS:** Analysis was based on a previously validated Markov model, describing the progression of the disease over a lifetime, adapted to population characteristics specific to Poland and cost parameters obtained via questionnaire studies completed by clinical practitioners. The model comprises the following health states: mild CHC without/with SVR (remission), moderate CHC without/with SVR, cirrhosis without/with SVR, antiviral therapy, decompensated cirrhosis, HCC, liver transplantation, post-liver transplant, CHC related death. The following treatment strategies were considered: PEG++ RBV therapy for 48 weeks; TVR for 12 weeks with PEG+RBV (response-guided therapy in TN and 48 weeks in TE patients). A cost-utility analysis was conducted

to calculate the incremental cost-utility ratio (ICUR) for triple therapy. A subgroup analysis was conducted to evaluate cost-effectiveness of TN patients with IL28B T/T; Scheuer ≥ 2 and in TE patients with Scheuer ≥ 2. **RESULTS:** In the overall TN population, ICUR is 80917 PLN/QALY (»€19736/QALY). ICURs in IL28B T/T and Scheuer ≥ 2 subgroups were 42407 PLN/QALY (»€10343/QALY) and 86984 PLN/QALY (»€21216/QALY), respectively. In the overall TE population, ICUR is 81793 PLN/QALY (»€19950/QALY). For Scheuer ≥ 2 subgroup ICUR = 72448 PLN/QALY (»€17670/QALY). Calculated values are below the cost-effectiveness threshold of 105801 PLN/QALY (»€25805/QALY) in Poland. Results for relapsers, partial responders and null responders are also presented. **CONCLUSIONS:** Based on the cost-utility analysis, telaprevir combination therapy is cost-effective compared to PR alone in Polish settings.

PIN108

COMPARATIVE COSTS ANALYSIS OF CONVENTIONAL STRATEGY VERSUS STEP-DOWN STRATEGY WITH LINEZOLID IN THE TREATMENT OF NOSOCOMIAL PNEUMONIA CAUSED BY GRAM POSITIVE BACTERIA IN MEXICO

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OBJECTIVES: To estimate the cost difference between use and absence of use of Step-Down Strategy (SDS) with linezolid for treatment of nosocomial pneumonia (NP) caused by Gram Positive Bacteria (GPB) in Mexico, from public health care institution perspective. **METHODS:** To evaluate the potential cost savings between the two strategies, a microcosting was made along three phases: (1) characterization of therapeutic protocol, (2) assessment of resources and (3) estimation of the unit costs of medical care. The temporal horizon of the analysis was set to 14 days. Costs were estimated for the year 2013, expressed in US$ and consider the following medical services: days of hospitalization, consultation with specialists, route of administration, laboratory and imaging tests as well as outpatient control, based on unit costs by level of care reported by Instituto Mexicano del Seguro Social. The frequency of use of these resources were determined from Delphi method with a panel of 10 experienced infectologists. We calculated the differences between average total costs (ATC). The stastistical significance difference between strategies was evaluated by Student's t statistic. **RESULTS:** The ATC of patients using SDS was $10,116, [95%CI $9,344.6 - $10,887.3] and the ATC of patients not using this strategy was $17,251.6 [$16,379.4 - $18,123.8]. The average potential savings due the use of SDS over conventional therapy (only intravenous) are $ 7,135.6, (p<0.001). **CONCLUSIONS:** The use of step down strategy could significantly reduce the costs of treatment of NP in terms of hospitalization, physician visits, laboratory and imaging tests, and drug administration, not as well the resources used in the outpatient control. In a challenging setting of cost containment policies, the use of step down strategy in suitable patients represents the opportunity to invest health care resources in a more efficient way.

PIN109

RESOURCE USE AND OUTCOMES OF PATIENTS TREATED WITH VANCOMYCIN OR LINEZOLID IN A TERTIARY HOSPITAL IN SHANGHAI

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OBJECTIVES: Vancomycin and linezolid are amongst the most commonly prescribed antibiotics for hospital-acquired infections in China. The aim of this study is to estimate and compare the baseline characteristics, hospitalization costs, length of stay (LOS), length of therapy (LOT) and all-cause in-hospital mortality of patients treated with vancomycin or linezolid. **METHODS:** Data were extracted from the electronic medical records (EMR) of a tertiary hospital in Shanghai (bed size 1700). The analysis included patients admitted for any underlying cause who received either vancomycin or linezolid between January 2009 and July 2012. Continuous variables were compared with *t* test and *chi-square* for categorical variables. **RESULTS:** Of the total 3234 patients identified, 93.6% were treated with vancomycin (female: 40.6%, mean age: 55.8 years) and 6.4% were treated with linezolid (female: 22.2%, mean age: 62.3 years). Cardiac Surgery was the most frequent admitting department for the both groups, while cardiovascular disease was the top admission reason for the vancomycin group and pulmonary infection for the linezolid group. The average daily dose was 1.6±1.1 g for vancomycin and 1.2±0.5 g for linezolid. The all-cause in-hospital mortality was lower in the vancomycin group compared to the linezolid group (4.2% vs. 21.7%, p<0.001). The vancomycin group had shorter LOS and LOT compared to the linezolid group (23.6±24.4 vs. 37.1±40.8 days, p<0.001; 7.0±8.8 vs. 8.7±10.6 days, p=0.025). The vancomycin group had lower total hospitalization costs, medication costs and antibiotics costs compared to the linezolid group (RMB 68788±64956 vs. 125425±117055, p<0.001; 33258±39792 vs. 70372±69115, p<0.001; 15206±18957 vs. 34681±33184, p<0.001). **CONCLUSIONS:** Vancomycin was more frequently prescribed than linezolid and was more likely to be used in females and younger patients. When compared to those patients treated with linezolid, vancomycin treatment was associated with a shorter LOS and LOT, decreased total hospitalization costs and decreased total medication and antibiotics costs.

PIN110

WHAT CLINICAL BENEFITS COULD BE EXPECTED FROM THE IMPLEMENTATION OF A ROTAVIRUS VACCINATION PROGRAMME IN FRANCE?

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OBJECTIVES: Rotavirus vaccines have shown great potential for reducing the disease burden of the major cause of severe childhood gastroenteritis. Real-life observational studies also confirmed the indirect protection provided by rotavirus vaccination in countries where rotavirus vaccination programmes have been introduced. France has not yet implemented such a programme. Previously reported models in France do not include herd protection, thus underestimating the effectiveness of vaccination. Our study uses a dynamic transmission model to account for herd protection and therefore better predict the effect of an oral rotavirus pentavalent vaccination programme in France. **METHODS:** We developed a dynamic model to account for susceptibility of rotavirus infection as a function of both age and the number of previous infections. It was parameterized with French data on rotavirus gastro-enteritis (RVGE) incidence and age-specific contact rates. We evaluated the direct and indirect effects of vaccination on disease incidence and clinical outcomes. A three-dose vaccine course was assumed to be administered to 75% of infant annually. **RESULTS:** Our model predicts that vaccination can reduce the burden of RVGE by 66% in the four years following vaccine introduction, gradually increasing to 73% in the long term for children under 5 years of age. Our calculations show that herd immunity accounts for 11% to 20% of the overall RVGE reduction in children. Incidence in the unvaccinated adult population would also be reduced by more than 40% through herd protection. Vaccination is also predicted to reduce pressure on the health care system with the model estimating an annual reduction of 84% and 82% in the number of hospitalization/nosocomial and outpatient visits for RVGE respectively. **CONCLUSIONS:** The use of dynamic models is critical to account for the indirect effects of rotavirus vaccination via herd protection and thus for policymakers to understand the true effectiveness of a country-wide rotavirus vaccination programme.

PIN111

COSTS ASSOCIATED WITH COLD CHAIN USED TO STORE AND TRANSPORT THERMALLY UNSTABLE ANTIRETROVIRAL DRUGS

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OBJECTIVES: In Russia free access to high quality health care for patients with AIDS and HIV infections guaranteed by state. Some antiretroviral (ARV) pharmaceuticals need to be transported and stored in special cold chain conditions that significantly increase the burden on the state budget. Use of thermally stable formulation if available may be efficient due to fewer expenses for cold chain provision. To estimate the costs associated with the cold chain conditions in Russian health care. **METHODS:** We calculated the difference in costs associated with ARV drug lopinavir+ritonavir thermally stable and unstable form transporting and storage. Thermally unstable form requires cold chain conditions that drives the cost difference. Costs for additional equipment, electricity, staff salaries were estimated.We used prices and tariffs that were valid in 2011. Calculations were based on the assumption that all eligible registered HIV-infected patients in all regions of Russia receive lopinavir+ritonavir, the number of patients was extracted from state statistics for 2011with a forecast for 2012. **RESULTS:** The difference in annual total costs of shipping toregional centers and storage till the moment patient gets the drug between thermally unstable and thermally stable form is 820,000 Euro. **CONCLUSIONS:** Choice of thermally stable form of ARV drug lopinavir+ritonavir which do not require cold chain conditions of transportation and storage can reduce the economic costs associated with the treatment of HIV infection in Russian health care.

PIN112

RE-ESTABLISHING THE SOCIETAL VALUE OF PEDIATRIC COMBINATION VACCINES

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OBJECTIVES: Over the past decades, the number of vaccinations recommended for infants has increased significantly, in an effort pursuing wider protection against severe infectious diseases. In their first year, infants would typically get more than 50 injections. The use of combination vaccines provides one solution to the problem of high injection burden but may be undervalued due to the underestimation of vaccine-preventable diseases' seriousness and vaccination benefits. Our objective is to investigate the societal value of pediatric combination vaccines. **METHODS:** A literature search was performed using MEDLINE for relevant articles from 1990 to today, focusing on industrialized countries. A grey literature search on public health websites was used to complement the peer-reviewed literature. **RESULTS:** A total of 86 articles, of which 34 from the peer-reviewed literature, met the inclusion criteria and were analyzed. Many articles presented qualitative argumentation but no quantitative evidence. Public health benefits included improved compliance, timeliness and vaccination coverage thanks to reduced injections and better acceptability by parents. Economic benefits were linked to the improvement of daily practice efficiency through reduced administration burden (less visits, simplified record-keeping, handling, inventory management) and less administration-related errors such as the need for fewer syringes reducing risk of needle-stick injury. Combination vaccines could also enhance efficiency at health care system-level through reduced costs of transport, cold chain, storage and wastage. **CONCLUSIONS:** This review supports the broader value of pediatric combination vaccines which may plausibly generate time and money savings in the short and longer term, and enhance efficiency at both micro and macro levels in the health care system. Findings often stemmed from US settings, the portability to other industrialized countries being therefore plausible but subject to some uncertainty. While there is a paucity of quantitative data to support these arguments, they have significant economic implications and warrant further investigation in future economic evaluations of pediatric combination vaccines.

INFECTION – Patient-Reported Outcomes & Patient Preference Studies

PIN113

ADHERENCE INTERVENTIONS TO IMPROVE ADHERENCE TO ANTIRETROVIRAL THERAPY IN LOW INCOME SETTINGS: AN INDIVIDUAL PATIENT DATA NETWORK META-ANALYSIS

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OBJECTIVES: To determine the comparative effectiveness of different interventions for improving antiretroviral medication adherence in low-income settings. **METHODS:** We obtained individual patient data from all randomized trials that have evaluated an adherence intervention to promote antiretroviral adherence within low-income countries. We created a treatment network of the differing interventions by pooling the individual patient data from comparable treatments and comparing them across the individual interventions using a Bayesian network meta-analysis approach. Outcomes included self-reported adherence and viral suppression. **RESULTS:** We obtained data on 11 randomized, involving 5432 patients. Interventions included daily and weekly text messaging, calendars, peer supporters, alarms, counseling, and basic clinical care. For self-reported adherence, we found compelling evidence for the role of weekly text messages (Odds ratio [OR] 1.57, 95% Confidence Intervals [CI] 1.22-2.02), counseling (OR 1.43, 95% CI, 1.06-1.94), and peer supporters (OR 1.72, 95% CI, 1.28-2.29). We found no compelling evidence for daily text messaging, alarms, calendars, or unsupported clinical care. Results were similar when using viral suppression as an outcome, although not all trials reported viral outcomes. Treatment supporters (OR 1.36, 95% CI, 1.02-1.82) and weekly text messages (OR, 1.56, 95% CI, 1.01-2.39) were superior to basic clinical care. **CONCLUSIONS:** Using individual patient data allowed us to increase precision to determine what interventions appear to work. Several common recommendations for improving adherence are unsupported by the available evidence. These findings should influence guidance documents on improving antiretroviral adherence in poor settings.

PIN114

HEALTH CARE RESOURCE UTILIZATION AND ADHERENCE TO ANTIRETROVIRAL TREATMENT (ART) BY HIV PATIENTS: AN ANALYSIS WITH THE QUEBEC (CANADA) PUBLIC DRUG PLAN DATABASE

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OBJECTIVES: Adherence to ART is a key success factor for achieving optimal clinical outcomes in HIV disease. The objective was to assess differences in compliance rates and health care resource utilization between patients receiving a once daily single tablet regimen (STR) vs. a multiple tablets per day regimen (MTR). **METHODS:** This retrospective study included patients covered by the Quebec provincial drug reimbursement program (RAMQ) who have received at least one script for an ART from January 1st, 2006 to June 30th, 2012. For each patient, the index date was defined as the date of the first script for an ART and compliance rates were estimated over a 1-year period. Patients were considered compliant if their medication possession ratio (effective treatment duration over expected treatment duration) was equal or greater to 90%. Medical costs (hospitalizations and ER, outpatient clinic, ICU and physician's visits) were compared between the STR group vs. the MTR group. Regression analyses were performed to assess the relationship between compliance, hospitalization rates and medical costs with the ART regimen, adjusting for age, gender, comorbidities scores, mental disorders diagnosis and drug and alcohol abuses. **RESULTS:** The study included 4,996 HIV patients (mean age: 42.4 years, 74.8% males). A higher proportion of patients were compliant (88.4% vs. 75.8%) in the STR group compared to the MTR group ($p<0.001$). Patients receiving a MTR were 2.0-fold more likely to be non-compliant than patients receiving a STR ($p<0.001$). Moreover, hospitalization rates (25.8% vs. 15.9%, $p<0.001$) and medical costs (CAD$2,785 vs. CAD$1,909, $p=0.008$) were higher for patients receiving a MTR than a STR. Linear regression analyses also showed a positive relationship between MTR (vs. STR) and hospitalization rates ($\beta=0.081$, $p=0.001$) and medical costs ($\beta=0.151$, $p<0.001$). **CONCLUSIONS:** Patients receiving a STR are more compliant than patients on a MTR and have lower hospitalization rates and medical costs.

PIN115

TOBRAMYCIN POWDER FOR INHALATION FOR THE TREATMENT OF CYSTIC FIBROSIS: ANALYSIS OF THE RAMQ DATA

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OBJECTIVES: To describe treatment patterns and measure real-world outcomes with tobramycin powder for inhalation (TIP), tobramycin inhalation solution (TIS), and other tobramycin formulations (OTF), using the provincial public drug reimbursement program database of the *Régie de l'assurance maladie du Québec*(RAMQ). **METHODS:** Patients with a diagnosis of CF covered by the RAMQ drug reimbursement program who had used TIP, TIS, or OTF on at least one occasion during the period from January 1st 2011 to June 30th 2012 were selected. Patient's characteristics, drug utilization patterns and resource utilization were analyzed. **RESULTS:** Data were available for a sample of 244 eligible patients. The average age of the study population was 24.3 years (SD=12.5). While the maximum medication possession ratio (MPR) for alternate month administration is 50%, patients on TIP had an average MPR of 52.8%, while patients on TIS and OTF had an average MPR of 41.4% and 39.7%, respectively. Treatment persistence at 3 months was estimated at 85.5%, 69.0%, and 65.2% for patients on TIP, TIS, and OTF, respectively. Treatment persistence at 6 months was estimated at 78.4%, 62.8%, and 56.5%, respectively for patients on TIP, TIS, and OTF. Higher CF medication treatment costs with TIP were partially offset by lower costs associated with the use of antibiotics, other medications and additional health care resource utilization. The median monthly cost per patient in terms of other medications was of $1,159 (including $79 for other antibiotics), $1,350 ($172), and $1,495 ($240) for patients on TIP, TIS, and OTF, respectively. The median monthly additional health care resource utilization cost per patient was estimated at $56, $188, and $220, respectively for TIP, TIS and OTF cohorts. **CONCLUSIONS:** In a real life setting, TIP was associated with a high level of treatment adherence and limited utilization of additional health care resources.

PIN116

ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG HIV-INFECTED PATIENTS ATTENDING TO A UNIVERSITY INFECTIOUS DISEASES CLINIC IN VENEZUELA

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OBJECTIVES: To determine adherence levels and factors influencing adherence to antiretroviral therapy among HIV-infected patients in Venezuela. **METHODS:** A sample of 46 HIV-infected HIV patients attending an infectious diseases clinic at the Central University of Venezuela were interviewed by the investigators for 20 to 25 minutes. The interview was guided by a structured questionnaire that included questions on sociodemographic and clinical characteristics, medication use, and health behaviors. Adherence was assessed retrospectively based on a 4-day recall as used in Adult AIDS Clinical Trials Group (AACTG) follow up questionnaire. All data analyses were performed using SSPS for Windows Version 19.0. **RESULTS:** Of 46 participants, 30 (65.2%) were male and 16 (34.8%) were female. The mean age was 43.17 years (Range 26-73, SD= 9,790). From 46 participants 69.7% reported adherence $\geq$ 95%. Forgetting to take the medications, alcohol use, and problems with the medications supply were main barriers for adherence in the present study. **CONCLUSIONS:** A group of patients at this clinic reported unsatisfactory adherence. Forgetfulness was reported to be the major cause of non-adherence. Since adherence to antiretroviral therapy in critical to achieve optimal treatment outcomes, health care providers must identify possible barriers to adherence at the earliest and provide appropriate solutions.

PIN117

HEPATITIS C VIRUS INFECTION TREATMENT COMPLETION: AN ANALYSIS OF THE QUEBEC PROVINCIAL REIMBURSEMENT PROGRAM DATABASE

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OBJECTIVES: Hepatitis C virus (HCV) infection treatment completion is a key success factor for achieving optimal clinical outcomes. The objective of this study was to assess HCV treatment completion rates in a real life setting. **METHODS:** A retrospective study of the Quebec provincial drug reimbursement program (RAMQ) was conducted using a random sample of patients who filled at least one script at the pharmacy for an HCV medication (pegylated interferon and ribavirin (peg-Riba) +/- boceprevir or telaprevir) from January 2007 to December 2012. Treatment completion rates were calculated at week 12, 24 and 28 according to HCV medication type in order to assess the proportion of patients treated beyond the 12-week futility threshold and the minimal expected treatment duration of 24 weeks (28 weeks for Peg-Riba + boceprevir). **RESULTS:** A total of 1,081 patients who used at least one HCV medication were included in the study. The average age was 46.4 years (SD=10.7) and the proportion of men was higher (64.8%). During the study period, the number of patients who used Peg-Riba only, Peg-Riba + boceprevir and Peg-Riba + telaprevir was 1,029 (95.2%), 50 (4.6%) and 18 (1.7%) respectively. The proportion of patients on Peg-Riba only who completed at least 12 and 24 weeks of treatment was 89.7% and 62.2% respectively. There were 96.0% and 58.0% of patients on Peg-Riba + boceprevir who remained on treatment at week 12 and 28 respectively. The percentage of patients on Peg-Riba + telaprevir on treatment at week 12 and 24 was 50.0% and 11.1%, respectively. **CONCLUSIONS:** The proportion of HCV patients who were still on treatment decreased with time with high discontinuation rates especially after week 12. Treatment completion was not achieved by a significant proportion of patients, regardless of HCV medications.

PIN118

PATIENT SATISFACTION WITH HIV THERAPIES: FOCUS ON ADHERENCE TO TREATMENT

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OBJECTIVES: Over the course of last decade the introduction of highly effective antiretroviral (ARV) therapies has transformed a once life-threatening disease into a chronic condition. However, maintaining patient adherence to therapy, in the long-term, is challenging. Despite the enormous benefits offered by current ARVs, evidence suggests that adherence to treatment regimens remains an issue. Numerous factors have been identified which compromise long-term adherence, including drug-drug interactions, therapy regimen, side-effects, and the overall demands of therapy. The aim of this study is to further understanding of the determinants of treatment satisfaction for HIV patients receiving ARV therapies. **METHODS:** A programme of research was developed in order to firstly establish the relationship between patients' views of their current therapies and the adherence to ARVs.

The initial step involved undertaking a review of published literature detailing HIV patients' experiences of receiving ARV therapy. These findings formed the basis of a meeting of leading European HIV clinical experts, prominent HIV organisation representatives and patients themselves. **RESULTS:** The literature revealed numerous factors such as convenience, tolerability, relationship with physician and disease characteristics which influences patients' satisfaction with treatment. Discussion between the clinicians, representative from patient organisations emphasised the importance of patient preferences as they relate to adherence with HIV therapy. This additional insight emphasised the under-recognised role played by individual differences and therapeutic knowledge in defining attitudes to treatments. **CONCLUSIONS:** Treatment satisfaction is a complex issue. The work undertaken so far has highlighted that despite the advances in ARVs there are still concerns for PLWH. The next stage of research involves undertaking a series of in-depth qualitative interviews with patients across Europe and examining attributes of HIV treatment using the discrete choice experiment methodology.

PIN119

PARENTAL PREFERENCES FOR ROTAVIRUS VACCINATION AND POTENTIAL VACCINATION COVERAGEIN YOUNG CHILDREN: A DISCRETE CHOICE EXPERIMENT

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OBJECTIVES: To determine parental preferences concerning rotavirus vaccination for their newborn baby, and to calculate the potential vaccination coverage for different vaccine scenarios. **METHODS:** A Discrete Choice Experiment (DCE) questionnaire was sent to the parents of 1,250 newborns aged 6 weeks in The Netherlands. The DCE included nine D-efficient designed choice tasks. Panel-mixed-logit models were used to estimate the relative importance of the five included rotavirus vaccine attributes; vaccine effectiveness, frequency of severe side effects, protection duration, location of vaccine administration, out-of-pocket costs. The potential uptake or vaccine coverage was calculated for different vaccine scenarios. **RESULTS:** All attributes showed a significant estimate (P<.05). Parents were more likely to get their newborn vaccinated if the vaccine effectiveness increased, parents preferred a frequency of 1 in 1,000,000 children that suffer from severe side effects over a frequency of 1 in 10,000. Protection duration of 3 years was preferred over 1 year and parents preferred to get their child vaccinated at the GP's office. Finally, increasing out-of-pocket costs were associated with decreased willingness to vaccinate. With respect to the relative importance of these attributes, vaccine effectiveness was most decisive for parents, followed by out-of-pocket costs, protection duration and frequency of severe side effects. Vaccination coverage rates ranged between 22.8% for the least preferred vaccine scenario and 87.5% for the most preferred scenario. **CONCLUSIONS:** When deciding whether to vaccinate their newborn baby against the rotavirus, parents are mostly driven by the effectiveness of the vaccine, the out-of-pocket costs, protection duration and the frequency of severe side effects. Differences in vaccine scenarios resulted in a large range in expected vaccination coverage. Therefore, the context and content of the implementation strategy of the vaccination is expected to strongly affect the vaccination coverage. Specifically requesting an out-of-pocket payment of parents should be considered carefully if a high vaccine coverage is desired.

PIN120

PATIENTS WITH CHRONIC HEPATITIS C VIRUS TREATED WITH SIMEPREVIR ADDED TO PEGINTERFERON AND RIBAVIRIN EXPERIENCED LESS TIME WITH FATIGUE, DEPRESSIVE SYMPTOMS, AND FUNCTIONAL LIMITATIONS: RESULTS FROM PATIENTS IN THE QUEST-1, QUEST-2, AND PROMISE STUDIES

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OBJECTIVES: To examine the value of adding simeprevir (SMV) to peginterferon and ribavirin (PR) for treatment of chronic hepatitis C virus infection using patient-reported outcomes (PRO) and their concordance with virology endpoints and adverse events (AEs). **METHODS:** Patients rated severity of fatigue (FSS), depressive symptoms (CES-D), and impairment in functioning (WPAI:HepC Productivity, Activity, Absenteeism) at baseline and throughout treatment/follow-up in three randomized, double-blind trials comparing addition of SMV or Placebo (PBO) during initial 12 weeks of PR treatment. PR was administered for 48 weeks (PBO group) and either 24 or 48 weeks (SMV group) (response-guided therapy [RGT]). Analysis of pooled data from the trials using a piecewise-linear mixed model compared the area-under-the-curve from baseline to Wk60 (AUC_{60}) between SMV/PR and PBO/PR for each PRO score. Subgroup analyses evaluated impact of Sustained Virologic Response 12 weeks post-treatment (SVR12), fibrosis level, and RGT on PRO scores. **RESULTS:** Of 1178 patients studied, analyses included 768 SMV/PR- and 393 PBO/PR-treated patients. 87.5% of the SMV/PR group met RGT and completed treatment in 24 weeks. Fatigue and anaemia AEs were comparable in both groups but FSS scores show clinically important increases in fatigue, lasting 6.9 weeks longer with PBO/PR ($p < 0.001$). No significant differences were observed for Absenteeism. Mean scores for all other PRO endpoints worsened from baseline to Wk4 in both groups and remained impaired to Wk24 (SMV/PR) and Wk48 (PBO/PR), resulting in significantly lower $AUC_{60}$and fewer weeks with clinically important worsening scores with SMV/PR. PRO scores indicated better outcomes for patients who met RGT criteria or achieved SVR12; differences in PRO scores associated with fibrosis level were only observed in the PBO/PR group. **CONCLUSIONS:** Greater efficacy of SMV/PR enabled reduced treatment duration and less time with PR-related side effects without adding to the severity of side-effects during treatment.

PIN121

PAPER-BASED AND ELECTRONIC ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE SPECIFIC TO HIV DISEASE: A RELIABILITY STUDY WITH THE PROQOL-HIV QUESTIONNAIRE

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OBJECTIVES: Electronic Patient Reported Outcomes (PRO) provide quick and reliable assessment of patients' health-related quality of life (HRQL). An electronic version of the PROQOL-HIV questionnaire was developed, and its face validity and reliability were assessed using standard psychometric methods. **METHODS:** A total of 70 French outpatients (63% males, mean age 47 years) were recruited. Hard copy and electronic questionnaires were completed in a randomized cross-over design (2-7 day interval). Biomedical data were collected. Questionnaire version and order effects were tested on full scale scores in a two-way ANOVA with patients as random effects. Test-retest reliability was evaluated using Pearson and intra-class correlation coefficients (with 95% confidence interval) for each dimension. Usability testing was carried out from patients' survey reports, specifically: general satisfaction, ease of completion, quality and clarity of user interface (UI) and self motivation for electronic measuring to monitor HRQL in clinical follow-up. **RESULTS:** Questionnaire version and administration order effects (N=58 complete cases) were not significant at the 5% level, nor interacting together (p=0.940). Reliability indices were acceptable, with Pearson correlations above 0.7 and intra-class correlations ranging from 0.696 to 0.926, and scores were not statistically different between the two versions. On 77% of complete surveys, 57% of patients reported being satisfied and interested in electronic assessment of their HRQL in clinical follow up. Individual ratings of PROQOL-HIV user interface (85-100% of positive responses) confirmed UI clarity and usability. **CONCLUSIONS:** The electronic PROQOL-HIV introduces minor modifications compared to the original paper-based version, following ISPOR ePRO Task Force guidelines, and it showed good reliability and face validity. Patients can complete the computerized PROQOL-HIV questionnaire as intended and scores delivered from paper or electronic version share comparable accuracy and interpretation.

PIN122

ATTITUDE OF PARENTS TOWARDS OBLIGATORY AND RECOMMENDED CHILDHOOD VACCINATION

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OBJECTIVES: The immunization is currently one of the most discussed topics in the population and the number of its opponents is increasing. **METHODS:** Opinion, awareness and knowledge of parents (n-parents=240, n-children=463) about childhood immunization through self-reported technique of a questionnaire survey was conducted, with respect of gender, age, education and profession of parents in regard of their professional connection with health care in case of obligatory and recommended childhood vaccination. **RESULTS:** In case of obligatory childhood vaccination all evaluated parameters influence and change opinion, awareness and knowledge of parents. Age ($p<0,01$, Degree of freedom (df)=10, Chi-squared distribution (χ^2)=81,08, table value of Chi-squared distribution ($t\chi^2$)=23,21); gender ($p<0,01$, df=2, χ^2=12,87, $t\chi^2$=9,21); education ($p<0,01$, df=10, χ^2=79,11, $t\chi^2$=23,21); health care profession ($p<0,01$, df=2, χ^2=13,75, $t\chi^2$=9,21. In case of recommended childhood vaccination all analyzed parameters influence and change parents' opinion, awareness and knowledge, except for those working in health care. Age ($p<0,01$, df=5, χ^2=13,29, $t\chi^2$=15,09); gender ($p<0,01$, df=, χ^2=79,82, $t\chi^2$=13,28); education ($p<0,01$, df=4, χ^2=49,10, $t\chi^2$=13,28); health care profession ($0,01<p<0,03$, df=1, χ^2=4,85, $t\chi^2$=6,64). **CONCLUSIONS:** Analysis confirms that age, gender, education and profession connected with health care influence and change parents' opinion, awareness and knowledge about obligatory childhood vaccination. Regarding the recommended childhood vaccination, age, gender and education influence and change parents' opinion, awareness and knowledge, although a profession connected with health care neither influences, nor changes opinion, awareness and knowledge of the parents.

PIN123

MINIMAL IMPORTANT DIFFERENCE (MID) OF RESPONSE TO THE HEPATITIS-C VIRUS PATIENT REPORTED OUTCOMES (HCV-PRO) INSTRUMENT IN A TRIAL OF PEGYLATED INTERFERON/RIBAVIRIN (PEGIFN/RBV) AND DIRECT-ACTING-ANTIVIRALS (DAA)

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OBJECTIVES: Both chronic HCV infection and current treatments negatively impact patient reported outcomes. PegIFN/RBV-based therapies decrease general HRQoL scores 10%-30% (on SF-36). Psychometric analyses of validity, responsiveness, and MID for the HCV-specific HCV-PRO instrument were performed. **METHODS:** Responses to the HCV-PRO (presented ILC2012), the SF-36, and EuroQol-5D (EQ-5D)+VAS were analyzed in the M11-602 trial of pegIFN/RBV with placebo (n=11) or DAA: ABT-450/ ritonavir (n=24), ABT-072 (n=23), or ABT-333 (n=16). DAAs were administered for 12 weeks, pegIFN/RBV for 48 weeks. PRO instruments were administered at baseline, week 8, end of DAA treatment (EODT), end of pegIFN/RBV treatment (EOT), and posttreatment week 24 (PT24). Convergent validity of HCV-PRO total score (range 0-100) was assessed through correlation (Pearson's) to SF-36 MCS/PCS and EQ-5D VAS scores. Discriminant validity was assessed by dichotomizing HCV-PRO responses on EQ-5D Anxiety/Depression dimension severity (none vs. some) and treatment emergent depression/fatigue adverse events (MedDRA terms). Responsiveness was assessed through analyses of effect size (ES). MID was assessed by standard error of the mean (SEM) and

Receiver Operating Characteristics (ROC) curves correlating HCV-PRO score to MID anchors on SF–36 MCS/PCS and EQ-5D VAS. **RESULTS:** Demographics (N=74): 22% female, 81% white, 51% >50 years of age, 74% Genotype 1a, 69% IL28B non-CC status. Convergent validity: HCV-PRO total score correlations with SF-36 MCS/PCS and EQ-5D VAS scores were 0.64-0.93 (all time points). Discriminant validity: HCV-PRO scores decreased 10-30 points more in subjects impaired by anxiety/depression (EQ-5D) or experiencing depression/fatigue events. ES showed an increasing impact during treatment (-0.66, week 8; -0.76, EODT; –0.93, EOT). At PT24, ES returned to -0.10. SEM and ROC analyses suggested an HCV-PRO MID approximating -10 points. **CONCLUSIONS:** The HCV-PRO is a valid, responsive, disease-specific instrument. In this study, an MID of approximately -10 points was identified. The HCV-PRO may enhance understanding of how HCV treatment impacts function/wellbeing.

PIN124

AN ASSESSMENT OF UNEMPLOYMENT AMONG PEOPLE LIVING WITH HIV/AIDS IN CANADA AND EUROPE

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OBJECTIVES: Neurocognitive impairment (NCI), depression, and duration of unemployment have been reported as barriers to obtaining employment among people living with HIV/AIDS (PLWHA) in the US. However, upon return to work, improvements in depression and health-related quality of life (HRQoL) have been observed. The objectives of this study were to examine the burden of unemployment among PLWHA in Canada and Europe by 1.) estimating the number of PLWHA who are unemployed and their duration of unemployment, and (2) determining patient characteristics associated with being unemployed, including NCI, depression, and HRQoL. **METHODS:** Data was derived from CRANIum (sCReen for Anxiety, depression, and Neurocognitive Impairment in HIV+ patients), a multicenter, cross-sectional study of PLWHA in 14 European countries and Canada between 2010 and 2011. Depression was assessed using the Hospital Anxiety and Depression Scale. NCI was assessed using the Brief Neurocognitive Screen, which consists of the Digit Symbol (DS) test and Trail Making tests A and B. HRQoL was assessed using the Medical Outcomes Study HIV Health Survey (MOS-HIV). Logistic regression was utilized in order to determine if these variables, in addition to demographic and clinical variables, were associated with unemployment. **RESULTS:** A total of 2754 PLWHA (mean age = 43; 62% male) were included in these analyses; 960 (35%) were unemployed. Regarding the unemployed, 110 (11%) had been unemployed for < 6 months, 99 (10%) for 6 to 12 months, and 737 (77%) for > 12 months. Logistic regression analyses indicated that NCI, lower scores on the MOS-HIV physical health subscale, previous psychiatric diagnoses, lesser education, Hepatitis B and/or C co-infection, older age and female gender were independently associated with unemployment. Current depression was not associated with unemployment. **CONCLUSIONS:** In tandem with previous reports, results from this multinational study suggest that NCI and HRQoL are salient issues with regards to employment among PLWHA internationally.

PIN125

VALIDATION AND PSYCHOMETRIC EVALUATION OF THE GERMAN-TRANSLATED HEPATITIS C VIRUS PATIENT REPORTED OUTCOMES (HCV-PRO) HEALTH AND WELLBEING INSTRUMENT IN GERMAN HCV-INFECTED PATIENTS TREATED WITH DIRECT ACTING ANTIVIRALS (DAAS) WITH OR WITHOUT RIBAVIRIN (RBV)

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OBJECTIVES: Chronic HCV infection and interferon-based treatments negatively impact PROs. The HCV-PRO is a validated disease-specific PRO instrument for patients with HCV. The purpose of this analysis was to ascertain the psychometric properties of the German-translated HCV-PRO. **METHODS:** Responses from German subjects to the HCV-PRO, SF-36v.2, and EQ-5D 5L+VAS were analyzed from the multinational AVIATOR trial of interferon-free oral DAA therapy in Genotype 1 patients. HCV-PRO was translated under Harmonization standards. Approved German-language validated versions of the SF-36 and EQ-5D were included for psychometric comparison. Internal consistency/reliability of HCV-PRO items and total score (range 0–100) were evaluated using Chronbach's alpha. Convergent validity of HCV-PRO total score was assessed through Pearson's correlation to SF-36 MCS/PCS and EQ-5D VAS scores (0.5–0.9 = moderate–strong). Discriminant validity was assessed by dichotomizing HCV-PRO total score on EQ-5D Anxiety/Depression and Pain/Discomfort dimensions by severity (none vs. some). Response range of HCV-PRO total score was examined. Analyses were performed at Baseline, week 8 (Wk8), End of Treatment (EOT), and 24 week follow-up (PTW24). **RESULTS:** Demographics (N=39): 46% female, 97% white, 46% ≥50 years of age, 36% Genotype 1a, 87% IL28B non-CC status. Clinical response was 92.3% of German patients achieving SVR24. Mean HCV-PRO, SF-36 MCS/PCS, and EQ-5D VAS scores were minimally changed during treatment (Wk8, EOT). Cronbach's alpha for HCV-PRO items and total scores over time were 0.92–0.96. HCV-PRO total score exhibited moderate-to-high correlation with SF-36 MCS/PCS and EQ-5D VAS total scores at each time period (r=0.42–0.85), with highest correlation with SF-36 MCS. HCV-PRO mean scores were lower in subjects with anxiety/depression or pain/discomfort vs. none (p<0.01). Mean HCV-PRO score at PTW24 was improved (p=0.038) over baseline. Baseline HCV-PRO floor (0%) and ceiling (10%) scores were acceptable. **CONCLUSIONS:** The German-translated HCV-PRO is a valid, responsive, disease-specific instrument for German-speaking HCV-infected people.

PIN126

REVISED SCORING OF THE WPAI:HEP C IMPROVES ASSESSMENT OF MISSED WORK AND WORK IMPAIRMENT IN HCV CLINICAL TRIALS

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OBJECTIVES: Trials comparing addition of simeprevir (SMV) or placebo to peginterferon/ribavirin for treatment of chronic hepatitis C virus (HCV) infection found that all patient-reported outcome (PRO) measures except Absenteeism scores from the Work Productivity and Activity Impairment questionnaire for Hepatitis C (WPAI:HepC) showed similar patterns over time and significantly better outcomes for the SMV groups. Absenteeism scores using recommended scoring were available only if a patient was in the workforce at baseline and subsequent study visits. To appreciate movement into and/or out of the workforce in HCV trials, we propose two alternative scores for the WPAI:HepC: Missed Work and Work Impairment. **METHODS:** A total of 711 subjects completed the WPAI:HepC in the QUEST1 and QUEST2 SMV trials during study visits at baseline and throughout treatment and follow-up. The WPAI:HepC assesses whether subjects were in the workforce during the past 7 days; and if so, number of hours missed from work due to HCV or its treatment/number of hours scheduled to work (Absenteeism); and how much productivity was impaired when working (Productivity Impairment). Revised scoring produced Missed Work scores (% hours not working in past week) and Work Impairment (Missed Work x Productivity Impairment) for all subjects at each study visit by setting scores for subjects not in the workforce to 100 (range 0 to 100% Missed Work or Work Impairment). **RESULTS:** WPAI Missed Work score results showed modest differences between treatments but Work Impairment scores were significantly better for the SMV group with a pattern over time consistent with other PRO endpoints in the trials (p=0.034). **CONCLUSIONS:** Methods for evaluating impact of HCV treatment on work life in clinical trials need to provide data for all subjects in order to capture work force participation and productivity when working. Revised scoring of the WPAI:HepC enable more accurate comparison of treatment in clinical trials.

INFECTION – Health Care Use & Policy Studies

PIN127

ASSESSING THE FISCAL CONSEQUENCES OF IMMUNIZING THE FEMALE AND MALE POPULATION AGAINST HUMAN PAPILLOMAVIRUS (HPV) IN GERMANY

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OBJECTIVES: It is well recognized that HPV infection causes a substantial burden in females. The infection also causes a substantial burden in males as it is associated with HPV-related cancers. Traditional economic evaluations focus only on quantifying cost-effectiveness, however, it is increasingly recognized that immunizations may generate broader benefits not captured in cost-effectiveness analysis. This research aimed at developing a government-perspective health investment model to estimate the fiscal impact of immunizing males and females with the quadrivalent HPV vaccine in Germany. **METHODS:** Methodologies from generational accounting, human capital and health economics were combined to estimate the fiscal benefits of HPV immunization. Cohort models were developed simulating the medical costs and average lifetime fiscal transfers between the government and cohorts of 13-year-old immunized and non-immunized individuals. To estimate tax revenue attributed to immunization-related changes in morbidity and mortality, direct and indirect tax rates were linked to differences in age- and gender-specific earnings. **RESULTS:** The lifetime discounted gross tax for the immunized male and female cohorts (n=400,000 each) were €208.7 billion and €130.4 billion, respectively. Over the lifetime of the female and male birth-cohorts, it was estimated that immunization with the quadrivalent HPV vaccine would result in the prevention of 986 female and 296 male HPV-related deaths. Compared to the non-immunized cohorts of 13-year old males and females, the immunized cohorts resulted in higher total net discounted tax by €106.1 million and higher total gross discounted tax by €80.4 million. **CONCLUSIONS:** The combined vaccination of males and females in Germany results in positive lifetime net and gross discounted tax revenues for the government. The vaccination of males and females with the quadrivalent HPV vaccine is likely to have positive effects on public finances and economic growth over subsequent generations.

PIN128

DYNAMIC NETWORK MODEL OF CLOSTRIDIUM DIFFICILE INFECTION TO EVALUATE TREATMENT INTERVENTIONS AND COSTS

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OBJECTIVES: To date, efforts to model Clostridium difficile infection (CDI) have been limited. Most models do not address the contribution of asymptomatic carriers as sources of new infections and are restricted to hospital acquired CDI. We aim to develop a simulation model to systematically examine the dynamic relationship between three major subpopulations of CDI transmission: hospitals, communities, and long-term facilities, to evaluate treatment effectiveness and costs. **METHODS:** We conducted a systematic investigation to determine the key epidemiological factors influencing CDI transmission according to the three major subpopulations: hospitals, communities, and long-term care facilities. We have developed a stochastic agent-tracking meta-population network model of CDI transmission, and identified parameters that would capture transmission from symptomatic and asymptomatic carriers to uninfected individuals among the subpopulations. **RESULTS:** We identified eight infection states: susceptible, gastrointestinal exposure, colonized, diseased, deceased, clinically resolved colonized, relapse of CDI, and cleared. Key parameters include; health outcomes of target populations, time horizon, diagnostic characteristics, treatment effectiveness, transmission rates, susceptibility rates, recurrence rates, and costs. Initial treatments of CDI do not induce a lasting response in 15%-25% of patients. The estimated effectiveness of antibiotic therapy for a first recurrence is 60% and declining with multiple recurrences. Major predictors of recurrences were advanced age and duration of initial hospitalizations. Recurrences of CDI were associated with major increases in hospital LOS and costs. **CONCLUSIONS:** Our dynamic network model of CDI transmission will improve the capacity to project and to quantify the impact of a CDI outbreak in terms of clinical burden and costs.

PIN129

CONSIDERING ECONOMIC ANALYSES IN THE REVISION OF THE PREVENTIVE VACCINATION LAW: A NEW DIRECTION FOR HEALTH POLICY-MAKING IN JAPAN?

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OBJECTIVES: Evidence of a significant vaccine policy shift can be witnessed not only in the number of new vaccines available in Japan but also in the way vaccine policy is being formulated. In 2010, policy makers decided for the first time ever to commission economic analyses as a reference in their consideration of subsidy allocation. This research offers a firsthand account of the recent changes in vaccine policies by examining the decision-making process from the perspective of researchers for economic evaluations. **METHODS:** In order to understand the vaccine policy-making process, we analyzed all the documents that were distributed and discussed during the government committee meetings starting from February 2010 when the revision of the Preventive Vaccination Law was initially proposed to May 2012 when the final recommendations were made. We then created a time-series table to summarize the main issues of the discussions and final conclusions from official reports and other relevant information recorded in the minutes. **RESULTS:** Economic evaluations were conducted for seven vaccines under consideration for the routine immunization program (Hib, PCV for children and adults, HPV, varicella, mumps, hepatitis B). The findings suggested most of them were cost-effective options. However, for the Hib vaccine, the expected savings was less than the additional costs required (23.8 billion yen increased), and for the hepatitis B vaccine, the incremental cost-effectiveness ratio was far beyond the acceptable range (18.3 million yen per QALY). Nevertheless, all the vaccines were equally recommended for inclusion in the routine immunization program. **CONCLUSIONS:** The findings included reasons why policy makers decided to commission economic evidence in the first place, the importance of external influences, the choice of evaluation methods, the extent to which policy makers actually incorporated the economic evidence into new vaccine policies, and the implications of using cost-effectiveness analyses on the future of Japanese health policy-making.

PIN130

HEPATITIS A VACCINE POLICY PROCESS IN 6 COUNTRIES – FACTORS INFLUENCING POTENTIAL ADOPTION

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OBJECTIVES: Until recently, there has not been a global focus on getting hepatitis A vaccines on country policy agendas. Using a vaccine policy adoption framework, we sought to identify drivers and barriers of hepatitis A vaccine adoption in six countries. **METHODS:** We applied a four-part framework to identify the public vaccine adoption process and drivers and barriers for hepatitis A vaccine adoption: 1) evidence in support of hepatitis A vaccine adoption; 2) existence of supportive policies; 3) political priority of hepatitis A within the country; and 4) whether or not the stakeholders were empowered and willing to act. Data were collected using a qualitative policy survey and a systematic literature review in Chile, India, Mexico, Russia, South Korea, and Taiwan between November 2011 and June 2012. **RESULTS:** Because hepatitis A is more of a concern during periods of economic transition for most countries, and because it is often perceived as a non-serious illness, countries struggle to align all of the factors necessary for adoption. Even where solid data exist, political support is often waning due to apparent transition to low endemicity for hepatitis A and a reduced threat. Where data are lacking, other vaccines take priority. Where economic studies exist, narrow perspectives fail to capture the broader threat of the disease to regional or country economies. Hepatitis A vaccination policy is further complicated by the fact that as countries transition to lower endemicity, the major threat is in older age groups. This trend leads to a subtle shift in stakeholders from the pediatric vaccine community to those more focused on the adult health community. **CONCLUSIONS:** Although the vaccine adoption process is the same for hepatitis A as for other pediatric vaccines, this study suggests that drivers of hepatitis A vaccine adoption may come from sectors outside the traditional pediatric vaccine community.

PIN131

BARRIERS UNDERLYING LIMITED UTILISATION OF VACCINES THROUGHOUT LIFE (LIFESPAN IMMUNISATION)

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OBJECTIVES: Vaccination constitutes a standard element of public health preventative programmes worldwide; however, majority tend to concentrate on early stages of life, limiting opportunity for other population groups (adolescents, adults and elderly) to fully benefit. The goal of this study was to uncover barriers underpinning limited and inconsistent utilisation of vaccination at all stages of life (lifespan immunisation). **METHODS:** Current access to vaccination was evaluated using publically available government websites in five market archetypes based on purchase and delivery mechanisms. A web-based survey and subsequent in-depth interviews were conducted with 22 country- and European-level vaccine stakeholders to identify perceived barriers. **RESULTS:** Key barriers: constrained finance and competing health care priorities; policy decisions undertaken at disease level; national immunisation programme (NIP) recommendations based on age and risk; poor influence on policy by public health practitioners and lack of vaccination advocacy groups; constrained finances to implement effective immunisation programmes at local level; inadequate data collection and follow-up process at later stages of life; poor awareness of immunisation schedule by health care practitioners (HCPs); lack of structural and operational policies to promote and deliver vaccination at later stages of life; infrequent interactions with the health care system during adult-hood; limited and inconsistent information dissemination by HCPs and government; negative messages on vaccination through media; complacent public attitude towards the risk posed by vaccine preventable diseases. **CONCLUSIONS:** Three main domains of barriers exist: low institutional facilitation to recommend lifespan immunisation as part of NIP; inadequate mechanisms at regional and local level to facilitate citizen access to immunisation / vaccination; low patient demand for immunisation at older stages of life. To overcome these barriers a broad-ranging approach based on awareness is required, which includes providing comprehensive pharmacoeconomic evidence to policy makers and payers, developing information tracking systems that enable follow up, and HCP education to facilitate information dissemination.

PIN132

ECONOMICAL JUSTIFICATION OF THE INNOVATION METHOD OF LABORATORY DIAGNOSTIC OF THE STRUCTURAL AND FUNCTIONAL CHANGES OF SERUM ALBUMIN IN SEPTIC COMPLICATIONS (ATA-TEST)

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OBJECTIVES: The topicality of septic complications (SC) in early period after surgery reminds very high despite the antibiotic prophylaxis. The prediction of SC can be provided by ATA-test (DTE index) by the registration the structural and functional changes of serum albumin. **METHODS:** Prospective observational controlled study of typical practice for cancer patients. Inclusion criteria: cancer patients; age – over 18 years; major operations. Exclusion criteria: inflammation diseases during 3 months before surgery; extended operations on pancreas, liver and bile ducts; renal and/or hepatic failure. ATA-test was made ones a day during 7 days in patients without SC, 14 days – with SC. Data about direct medical costs was collected via medical charts. Analysis was performed with methods of descriptive statistic, parametric and non-parametric criteria. **RESULTS:** Data on 104 patients were obtained: 11 had SC. Ratio (male:female) was 1:1,4. Average age – 61.2±12.5 years. Average level DTE in first 2 hours after surgery in patients with SC was 15.4±7.2%, without SC -31.8±14%, in case SC it didn't increase till normal meanings (40-175%) during 7 days. Direct medical cost of patient with SC – 8838$: 5352$ - cost for medicines, 1949$- hospitalization during 36.5 days (7.5 days in ICU), 1537$-medical services; without SC – 2992$: 534$-medicines, 1309$-hospitalization during 30 days (3 days in ICU), 1149$-medical services. **CONCLUSIONS:** SC can be predicted by ATA-test (DTE index) in first hours after surgery. It provides economy in 10 times for medicines and in 3 times in common direct medical costs.

PIN133

MODELLING STAFF RESOURCE USE IN AMBULATORY HIV CARE

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OBJECTIVES: Information on staff resource requirements for outpatient HIV care is useful for effective planning of the service, especially given the increasing and increasingly complex patient population. The aim of this study was to estimate the staff resources used in the HIV outpatient clinic in Cork University Hospital (CUH). **METHODS:** Staff in the CUH HIV outpatient clinic completed time sheets for 6 consecutive clinics (March-April 2013). Patient identifiable data were not collected, however basic patient characteristics (gender, route of transmission, age > 50 years, Irish nationality, late diagnosis) and clinical information (type of visit and complexity) were included. **RESULTS:** Over the study period 83% (127/153) of doctor visits were timed. 46% of patients were seen by a senior doctor. The average length of time spent with each patient by senior doctors was 14.5 minutes, while NCHDs spent an average of 24.1 minutes per patient. Patient gender, age, route of infection, nationality, late diagnosis and visit type had little impact on the average length of doctor visit, but visit length was affected by doctor type and complexity. In addition, clinical nurse specialists saw 62% of patients, and spent 14.3 minutes on average per patient. **CONCLUSIONS:** Time spent with patients varies with the experience level of the doctor. Visit length was also affected by the individual complexity of the visit. The results of this study will be fed into a wider study estimating the factors influencing the cost of providing ambulatory HIV care in Ireland.

PIN134

UNITED STATES POLICY IMPLICATIONS OF GENERIC SUBSTITUTION OF BRANDED HUMAN IMMUNODEFICIENCY VIRUS MEDICATIONS

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OBJECTIVES: Increasingly, human immunodeficiency virus (HIV) infection is managed as a chronic condition. Payers in the United States (US) typically manage chronic conditions as cost-effectively as possible. One element of cost containment is to institute policies driving utilization of less-expensive generic medications. As generic HIV drugs become available, concerns arise that "de-simplifying" HIV treatment by incentivizing use of generic components of fixed-dose combination (FDC) treatments will impact adherence, resulting in adverse treatment effects. This study evaluated US payers' likelihood to incentivize patients/physicians from branded FDCs toward a combination of generic single-dose drugs. **METHODS:** We conducted targeted research of published literature and payer Web sites to identify information relevant to HIV coverage polices. This informed a discussion guide for one-on-one interviews with 10 payers from US commercial health insurance companies. Participants were recruited to ensure diversity from organizational sizes and geographical regions; interviews were double-blinded (i.e., payer and pharma). **RESULTS:** Payers indicated HIV management is increasingly perceived as

chronic (e.g., diabetes, hypercholesterolemia, schizophrenia) rather than life-threatening and that treatments, while costly, lead to significant savings in medical benefits and ultimately leave medication decisions to specialists. Payers are cautiously examining potential savings and were willing to institute modest management for generics (tier 1) while keeping branded FDCs on preferred tier 2 (branded preferred copay). Payers were unwilling to institute, high cost-sharing co-insurance, prior authorizations, or require failure for members to access branded HIV medications presently or in the near future. **CONCLUSIONS:** Payers recognize the complexity of treating HIV, the role of adherence, the high cost of failure and the public health component of preventing resistance. We found payers to cautiously look at potential cost savings in medication management until all FDC components become generic. We found no widespread desire to drive generic adoption in HIV treatment, and little interest in the "de-simplification" of currently available FDCs.

PIN135

THE HEALTH AND ECONOMIC EFFECTS ON PUBLIC HEALTH DUE TO PATIENTS' DEFAULT IN TUBERCULOSIS TREATMENT IN MALAYSIA

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OBJECTIVES: Inadequate or partial treatment of Tuberculosis (TB) is a known factor that would promote drug resistance, thus increasing the overall cost of TB management. The study objectives are to identify the general characteristics of defaulting patients and to estimate the cost impact on health authorities as compared to non-defaulters. **METHODS:** A retrospective case-control study was carried out in public treatment centres in Selangor, Malaysia. Defaulter is defined as TB patient who has interrupted treatment for two consecutive months or more and did not complete their treatment. All subjects were selected from 2011 TB District Registry database. Patients' medical case notes and baseline characteristics were reviewed and analysed. The direct costs of TB management were estimated from public health cost references. The study was performed from a government's perspective. **RESULTS:** A total of 176 defaulters and 204 non-defaulters were studied. Foreign-born patients showed a higher risk (OR= 5.929; p <0.01) of defaulting treatment. Unemployed patients were also more likely to default treatment (OR=1.521 p>0.05). Defaulters were more likely to default treatment during intensive phase as compared to maintenance phase (68.1% vs. 31.9%; p<0.05). No other significant findings were observed between the two groups including age, ethnicity, severity of x-ray changes, type of TB and overall medical risk factors. Mean cost of the non-defaulter group is higher than the defaulter group due to a complete treatment (RM 1,259.62 vs. RM 575.58; p<0.05). No significant treatment cost difference was observed in foreign-born defaulters as compared to local Malaysians (mean: RM 576.43 vs. RM 573.78; p>0.05). **CONCLUSIONS:** Data from this study suggest TB treatment should be completed to avoid a potential huge waste of resources. More attentions are required for foreign-born defaulters due to overall consequence in public health and management cost. Additional costs would be required if susceptible TB strains of the defaulters turned into more virulent strains.

PIN136

THE DISEASE BURDEN OF INFLUENZA IN GERMANY

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OBJECTIVES: To describe the burden of influenza for children and adults diagnosed with seasonal influenza in Germany. **METHODS:** The study was based on a retrospective database analysis, using a longitudinal electronic medical records database (IMS® Disease Analyzer). Patients with influenza episodes (ICD-10 diagnosis J09-11) being observable 12 months before index date and 1 month afterwards were included. The selection window was May 2010 to April 2012 to cover two influenza seasons. **RESULTS:** A total of 23,068 influenza episodes (19,446 patients) managed by primary care practitioners (PCP) and 7,295 episodes (5,988 patients) managed by pediatricians were eligible. Mean age of patients was 43±20 years in the PCP panel and 7±4 years in the pediatrician panel. The presence of clinical risk factors was documented for 40% of episodes in adults and 31% of episodes in children. The most common risk factors were cardiovascular diseases in adults (28%) and chronic respiratory diseases in children (26%). The presence of risk factors correlated with the number of episodes/patient. Influenza episodes were frequently accompanied by complications (adults: 38%; children: 57%). Bronchitis (adults: 16%, children: 20%) and acute upper respiratory infections (adults: 15%, children: 21%) accounted for the most frequent complications. Mean number of physician visits was 1.2± 0.5 in adults and 1.5±0.8 in children. Nevertheless one in three children (34%) had more than one visit/episode due to complications. About 60% of episodes (adults: 60%; children: 64%) with at least one complication were reported in patients without risk factors. About 50% of patients received drug prescriptions related either to influenza diagnosis or complications. **CONCLUSIONS:** This study demonstrates that in Germany seasonal influenza is associated with a substantial disease burden and considerable resource utilization, which can be preventable by vaccination. The findings may suggest the modification of the current vaccination recommendation for at risk populations.

PIN137

HIV REGULATORY PRACTICES AND THEIR INFLUENCE OVER REIMBURSEMENT DECISIONS

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OBJECTIVES: This analysis compares the studies that four regulatory agencies used to make their decisions and compares the relationship between the reasons for regulatory decisions and reasons for reimbursement decisions. **METHODS:** The scientific discussions and the studies used to make regulatory decisions for 15 different HIV drugs approved over the last 12 years (2000-2012) were compared for the FDA, EMA, Health Canada and Australia the Australian Therapeutic Goods Administration. The studies used to make regulatory decisions were then compared to the studies used in the reimbursement decisions of France, Scotland, Canada and Australia. **RESULTS:** In all 15 cases reviewed the FDA, EMA and Health Canada used at least one of the same studies to come to their decision and in 13 of the cases Australia also used that same study. In 14 cases the FDA approved the drug before the other regulatory authorities; the longest time before another regulatory agency approved a drug was 15 months for rilpivirine. In six cases the FDA commissioned studies that other regulatory bodies and reimbursement agencies used later. All of the studies were interventional studies. Reimbursement agencies always used studies that were previously cited in regulatory documents. These agencies would also use studies intended for the regulatory approval of another drug as a source for information in a review. **CONCLUSIONS:** Reimbursement agencies and other regulatory agencies are influenced by the FDA in the studies they consider, as illustrated by at least six cases in which other agencies used studies commissioned by the FDA after approval. This influence is easier to see in the last five years, but may be older than that due to improvements in published reports.

PIN138

ATTITUDES, BELIEFS AND BEHAVIOURS OF GENERAL PRACTITIONERS REGARDING VACCINATION: DEVELOPMENT OF A CHARACTERISATION TOOL – QUALITATIVE STEPS

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OBJECTIVES: General practitioners (GPs) play an essential role in France in the prescription and administration of vaccines. Understanding factors that influence GPs' opinions regarding vaccination would help improve vaccination rate in the general population. The study objectives were to understand and describe GPs' attitudes, beliefs and behaviours regarding vaccination, to develop a self-report tool enabling characterisation of GPs, to assess the prevalence and determinants of vaccination behaviours and to identify the modifiable barriers regarding vaccination. **METHODS:** Focus groups with French GPs (n=36) were conducted following a semi-structured interview guide. Main themes of the guide were identified through a literature review. Qualitative analysis enabled development of a conceptual framework based on the theory of planned behaviour (TPB). Items were then generated based on GPs' quotations. Cognitive debriefing interviews with GPs (n=10) were conducted to assess understanding, acceptability and content validity of the tool. Research methods and results were approved by a committee involving GPs, vaccination and tool development experts. **RESULTS:** Focus groups revealed that GPs' attitudes, beliefs and behaviours regarding vaccination varied depending on target disease and population. GPs were influenced by factors classified in 6 themes: vaccine characteristics, disease characteristics, practical aspects, expected benefits, personal background and relationship with patients. These qualitative findings supported item generation of the tool to capture 39 detailed concepts. The tool was developed to be generic for any disease that could be prevented by vaccination. Comprehension testing to confirm the relevance and understanding of the tool is underway. **CONCLUSIONS:** The tool was developed following rigorous methodology based on documented qualitative research. The TPB seems appropriate for organising qualitative research findings. Characterisation of GPs based on their attitudes, beliefs and behaviours regarding vaccination is expected to predict their intention to vaccinate and thus enable development of efficient programs promoting vaccination. The next step is to perform psychometric validation.

PIN139

A CASE STUDY OF FDA PRACTICES AND ITS INFLUENCE ON REGULATORY AND REIMBURSEMENT DECISIONS FOR DARUNAVIR

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OBJECTIVES: It is assumed that agencies influence one another but little has been written on the extent of this influence. This analysis aims to explore how regulatory decisions affect reimbursement decisions within one HIV drug, darunavir. **METHODS:** Documents from the FDA, European Public Assessment Report (EPAR), Health Canada, and the Australian Register of Therapeutic Goods together with the reimbursement decisions from France, Scotland, Canada and Australia were analyzed. The clinical trials found in these documents were compared. **RESULTS:** The FDA approved darunavir ethanolate on June 23, 2006 based on the POWER 1, 2 and 3 clinical trials. After approval, the FDA also required further reports (to be completed by December 31, 2007) on two Phase III studies, ARTEMIS and TITAN. Health Canada approved darunavir on July 28, 2006 and used the POWER studies along with the ARTEMIS and TITAN studies in its decision. The EMA approved darunavir on December 2, 2007 but gave conditional authorization a year earlier. EPAR also used the TITAN and POWER studies to make its decision. The French reimbursement agency used the ARTEMIS and TITAN studies in two recommendations. Scotland and Canada cited the ARTEMIS study in their recommendations. Australia used the POWER and TITAN studies in two recommendations and the ARTEMIS study in its one negative recommendation, citing an inappropriate comparator for the population under review. **CONCLUSIONS:** Studies that required further review by the FDA after approval were key in determining regulatory decisions by Health Canada, EMA and Australia. The reimbursement decisions of France, Scotland, Canada and Australia also relied on these commissioned studies.

PIN140

CLINICAL GUIDELINES EVIDENCE AS A CRITERION FOR CHANGES IN THE LEGISLATION COMBATING TUBERCULOSIS

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OBJECTIVES: Modern medicine provides continuous improvement of diagnosis, treatment and prevention methods in accordance with the requirements of best medical practice. The system of medical care standardization with regard of the evidence-based medicine is focused on developing medical and technological documents that assist a doctor to act effectively in specific clinical situations, avoiding inefficient and false interventions. In view of this, the Ministry of Health of Ukraine has approved the methodology for development of medical and technological documents on the basis of evidence. **METHODS:** Evidence of clinical effectiveness is the main criterion in choosing the treatment methods combating tuberculosis. **RESULTS:** Ukraine has recently introduced the methodology of developing unified clinical protocols of medical care based on adapted clinical guidelines, which in turn are the result of adaptation of the best international practice. In particular, within the project of combating TB the adapted clinical guidelines was developed based on the documents of NICE and WHO. In developing the protocol there identified found differences in the tuberculosis treatment in Ukraine compared to the best practice, which resulted in amendments to the corresponding regulations in health care. **CONCLUSIONS:** Practical recommendations derived from the evidence-based medicine allowed the change of approaches to diagnosis and treatment of tuberculosis in Ukrainian regulations. 3-time examination by sputum smear and culture microscopy is replaced by 2-time, the duration of the basic course of chemotherapy is reduced from 8 to 6 months and its intensity is reduced from 5-component to 4-component treatment for the treatment of new and recurrent cases of tuberculosis with sensitive mycobacteria. In order to integrate these changes into clinical practice local protocols and critical pathways for management of tuberculosis are developing in all health care facilities taking into account peculiarities of the region and available resources of the hospitals.

RESPIRATORY-RELATED DISORDERS – Clinical Outcomes Studies

PRS1
CHARACTERISTICS OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) RECEIVING INHALED CORTICOSTEROID/LONG-ACTING β2–SS2-AGONIST (ICS/LABA) FIXED COMBINATION PRODUCTS IN ENGLISH PRIMARY CARE

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OBJECTIVES: ICS/LABA fixed combinations are used in patients with COPD with a history of repeated exacerbations i.e. worsening of disease including infections and who have significant symptoms despite regular bronchodilator therapy. This study describes the characteristics of COPD patients initiating ICS/LABA in English primary care. **METHODS:** Patients with first prescription (index date) of fluticasone/salmeterol (FP/SM) or budesonide/formoterol (BUD/FM) between 01.01.2005-31.10.2011 and a prior COPD record were selected from CPRD primary care records linked to Hospital Episode Statistics. Baseline characteristics prior to first ICS/LABA prescription were described as proportions, means and rates (95%CI). Prior exacerbations were defined as: antibiotic or oral corticosteroid prescriptions or COPD hospitalisation; multiple events within 14 days were treated as one event. **RESULTS:** 26,875 patients age≥40 at index were included with 75.9% initiating FP/SM and 24.1% BUD/FM; mean age 70.3(70.1-70.4) and 69.0(68.8-69.3) years, respectively. In both cohorts 54% were male, approximately 36% current smokers, and 56% past smokers. Pneumonia within 1-year prior to index was slightly higher in FP/SM patients (1.9%(1.9-1.9)) compared to 1.4%(1.4-1.4) in BUD/FM), as was prior mean annual COPD hospitalisation rate (0.17(95%CI:0.16-0.17); 0.11(95%CI:0.10-0.12)). Amongst FP/SM patients 12.7%(95%CI:12.6-12.9) had COPD hospitalisations 1-year prior with 9.2%(95%CI:8.9-9.4) amongst BUD/FM. 37.2%(95%CI:36.7-37.7) of FP/SM patients received tiotropium 1-year prior with 35.4%(95%CI:34.5-36.2) amongst BUD/FM. The majority of patients had received short-acting ß2-agonist; FP/SM patients: 89.8%(95%CI:88.6-91.1), BUD/FM patients: 84.8%(95%CI :82.7-86.8). Proportions receiving inhaled-corticosteroids within 1-year prior was 50.9%(95%CI:50.3-51.6) and 48.0(95%CI:46.8-49.2) for FP/SM and BUD/FM, respectively, oral-steroids figures were 42.2%(95%CI:41.7-42.8) and 39.8%(95%CI:38.8-40.8), respectively, and mean annual exacerbation rate was 2.15(95%CI :2.12-2.18) and 2.02(95%CI:1.96-2.07), respectively, with 75.3%(95%CI:74.2-76.3) and 73.9%(95%CI:72.1-75.7), respectively, having exacerbations. **CONCLUSIONS:** Both groups had similar burden of COPD disease prior to starting fixed combination. The crude prevalences for some baseline characteristics were slightly higher in FP/SM vs. BUD/FM highlighting the need for rigorous propensity score matching in any comparative outcomes research.

PRS2
THE EFFICIENCY OF PREOPERATIVE PHYSIOTHERAPY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE UNDERGOING OPEN HEART SURGERY

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OBJECTIVES: Chronic Obstructive Pulmonary Disease (COPD) associated with heart disease is common; this fact leads to increase the number of postoperative complications. The aim of this study was to evaluate the benefits of preoperative physiotherapy (PT) among patients with COPD. **METHODS:** Thirty-seven patients with COPD were included in the study those who underwent open heart surgery. Group1 (n=17) participated in pre- and postoperative PT while Group2 (n=20) received only postoperative PT. Inclusion criteria: open heart surgery and patients diagnosed with COPD or have FEV_1<80%. Spirometric measurements (vital capacity=VC, forced expiratory volume=FEV_1, maximum expiratory pressure=PEF) performed preoperatively and on the 3rd and 7thpostoperative days. Operative data, duration of mechanical ventilation, average stay of intensive care unit, incidence of atelectasis were also assessed. IBM SPSS Statistics 20 software was used for statistical analysis; t-test and Pearson-correlation was applied (p<0.05). **RESULTS:** VC, FEV_1, PEF showed significantly decrease in Group1 (21.29±13.40%; 19.71±17.96%; 4.18±20.09%) compared to Group2 (34.70±17.54%; 32.85±11.95%; 24.65±21.65%), (p_1=0.013, p_2=0.011, p_3=0.002). Compared to the preoperatively measured, the fail of the three measured respiratory functional values on the 7th postoperative day was significantly smaller in Group1 than Group2 (VC, FEV_1, PEF; Group1: 14.18±12.61%; 12.82±14.31%; -6.29±18.46%; Group2: 25.60±16.11%; 23.05±14.93%; 13.70±19.28%; p_1=0.043, p_2=0.046, p_3=0.004). There was no difference between groups in duration of mechanical ventilation and average stay of intensive care unit. Incidence of atelectasis was 10% in Group1, while 0% in Group2. Pre- and postoperative respiratory functional values did not correlate significantly with extubation time (p>0.05). **CONCLUSIONS:** The applying of preoperative PT to cardiac surgical patients with COPD is effective since the examined respiratory functional values reduced less and increased better in the postoperative period at the preoperatively treated group.

PRS3
RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS IN THE CANADIAN REGISTRY FOR SYNAGIS (CARESS)

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OBJECTIVES: Paediatric advisory committee guidelines recommend palivizumab prophylaxis for infants at high risk for respiratory syncytial virus (RSV) infection. The objective of this study is to compare the hospitalization rates for respiratory illness (RIH) and RSV-positive hospitalizations (RSVH) among infants who received palivizumab for various indications. **METHODS:** The Canadian Registry for Synagis (CARESS) is a prospective registry of infants who have received ≥1 dose of palivizumab per RSV season across Canada. Demographic data were collected in 32 Canadian national sites during the 2005-2012 RSV seasons. Respiratory illness related hospitalization events were recorded monthly. Standard risk indications that qualified for RSV prophylaxis were categorized as prematurity (≤35 completed weeks gestational age), chronic lung disease or bronchopulmonary dysplasia (CLD), hemodynamically significant congenital heart disease (CHD), and other serious underlying medical disorders (MD). A Cox proportional hazards analysis was conducted to examine differences in hospitalization rates between the indications. **RESULTS:** Of the 13,310 infants enrolled, 8751 were premature, 1048 had CLD, 1414 had CHD, and 2097 qualified with MDs. The overall RIH rate was 6.6% (n=875) with premature infants having a significantly lower rate than the other groups (4.4% vs. 12.2% [CLD], 10.3% [CHD], 10.3% [MD]; B=-0.770, df=1, p<0.0005). Details of hospitalizations did not differ between groups, except the number that were admitted to the Intensive Care Unit which was significantly different between groups (χ^2=11.420, df=3, p=0.010). The overall RSVH rate was 1.55% but was also significantly lower for prematurity (prematurity, 1.36%; CLD, 1.64%; CHD, 2.05%; MD, 2.03%; p<0.0005), with no significant differences between the groups in terms of time to RSV hospitalization (χ^2=1.833, df=3, p= 0.608). **CONCLUSIONS:** RIH and RSVH rates were dissimilar across the groups with premature infants being significantly lower compared to the others. However there were no identified group differences regarding time to first RSVH.

PRS4
THE EFFICACY OF THE EXTRA FRONT LOADING SMOKING CESSATION COUNSELLING SESSIONS ON THE ABSTINENCE RATE COMPARED WITH USUAL CARE USED IN QUIT SMOKING CLINIC IN PENANG, MALAYSIA

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OBJECTIVES: To assess the impact of the front loading phone calls counselling on the abstinence prevalence at 3 and 6 months after quit date among smokers in Penang, Malaysia. **METHODS:** The study was carried out at Quit Smoking Clinic of two major hospitals in the state of Penang, Malaysia. All the eligible tobacco users who attended the clinics between February 1 and October 31, 2012 were invited. Participants were randomly assigned to receive either the usual care (a combination of nicotine gum for the first 2 weeks and cognitive behaviour therapy); (control group), or the previous combination plus extra counselling sessions through phone calls during the first month of quit attempt (intervention group). **RESULTS:** Two hundred thirty-one subjects were recruited during the period under review. The mean age of starting smoking in the study population was 17.38 ± 3.9 years. The vast majority of our cohort (96.1%) was male. Participants smoked about 14 cigarettes per day on average (mean = 13.78 ± 7.0). At 3 months follow-up point, control group was less likely to quit smoking compared to intervention group but this did not reach statistical significance (OR = 0.669; 95% CI = 0.395-1.133, *P* = 0.86). However, at 6 months, the abstinence rate significantly differed between the standard care and combination of standard care and extra phone calls after verification with exhaled carbon monoxide (48.6% vs. 71.7%, respectively: < 0.001). The control group were significantly less likely to quit smoking (OR = 0.375; 95% CI = 0.217-0.645, P< 0.001). **CONCLUSIONS:** Smoking cessation intervention consisting of phone calls delivered counselling during the first month of quit attempt results in significantly higher abstinence rates compared with a standard care approach. Therefore, the front loading counselling is a promising treatment strategy that should be evaluated further.

PRS5
RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATION IN INFANTS WITH CONGENITAL AIRWAY ANOMALIES IN THE CANADIAN REGISTRY OF SYNAGIS® (CARESS) FOLLOWING PROPHYLAXIS (2005-2012)

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OBJECTIVES: Palivizumab is recommended for respiratory syncytial virus (RSV) prophylaxis. CARESS tracks palivizumab use and respiratory outcomes in high-risk infants, including those with congenital airway anomalies (CAA). Our objective was to compare hazards for hospitalization for respiratory illness (RIH) and RSV (RSVH) in CAA infants versus those prophylaxed for: 1) other medical disorders (MD) and 2) standard indications (SD). **METHODS:** Infants were prospectively recruited from 32 Canadian sites who received ≥1 dose of palivizumab during the 2005-2012 RSV sea-

sons. Utilization and hospitalization outcomes were collected monthly throughout respective seasons. **RESULTS:** A total of 13,310 infants were enrolled (309 CAA, 1816 MD, 11185 SD). There were statistically significant group differences ($p<0.05$) in: enrolment and gestational age, birth and enrolment weight, proportions of: Caucasians, daycare attendance, smoking exposure, siblings, multiple birth, household crowding, and atopy. Compliance, calculated by inter-dose intervals, was similar across the groups - overall rate 73.2%. CAA infants had a RIH rate of 12.9%; MD (9.9%); SD (5.9%) with significantly increased hazard of hospitalization compared to MD (HR = 1.47, 95%CI: 1.04-2.10, $p = 0.030$) and SD (HR = 1.92, 95%CI: 1.39-2.67, $p < 0.0005$). 40/309 CAA infants were hospitalized for RI, 32 were tested for RSV; 4 were positive (RSVH rate: 1.61% versus 2.06% (MD), 1.47% (SD). By Cox proportional hazard analysis, CAA did not increase hazard of first RSVH compared to MD or SD infants ($\chi^2 = 0.79$, df = 2, $p = 0.67$). After risk factor adjustment for daycare attendance, siblings, smoking exposure and crowding, the model was significant ($\chi^2 = 66.1$, df = 10, $p < 0.0005$); however, individual groups as risk factors remained insignificant ($p = 0.73$). **CONCLUSIONS:** This is the largest report of CAA infants who have received palivizumab world-wide. Despite differences in risk factors, the groups appear to have similar hazards in terms of RSVH.

PRS6

SYSTEMATIC REVIEW OF COLISTIMETHATE SODIUM DRY POWDER AND TOBRAMYCIN DRY POWDER ANTIBIOTICS FOR PSEUDOMONAS AERUGINOSA LUNG INFECTION IN CYSTIC FIBROSIS

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OBJECTIVES: To evaluate the clinical effectiveness of colistimethate sodium dry powder for inhalation (DPI) and tobramycin DPI for the treatment of Pseudomonas aeruginosa lung infection in cystic fibrosis. **METHODS:** Electronic bibliographic databases were searched in May 2012 (MEDLINE, MEDLINE in-Process, EMBASE, Cochrane Library databases, CINAHL, Web of Science and Conference Proceedings Citation Index, BIOSIS Previews). Randomised controlled trials were selected for inclusion in the review if they included at least one of the interventions of interest and reported at least one of the following outcomes: rate and extent of microbial response (e.g. sputum density of Pseudomonas aeruginosa); lung function (e.g. forced expiratory volume in one second % predicted (FEV1%); respiratory symptoms; frequency and severity of acute exacerbations; health-related quality of life; and adverse events of treatment (including rate of resistance to antibiotic treatment). **RESULTS:** Three poor to moderate trials were included in the review. Both dry powder formulations were reported to be non-inferior to nebulised tobramycin in terms of clinically relevant changes in FEV1%. However, follow up may not be long enough to detect slowing of the rate of decline in respiratory function and exacerbation rates were not always reported. It was not possible to draw any firm conclusions as to the relative efficacy of the treatments. **CONCLUSIONS:** Whilst both dry powder drugs were reported to be non-inferior to nebulised tobramycin, some results should be interpreted with caution due to the means by which they were analysed, the length of follow up, and concerns about the ability of FEV1% to accurately represent changes in lung health. The clinical trials should have considered FEV1% alongside other clinically relevant outcomes, such as acute exacerbations. This study illustrates the difficulty in assessing new technologies where the evidence base is poor.

PRS7

ASSESSING NON-INFERIORITY OF ACLIDINIUM BROMIDE 400 μG BID VERSUS TIOTROPIUM 18 μG AND 5 μG QD IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) BY MEANS OF A NETWORK META-ANALYSIS

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OBJECTIVES: To assess non-inferiority (NI) of aclidinium bromide 400 μg BID (AB400), to tiotropium bromide 18 μg (TIO18) and 5 μg (TIO5) QD in patients with COPD. **METHODS:** A systematic literature search identified 21 RCTs: TIO18 (16 trials), TIO5 (3 trials) and AB400 (2 trials). All trials were analysed using a Bayesian network meta-analysis (NMA) and relative treatment effects between all regimens were obtained for change from baseline (CFB) in FEV_1 trough, SGRQ total score, and TDI focal score, at 24 weeks. The posterior distributions of the relative treatment effects were used to estimate the probability of non-inferiority, based on the NI margins. Two approaches used for margin selection (a) NI_{MCID}: 50% of the Minimum Clinically Important Difference (MCID) (b) NI_{NMA}: 50% of the difference between TIO18 and placebo (PLA), based on the NMA results. AB400 was considered non-inferior if it could maintain at least 50% of this difference with a probability >99%. **RESULTS:** For FEV_1 the MCID is 100mL, while the CFB for TIO18 vs. PLA is 104.1mL giving NI_{MCID}=50mL, NI_{NMA}=52.05mL. AB400 is shown to be non-inferior to TIO5 and TIO18, for both margins. For SGRQ, a change of 4 points is the MCID and CFB for TIO18 vs. PLA is 2.65, thus $NI_{MCID} = 2$ and $NI_{NMA} = 1.325$. AB400 was shown to be non-inferior to TIO5 and TIO18 for both margins. A difference of 1 unit is the MCID for TDI, while the CFB for TIO18 vs. PLA is 0.90 unit, giving $NI_{MCID} = 0.5$, $NI_{NMA} = 0.45$. For these margins, the probability of aclidinium been non-inferior is 97% for the NI_{MCID}, and 96% for the NI_{NMA}. **CONCLUSIONS:** This analysis suggests that treatment with AB400 in COPD is non-inferior to TIO18 and TIO5 with respect to lung function, health status, and to breathlessness with a probability >95%.

PRS8

EFFECTIVENESS OF MONTELUKAST ON ASTHMA CONTROL IN INFANTS: METHODOLOGY OF A CLAIMS DATA STUDY

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OBJECTIVES: Montelukast 4mg (MTL-4) is a recent add-on therapy for young asthmatic children. French regulators have requested real-world evidence on effectiveness of MTL-4 in infants (6-24 months), compared to inhaled corticosteroid (ICS) therapy. National claims data (SNIIR-AM) are now available to public investigators. SNIIR-AM records exhaustive medical resource utilization of the French population, i.e. 65.4 millions. Due to the limited population of infants exposed to MTL-4 from 2010 (i.e. 78 000 children 6-24 months old), SNIIR-AM represents a good tool to investigate its effectiveness. We first tested the feasibility of such a study in a pilot phase conducted on a 1/97th representative sample of the full data set (EGB: Representative Sample of Beneficiaries), to validate identification and evaluation criteria, and to identify potential pitfalls in the methods or insufficient statistical power for groups comparison, in order to take them into account in the finalized version of the protocol. We present hereafter the main conclusions of the pilot project. **METHODS:** We preselected infants receiving ≥ 2 consecutive dispensations of any respiratory drugs (R03 ATC classification) and presenting an initial exacerbation within 6 months following the first dispensing. Asthma exacerbation was identified by asthma-related hospitalizations, dispensing of oral corticosteroids, addition of short-acting beta agonist to existing respiratory therapy, switch to an ICS therapy with higher dosage, or switch to nebulized CS. **RESULTS:** Our sample included 1,149 infants (mean age 13 months, 64% boys). Among them, 51 and 768 were assigned to Montelukast and ICS groups, respectively. Infants with a exacerbation during the 6 months post inclusion were 78.8% and 78.4% in each group, respectively (51% and 62% for oral costicosteroids only). **CONCLUSIONS:** The results of this pilot study support the feasibility of our SNIIR-AM project, regarding inclusion criteria and identification of outcomes. These data allowed us to finalize the SNIIR-AM study protocol that is ongoing.

PRS9

CURRENT CHARACTERISTICS, TREATMENT AND HEALTH CARE CONSUMPTION OF PATIENTS WITH ASTHMA OR COPD IN THE NETHERLANDS

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OBJECTIVES: To investigate the characteristics, medication persistence and health care consumption of asthma and COPD patients in The Netherlands in 2011. **METHODS:** Data were obtained from the PHARMO Database Network, including outpatient drug dispensings, hospitalization records and information from general practitioners (GP). From the GP-database, patients with a recorded ICPC-code for asthma or COPD (period 2001-2010) were selected and included if they were continuously registered in 2010-2011 and had ≥1 respiratory dispensing in 2010. Persistence with any respiratory medication was determined among new patients and defined as the number of days of uninterrupted use. **RESULTS:** The study included 6037 asthma and 4489 COPD patients. In 2011, most asthma patients were most often categorized into GINA I (n=1727), female (60%) and had a mean age of 45 (SD±18) years. COPD patients were classified as GOLD II (n = 1485), male (54%) and had a mean age of 67 (SD±11) years. On January 1, 2011, most common used respiratory treatment among asthma patients was fixed-dose combination of LABA+ICS (FDC) (25%), whereas COPD patients mostly either used FDC (14%), LAMA (14%) or both (15%). 30% Of asthma and 16% of COPD patients did not use respiratory medication. Among new asthma patients, after six and twelve months, 22% and 10% of patients were persistent with respiratory medication. These proportions were 42% and 30% for COPD. Most common selected co-morbidities among both groups were hypertension, hypercholesterolemia, and depression. In 2011, asthma patients consulted their GP on average 5.3 times and COPD patients 7.7 times. On average, asthma patients were 0.4 days hospitalized and COPD patients 1.2 days. Cost calculations for health care consumption are available in November. **CONCLUSIONS:** This study provides an overview of the characteristics and health care consumption of asthma and COPD patients in The Netherlands, and emphasizes the need for more research regarding persistence among these patients.

PRS10

ESTIMATION OF THE NUMBER OF CASES OF NOSOCOMIAL PNEUMONIA IN ADULTS CAUSED BY GRAM-POSITIVE BACTERIA IN PUBLIC HOSPITALS IN MEXICO

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OBJECTIVES: To estimate the number of cases of nosocomial pneumonia (NP) in adults caused by Gram-positive bacteria (GPB) in public hospitals in Mexico. **METHODS:** To estimate the number of hospital discharges for each public institution in ≥ 18 years, databases from the National Health Information System (SINAIS) were consulted. We apply the nosocomial infection (NI) rate (5.97 cases per 100 discharges) issued by Instituto Mexicano del Seguro Social (IMSS) during the period 2011-2012. Through a systematic literature review and critical reading of studies developed in the Mexican setting (using the Critical Appraisal Skills Programme guidelines) we assessed the type of infection and determined the proportion of cases in which microbiological culture was obtained, as well as the proportion giving positive isolates; subsequently, etiologic agent was disaggregated according to their Gram staining characteristics. **RESULTS:** In the year 2011 there were 5,517,139 discharges from public hospitals, applying a rate of 5.97 NI cases/100 discharges, resulted in 329,373 NI cases (16.9% under 18 years and 83.1% in adults). The NP represented 33.2% of NI (90,882 cases), of these, only in 63% of cases a microbiological culture was obtained (57,256) and pathogens were isolated in 87.0% of microbiological cultures (49,813), among these, GPB we identified in 30.4% . According to our estimates the number of cases of adult NP caused by GPB is 15,135 and the pathogens reported were *Staphylococcus aureus* (74.3%), Streptococcus pneumoniae (15.6%), Enterococcus spp. (6.3%) and others (3.8%). **CONCLUSIONS:** In

spite of high heterogeneity found in NI reports (which may decrease the quality of the information recorded), the local data reported in this study can help clinicians in the choice of first line antibiotics in order diminish the probability of unsuccessful treatment and additionally to reduce the emergence of resistant organisms, which could cause negative economic impact in the health care institutions.

PRS11

FACTORS ASSOCIATED WITH COMPLIANCE WITH PALIVIZUMAB PROPHYLAXIS IN THE CANADIAN RSV EVALUATION STUDY FOR SYNAGIS (CARESS) REGISTRY (2005-2012)

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OBJECTIVES: Palivizumab prophylaxis against respiratory syncytial virus (RSV) is provided monthly during the RSV season. CARESS is a prospective registry of infants who received ≥1 dose of palivizumab across 32 Canadian sites during 7 seasons. The objective is to determine factors associated with palivizumab compliance. **METHODS:** Neonatal and demographic data were collected at enrolment. Palivizumab utilization, compliance, and outcomes related to respiratory illness (RI) and RSV hospitalization were collected monthly. Compliance was defined as receipt of all expected injections at 25–35 day intervals during the RSV season. **RESULTS:** A total of 13,310 infants were enrolled. Infants received 89.0% ± 18.23% of their expected injections and 9745 (73.2%) were administered within appropriate inter-dose intervals.Compliant versus non-compliant infants had a rate of 9.2 RSV and 57.5 RI versus 11.7 RSV and 65.5 RI hospitalizations / 100-patient-years respectively. Compliance differed between prophylaxis indications (χ^2=24.6, p<0.0005); with congenital heart disease the most non-compliant (CHD; n=668, 47.2%), followed by chronic lung disease (CLD; n=470, 44.8%), prematurity (≤35 weeks gestational age; n=3643, 41.6%) and other medical disorders (n=831, 39.6%). A greater proportion of non-compliant infants were Aboriginal (4.8% vs. 2.4%, χ^2=57.8, p<0.0005), attended daycare (4.0% vs. 3.3%, χ^2=5.0, p=0.03), had a mother who smoked (17.1% vs. 12.0%, χ^2=69.0, p<0.0005), and lived with ≥1 smoker (31.7% vs.26.1%, χ^2=49.7, p<0.0005). Significant factors independently associated with compliance (OR, 95%CI) were: maternal education (1.38, 1.22–1.58), Aboriginal descent (0.57, 0.47–0.70), smoke exposure (0.70, 0.52–0.94), CLD (0.74, 0.56–0.99), maternal smoking (0.79, 0.68–1.01), daycare (0.82, 0.68–0.99), and indication for prophylaxis. Compliance by both expected number of injections and inter-dose intervals was associated with lower hazard rates of RI hospitalization (HR=0.86, 95%CI=0.74-0.99, p=0.04). **CONCLUSIONS:** Higher maternal education and lower RI hospitalization was associated with full compliance where as non-compliance was associated with other demographic factors and differed by palivizumab indication.

RESPIRATORY-RELATED DISORDERS – Cost Studies

PRS12

BUDGET IMPACT ANALYSIS OF A NEW FIXED-DOSE COMBINATION INHALER FOR A CLINICAL COMMISSIONING GROUP WITHIN THE NATIONAL HEALTH SERVICE IN ENGLAND

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OBJECTIVES: The economic burden of asthma on the UK National Health Service (NHS) is the largest amongst allergic diseases, costing approximately £800 million per year. Current Global Initiative for Asthma guidelines recommend adding a long acting β2-agonist (LABA) to a low-dose inhaled corticosteroid (ICS) in patients who are on ICS monotherapy and have uncontrolled asthma. The fixed-dose combination of fluticasone propionate and salmeterol (FLUT/SAL), available in a pressurized metered dose inhaler (pMDI) device, is the most commonly prescribed ICS/LABA combination. A new fixed-dose combination of fluticasone propionate and formoterol fumarate (FLUT/FORM) in pMDI is now available. In a 12 week non-inferiority study, FLUT/FORM demonstrated comparable efficacy to FLUT/SAL. This study estimates the budget impact of using FLUT/FORM as an alternative to FLUT/SAL for an average NHS clinical commissioning group (CCG) within England. **METHODS:** Current pMDI prescribing data were taken from a real-world UK patient database (Cegedim Strategic Data). Annual costs to the NHS for drug acquisition, administration, and monitoring were estimated for FLUT/FORM and FLUT/SAL. Annual cost data were used to estimate the potential budget impact for the use of FLUT/FORM versus FLUT/SAL, based on an estimated average population size for a CCG (260,000 persons or 0.41% of the UK population). **RESULTS:** Assuming similar levels of ICS use with both combination regimens, annual drug acquisition costs per person were lower with FLUT/FORM (£411.58) than with FLUT/SAL (£509.06). The difference in acquisition costs and otherwise comparable input costs between the treatments, results in potential annual savings of £61,952.14 for an average CCG, assuming uptake of FLUT/FORM over FLUT/SAL in 50% of existing patients. **CONCLUSIONS:** The comparable efficacy and lower acquisition costs for FLUT/FORM compared to FLUT/SAL make it a cost-saving option, from a NHS England CCG perspective, for the treatment of asthma patients requiring combination maintenance therapy using a pMDI.

PRS13

BUDGET IMPACT ANALYSIS OF STEP-DOWN STRATEGY VERSUS CONVENTIONAL THERAPY IN THE TREATMENT OF NOSOCOMIAL PNEUMONIA CAUSED BY GRAM POSITIVE BACTERIA IN MEXICO

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OBJECTIVES: Previous reports of national literature estimated 15,135 cases of nosocomial pneumonia caused by Gram-positive bacteria (GPB) in Mexico, of which approximately 51% (95%CI 43%-59%) are candidates to use the step-down strategy (SDS) with linezolid. The aim of the study was to estimate the budget impact of SDS vs conventional strategy (CS, only intravenous) with linezolid in Mexico, from the perspective of Instituto Mexicano del Seguro Social (IMSS). **METHODS:** Budget impact analysis (BIA) considered direct medical costs of linezolid (intravenous and tablets), length of stay, physician visits, route of administration, laboratory and imaging tests, as well as outpatient control (unit costs extracted from IMSS sources). Costs are expressed in 2013 US$ (1US$:€0.719). The resource use profile was estimated by Delphi method in a panel of 10 experienced infectologists. A BIA considering two scenarios was performed: i) budget impact of use CS in 100% of cases of nosocomial pneumonia caused by GPB (15,135) and ii) budget impact of use of SDS only in candidates (7,718 cases), based on the National budget allocated to health in 2013. **RESULTS:** The per-patient average treatment cost (ATC) of SDS was $10,116 ($9,345-10,887) whereas the per-patient ATC of CS was $17,251 ($16,379-18,124). The scenario i) represents 2.79% of National budget allocated to health, whereas scenario ii) represents 2.19%. This means potential savings of 0.6% of National budget allocated to health ($55,078,697). With these resources, CS treatment could be provided to 3,192 additional nosocomial pneumonia patients caused by GPB in Mexico. **CONCLUSIONS:** In the Mexican setting, SDS with linezolid in suitable patients is an intervention that could promote significant savings regarding the use of only intravenous form of the drug, which represents an opportunity to allocate scarce resources in a more efficient way.

PRS14

POTENTIAL OF OMEGA-3 FATTY ACID IN PARENTERAL NUTRITION IN GERMANY: A BUDGET IMPACT ANALYSIS

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OBJECTIVES: The costs to the German hospitals of intensive care (ICU) patients and of surgical patients not admitted to the ICU were estimated in a previous cost-effectiveness analysis of omega-3 FA-supplemented compared to standard PN regimens. The supplementation with Omega-3 FA results in shorter LOS and reduced infection rate, with cost savings for 3,277 € per ICU patient and 1,515 € per not-ICU patients. We aimed to estimate the economic consequences of increasing the rate of omega-3 fatty acids (FA) supplemented parenteral nutrition (PN) regimens in German hospitals **METHODS:** IMS-data recorded about 3 million lipid-containing PN days for Germany; the total number of patients in ICU or in ward receiving PN with lipids was estimated on average PN duration from the cost-effectiveness analysis The costs related to the current use of omega-3 FA (about 29% of total lipid PN days) were compared with those expected with increasing percentages of omega-3 FA-containing PN rates. **RESULTS:** The yearly cost of the patient population (104,022 ICU patients and 427,986 not-ICU patients) treated with current PN regimens mix amounts to about 6 billion Euro. The increase of omega-3 FA-containing PN proportion up to 50% results in a saving of about 210 million Euro (2.7%); the exclusive use of omega-3 FA-containing PN regimes results in savings of 704 million Euro (11.6%). Encouraging omega-3 FA supplemented PN regimens is expected to save costs, because the use is associated with a reduction in hospital LOS (~ 850,000 days saved in the best scenario) and the number of nosocomial infections (~ 40,000 infections avoided in the best scenario). **CONCLUSIONS:** The potential of PN including omega-3 FAs in contributing to an improved quality of care/patient recovery and significant cost savings is not fully exploited in German hospitals.

PRS15

REDUCTION OF COSTS ASSOCIATED WITH A NEW DRY-POWDER INHALER FORMULATION WITH BECLOMETHASONE DIPROPIONATE AND FORMOTEROL COMBINATION FOR THE TREATMENT OF ASTHMA

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OBJECTIVES: A new dry-powder inhaler combination for the treatment of asthma has appeared. The objective of the present study is to analyze the cost impact of the introduction of the new dry-powder inhaler (DPI) –beclomethasone dipropionate with formoterol combination (BEC/FOR) - in the treatment of the moderate to severe persistent asthma **METHODS:** A mathematical model was designed to estimate the financial impact of the partial substitution of DPI budesonide with formoterol (BUD/FOR) and DPI fluticasone propionate with salmeterol (FLU/SAL). Only direct health care costs were considered because the perspective of Spanish National Health Service (NHS) was adopted. The time horizon was four years **RESULTS:** The prevalence is 4.6% and it increases 0.26% yearly. Current annual total cost of treatment with BUD/FOR and FLU/SAL is estimated in around 512; 538; 565 and 591 million € for 2013-2017 respectively. The new total cost is estimated in about 511; 537; 562 and 587 million € with the introduction of BEC/FOR. The major determinants of costs were the exacerbations of asthma (44.5% of total cost), and the antiasthmatic drugs (40.2%). The pharmacological cost of BEC/FOR represented the 37.02% of the total of this option while those of FLU/SAL and BUD/FOR were the 39.75% and 41.27%, respectively. Finally, the introduction of BEC/FOR (share of 2; 4; 9 and 14% for 2013-2017) was associated with a roughly saving of 0.7; 1.2; 2.8 and 4.5 million € in the same time **CONCLUSIONS:** The utilization of beclomethasone dipropionate and formoterol in substitution of fluticasone and salmeterol, and budesonide and salmeterol, all of them as dry-powder inhaled, results in important savings of costs for the NHS

PRS16

THE INFLUENCE OF IMPROVED ADHERENCE AND PERSISTENCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) COSTS: SYSTEMATIC REVIEW OF THE LITERATURE

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OBJECTIVES: The lack of treatment adherence and persistence is associated with poor clinical outcomes and higher costs. The aim of this study is to estimate the variation on COPD costs that may take place as a consequence of improving

patients' treatment adherence and persistence. **METHODS:** A systematic review of the literature was performed in MedLine/PubMed, Cochrane Library, ISI WOK, MEDES, IBECS, CSIC, Google Scholar (2002-2012) to identify articles referred to direct COPD cost and treatment persistence and adherence. Based on the direct cost data extracted, the annual cost difference between an adherent and non-adherent and a persistent and non-persistent patient in Spain was estimated. Costs were updated to €, 2012. **RESULTS:** A total of 48 articles were included (9 Spanish; 39 international). The mean annual direct cost of a COPD patient in Spain varies between €301 and €4.226, depending on the publication. Patients' adherence and persistence on COPD treatment and their annual costs was analyzed in 3 articles (no Spanish publications identified). Multiple inhaled treatments and devices of complex use contribute to poor adherence and persistence and to higher medical resources use and more exacerbations. Treatment adherence and persistence implies a 9% and 3% decrease in mean annual direct cost of a COPD patient, respectively, while non-adherence and non-persistence means an increase of 5% and 13%. The difference between the mean annual direct cost associated to adherent and to non-adherent patient varies from €43 to €601 (depending on the selected publication) and rises up to €89 to €1.674 in severe COPD patients. A difference between annual direct cost in persistent and non-persistent patient was estimated in €47 to €666 that reached €99 to €1.855 in severe COPD patients. **CONCLUSIONS:** Treatment adherence and persistence information is scarce. Therapeutic strategies improving patient adherence and persistence may optimize outcomes contribute to COPD costs contain.

PRS17

THE BURDEN OF PNEUMONIA IN MALAYSIA, INDONESIA AND PHILIPPINES

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OBJECTIVES: The Casemix databases contain clinical costing information from hospitals in Malaysia, Indonesia and the Philippines. The objective of this study was to determine burden of pneumonia in these three countries. **METHODS:** Pneumonia cases occurring in a single year were identified using ICD10 codes, J10-J18. Patients were further categorized into community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP); CAP if they had 1) a primary diagnosis of pneumonia, or 2) secondary diagnosis of pneumonia with primary diagnosis of a respiratory condition; HAP cases had pneumonia in any of the secondary diagnosis fields with non-respiratory primary diagnoses. Descriptive analysis was performed to ascertain patient age groups, mean age, mean length of stay (LOS) and case fatality rates (CFR). **RESULTS:** A total of 15,851 pneumonia cases in year 2010 for Indonesia and Philippines and 2011, for Malaysia were included in the analysis. The mean age of patients was 47.5 years in Malaysia, 36.6 years in Indonesia and 23.5 years in Philippines. There was a preponderance of CAP cases among the very young and the very old while HAP cases were more likely to occur in older persons. The overall CFR of all pneumonia hospitalizations was 11.5% for Malaysia, 5.2% for Indonesia and 3.6% for Philippines. The cost of hospitalization was USD 1,177.50, USD 1,103.80 and USD 254.30 in Malaysia, Indonesia and Philippines respectively. The mean LOS in days was 9.2, 8.0 and 6.6 in the three countries, respectively. **CONCLUSIONS:** Our study is the first to utilize these databases to study and compare the burden of pneumonia across three countries in Asia. The CFR and LOS varied in each of the countries likely due to a variety of reasons including differences in socio-economic conditions, patterns of infection as well as health system differences. In conclusion, pneumonia is significant burden in the South East Asian countries studied.

PRS18

COST AND COST-EFFECTIVENESS ANALYSES FOR MODERATE AND SEVERE COPD PATIENTS TREATED UNIQUELY WITH TIOTROPIUM 18 MCG OD FOR TWENTY-FOUR MONTHS

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OBJECTIVES: To evaluate cost and cost-effectiveness of tiotropium monotherapy administered for 24 months (18 mcg die) in patients suffering from mild-to-moderate and severe chronic obstructive pulmonary disease (COPD). **METHODS:** A recent published study showed that tiotropium monotherapy enables a significant minimization of morbidity in two groups of patients corresponding to predicted FEV1 baseline values ≤ 50% (A) and > 50% (B). Clinical outcomes (days in hospital, visits in general ward, cycles of systemic steroids, cycles of antibiotics and maintenance therapy drugs) were evaluated from the Italian NHS perspective. In order to perform cost-effectiveness analysis, FEV1 value, available for each patient, was converted in SGRQ score using a published multivariate linear model; then utilities were obtained through the Ståhl equation. **RESULTS:** Results from comparison between 24 months of standard therapy and subsequent 24 months of tiotropium monotherapy show that hospitalization cost, which represents the driving treatment cost, drops from 74.1% to 67.3% (A) and from 64.5% to 31.6% (B) of the total cost; differently maintenance therapy cost increases but it is more than offset by the savings accruing from the shortening of hospitalization. Furthermore, cost-effectiveness results reveal a mean saving of 216 € (A) and 900 € (B) other than a mean gain of 0.07 QALY(A) and 0.03 QALY(B). Dominance of tiotropium calculated only with patients completing treatment course reveal that in almost 30% (A) and 37% (B) of subjects tiotropium strategy is dominant while only in 2% (A) and 7% (B) of cases are associated to costs increment and worsening on quality of life. **CONCLUSIONS:** These results suggest that adoption of tiotropium as unique treatment in selected mild-to-moderate and severe COPD patients yields significant costs savings and has a beneficial effect on evaluated quality of life.

PRS19

DOUBLING OF HEALTH CARE COSTS AMONG ASTHMA PATIENTS WITH COPD DIAGNOSIS AND ITS ASSOCIATED CO-MORBIDITIES IN A CLAIMS DATABASE IN THE UNITED STATES

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OBJECTIVES: To estimate health care costs for asthma patients with and without a COPD diagnosis. **METHODS:** Asthma patients with and without diagnosed COPD were selected from the HealthCore Integrated Research Database covering administrative claims from approximately 27.6 million people in the USA. The index event was a patient's first exacerbation defined as oral corticosteroid prescription fills or emergency department visits or inpatient visits with a primary diagnosis of asthma. Eligibility criteria were ≥1 asthma diagnosis, ≥1 exacerbation and 12 months of continuous health plan enrolment on each side of the index date. Total all-cause and asthma-related direct health care costs for 12 months before and after the index date were calculated for all patients and those with and without a COPD diagnosis. **RESULTS:** A total of 94,883 patients met all eligibility criteria, of these 15,127 (15.9%) had both asthma and COPD diagnoses. The mean patient age was 41.6 years and 62.4% were female. Co-morbid conditions were more common among asthma patients with a COPD diagnosis. Asthma-related direct costs represented 25-30% of all-cause direct health care costs for all patients. Among asthma patients, COPD and its associated co-morbidities roughly doubled all-cause and asthma related direct health care costs: mean annual pre-index all-cause health care costs were $20,012 (COPD diagnosis) versus $8,938 (no COPD diagnosis); mean annual pre-index asthma related costs were $5,623 (COPD diagnosis) versus $2,600 (no COPD diagnosis). Mean annual post-index costs were almost unchanged: all-cause costs of $21,692 (COPD diagnosis) versus $10,787 (no COPD diagnosis) and asthma-related costs of $5,242 (COPD diagnosis) versus $3,016 (no COPD diagnosis). **CONCLUSIONS:** The economic burden of asthma among patients with a COPD diagnosis in a US claims database is twice as high as those without a COPD diagnosis. Further research could adjust for the effects of age on the prevalence of co-morbidities among the different groups.

PRS20

THE IMPACT OF SMOKING ON HOSPITAL COSTS IN TIMES OF CRISIS; AN ADDITIONAL BURDEN TO THE VULNERABLE GREEK HEALTH CARE SYSTEM

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OBJECTIVES: Smoking has a tremendous impact on public health and has been a cause of major concern in Greece for more than twenty years. In times of economic recession when household income drops and health spending is decreasing, the demand for health services is transferred to the public sector. In light of the above, the aim of this study was to measure the number of smoking-related hospitalizations and the additional hospital costs for the treatment of smoking-attributable diseases. **METHODS:** A prevalence-based disease specific approach was used for the calculations. Greek-specific smoking-attributable fractions (SAFs) were calculated for all smoking-related diseases, coded according to the International Classification of Diseases ICD-10. Smoking attributable morbidity was obtained by applying the SAFs to all public hospital admissions for 2011. Total hospital costs associated with smoking were calculated by applying the smoking-attributable admissions to each DRG rate. **RESULTS:** For Greece, lung cancer (C33-C34), bronchitis and emphysema (J40-J42, J43) presented the highest disease-specific SAF with a value of 88.4% and 88.1% respectively. In 2011, smoking was responsible for 199,028 hospital admissions (8.9 % of total). Smoking-attributable hospital costs, based on the current pricing DRG system, has reached 400,011,801€ representing 7.7% of public hospital budgets. Ischemic heart disease (I20-I25) was found to be the main cost driver (90.3 million €), followed by other circulatory diseases (I00-I09, I26-I51) (55.8 million€) and pneumonia, influenza (J10-J18) (52.6 million €). **CONCLUSIONS:** Despite evidence of a decreasing trend, smoking is still a considerable public health issue in Greece and has a great impact on public health care system. Vigorous efforts have been implemented to promote a smoke-free environment and to enforce existing anti-smoking legislation however the Greek society still experiences a high proportion of smoking-attributable admissions and hospital treatment costs. The findings of this study further corroborate a call for stronger support of cost-effective tobacco control policies.

PRS21

IMPACT OF CHRONIC PAIN ON HEALTH CARE COSTS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS COMPARED TO OTHER CHRONIC DISEASES

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OBJECTIVES: Surveys have found high rates of pain medication use among COPD patients. However, few data exist on how chronic pain affects health care utilization. We examined how chronic pain affects direct medical costs in COPD and a matched cohort of patients with other chronic diseases. **METHODS:** We conducted a retrospective analysis using claims data from one managed care system. COPD patients were matched by age, sex, insurance type, and encounter type to persons with other chronic conditions but without COPD [Alzheimer's, atrial fibrillation, cancer, kidney disease, acute myocardial infarction, diabetes, heart failure, ischemic heart disease, rheumatoid/osteoarthritis (RA/OA), and stroke]. Chronic pain was indicated by pain-associated diagnoses, procedures for pain interventions, or prescription fills for pain medications. **RESULTS:** The study cohort (7,952 COPD patients, 15,904 non-COPD) was 58% female; mean age, 69. A higher percentage of COPD patients were chronic users of any pain medication (41.2% vs 31.5%, P<0.0001). The only

chronic disease with a greater use of pain medications was RA/OA (44.8% vs 41.2%, P<0.0001). COPD patients had more chronic use of short-acting opioids (24.2% vs. 15.1%, P<0.0001) and long-acting opioids (4.4% vs. 1.9%, P<0.0001). Among COPD patients, those with chronic pain had higher mean annual direct cost [$24,261 vs. $10,390 (p<0.0001)] which was largely attributable to increased hospitalizations (42.7% vs 25.4%, p<0.0001). By comparison, the mean total medical cost for the matched cohort was $17,681 for those with chronic pain compared to $6,543 for individuals without chronic pain (P<0.0001). Pain-related utilization was approximately 20% of COPD patients' annual direct cost. **CONCLUSIONS:** COPD patients have increased prevalence of and utilization for chronic pain as compared to all other chronic illnesses except RA/OA. Individuals with chronic disease and chronic pain have more than double the cost of those without chronic pain, and this difference is even higher among individuals with COPD.

PRS22

COSTS OF COPD IN FRANCE: A NATIONAL DATABASE ANALYSIS

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OBJECTIVES: To describe the direct costs to society of COPD per severity grades using the "Echantillon Generaliste de Beneficiaires"(EGB). EGB is a database which contains all health care resources used by a random 1/97 permanent sample of the French population covered by the national health care insurance system. **METHODS:** Several algorithms were developed to identify patients with COPD and to distinguish patients between four severity grades (1-4) based on health care consumption. These algorithms were based on age, rate and history of hospitalizations, treatments and tests received by the individuals. Exacerbations as well as their severity were identified through both antibiotics/corticosteroids drugs prescribed and hospitalizations. Total health care costs were calculated and a case-control approach was then used to estimate the cost of COPD. Exacerbations costs were calculated through a linear regression analysis including age and gender. **RESULTS:** Based on the 10,715 COPD patients identified in the EGB, its prevalence was estimated to 4.2% of the population beyond 40 years. The mean annual overall direct health care cost in this population was estimated to be €9,382. Annual average costs were €7,628; 10,770, 14,979 and 20,747 for severity grade 1-4 (severity data-base defined) respectively. The yearly cost of COPD itself was 5,516€: 45.5% related to hospital care and 20.0% to pharmaceuticals (6.0% to long-acting bronchodilators). The average exacerbation cost was €1,664 (SD: €86.6). The global economic burden of COPD in France was therefore estimated over €7 billions (4% of the national health care expense). **CONCLUSIONS:** Our study provides new solutions to estimate the burden of COPD in France using existing national databases. It confirms that COPD is associated with significant economic burden and the striking direct relationship between the cost of care and severity of the disease.

PRS23

HEALTH CARE RESOURCES UTILIZATION AND ASSOCIATED COSTS IN PATIENTS WITH COPD WITH OR WITHOUT ASTHMA: A RETROSPECTIVE, POPULATION-BASED OBSERVATIONAL STUDY

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OBJECTIVES: Chronic Obstructive Pulmonary Disease (COPD) is a highly prevalent chronic inflammatory disease. Some COPD patients show a co-diagnosis of asthma (COPD-A). This real-life observational study assessed the frequency of exacerbations, the use of health care resources and their associated costs in patients with COPD only and COPD-A. **METHODS:** Medical records from 6 Primary Care (PC) and one general hospital were reviewed and data from 2011 were collected from COPD and COPD-A patients aged 40 year or older who met specific inclusion/exclusion criteria. Main study variables were demography, co-morbidities, exacerbations and resources utilization. **RESULTS:** A total of 1210 COPD and 102 COPD-A, mean age (% male) 71.8 (85.5) and 71.2 (65.7) years, respectively, were included. Mean co-morbidity burden was similar in both groups with 7.9 and 7.8 diseases per patient. Most frequent co-morbidities (% in COPD; % in COPD-A) were dyslipidemia (63.0; 60.8) and arterial hypertension (59.5; 62.7) whereas the proportion of exacerbations (%) were 35.0 and 42.2, respectively. Mean number of exacerbations per patient per year was 1.2 in COPD and 1.6 in COPD-A. The frequency of severe exacerbations (%) requiring hospitalizations was 0.4 and 0.7, while those requiring oral corticosteroids was 24.4 and 33.0, respectively. Mean per patient, per year health care resources costs (Euro) were 2152.2 and 2207.5 for PC-associated costs, and 1361.6 and 1754.3 for specialist care-associated costs, respectively. **CONCLUSIONS:** Exacerbations are frequent complications in COPD and COPD-A patients. Both groups show high proportion of co-morbidities and use of health care resources which were higher in the COPD-A group. Health care-related costs are high and are mainly related to hospitalizations and drug therapy.

PRS24

ECONOMIC BURDEN IN DIRECT COSTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN TURKEY: A PAYOR PERSPECTIVE

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OBJECTIVES: COPD has a major burden on Turkey's health care system. It leads to high mortality, morbidity and frequent use of health care resources. This study determined the total direct health care costs for the management of COPD patients with differing degrees of disease severity. The study also aimed to find the key cost drivers in the management of COPD in Turkey. **METHODS:** The methodology was based on a study conducted by European Respiratory Society in which Turkey and 11 other countries had been included. COPD patients were recorded from a territary care hospital in 2012. One-year costs were identified by applying cost data to medical information obtained by medical records. The cost analysis was based on cost of illness methodology. Costs included those for medications, laboratory and diagnostic tests, outpatient visits and hospital stays. **RESULTS:** There were 612 patients recruited. Patients were categorized by GOLD classification: 14.29% GOLDI, 15.28% GOLDII, 38.21% GOLDIII, 32.23% GOLD IV. The median of hospitalization day was 9 days. 36.1% of patients were rehospitalized in 90 days. The mortality rate was 3.1% because of exacerbation. The mean total direct costs was €4,135.60 per patient in a year. The total annual cost was correlated with disease severity. Hospitalization contributed the major portion of cost and also correlated with disease severity. The average outpatient cost was € 98.62, hospitalization cost including intervention was €1,548.56, laboratory and diagnostic tests cost were €103,03, comorbidity and complication cost were €1.493,88, medication cost with side effects were €903,59. **CONCLUSIONS:** There is a significant correlation between the cost of COPD and disease severity with hospitalization leading to disease exacerbation being a major contributor to cost. The keys to reducing health care costs lie beneath reducing the frequency of exacerbations and disease severity. As expected, the highest cost component was hospitalization, comorbidity and complication cost respectively.

PRS25

PAEDIATRIC TUBERCULOSIS - COSTS TO THE IRISH HEALTH CARE PAYER

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OBJECTIVES: Ireland currently administers a universal BCG vaccination programme to infants. In order to assess the cost effectiveness of this programme, it is vital to have accurate cost estimates of the burden of tuberculosis (TB) illness in infants. The aim of the current study was to cost the diagnosis and treatment of an episode of the following health states; pulmonary TB, extrapulmonary TB, TB meningitis and latent TB, from the health care payer's perspective. The cost of contact tracing per primary case of TB was also estimated. **METHODS:** Decision trees were constructed to reflect typical episodes of care in the diagnosis and treatment of each health state. Resource use and unit cost data were applied to each node in the decision tree. The probabilities of events occurring were derived from the literature and expert clinical opinion. Main costs included were inpatient medical/surgical costs, pediatrician outpatient appointments, medications, laboratory tests and x-rays. Each health state included a cost for a Directly Observed Therapy programme. Direct medical costs were calculated and the 2012 price year was used. **RESULTS:** The direct medical costs of diagnosing and treating a case of pulmonary TB, extrapulmonary TB, TB meningitis and latent TB were estimated to be approximately €8153, €12224, €15752 and €894 respectively. The main drivers in the costs are the length of hospital stay and the number of pediatrician visits. The cost of contact tracing per primary case of TB was estimated to be approximately €4,248, which was based on a mean number of 9.4 contacts examined per primary TB case. **CONCLUSIONS:** To our knowledge this is the first investigation of costs associated with paediatric TB within the context of the Irish health care setting and will allow for a more robust estimation of the cost effectiveness of BCG vaccination programmes, which will benefit the health care payer.

PRS26

PHARMACOECONOMIC ASSESSMENT OF DIFFERENT TACTICS OF COPD TREATMENT IN RUSSIA

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OBJECTIVES: Comparative pharmacoeconomic assessment of COPD therapy of patients in GOLD 2-3 stages in Moscow health care system. **METHODS:** Retrospective analysis of 130 cases during 1 year routine practice of patients with COPD in Moscow outpatients departments. Basic therapy strategies were obtaned: 1) monotherapy with indacaterol (14 pts. Low # of pts is because of the product was launched less than year ago); 2) monotherapy by tiotropium (33 pts), 3) fixed combination LABA + ICS (38 pts); 4) tiotropium plus fixed combination of LABA and ICS (45 pts). Cost of illness via calculation of direct medical costs on diagnostic, hospitalization, treatment of main disease and complications based on Federal Standards of COPD treatment and regional tariffs on cervices was estimated. Data on prices on medical products were obtained from State Register of medical products and www.aptechka.ru. **RESULTS:** The most expencive strategy is management of group 4 - 86.5 KRUR/pt/year (1 Euro - 40 RUR) where 67% are costs on base drugs and 31% are hospitalization expenses. Usage of fixed combinations LABA + ICS is comparable with monotherapy by tiotropium, total costs are 47 and 49 KRUR/pt/year accordingly. But if the reason of main part of the costs in group 3 is hospitalization due to exacerbation - 69%, for group 2 - 61% are expenditures on tiotropium. The most preferable is treatment of group 1 - 32847 RUR/pt/year, where 55% - part on indacaterol, 42% - hospital treatment, 3% - urgent care. **CONCLUSIONS:** In spite of high price, indacaterol is the most economic preferable product for basic COPD treatment of patients in GOLD 2-3 stages

PRS27

PREDICTING HEALTH CARE COSTS IN ASTHMA USING THE EQ-5D INDEX SCORE

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OBJECTIVES: To predict health care costs in asthma using the EQ-5D health-related quality-of-life (HRQoL) index score. **METHODS:** We extracted data from the 2000-03 Medical Expenditure Panel Survey (MEPS) on adult respondents who had EQ-5D index scores. Asthma patients were identified using ICD-9 (=493) and self-report on disease (n=3,783). To account for non-random selection of positive spending, the

Heckman two-step selection model was used. The EQ-5D index score was categorized into categories with 0.1 gradations. Marginal effects (ME) were estimated to quantify the marginal changes in costs corresponding to, for instance, 0.1 increments in the EQ-5D index score, or the presence of asthma or asthma treatment. All costs were adjusted to 2003 dollars. **RESULTS:** The EQ-5D index score was a significant predictor of health care costs in all models, as were asthma, asthma treatment and other covariates ($p<0.01$). The Heckman model suggested a significant positive spending bias ($p<0.01$). For the 3 groups considered--non-asthma, asthma and asthma with treatment--the mean EQ-5D index scores were 0.848, 0.755 and 0.706, respectively. The actual mean costs were $2,355, $4,284 and $5,577, respectively. The predicted mean costs using Heckman model were $2,673, $4,431 and $5,618, respectively. On average, a 0.1 unit improvement in EQ-5D score was associated with $502 cost reduction in asthma and $693 cost reduction if asthma patients had treatment ($p<0.01$). However, after adjusting for positive spending bias, the cost reduction was $891 and $961 ($p<0.01$) for these two groups respectively. Greater cost reductions were associated with improving EQ-5D scores at the lower end (<0 to 0.3) and the mid-range (0.5 to 0.7). **CONCLUSIONS:** HRQoL is an important component of health care resource utilization. The findings suggest a significant relationship exists between health care costs and HRQoL data. The EQ-5D significantly predicts costs in asthma and asthma treatment, especially after adjusting non-random positive health care spending.

PRS28

EFFECT OF SMOKING STATUS ON HEALTH CARE COSTS AND RESOURCE UTILIZATION IN PATIENTS WITH CHRONIC-OBSTRUCTIVE-PULMONARY-DISEASE IN CLINICAL PRACTICE: A RETROSPECTIVE NESTED CASE-CONTROL ECONOMIC STUDY

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OBJECTIVES: Chronic-Obstructive-Pulmonary-Disease (COPD) is a prevalent health condition mainly associated with smoking habit, which is considered the reason for higher health care resources utilization and related costs in the National health System. The aim of this study was to analyze and compare health care resource utilization and costs according to smoking status in patients with COPD in clinical practice in Spain. **METHODS:** A retrospective cohort nested case-control study was designed. Cases were current smokers, while two controls (former smokers) per case matched for age, sex, duration of COPD, and burden of comorbidity (number of diagnosis and Charlson index) were included using data from medical records. Non-institutionalized COPD, both genders, 40 years of age and older, seen consecutively over a period of 4 years before the index date and fulfilling eligibility criteria were considered eligible for analysis. Analysis used regression and general linear models with covariates to compare direct and indirect costs and resource utilization. **RESULTS:** A total of 930 COPD medical records were analyzed: 310 corresponding to cases (current smokers) and 630 to controls (former smokers). Mean age was 69.4 years (84.6% male). COPD was more severe in cases; Odds ratio (OR)=1.7 (95% CI 1.1;2.1), and higher percentage of current smokers had exacerbations [OR=2,7 (2.0;3.8)], with 4.2 vs. 1.7 exacerbations per year, respectively, on average ($p<0.001$). Smokers used more physicians visits both at primary care and specialized level, and emergency room as well. Drugs-based therapies were more common in current smokers COPD subjects. As a consequence, smokers had higher average annual health care costs; €3,784 (1,888) vs. €2,302 (2,451) in former smokers ($p<0.001$). **CONCLUSIONS:** COPD smoker patients had more exacerbations and higher severity of disease. Also, used more health care resources, particularly physicians visits and drugs-based therapies resulting in higher health care costs to the national health System.

PRS29

COSTS AND EFFECTIVENESS OF NON-SMOKING CLINIC

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OBJECTIVES: In Finland a new Tobacco Act entered into force in October 2010 with the aim of limiting marketing and supply of tobacco products. The long-term objective of the Finnish government is to make Finland tobacco-free by 2040. Several work places and organizations have declared themselves non-smoking. The city of Mikkeli with a population of 55 000, has declared itself a non-smoking city and has established a non-smoking clinic in September 2011. Citizens contacting public health care and willing to quit smoking will be referred to the clinic. **METHODS:** Cross-sectional data was gathered 12 months after the establishment of the clinic. Costs related to investment and clinic's resource utilization were estimated. A health care perspective was applied. **RESULTS:** We studied 74 citizens, who had a least one visit during the first year since the establishment of the clinic. Of them 37% managed to quit smoking. Investment costs related to planning and training of nurses were 168€ per quitter. Operational costs were 141-167€ per quitter. Total costs per quitter were 309-335€. In the future investment costs per customer will decrease as investment costs were nonrecurring. **CONCLUSIONS:** Our results were slightly better than what was achieved in an occupational health care non-smoking project in Finland (37% vs. 31%). In 2010 the average total costs of occupational health care were 340€ per employee in Finland. This is almost the same as the costs per quitter in this study. Cost of cigarettes is about 1800€ per average smoker in Finland. Health care costs related to lung cancer and stroke are about 18500€ per case during the first year. Pharmacological treatment costs about 200-400€ to quitter in average. Investing in smoking clinic is justified from economic and effectiveness point of views. The non-smoking clinic is still in operation.

PRS30

THE LIST OF MEDICINES FOR COPD TREATMENT IN STATE FORMULARY OF UKRAINE AND RELATED COSTS

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OBJECTIVES: According to the GOLD-2011 report pharmacotherapy in stable COPD is used to reduce the symptoms, frequency and severity of exacerbations, improve health status and exercise tolerance. **METHODS:** Our aim was to assess the list of medicines, which are available in Ukraine for COPD treatment. We compared the medications included in the State Formulary of Ukraine with the dosage forms and typical doses of COPD medications list provided by GOLD-2011. Also we calculated annual course costs for each drug in different dosage forms. The annual course was considered as amount of medicine for 365 days in appropriate for COPD basis dosing. Information about the medicine prices was obtained from the ukrainian electronic pricing database "MORION". The EUR/UAH exchange rate was 1 EUR = 10.53 UAH (20.06.2013) **RESULTS:** The State Formulary of Ukraine (SFU) contains 19 medicines for INN provided by GOLD-2011: 5 INN are in metered dose inhalers (MDI), 5 - in dry powder inhalers (DPI), 1 - in smart mist inhaler (SMI), 5 solutions for nebulizer and 3 - in tablets. Salbutamol, salmeterol, indacaterol, fluticasone, beclomethasone in DPI are not included in the list of SFU, formoterol in MDI and aminophylline, prednisone in tablets are not included in this list as well. The most expensive drug is tiotropium with annual costs 604.46 EUR for SMI and 533.81 EUR for DPI. The annual costs of salmeterol in MDI and formoterol in DPI are 318.55 and 277.30, respectively. The cheapest medicine is salbutamol in MDI with 22.13 EUR annually but annual costs of salbutamol solution for nebulizer amount 464.48 EUR per year per patient. **CONCLUSIONS:** The State Formulary of Ukraine should be reached by medicines for COPD management recommended by GOLD. Annual COPD basis costs are depending not only from kind of medicine but from it dosage forms as well.

PRS31

COMPARING COSTS AND CONSEQUENCES OF TREATING CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH BUDESONIDE/FORMOTEROL AND FLUTICASONE/SALMETEROL

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OBJECTIVES: Inhaled corticosteroids in fixed combination with long-acting B_2-agonists could prevent and reduce chronic obstructive pulmonary disease (COPD) exacerbations. The aim of this analysis is to compare clinical consequences and direct health care costs related to treatment with budesonide/formoterol and fluticasone/salmeterol for COPD considering the Italian National Health Service (INHS) perspective. **METHODS:** Effectiveness data by the PATHOS study, a population-based, retrospective, observational registry study conducted in Sweden, in terms of reduction in COPD hospitalizations and COPD-related emergency departments (ED) visits were considered in order to estimate the differences in resource consumption between patients treated with budesonide/formoterol versus fluticasone/salmeterol. Base case considers the dosages of the 2 drugs from the PATHOS study, the cost of drugs in charge to INHS, COPD hospitalizations costs from Italian real world data and Italian national tariffs for COPD-related ED visits. **RESULTS:** The real world study PATHOS demonstrated a significant reduction in COPD hospitalizations and COPD-related ED visits with budesonide/formoterol versus fluticasone/salmeterol (-29.1% and -21%, respectively); average dosages reported were 568 mcg/day for budesonide/formoterol (as budesonide dosage) and 783 mcg/day for fluticasone/salmeterol (as fluticasone dosage). In the base case, the treatment for 1 year of 100 patients with budesonide/formoterol lead to a saving of 43.892€ (21.859€ for drugs, 21.864€ for COPD hospitalizations and 169€ for COPD-related ED visits) corresponding to -25.2% compared with fluticasone/salmeterol treatment. In the most conservative sensitivity analysis which consider the DDD dosages for the 2 drugs and COPD hospitalizations and COPD-related ED visits costs from national tariffs, the treatment for 1 year of 100 patients with budesonide/formoterol lead to a saving of 15.523€ (5.754€ for drugs, 9.600€ for COPD hospitalizations and 169€ for COPD-related ED visits) corresponding to -12.5% compared with fluticasone/salmeterol treatment. **CONCLUSIONS:** Treatment with budesonide/formoterol compared to fluticasone/salmeterol could lead to a reduction in direct health care costs with relevant improvement in clinical outcomes.

PRS32

UPDATE ON PHARMACOECONOMICS IN NUTRITION: PARENTERAL GLUTAMINE SUPPLEMENT IN INTENSIVE CARE UNIT PATIENTS

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OBJECTIVES: To re-evaluate the economic consequences of parenteral glutamine supplementation (PGS) in light of the recent metaanalysis confirming that PGS at a dose >0,20 g/kg body weight per day in intensive care unit (ICU) patients is associated with reduced mortality, infection rate (IR) and length of stay (LOS). **METHODS:** A simulation model was updated with the new meta-analysis data and clinical inputs for the control group from Italian ICU population reported in "Progetto Margherita". Costs are evaluated from the perspective of the Italian hospital and derive from official sources. Sensitivity analyses are undertaken to test results' reliability **RESULTS:** PGS is predicted to reduce mortality rates (-29.0%), IR (-21.2%) and overall LOS (-1.07 days/patient), yielding a saving of € 1,047 per patient treated. Treatment costs are completely offset by the reduction in hospital stay costs and antibiotic costs. Probabilistic sensitivity analysis indicates PGS strategy as dominant in more than 90% of cases. **CONCLUSIONS:** Also with contemporary comparative efficacy data is PGS in ICU patients expected to be effective in improving outcomes and containing costs in Italian hospitals providing intensive care.

PRS33

COST-EFFECTIVENESS OF GLYCOPYRRONIUM COMPARED TO TIOTROPIUM IN COPD PATIENTS FROM A SWEDISH SOCIETAL PERSPECTIVE

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OBJECTIVES: To estimate the cost-effectiveness of a novel LAMA, glycopyrronium (Seebri® Breezhaler), compared with tiotropium (Spiriva®) in COPD patients from a Swedish societal perspective. **METHODS:** A probabilistic Markov model was utilized to

simulate the progressive course of COPD and its impact on quality adjusted life years (QALYs) in moderate to severe patients. Effectiveness was based on initial FEV1 increase included by using patient level improvement in one or more disease severity stages (according to GOLD guidelines) and annualized risk for exacerbation as observed in a 1-year head-to-head randomized controlled trial (GLOW2). Initial FEV1 increase during the first year was followed by a constant decline in FEV1 in subsequent cycles. Based on list prices, annual drug costs were 3'825 Swedish krona (SEK)/447 EUR for glycopyrronium and 5'040 SEK/589EUR for tiotropium. Direct and indirect maintenance and exacerbation costs as well as utilities were extracted from published literature. Primary outcomes were QALYs and societal costs over 3 years, discounting future costs and benefits at 3%. Both one way and probabilistic sensitivity analysis have been performed. **RESULTS:** Over 3 years, glycopyrronium was found to be dominant (i.e. less costly and more effective) compared with tiotropium. Treatment with glycopyrronium resulted in a minor QALY gain of 0.005 compared with tiotropium. Total costs per patient were estimated at 73'752SEK / 8'630 EUR for glycopyrronium and 79'357 SEK /9'286 EUR for tiotropium, resulting in an average cost saving of 5'605SEK /656 EUR per patient after 3 years. Univariate sensitivity analyses showed that base-case results were robust and probabilistic sensitivity analyses resulted in 99% of generated samples with glycopyrronium to be dominant. **CONCLUSIONS:** From a Swedish societal perspective, glycopyrronium was estimated to be cost-effective compared with tiotropium based on the progressive course of COPD and risk for exacerbation in moderate to severe patients as observed in the head-to-head study GLOW2.

PRS34

COST-EFFECTIVENESS ANALYSIS OF CARBAPENEMS IN TREATMENT NOSOCOMIAN PNEUMONIA IN UKRAINE

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OBJECTIVES: To conduct a cost-effectiveness analysis of carbapenems use (imipenem, meropenem, and doripenem) in treatment nosocomial pneumonia. **METHODS:** Cost-effectiveness analysis based on decision-tree model was conducted from patient's (out-of-pocket drugs costs) and state (drugs costs and hospitalization expenses) perspectives. The input data on therapy duration and drugs' doses were retrieved from randomized controlled trials and clinical standards. The drugs doses were equal to: 2.0g /day from imipenem/cilastatin, 3.0g /day for meropenem, and 1.5g/day for doripenem. The model considered that in the case of drugs effectiveness the treatment continued till successful outcome, and in a case of non-effective treatment, the second line therapy (vancomycin or colomycin depending on type of infection) was applied. The data on infections resistance and empirical effectiveness of antibiotics were retrieved from the largest microbiologic study conducted in Ukraine. **RESULTS:** The lowest cost- effectiveness ratio correspond to the initial therapy with imipenem/cilastatin (CER 910$/1158$ vs. 1280$/1648$ for meropenem and 1317$/1712$ for doripenem from state and patient's perspectives accordingly). **CONCLUSIONS:** Thus, empiric therapy with meropenem increases the costs of medical treatment by 29 %, with doripenem – by over 35 %. Sensitivity analysis of the results of calculations versus changes of level of MRSA-resistant and carbapenem-resistant strains demonstrated reliability of the received results.

PRS35

COST-EFFECTIVENESS ANALYSIS OF PALIVIZUMAB AS A PROPHYLAXIS FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN HIGH-RISK LATE PRETERM INFANTS IN THE NETHERLANDS

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OBJECTIVES: To determine the cost-effectiveness of palivizumab for the prevention of serious lower respiratory tract infection requiring hospitalization caused by RSV compared to no prophylaxis in high-risk infants born at 33-35 weeks of gestational age (wGA) according to the Dutch RISK model. **METHODS:** A decision tree model was developed using data from published literature, palivizumab clinical trials, the Dutch RISK score model, official price/tariff lists and Dutch national population statistic. The comparator was no prophylaxis. The primary perspective of the study was that of the society in The Netherlands. Time horizon was lifetime. The cost valuation is based on the direct health care costs, direct nonmedical costs and indirect costs. Costs were assessed in 2012 Euros. The costs and utilities are discounted by 4% and 1.5%, respectively, from the second year onwards, and no discounting is applied in the first year. **RESULTS:** The base case results show that the use of palivizumab leads to an additional cost of € 4,116, whereas the use of palivizumab leads to a gain of 0.201 life years and 0.265 QALYs. Although the use of palivizumab increases the costs compared with no prophylaxis, palivizumab-treated patients experienced more QALYs and a gain in life years. Subsequently, palivizumab results in an ICER of € 15,520 per QALY gained compared to no prophylaxis. The ICER in cost per LYG is € 20,440. **CONCLUSIONS:** This analysis showed that palivizumab was cost-effective as a prophylaxis against RSV infection requiring hospitalisation in high-risk late premature infants compared to no prophylaxis. Extensive sensitivity analyses and explored scenarios underline the robustness of the demonstrated base case cost-effectiveness.

PRS36

COST-EFFECTIVENESS ANALYSIS OF GLYCOPYRRONIUM BROMIDE IN THE TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN SPAIN

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OBJECTIVES: To assess the cost-effectiveness and cost-utility of glycopyrronium bromide versus tiotropium bromide in Chronic Obstructive Pulmonary Disease (COPD) patients, from the Spanish National Health System perspective. **METHODS:** A Markov model was developed to compare glycopyrronium bromide and tiotropium therapies. Progression of a COPD patient cohort was simulated for a 5-year time horizon (3 months-cycle duration). The health states included were defined according to the severity of COPD: mild, moderate, severe, very severe and death (absorbent). Three additional sub-states: without exacerbation, mild and severe exacerbation were considered. The effectiveness of treatment options and utilities for each health state were taken from the literature. Only direct health care costs were considered. Disease management and exacerbation costs were obtained from the literature. Drug costs were calculated based on ex-factory prices with mandatory 7.5% rebate. All costs were updated to €2012. A 3% annual discount rate on costs and health outcomes was applied. Incremental ratios in terms of cost per life-year gained (LYG) and cost per quality-adjusted life-year gained (QALY) of the most effective therapy versus the comparator were calculated. One-way sensitivity analyses were performed modifying the following parameters: time horizon (10 years, lifetime), discount rate (0%, 5%), drug costs (±10%, ±20%) and utilities (±10%). Probabilistic sensitivity analysis (PSA) was also performed. **RESULTS:** At 5 years, glycopyrronium bromide accounted a total cost of €2,225.18 compared to €2,374.81 accounted for tiotropium bromide. Glycopyrronium bromide yielded higher health benefits (4,321 LYG and 3,388 QALY) than tiotropium bromide (4,315 LYG and 3,377 QALY). In all one-way sensitivity analyses performed and in 100% of PSA simulations (1,000 iterations), glycopyrronium bromide compared to tiotropium bromide remained as a dominant strategy. **CONCLUSIONS:** Glycopyrronium bromide therapy in COPD patients is associated to less costs and higher health benefits than tiotropium in Spain.

PRS37

INHALED CORTICOSTEROIDS (ICS) IN TREATMENT OF MODERATE AND SEVERE ASTHMA IN RUSSIAN FEDERATION – COMPARATIVE PHARMACOECONOMIC STUDY

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OBJECTIVES: We conducted this pharmacoeconomic study to compare mometasone furoate (M/F), fluticasone propionate (F/P) and budesonide (BUD) in treatment of moderate and severe asthma. **METHODS:** Initially we conducted indirect comparison of efficacy and safety of studied therapies through the review of clinical data publications. We used cost minimization and cost effectiveness analysis for the pharmacoeconomic research. In the study we considered the direct costs of the three ICS and additional costs of β2-adregenic agonist (salbutamol). We made calculations of costs for the most common treatment regimens in Russia: M/F 400 µg 1 dose once a day and F/P 125 µg 2 doses twice a day; M/F 400 µg 1 dose twice a day and F/P 250 µg 2 doses twice a day; M/F 200 µg, 400 µg 1 dose twice a day and BUD 200 µg 2 doses twice a day. **RESULTS:** The review of clinical data demonstrated that M/F has similar efficacy to F/P and superior efficacy to BUD. The three ICS have similar safety profile. Use of M/F presents 10105 RUR (316 USD) in direct annual per patient costs for the treatment of moderate asthma and 20210 RUR (632 USD) for severe asthma. Cost minimization analysis showed, that the considered treatment regimens of M/F are cost effective compared to F/P 125 µg and 250 µg. M/F will save the health care system 28 to 50 USD per patient annually, though these results are price sensitive. Cost effectiveness analysis demonstrated that M/F has favorable CER compared to BUD: for 1% of FEV1 increase M/F 200 µg is 12 USD, M/F 400 µg is 24 USD and BUD is 32 USD. These results are insignificantly price sensitive. **CONCLUSIONS:** M/F is the most cost effective of the three ICS as demonstrated by the results of cost minimization and cost effectiveness analyses.

PRS38

THE COST-EFFECTIVENESS OF DRY POWDER ANTIBIOTICS FOR THE TREATMENT OF PSEUDOMONAS AERUGINOSA IN PATIENTS WITH CYSTIC FIBROSIS

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OBJECTIVES: To evaluate the cost-effectiveness of colistimethate sodium dry powder for inhalation (DPI) and tobramycin DPI versus nebulised tobramycin for the treatment of Pseudomonas aeruginosalung infection in patients with cystic fibrosis. **METHODS:** We developed a state transition model based on transitions between strata of lung function measured in terms of Forced Expiratory Volume in 1 Second (FEV_1) % predicted. Health states representing post-lung transplantation and dead are also modelled. The model was informed by systematic reviews of evidence concerning potential relationships between intermediate and final outcomes. The model assumes that treatment impacts on FEV_1which manifests as changes in health-related quality of life. No survival benefit is assumed due to the absence of robust evidence. Model parameters were informed by two RCTs and best available evidence from the literature. Resource costs associated with drug acquisition, management of exacerbations and nebuliser maintenance were drawn from reference sources and expert opinion. Additional analyses of Patient Access Scheme (PAS) price discounts offered by the manufacturers of both DPI products were also undertaken. **RESULTS:** Colistimethate sodium DPI is expected to produce fewer QALYs than nebulised tobramycin. Based on its list price, nebulised tobramycin is expected to dominate colistimethate sodium DPI. When the PAS is incorporated, the ICER for colistimethate sodium DPI versus nebulised tobramycin is expected to be approximately £288,600 saved per QALY lost. Based on its list price, the ICER for tobramycin DPI versus nebulised tobramycin is expected to be approximately £124,000 per QALY gained. When the proposed PAS is included, tobramycin DPI is expected to dominate nebulised tobramycin. **CONCLUSIONS:** Under their list prices, neither DPI product is likely to represent good value for money given current UK cost-effectiveness thresholds. The price discounts significantly improve the economic attractiveness of both products. The cost-effectiveness of the DPIs against other nebulised antibiotics remains unclear.

PRS39

EMPIRICAL THERAPY FOR RESPIRATORY TRACT INFECTIONS IN AN ERA OF INCREASING ANTIMICROBIAL RESISTANCE: A DECISION AND COST ANALYSIS

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OBJECTIVES: To analyze the costs of macrolides use compared to cephalosporines for treatment of Acute Bacterial Sinusitis (ABSs) in the era of increasing resistance to *Streptococcus pneumoniae*. **METHODS:** We used a decision analysis model (TreeAge Pro 2013) to perform a cost-minimization and sensitivity analysis to determine what level of macrolide resistance in a community would trigger cephalosporine use. Costs and clinical outcomes of ABSs were extracted from a systematic review of the literature and official local databases. Clinical response was derived from prospective clinical trials, investigations and from clinical experts experience, were we had ≤1 source. **RESULTS:** We have found that the mean cost of empirical treatment with macrolides for ABSs was 79 EUR when community *S. pneumoniae* resistance was at 0%; 77 EUR at 10%; 82 EUR at 20% and 88 EUR at 30%. Cephalosporines were found to be cost-minimizing when the prevalence of macrolide resistance to *S. pneumoniae* exceeded 15%. Sensitivity analysis variables that had a significant impact on our cost-minimization threshold included proportion of macrolide resistance to *S. pneumoniae*, cost of antibiotics and probabilities of clinical cure with antibiotics. **CONCLUSIONS:** We believe we have performed the first cost-based model and sensitivity analysis to determine what level of macrolide resistance in the community could trigger a switch of empirical therapy for ABSs from macrolides to cephalosporines in Slovakia. Our investigation is to our knowledge also locally the first to employ decision analysis to explore the relationship between antimicrobial resistance and clinical decision making in ABSs. From a payer perspective, cephalosporines appears to be a reasonable alternative to macrolides for empirical treatment of ABSs, especially given the current prevalence of macrolides resistance among *S. pneumoniae* in community that reached 30% level, nationwide.

PRS40

ECONOMIC EVALUATION OF MANDIBULAR ADVANCEMENT DEVICE TO TREAT OBSTRUCTIVE SLEEP APNEA

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OBJECTIVES: In the treatment of obstructive sleep apnea/hyoponea syndrome (OSAHS) moderate patients are primarily offered Continuous Positive Airway Pressure (CPAP). This study aims to assess the cost-effectiveness of mandibular advancement device (MAD), a commonly suggested alternative, as compared to CPAP for moderate OSAHS patients in The Netherlands. **METHODS:** The prognosis of a hypothetical cohort of 50-year-old patients with moderate OSAHS was simulated with a Markov model to estimate the costs and quality-adjusted life-years (QALYs) for both CPAP and MAD. A distinctive factor incorporated in the model was switch of therapy. All input parameters, including the risks of experiencing myocardial infarction, stroke and motor vehicle crashes (MVC) were based on literature and clinical expert opinion. Costs and effects were estimated over a 5-year time horizon using a health care provider perspective and were discounted at a rate of 4% and 1.5%, respectively. Robustness of the results was investigated with several sensitivity and scenario analyses. **RESULTS:** Compared with CPAP, MAD is less expensive (€4,511 vs. €5,302) and only slightly less effective (3.44 vs. 3.49 QALYs) resulting in an incremental cost-effectiveness ratio (ICER) of €15,393 saved per QALY lost. The most influential parameter was the cost of MAD device and its titration. Quality-of-life values, compliance rates, costs and the probabilities of switching treatment, cardiovascular events and MVC were varied in the scenario analyses. Under the majority of the scenarios MAD remained less cost-effective compared to CPAP. **CONCLUSIONS:** Over a 5-year time horizon, MAD therapy may be considered not cost-effective in the treatment of moderate OSAHS patients in The Netherlands. Further research on the impact of both treatments on long-term risks and improvement in the quality of life is required. Similarly, more long-term studies using a uniform compliance definition are needed to inform future cost-effectiveness analyses.

PRS41

INTEGRATING THE LONG-TERM HEALTH BURDEN OF ORAL CORTICOSTEROIDS IN THE COST-EFFECTIVENESS OF OMALIZUMAB

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OBJECTIVES: Omalizumab offers an alternative to maintenance oral corticosteroids (OCS) in the treatment of severe persistent asthma. Despite widespread recognition of the adverse effects from OCS, there is little quantitative evidence on their health burden or costs. Failing to account for the adverse effects of OCS may underestimate the cost-effectiveness of innovative steroid-sparing medicines such as omalizumab. This study aims to explore the possibilities for integrating evidence on the burden of OCS in cost-effectiveness analysis using omalizumab as a case study. **METHODS:** A model was developed to evaluate the long-term cost-effectiveness of omalizumab in patients requiring maintenance OCS. Costs were from a health service perspective and outcomes were measured as quality-adjusted life years (QALYs). The burden from maintenance use of OCS was quantified with population-based approach, with a decision model and with threshold analysis. **RESULTS:** The incremental cost-effectiveness ratio (ICER) was £37,987 per QALY gained, which is above conventional thresholds used in the UK. Threshold analysis showed that the annual health losses from maintenance use of oral corticosteroids would need to be 0.12 QALYs per year. This is double the quantifiable health losses with the population-based approach and with the decision model and 10% of the health gains achieved with omalizumab. **CONCLUSIONS:** The burden from maintenance OCS can be integrated in cost-effectiveness analysis but the extent to which these estimates account for their full impact on health depends on the approach used and underlying assumptions. The challenges arise from sparse randomised evidence, time lag in the adverse effects and unclear relationship between risk and long-term steroid load. These are empirical questions which can be answered with further research. Such research would be valuable not only for decision making in severe asthma but also for other conditions treated with maintenance OCS.

PRS42

ECONOMIC IMPACT OF A SMOKING CESSATION PROGRAM IN MEXICO: ENROLLING EMPLOYEES AND EMPLOYERS

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BACKGROUND: Smoking costs at work affect both employers and employees. These costs are a result of a combined loss of productivity, time off work due to illness, smoking breaks and increasing insurance costs. **OBJECTIVES:** This study aims to evaluate the economical impact of a 12 week smoking cessation program with varenicline from an employer perspective in a medium size Mexican-Corporate setting. **METHODS:** A decision tree was built in order to estimate the two endpoints of the program: resource used in terms of costs and productivity gains in labor hours, in a three year horizon. Smokers enrolling in the program were assumed to be the proportion of people who reported being very much indeed interested on quitting smoking in a 2005 UK survey (27%). A promotional cost of a 12 week combo-pack of varenicline was provided by the manufacturer. A literature review was performed in order to obtain smoking specific data of the country and response rates. Labor costs were retrieved from the Mexican National Institute of Statistics and Geography (INEGI). A base scenario of a medium sized company (250 employees) was assumed to show the potential benefits of the program. **RESULTS:** Assuming a 250 employees company and a shared proportion of 50% of the costs of the program between employees and employers, companies would have to invest US$178 per employee only at the first year, and have potential savings of US$228 for each of them after 3 years. At the same circumstances the net productivity gains per programme participant would be in an amount of 70.8 hours. **CONCLUSIONS:** This research showed that if mexican employers invest in a smoking cessation program, significant productivity gains and savings could be reached in a 3 year horizon.

RESPIRATORY-RELATED DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PRS43

THE RELATIONSHIP BETWEEN TREATMENT SATISFACTION AND ADHERENCE IN COPD PATIENTS IN 5 COUNTRIES

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OBJECTIVES: To assess the relationship between treatment satisfaction and adherence in chronic obstructive pulmonary disease (COPD) in European patients, and whether the strength of this relationship varies according to country. **METHODS:** Data were taken from the 5EU (France, Germany, Italy, Spain, and UK) 2011 National Health and Wellness Survey (NHWS), a cross-sectional survey representative of the total adult populations in each 5EU country. The current analysis included all respondents taking one or two treatments for COPD (including chronic bronchitis, COPD, and emphysema; n=914). Satisfaction with medication was measured using a single item per treatment, and averaged for respondents taking two treatments. Adherence was measured using a single 4-item Morisky Medication Adherence Scale (MMAS) for all COPD treatments used. Spearman correlations were used to assess the relationship when adherence was considered as an ordinal variable, and binary logistic regressions were used to assess the relationship between the two constructs when adherence was dichotomized. Regressions included age and gender as covariates. **RESULTS:** Bivariate correlations demonstrated a modest relationship between satisfaction and adherence within COPD patients across the five countries $r_s = .133$, $p<0.001$). The strength of this relationship ranged from a low of $r_s = 0.05$ in France ($p = 0.60$) to a high of $r_s = .37$ in Spain ($p<0.001$). A significant interaction between country and satisfaction confirmed that the relationship varied by country. When the relationship was examined within each country, satisfaction was a significant predictor of adherence only in Spain and the UK (both $p<0.05$). **CONCLUSIONS:** Mean level of adherence to COPD treatments differed across European countries. Higher satisfaction was generally associated with greater adherence, but the strength of this relationship varied. Ensuring treatments are satisfactory to the patient may promote greater adherence, but the strength of the impact is likely to vary across populations.

PRS44

FACTORS RELATED TO ADHERENCE AFTER A MULTIFACTORIAL INTERVENTION TO IMPROVE IT IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). ICEPOC STUDY

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OBJECTIVES: To identify factors related to adherence after a multifactorial intervention in patients with COPD. **METHODS:** Design: Randomized Controlled Trial (ISRCTN 15106246) Patients: 146 subjects randomly allocated (random blocks of 4 patients) in two groups (intervention group-IG, control group-CG). Intervention components: 1) Motivational aspects: beliefs-behaviour about COPD (group and individual interviews); 2) Cognitive aspects: information about illness; and 3) Skills: inhaling techniques training. Follow-up: 1 year, 5 visits/group. Primary Outcome: adherence (pill/doses count); Secondary Outcomes: functional status (spirometry), quality of life (Saint George Respiratory Questionnaire-SGRQ); Independent variables: intervention, age, sex, educational level, comorbidity, COPD severity stage (SEPAR guidelines), prescribed medication. Statistical analysis: Four partial logistic regression models, fixed- and random effects estimation, were carried out, a final model was built considering them. Statistical packages SPSS 15.0 and Stata 11.1. **RESULTS:** Predominance of males (91.8%), mean age 69.08 years (CI95%,67.58-70.44); low cultural level (78.1%), 32.2% current smokers (62.84 pack-years [CI95%,55.34-70.34]), Body Mass Index 30.78 kg/m2 (CI95%,28.78-32.78), 81.2% mild-moderate severity stage, predominance of obstructive respiratory pattern; FEV1 (mean)= 67.58% (CI95%,64.58-71.08), 0.87 exacerbations/year [CI95%, 0.68-1.06]. Pharmacological treatment: inhaled-beta2-adrenergic (80.1%); inhaled-anticholinergic (77.4%); inhaled-corticosteroids (70.5%); mucolitycs (11.6%); xanthine (8.2%); oxygen therapy (4.8%); oral-corticosteroids (0.7%). Adherence was 41% (41.2CG/40.8IG).

Both groups were similar at baseline. Drop out was 28.8%. Intention to treat analysis. Adherence increased significantly in IG (p=0.046), NNT=6.37 (CI95%,3.25-142.8). Factors related to adherence: intervention (OR=1.88, CI95%,1.01-3.52), number of exacerbation (OR=0.66,CI95%,0.48-0.91), number of visits to health centre (OR=0.93,CI95%,0.87-1.00), severity (OR=0.677,CI95%,0.43-1.04), number of devices (OR=2.4,CI95%,1.09-5.30), SGRQ-Activity scale (OR=0.978,CI95%,0.95-1.00), SGRQ-Impact scale (OR=1.03,CI95%,1.00-1.06), inhaled-beta2-adrenérgic (OR=0.16, CI95%,0.059-0.43), xanthine (OR=0.199, CI95%,0.05-0.77). Rho coefficient=$6.07x10^{-6}$ (p=0.498). **CONCLUSIONS:** The more adherent patient was that who showed a lower number of visits to health centre, exacerbations, number of devices, level of severity, and impact on daily activities but with higher disease impact. The beta-2-adrenergic and xanthine treatment are associated with no adherence.

PRS45

HOW DO PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) USE THEIR INHALERS? COMMON MISTAKES. TECEPOC STUDY

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OBJECTIVES: To test the inhaler use in COPD patients. Frequent mistakes. **METHODS:** Design: Cross-sectional study at the beginning of a Multicenter patients' preference trial (ISRCTN15106246) Patients: 465 COPD patients from 9 health care centres, with inhaled treatment, written consent. Non-probabilistic consecutive sampling. Variables: inhaler devices, performance of correct inhalation technique, type of mistakes. Age, sex, Inhalatory pick flow, COPD severity stage, prescribed medication. Basal dyspnea index (BDI). Statistical analysis: Mean, frequency. 95% confidence interval. **RESULTS:** Predominance of males (91.4%), mean age 69.8 years (CI95%,69.00-70.59); FEV1(mean)=55.91%(IC95:53.62-58.2), mixed respiratory pattern (65.9%). Severity stage: 15.7% mild, 44.1% Moderate, 40.3% Severe. Pharmacological treatment: inhaled-beta2-adrenergic (88.8%); inhaled-corticosteroids (76.7%); inhaled-anticholinergic (70.7%); mucolitycs (19.4%); xanthine (7.3%); oral-corticosteroids (1.3%). BDI: grade 2. Inhalation technique: 84.9% had received instruction about inhalation techniques (48.6% from neumologist, 42.1% from general practitioner). The instruction was an explanation without device (59.6%). 67.3% of patients used Handihaler, 54.8% Accuhaler, 31.8% Turbuhaler, 26.9% pressurised metered dose inhaler (pMDI). The 91.3% of patients performed an incorrect inhalation technique with handihaler, 89.5% with Turbuhaler, 85.6% with Accuhaler and 91.7% with pMDI. The most common mistakes in all devices were related to the action consist on: emptying or almost emptying the lungs before activating the spray (79.8%) and holding breath for at least 8-10 seconds or for as long as possible when inhalation is complete (69.5%). The most common mistakes per device were related to: repeating the inhalation with Handihaler (10%), Loading the dispenser correctly in Accuhaler (8.2%) or Turbuhaler (16.6%) and hand-breath coordination in pMDI (52.8%). **CONCLUSIONS:** A high percentage of patients with COPD performed an incorrect inhalation technique although they had been received instruction about this. The most common mistakes are more related to the patient's attitude than to the type of device.

PRS46

TECEPOC STUDY. HOW TO IMPROVE THE INHALATION TECHNIQUES IN PATIENT WITH COPD. THE INFLUENCE OF PREFERENCES

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OBJECTIVES: to test the efficacy of two educational interventions to improve the inhalation techniques in patients with COPD and the influence of patient' preference. **METHODS:** Design: Multicenter patients' preference trial or comprehensive cohort design ISRCTN15106246. Patients: 465 COPD patients (to detect a difference between groups of 25%, 80% statistical power, 95% confidence level, 40% expected losses), with inhaled treatment, written consent. Non-probabilistic consecutive sampling. Allocation: Patients without strong preferences for a treatment are randomised: RCT group (block randomization), and those with strong preferences are given their choice: PPS group. Variables: Primary outcomes: Performance of correct inhalation technique. Secondary outcomes: Pick flow, dyspnea (Baseline dyspnea index), Functional status (forced spirometry). Interventions: Intervention-A: Written information. A leaflet with the correct inhalation technique for the main inhaler devices used in our area. *Intervention-B:* Intervention-A + individual training (by instructors). Follow-up: 3 month, visits: baseline, 1 month, 3 month. Statiscal analysis: Mean, frequency, 95% confidence interval at baseline. Number Needed to Treat for a benefit (NNT) was calculated. Intention to treat analysis. **RESULTS:** Predominance of males (91.4%), mean age 69.8 years (CI95%, 69.00-70.59); FEV1(mean)=55.91% (IC95%, 53.62-58.2), mixed respiratory pattern (65.9%). Severity stage: 15.7% mild, 44.1% Moderate, 40.3% Severe. Pharmacological treatment: inhaled-beta2-adrenergic (88.8%); inhaled-corticosteroids (76.7%); inhaled-anticholinergic (70.7%); mucolitycs (19.4%); xanthine (7.3%); oral-corticosteroids (1.3%). BDI: grade 2. Primary outcome: better inhalation technique (p=0.002) in the PPS group, NNT=7.4 (IC95%, 4.52-20). Among the RCT cohorts: there was no difference between control and intervention A and there were statistically significative differences between intervention B versus control (p<0.0001), NNT=2.44 (IC95%, 1.87-3.5) and versus intervention A, NNT=2.85 (IC95%, 2.08-4.56). In the PPS cohorts: there was a difference (p<0.0001) between intervention B versus intervention A, NNT=2.33 (IC95%, 1.5-3.2). **CONCLUSIONS:** The performance of a correct inhalation Technique improves with monitor training. The patients' preferences enhance the efficacy of intervention.

PRS47

RELATIONSHIP BETWEEN MEDICATION ADHERENCE AND QUALITY OF LIFE IN COPD – SYSTEMATIC REVIEW

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OBJECTIVES: Adherence and health-related quality of life (HRQoL) are two important indicators in determining success of drug treatments. Although medication adherence and HRQoL have been studied intensively, less is known about the association of these factors. This research aims to undertake a systematic review of the published literature on the relationship of medication adherence and HRQoL in patients with chronic obstructive pulmonary disease (COPD). No comprehensive review has been published in this topic so far. **METHODS:** Peer-reviewed English-language articles that examined the relationship between adherence/compliance/persistence to medication and HRQoL in COPD were identified through database (Medline, EMBASE) searches. Reports until April 2013 were screened. Papers related to oxygen therapy were excluded. **RESULTS:** Of the 243 papers reviewed, eight studies met the inclusion criteria and were analyzed in our systematic review. Evidence suggests that relationship between medication adherence and HRQoL is dual. Non-adherence does not have a clear negative impact on HRQoL. Adherence to medication may affect HRQoL due to more factors, such as effectiveness/efficacy and side effects of the medication, daily life limitation and social stigmatization caused by the therapy. Effect of non-adherence on HRQoL can be derived from the resultant of these factors. Nevertheless, HRQoL may also influence patients' drug use; poor or good HRQoL may trigger non-adherence. Relationship between adherence and HRQoL may differ depend on the duration of the previous therapy (as therapy in newly diagnosed COPD patients may improve HRQoL more than in patients treated previously for longer durations) and on the study design (cross-sectional versus longitudinal follow-up study) as well. **CONCLUSIONS:** Association of medication adherence and HRQoL is multiple. Results from previous studies are limited. Further scientific evaluations are needed to better understand the dynamics between these factors. Such information would be critically important and needs to be considered when integrating adherence into health-economic evaluations.

PRS48

ESTIMATION OF GENERIC UTILITIES IN SPANISH CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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OBJECTIVES: Chronic obstructive pulmonary disease (COPD) is a major public health problem and one of the leading causes of chronic morbidity and mortality worldwide. This study aims at determining generic utilities for Spanish COPD patients stratified by international guidelines GOLD 2006 (airflow limitation) and GOLD 2013 (airflow limitation, exacerbation history and symptoms), and Spanish guidelines GesEPOC (clinical phenotypes). **METHODS:** Multicentre, observational, cross-sectional study, carried out in 15 Pulmonology Spanish public services, including patients aged 40+, diagnosed with COPD, who have not experienced an exacerbation in the previous 2 months and receiving pharmacological treatment for COPD. Utilities were derived from EQ-5D-3L scores. Medians, means and standard deviations (SD) were computed for groups of patients based on GOLD 2006, GOLD 2013 and GesEPOC classifications. Differences in median utilities between groups were assessed by means of Kruskal-Wallis tests. Post-hoc pair-wise comparisons were based on Wilcoxon tests (Bonferroni-adjusted). **RESULTS:** A total of 346 patients were included in the analysis. Statistically significant median differences in utilities by groups of patients were found. GOLD 2006: moderate (n=135, median=0.87, mean=0.81, SD=0.22); severe (n=145, median=0.80, mean=0.71, SD=0.29); very severe (n=66, median=0.67, mean=0.57, SD=0.35); (p<0.001). All pair-wise comparisons were statistically significant (p<0.001). GOLD 2013: group A (n=28, median=0.98, mean=0.94, SD=0.06); group B (n=66, median=0.87, mean=0.80, SD=0.22); group C (n=30, median=0.98, mean=0.87, SD=0.24); group D (n=222, median=0.74, mean=0.66, SD=0.30); (p<0.001). All pair-wise comparisons were statistically significant (p<0.002), excepting groups A and C comparison. GesEPOC: (A) non-exacerbator (n=215, median=0.84, mean=0.78, SD=0.23); (B) overlap COPD-asthma (n=21, median=0.80, mean=0.80, SD=0.19); (C) exacerbator with emphysema (n=46, median=0.74, mean=0.59, SD=0.40); (D) exacerbator with chronic bronchitis (n=64, median=0.74, mean=0.62, SD=0.33); (p<0.001). Pair-wise comparisons between phenotypes A and C (p<0.002) and phenotypes A and D (p<0.001) were statistically significant. **CONCLUSIONS:** Generic utilities are associated with airflow limitation, exacerbation history, symptoms and clinical phenotypes in a sample of Spanish COPD patients.

PRS49

PATIENT-REPORTED OUTCOME (PRO) CLAIMS IN PRODUCTS APPROVED FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASES (COPD) IN EUROPE AND THE UNITED STATES

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OBJECTIVES: 1) To identify COPD products approved with a Patient-Reported Outcome (PRO) labeling claim in Europe and the USA, and 2) to list the differences found in Europe vs. the USA in terms of products and labeling. **METHODS:** The search was performed on the FDA- and EMA-approved medicinal product labels and medical reviews/scientific discussions (from January 1995 - February 2013 inclusive). **RESULTS:** A total of 25 COPD products were retrieved: 11 were approved by the EMA and 14 by the FDA. Only three INN were approved by both agencies (aclidinium bromide, indacaterol, and roflumilast), representing 11 products (EMA, n=8; FDA, n=3). Out of the 25 products approved, 15 have a PRO claim (EMA, n=8; FDA, n=7). When focusing on the INN approved by both agencies, the review showed that the FDA and the EMA agreed on the granting of a PRO claim (i.e., "yes" for aclidinium bromide and indacaterol, and "no" for roflumilast). The FDA and the EMA reviewed the same clinical studies. However, the labeling text differs between the agencies. The FDA label of aclidinium bromide does not provide any mention of results measured by the St. George's Respiratory Questionnaire (SGRQ) and the Transition Dyspnoea Index (TDI), while the EMA label does. As for indacaterol, the FDA label does not mention any TDI results, while the EMA label does. Reasons for these discrepancies are found in the FDA medical reviews. The TDI has been assessed as inadequate for use as a CT endpoint. As for the SGRQ, the results met the threshold of clinically meaningful improvement in only

one study. **CONCLUSIONS:** Our review showed that PROs are often included in COPD product labels in Europe and in the USA. Although the FDA and the EMA agree on a general level, the FDA seems more restrictive in the label wording.

PRS50

STUDY OF QUALITY OF LIFE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND SYMPTOM ASSESSMENT DIFFERENCES BETWEEN PATIENTS AND FAMILY MEMBERS

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OBJECTIVES: To assess the relationship between the questionary of quality of life "COPD assessment test" (CAT) and clinical, functional and comorbidity parameters and compare patient perceptions of symptoms with that of their family members. **METHODS:** We analysed demographic (age, sex, BMI), lung function (FEV_1%) and comorbidity variables (Charlson index) in patients with stable COPD. Patients and family members independently completed the CAT (family members reported their observations of the patient). **RESULTS:** We included 70 patients (83% men, mean age 72±9.4 years, BMI 27.8±4.2 kg/m^2, Charlson index (ChI) 2.41±1.7, mean FEV_1% 57.1±15.1%. Air flow limitation (GOLD): 7 patients (9%) mild, 36 (53%) moderate, 24 (34%) severe and 3 (4%) very severe. There was a significant negative correlation between CAT and FEV_1% (r=-0.265, p<0.0028) but no correlation between CAT and ChI, age or BMI. A comparison of CAT scores between the patients and their family members showed that 61% of the patients underestimated and 33% overestimated their symptoms (CAT scores: 15.5±7.9 (patient) vs. 17.1±7.7 (family) (p<0.038); correlation: (r=0.72; p<0.001). We observed correlations in the 8 CAT items. We found significant differences between the patients and their family members in items 1: coughing (p<0.015), 3: chest tightness (p<0.005) and 6: confidence leaving home (p<0,015) and in overall score (p<0.038). **CONCLUSIONS:** 1. We found a negative correlation between the CAT and FEV_1but not between the CAT and Charlson index. 2. Patients underestimate their symptoms. Cough, chest tightness and confidence leaving home are the issues items that had the greatest discrepancy between patients and family members.

PRS51

COMPARISON OF TREATMENT SATISFACTION IN PATIENTS WITH ASTHMA TAKING LEUKOTRIENE MODIFIERS VERUS THOSE TAKING INHALED CORTICOSTEROIDS

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OBJECTIVES: To assess treatment satisfaction between patients with self-reported asthma for two classes of asthma treatments, leukotriene modifiers (LM group) and inhaled corticosteroids (IC group), using a novel patient community in the U.S. **METHODS:** Participants were identified via MediGuard, a digital patient platform where patients enroll online to be part of a digital patient community. All information was obtained through participant self-report. Patients were invited to complete the Treatment Satisfaction Questionnaire for Medication (TSQM), a patient reported outcome (PRO) instrument, at random time points between 2009 and 2011. Domain scores of the TSQM were compared between the IC and LM groups using regression analyses, adjusting for age, gender, self-reported severity and number of co-medications. **RESULTS:** A total of 736 patients were included for the IC group, and 647 for LM group. Average ages were comparable (56.3 years (SD=13.8) for IC; 54.9 (13.5) for LM). Both groups were predominantly female (76.3% IC; 83.2%, LM). Effectiveness domain scores were similar between IC and LM groups (p=0.502). LM users reported significantly higher scores (i.e., increased satisfaction) for other domains: side effects (97.1 (SD=0.8) vs. 93.5 (0.7), resp.); convenience (89.2 (0.8) vs. 81.6 (0.7), resp.); global satisfaction (72.3 (1.1) vs. 67.3 (1.0). **CONCLUSIONS:** Patients in the LM group reported higher satisfaction in the convenience and global satisfaction domains than the IC group. Patients in the LM group reported less interference with side effects than the IC group. Providing patients with information on population-based satisfaction scores for these two medications could help inform patients' treatment selection decisions.

PRS52

SYMPTOMS OF COPD IN URBAN RUSSIA AMONG ADULTS 40 YEARS AND OLDER

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OBJECTIVES: Chronic obstructive pulmonary disease (COPD) is a major cause of disability worldwide, but awareness of COPD and information regarding the burden of this disease are lacking worldwide, including Russia. The aim of the current study was to assess the prevalence of COPD symptoms (cough with mucous, wheezing, and shortness of breath) among a representative sample of adults aged 40 and above in major cities in Russia. **METHODS:** Data was obtained from the 2011 Russia National Health and Wellness Survey, a cross-sectional survey of the adult population in the city adult population in Russia which includes information on awareness, experience, and diagnosis of medical conditions, health care-related attitudes, demographic characteristics, and health outcomes. The frequency of COPD symptoms was assessed using the Lung Function Questionnaire, and health status was assessed using the SF-12v2. Those experiencing a symptom at least 'sometimes' were compared to those who experienced the symptom 'rarely' or less using independent-samples t-tests. **RESULTS:** A total of 5920 adults aged 40 and older completed the survey. After weighting, 45%, 27%, and 18% reported shortness of breath, coughing up mucous, and wheezing, respectively, and 54% reported at least one symptom. Only 23% of those surveyed were aware of COPD; awareness of COPD was greatest among those with the most symptoms but even among those with all three symptoms, only 31% were aware of the condition. Experience of each symptom was associated with worse mental and physical component summary scores on the SF-12v2, with decrements ranging from 2-6 points depending on the symptom and score considered. **CONCLUSIONS:** Respiratory symptoms are common among adults living in Russian cities, which may indicate high COPD incidence. Awareness of COPD in Russia is lacking. A high proportion of adults aged 40 and older in Russia report frequent respiratory symptoms, and these symptoms are associated with significantly worse health status.

PRS53

THE RELATIONSHIP BETWEEN COPD ASSESSMENT TEST (CAT) AND EQ-5D IN A REAL WORLD PATIENT POPULATION

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OBJECTIVES: COPD is a chronic lung disease that has a detrimental effect upon patient's quality of life. The COPD Assessment Tool (CAT) has been developed to measure the impact of the disease. This research explores the relationship between the disease-specific CAT, and the general health related utility measure EQ-5D. **METHODS:** COPD is a chronic lung disease that has a detrimental effect upon patient's quality of life. The COPD Assessment Tool (CAT) has been developed to measure the impact of the disease. This research explores the relationship between the disease-specific CAT, and the general health related utility measure EQ-5D. **RESULTS:** A scatter plot relating CAT score to EQ-5D showed that the relationship is non-linear. Variance of the EQ-5D score increased with CAT score, suggesting the increasing influence of confounding factors for patients reporting a higher CAT score (CAT score range variance: 0-10: 0.013, 11-20: 0.026, 21-30: 0.050 and 31-40: 0.126). A generalized linear model was used to account for the non-linear relationship, and control for confounding influences of age, gender, physician-perceived COPD severity and number of concomitant conditions, with no assumption of constant variance. The relationship between CAT and reversed EQ-5D was positive and significant (coefficient 0.070, p-value <0.0001), illustrating higher CAT score was associated with lower EQ-5D. A one point increase in CAT score resulted in an approximate 7.2% relative decrease in EQ-5D score. Similarly, significant (p-value <0.0001) negative relationships observed for older patients (coefficient 0.016), female gender (coefficient 0.147), greater severity (coefficient 0.469), and a higher number of comorbidities (coefficient 0.070). **CONCLUSIONS:** Increasing COPD impact as measured by the CAT was associated with lower EQ-5D scores. However, the increasing variance of EQ-5D for patients with higher CAT scores demonstrates the need for both COPD impact and overall health status assessment.

PRS54

THE RELATIONSHIP BETWEEN ASTHMA-SPECIFIC QUALITY OF LIFE AND MEASURES OF ASTHMA CONTROL AND GENERIC QUALITY OF LIFE

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OBJECTIVES: Previous research has indicated a strong relationship between asthma symptoms and asthma-specific quality of life (QoL). However, past measures of asthma-specific QoL typically confound symptoms and functional impairment with QoL, which in turn may cause a misleadingly high inter-correlation. The current research uses a newly developed measure of asthma-specific QoL (the RAND-Impact of Asthma on Quality of Life; RAND-IAQL) that controls for asthma symptoms and functional impairment while assessing the degree of asthma impact or burden. Using this new measure, we model the relationship between asthma specific quality of life, generic quality of life, asthma control, and comorbid conditions commonly associated with asthma. **METHODS:** Using a diverse sample of adults with asthma (N=2032), we use structural equation models (SEM) to establish the relationships and suppression effects of asthma control, symptoms, comorbidities (e.g., COPD, Sinusitis), and multiple PROMIS QoL instruments (including anxiety and social QoL) on the prediction of asthma-specific QoL. SEM models will be presented sequentially in order to evaluate the relative utility of increasingly complex models using likelihood ratio tests and changes in the amount of IAQL variance that is accounted for by each added predictor (latent) variable. **RESULTS:** Close fitting SEM models suggest that "interference" caused by asthma, an indicator commonly used to measure asthma control, is most strongly related to asthma-specific QoL. Contrary to the research literature, symptoms of asthma (including shortness of breath, wheezing, and cough) and comorbid diseases are less strongly related to asthma specific QoL than are general assessments of interference and generic measures of anxiety and limitations in social functioning. **CONCLUSIONS:** Asthma-specific QoL is best understood as the degree to which asthma impacts or burdens ones daily life. While asthma symptoms, control, and general QoL are highly inter-correlated, asthma control (primarily interference) is differentially predictive of asthma-specific QoL.

PRS55

THE RAND NEGATIVE IMPACT OF ASTHMA ON QUALITY OF LIFE ITEM BANK AND SHORT-FORMS

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OBJECTIVES: In response to recommendations from the 2010 NHLBI Asthma Outcomes Workshop, we developed a new system for measuring the impact of asthma on quality of life (QoL) that avoids confounding QoL with asthma symptomatology and functional impairment. This presentation summarizes the process of developing and validating an item bank and short-forms that measure patients' perceptions of the impact or bother of asthma on their life. **METHODS:** Focus groups, supplemented by literature review and expert panel recommendations were used to identify key QoL dimensions and develop a pool of items which were refined based on cognitive interviews. Items were field-tested using a diverse national sample of adults with asthma (N=2032). Modern measurement theory was used to develop an item bank and short forms. We validated our short-forms against the Marks AQLQ; ACT; and generic QoL measures. Discriminant validity was examined by evaluating scores from respondents who differed according

to indicators of asthma severity, control, health care utilization and comorbidity. **RESULTS:** A total of 661 QoL statements were identified from focus group transcripts and subsequently used to generate a pool of 112 items in 16 different content areas. Psychometric evaluation of field test data yielded a 65-item unidimensional item bank, 4 and 12-item short forms (alpha = .86 and .93, respectively), and a simulated computer adaptive test suggesting that as few as 5-items are needed to obtain highly precise estimates of the impact of asthma on QoL (IAQL). Our measures correlated highly with Marks' AQLQ and more strongly with the PROMIS global physical than mental scale. IAQL was greater in persons with indicators of more severe asthma, less asthma control, and in persons with greater health care utilization. **CONCLUSIONS:** The RAND-IAQL item bank is a new freely available system for measuring the impact of asthma on Qol that will complement other patient-reported outcomes.

PRS56

HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN NORTH INDIA

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OBJECTIVES: Chronic obstructive pulmonary disease (COPD) is a major health problem in India and constitutes an important cause of mortality and morbidity. A cross sectional study was undertaken to assess health related quality of life (HRQL) and its determinants in COPD patients from India. **METHODS:** A total of 126 patients (73.81% male, 26.19% female) recruited using convenient sampling in a cross-sectional study. Eligible patients assessed for socioeconomic status, anthropometric measures, COPD severity, dyspnea, and health status using a validated Hindi (Regional Language) version of St. George Respiratory Questionnaire (SGRQ). Linear regression model was used to examine association between risk factors and HRQL with adjustment of age and sex. **RESULTS:** Mean total score for SGRQ was 52.66±12.89 showing marked impairment of HRQL. Impairment was associated with the severity of airway obstruction but within each GOLD stage the variation (SD) was wide [Stage I: 47.8±12.3 (n=14); Stage II: 49.28±11.69 (n= 47); Stage III: 53.47±11.69 (n= 44); Stage IV: 61.75±14.14 (n= 21)]. Regression analysis showed that body mass index, Forced expiratory volume in 1 minute (FEV_1), dyspnea grade and depression were associated with poor HRQL. **CONCLUSIONS:** HRQL of COPD patients was significantly impaired across all severities. Marked impairment of HRQL was found even in patients with milder disease.

RESPIRATORY-RELATED DISORDERS – Health Care Use & Policy Studies

PRS57

THE FIRST EXPERIENCES WITH REASSESSMENTS AND APPRAISALS OF CONDITIONALLY APPROVED EXPENSIVE AND ORPHAN DRUGS IN THE NETHERLANDS (2006-2013)

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OBJECTIVES: To provide an overview of the first experiences with reassessments and appraisals of expensive drugs after 4 years of coverage with evidence development (CED) in The Netherlands. **METHODS:** Completed assessments, reassessments and appraisals were summarized. Special attention was paid to the consistency of the conclusions at the initial assessment (T=0) with those at the reassessment (T=4), to the execution of the research proposals, and to the consequences of the reassessments and appraisals. **RESULTS:** From 2006 until 2012, 46 T=0 assessments have been performed: 36 were approved for CED and 10 were declined. By mid 2013, the 4 years' period of CED had ended for 25 drugs. For four drugs, T=4 assessments and appraisals have been completed: omalizumab and ranibizumab for treatment of patients with severe asthma and macula degeneration respectively; and the orphan drugs alglucosidase alfa and agalsidase for treatment of patients with Pompe's disease and Fabry's disease. Based on all the available evidence, conclusions regarding effectiveness were mostly consistent between T=0 and T=4 assessments. However, results from the requested outcomes research studies between T=0 and T=4 were of mixed quality and therefore of limited relevance for the T=4 assessment. Nevertheless, most data from the outcomes research were useful to evaluate appropriate usage in daily practice and resource use. The resource use data was applied in health economic models. In contrast, the input for the clinical effectiveness component in the cost-effectiveness assessment was generally derived from pivotal clinical studies already available at T=0. The T=4 appraisals led to a societal debate on the cost-effectiveness of these drugs. The appraisals resulted in pragmatic solutions like a pay-for-performance agreement and ongoing price negotiations. **CONCLUSIONS:** Outcomes research as part of a CED in The Netherlands has yielded some information regarding the costs and appropriate use in daily practice of expensive drugs. The results from these CED experiments (or lack thereof) have been used in the subsequent negotiations on financial or risk-sharing arrangements.

PRS58

HEALTH TECHNOLOGY ASSESSMENT OF COMPANION DIAGNOSTIC BIOMARKERS AS GATEKEEPERS FOR PERSONALIZED MEDICINE MARKET ACCESS

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OBJECTIVES: Personalized medicines (PM) are the subset of drug therapies whose efficacy and/or safety can be predicted or monitored based on the status of specific molecular biomarkers. In most cases, access to the applicable biomarker test (also called a companion diagnostic (CDx) if the biomarker/test is regulatory approved and included in the drug label) is critical for early patient access to the specific PM the biomarker status informs. Recent examples of PM and CDx/biomarker test combinations include crizotinib/EML4-ALK test in lung cancer; clopidogrel/CYP2C19 test in cardiovascular disease; natalizumab/ JC virus test in multiple sclerosis; maraviroc/HIV tropism test in HIV infection. To define key evidence required by health technology assessment (HTA) agencies and payers for reimbursement and access decision making, we evaluated global CDx/biomarker test HTAs. **METHODS:** HTA Watch conducted a search of global HTA agency websites for HTAs reviewing CDx/biomarker tests. HTAs were reviewed for key clinical, economic and other evidence criteria scrutinized or raised as concerns by agencies, and potential impacts/correlations of such evidence on agency reimbursement recommendations, distinguishing between true CDx and non-CDx biomarker tests. **RESULTS:** CDx/biomarker tests reviewed by HTA agencies included those used to inform oncology, cardiovascular or infectious disease, neurological disorder, and allergy/asthma treatments. Evidence scrutinized by HTA agencies included demonstration of clinical validity and utility versus competing tests or no test, cost-effectiveness and budget impact associated with implementing CDx testing, size of the responder population and, for solid tumor indications, the practicality of obtaining/availability of sufficient biopsy material for biomarker testing. **CONCLUSIONS:** CDx/biomarker tests are necessary gatekeepers for informing use of PM drugs, especially in early lines of treatment when alternative treatments exist. Since optimal PM market access requires CDx/biomarker test availability it is critical that the value of CDx/biomarkers is demonstrated through evidence development that addresses key HTA agency and payer needs.

PRS59

DIRECT AND INDIRECT BURDEN ASSOCIATED WITH PARENTS WHOSE INFANT HAS BEEN HOSPITALIZED FOR A LOWER RESPIRATORY TRACT INFECTION (LRTI) IN GREECE

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OBJECTIVES: Severe respiratory infections result in infant hospitalizations for LRTI, of which the most common cause is due to respiratory syncytial virus (RSV). The economic impact of pediatric hospitalizations for respiratory infections is substantial; however the socioeconomic burden it has on parents and caregivers is less understood. **METHODS:** Data was attained from the Parent Burden Study: A prospective multinational study to determine the humanistic and economic burden of infant LRTI hospitalizations during the RSV season. Direct health care resource utilization including length of hospitalization stay (LOS) and intensive care use (ICU) were obtained from medical chart reviews. Indirect economic burden borne by parents were measured in parent surveys administered at the time infants were discharged. Lost work productivity was assessed via the Work Productivity and Activity Impairment questionnaire, specific to caregivers of children hospitalized with respiratory illness. **RESULTS:** A total of 47 infants (35 term, 12 preterm), <1 year of age were included in the Parent Burden Study in Greece. A total of 74% of infants had a confirmed diagnosis of RSV. The mean LOS was 7.50 days (range: 0.66- 40.97, 6.33 days term, 10.91 days preterm). 8.5% (2.9% term and 25% preterm) required ICU admission and 85.1% had supplemental oxygen and/or mechanical ventilation support (80% term, 100% preterm). Among fathers, the average absenteeism (time away from work) was 19.2%, presenteeism (impaired productivity while at work) was 45.6%, and overall work impairment was 55.3%. For mothers, the average absenteeism was 47.0%, presenteeism was 35.0% and overall work impairment was 54.0%. On average, fathers reported 62.1% activity impairment and mothers reported 93.5% due to their child's hospitalization. A total of 51.1% of families required family or arranged childcare to assist siblings during the hospitalization. **CONCLUSIONS:** This study demonstrates, in addition to direct morbidity burden, infant LRTI hospitalizations have a substantial socioeconomic impact on parents and caretakers in Greece.

PRS60

PATTERNS IN ASTHMA MEDICATIONTREATMENT IN THE UNITED STATES

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OBJECTIVES: Despite evidence of medication adherence benefits, many patients do not take their medications as prescribed. The objective of this study was to understand asthma medication treatment patterns among asthma patients in the US by initial asthma treatment medication. **METHODS:** A retrospective database analysis was conducted using Marketscan Commercial and Medicare Supplement Data. Patients were identified between January 1, 2005 through March 31, 2011 based on asthma related hospitalization, emergency room visit or at least 2 office visits at different dates within 1 year. Asthma drug utilization patterns were analyzed among patients aged 12 years or older who were initiated on an asthma medication (without asthma maintenance therapy in the past 12 months) and had at least 24 months traceable insurance coverage information since their initiation of the medication. **RESULTS:** Among the selected patients (n=88,567) being followed up for 24 months, approximately 30% of patients switched treatments at least once regardless of their initial asthma treatment. The three most common medications were montelukast sodium (>90% Singulair), fluticasone propionate and salmeterol (Advair) 250/50mcg and 100/50mcg. One prevalent prescription change was to step down the steroid component. Patients initiating asthma treatment on combination therapy (i.e. Singulair and inhaled corticosteroids) is low (between 0.3% - 1.8%) and switch patterns show that over 50% of patients switch to Singulair monotherapy. Regardless of their initial treatment and medication switches, on average, asthma patients initiate their treatment with 2-3 months days supply; have a gap of over 6 months (~200days) and switch to another treatment. **CONCLUSIONS:** Our results show the high frequency of asthma medication patterns changes. Despite the avail-

ability of prescription of asthma medications, there appears to be an unmet need and further research is necessary.

PRS61

ECONOMIC EVALUATION OF ENHANCED ASTHMA MANAGEMENT: A SYSTEMATIC REVIEW

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OBJECTIVES: To evaluate, compare, and assess the quality of the studies on the cost-effectiveness of enhanced management (either as adjunct to usual care or alone) *vs.*usual care alone or none at all. **METHODS:** Scientific databases (ScienceDirect, Wiley Online Library, (EbscoHost – MEDLINE, CINAHL, PSYInfo), (OvidSP – EMBASE, MEDLINE), and Scopus) were searched for published journal articles in English language from year 1990 to 2012, using the search terms "asthma AND (intervene OR manage) AND (pharmacoeconomics OR economic evaluation OR cost effectiveness OR cost benefit OR cost utility)". Hand search was done for local publishings. Only studies with full economic evaluation on enhanced management (either as adjunct to usual care or alone) were included. Selected studies were data abstracted and assessed for their quality of economic evaluation using the Quality of Health Economic Studies (QHES) instrument, and quality of evidence. **RESULTS:** A total of 14 studies were included. There were three distinct modes reviewed: environmental control, self-management, education. Most of the enhanced managements were found to be cost-effective with ICER ranged from dominant to $26700.00 per unit of outcome. Overall, the mean score of QHES was 76.69% (SD 9.26). For the quality of evidence, 'clinical effect sizes, adverse events & complication', baseline clinical data, resourse use, and costs components were ranked mainly 1 or 2 (best or nearly best) in all studies. For 'utilities' component, one study ranked 5 because it used visual analogue scale to obtain patient preference values. **CONCLUSIONS:** Despite the low qualities of the reviewed studies, it overall suggests that enhanced management (either as adjunct to usual care or alone) is mostly cost-effective than the usual care or none at all; environmental control is considered the most cost-effective, and there is also strong evidence for self-management, but provided the mode of it is made available, affordable, and accessible then this shall be worth to be adapted in one's setting.

PRS62

ECONOMIC EVALUATION OF THE IMPACT OF NEW TREATMENT ALTERNATIVES ON MARKET DYNAMICS IN RESPIRATORY DISEASES; A CASE STUDY IN TURKISH HEALTH CARE SYSTEM

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OBJECTIVES: Economic evaluation of the change in market dynamics of a sample ProductA[1] through its inclusion in Therapeutic Equivalence Band (TEB) (with products B[2] and C[3]) between 2010 and 2012 in Turkish health care system. **METHODS:** IMS Dataview was analyzed for 2010-2012 unit sales values (market entry timeline for products A, B, C is 2006, 2009 and 2009, respectively) in the TEB. IMS Medical Index is used for estimating prescription data for the corresponding products. Assumptions on median patient adherence (receipt of prescribed treatment in pharmacy) are applied to prescription data in order to calculate unit sales (prediction). Deviation calculations and sensitivity analysis on market dynamics were performed in Microsoft Excel-2007. **RESULTS:** Deviations between unit sales predictions and realizations for products A, B and C occurred as +11.48%, -5.41% and -20.85% in 2010, -10.16%, +8.14% and -53.87% in 2011 and -31.89%, +28.92% and -67.76% in 2012 respectively. Negative deviation values indicate that receipt of prescription cannot be transformed to receipt of the prescribed product in pharmacy, however positive deviation values correspond to receipt of a product in pharmacy which is different from the content of the prescription. **CONCLUSIONS:** The TEB system allows receipt of a different product than prescription. This study shows alteration of market dynamics in pharmacy as a change from prescribed inhaler option (as negative deviation value), which is linked to receipt of another inhaler option (as a positive deviation value) within the same TEB. Real life data may be collected for further analysis of TEB system in dynamics of corresponding market. [1]Originator treatment in TEB-Novartis-Budesonide(400mcg)&Formoterol(12mcg), [2]Second treatment in TEB-Bilim Pharma, [3]Third treatment in TEB-Abdi Ibrahim Pharma.

PRS63

ESTIMATES OF PRICE AND INCOME ELASTICITY IN GREECE: GREEK DEBT CRISIS TRANSFORMING CIGARETTES INTO A LUXURY GOOD

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OBJECTIVES: Greece was long reported to show a smoking prevalence over 40% on adult population, as efforts to constrain smoking were rather ineffective. Following a sharp fall in cigarette consumption for 2012, our objective is to assess smokers' sensitivity to cigarette price and consumer income changes as well as to project health benefits of an additional tax increase. **METHODS:** Analysis includes the conventional model of demand, the myopic addiction model and the rational addiction model. Cigarette consumption for the period 1994-2012 was the dependent variable with Weighted Average Price as a proxy for cigarette price, GDP as a proxy for consumer income and dummy variables reflecting smoking restrictions and antismoking campaigns. Values were computed to natural logarithms and regression was performed. Then, 4 scenarios of tax increase were distinguished in order to calculate potential health benefits. **RESULTS:** Addiction models are unable to provide statistically significant information following a nearly 23.5% drop in consumption during 2012. Short-run price elasticity is estimated at -0.441 and short-run income elasticity is estimated at 1.040. Antismoking campaigns were found to have a statistically significant impact on consumption. Results indicate that, depending on the level of tax increase, annual per capita consumption could fall by up to 607.99 cigarettes; tax revenue could rise by at least €39 million, while up to 595,866 smokers could quit and up to 2,696 smoking related deaths could be averted. **CONCLUSIONS:** Price elasticity estimates are greater than previous studies in Greece and consistent with literature internationally, while income elasticity estimates are far greater. With cigarettes regarded as a luxury good, a great opportunity is presented for decison makers to counter smoking. Increased taxation, along with focused antismoking campaigns, law reinforcement (to ensure compliance with smoking bans) and intensive control for smuggling could inflict a massive blow to the tobacco epidemic in Greece.

PRS64

PREVALENCE OF COMORBIDITIES AMONG CHRONIC COPD PATIENTS IN THE UNITED STATES

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OBJECTIVES: COPD is the third leading cause of death with increasing mortality while other chronic condition mortality rates are decreasing. This may be due to the fact that COPD is a complex chronic condition with a complicated diagnosis and treatment guideline in an aging patient population with increasing comorbid conditions. The objective of this study was to understand the prevalence of comorbid conditions among COPD patients in the US. **METHODS:** A retrospective database analysis was conducted using Marketscan Commercial and Medicare Supplement Data from year 1/1/2010 to 12/31/2011. Patients were included if they had continuous medical and pharmacy benefits coverage for at least 12 months after their first COPD diagnosis defined as primary or ancillary ICD-9 codes of 491.xx, 492.xx, or 496.xx and were between the ages of 40 and 90 years old at the time of diagnosis. Univariate descriptive analyses were conducted to quantify comorbid disease prevalence. **RESULTS:** Among the selected patients (n=231,827), 95.1% (n=220,519) had medical claims (ICD-9 codes) for diagnoses beyond COPD within 12 months of their COPD diagnosis. The majority of patients were over 65 years old (61.4%, n=135,366). Over 60% (n=130,325) of the patients had more than 3 comorbid conditions. The most common were hypertension (64.9%, n=143,189) (ICD-9 codes 401.xx-405.xx, 415, 416, 416.8, 459.1x and 459.3x), hyperlipidemia (46.5%,n=102,498) (ICD-9 code 272.x), diabetes (27.8%, n=61,225) (ICD-9 code 249.xx, 250.xx, 253.5, 271.4, 357.2, 588.1, 790.29), coronary artery disease (27.4%, n=60,364) (ICD-9 code 414.0x, 414.3, 414.4), and asthma (22.7%, n=50,113) (ICD-9 code 493.xx). **CONCLUSIONS:** Our results show the significant prevalence of comorbid conditions among COPD patients. Further research on comorbid conditions impacting COPD patient treatment adherence, COPD pathogenic pathways and worsening overall prognosis are necessary. More evidence is required to estimate the role of comorbidities in COPD.

SYSTEMIC DISORDERS/CONDITIONS – Clinical Outcomes Studies

PSY1

EXAMINING THE BURDEN OF ILLNESS OF VETERAN PATIENTS DIAGNOSED WITH OBESITY IN THE UNITED STATES

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OBJECTIVES: To examine the burden of illness of diagnosed obesity in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration (VHA) Medical SAS datasets (01OCT2008-30SEPT2012). Patients diagnosed with obesity were identified (International Classification of Disease 9th Revision Clinical Modification [ICD-9-CM] diagnosis code 278.xx) with the first diagnosis date designated as the index date. A group of patients without obesity but with the same age, region, gender and index year were identified and matched by baseline Charlson Comorbidity Index as a comparator group. The index date for the comparator group was randomly chosen to reduce selection bias. Patients in both groups were required to be at least 18 years old, and have 1 year of continuous medical and pharmacy benefits before and after the index date. Study outcomes, including health care costs and utilizations, were compared between the disease and comparator groups by using 1:1 propensity score matching. **RESULTS:** A total of 1,525,218 patients were identified for the obesity and comparison cohorts. After applying 1:1 matching, a total of 634,257 of patients were included in each group, and the baseline demographic and clinical characteristics were balanced. The obesity cohort had higher percentages of health care utilizations for inpatient (6.21% vs. 2.92%, p<0.01), emergency room (11.96% vs. 7.28%, p<0.01), physician office (99.84% vs. 60.12%, p<0.01), outpatient (99.86% vs. 60.85%, p<0.01), and pharmacy visits (89.01% vs. 61.71%, p<0.01) than the comparator group. Patients diagnosed with obesity also incurred higher expenditures in inpatient ($1,812 vs. $875, p<0.01), emergency room ($117 vs. $69, p<0.01), physician office ($2,936 vs. $1,436, p<0.01), outpatient ($3,288 vs. $1,621) and pharmacy visits ($641 vs. $423, p<0.01) compared to non-obese patients. **CONCLUSIONS:** Study results suggest that patients diagnosed with obesity incurred significantly higher costs and utilizations than non-obese patients.

PSY2

CLINICAL EFFECTIVENESS ANALYSIS OF DEFERASIROX FOR THE TREATMENT OF IRON OVERLOAD DUE TO FREQUENT BLOOD TRANSFUSIONS

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OBJECTIVES: To compare clinical efficacy and safety of orphan drug deferasirox (DSX) versus deferoxamine (DFO) in the treatment of paediatric patients (age ≤ 18 years) with iron overload from repeated blood transfusions. The underlying conditions requiring transfusion included beta-thalassaemia, sickle cell disease and other congenital and acquired anaemias (myelodysplastic syndromes, Diamond-Blackfan syndrome, aplastic anaemia and other very rare anaemias). **METHODS:** We searched CENTRAL, MEDLINE and EMBASE for relevant randomized controlled trials (RCTs) published up to April 2012. The review was conducted in accordance

with the Cochrane Collaboration guidelines and the Polish Agency for Health Technology Assessment recommendations. Calculations were performed using the StatsDirect®2.6.8 statistical package. **RESULTS:** : As a result of the systematic literature search 2 primary RCTs (subtype II A), satisfying the inclusion criteria were found: Cappellini 2006 (patients with beta-thalassaemia) and Vichinsky 2006 (patients with sickle cell disease). The results of the performed analysis proved that once-daily oral deferasirox showed similar efficacy to parenteral deferoxamine therapy in terms of decreased in LIC (liver iron concentration) and SF (serum ferritin). Treatment adherence was similar in both DSX and DFO groups. Safety analysis showed that deferasirox was safe and well-tolerated therapy. The most frequent adverse events in the deferasirox group were diarrhea, nausea, vomiting, abdominal pain and skin rash. In most cases, analysed adverse events were mild and transient. Discontinuation rates were similar in both DSX and DFO arms. **CONCLUSIONS:** Deferasirox represents an important once-daily oral agent for the treatment of chronic iron overload due to blood transfusions. Once-daily oral deferasirox has acceptable tolerability and similar efficacy to parental deferoxamine in reducing iron burden in transfused paediatric patients. Moreover, deferasirox improves patients' quality of life, may improve patient's compliance with treatment and reduces morbidity and mortality from iron overload.

PSY3

META-ANALYSIS OF EFFICACY OF ROMIPLOSTIM FOR TREATMENT OF IMMUNE IDIOPATHIC THROMBOCYTOPENIA

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OBJECTIVES: Immune (idiopathic) thrombocytopenia (ITP) is an autoimmune condition characterized by increased platelet destruction and suboptimal platelet production, resulting in low platelet counts (thrombocytopenia). Romiplostim has shown efficacy in increasing platelet counts. The objective of this study was to conduct meta-analysis and present total evidence for Romiplostim for treatment of ITP. **METHODS:** For this meta-analysis we included randomized controlled trials (RCTs) evaluating Romiplostim for the treatment of ITP. We included RCTs that compared romiplostim versus placebo for management of ITP, had a treatment duration of at least 24 weeks, were doubleblind (patients and investigators blinded) and reported data on platelet response. A systematic literature search for Etanercept trials was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interventions, year, and the two outcomes overall and durable platelet response rate. For meta-analysis, random effects and fixed effects models were used to obtain cumulative statistics. **RESULTS:** Two RCTs with a total of 125 patients were identified. The pooled response rates for Romiplostim for overall platelet response rate were 82% (95% CI 73%-90%); and for durable platelet response rate were 48% (95% CI 26%-71%). The pooled response rates for placebo for overall platelet response rate were 7% (95% CI 0%-15%), and for durable platelet response rate were 2% (95% CI 0%-4%). For overall platelet response rate the cumulative relative risk with placebo versus Romiplostim was 0.09 (95% CI 4%-14%). For durable platelet response rate, the cumulative relative risk with placebo versus Romiplostim was 0.03 (95% CI 0%-6%). **CONCLUSIONS:** Meta-analysis shows Romiplostim offers patients with Immune idiopathic thrombocytopenia an effective therapeutic option for increasing platelet counts.

PSY4

BIS SENSOR VERSUS CONVENTIONAL ANESTHETIC MONITORING: SYSTEMATIC REVIEW ON PATIENT-ORIENTED OUTCOMES

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OBJECTIVES: Adult patients who receive general anesthesia may not remain totally unconscious during surgery despite of anesthetics and analgesics care received. The retention of memory due to intraoperative awareness may cause serious clinical complications, requiring 1071 patients monitored to prevent the occurrence of one event. The proper conventional maintenance of general anesthesia is assessed with clinical signs or expired gases (ETAC/ETAG/ETCO2). Bi-Spectral Index Monitoring or BIS Sensor is a neurophysiological evaluation system that continually analyzes EEG to determine the level of intraoperative awareness. **METHODS:** We have made a literature search in PubMed to identify systematic reviews and randomized controlled trials that studied level of consciousness intraoperative or postoperative memory when used these alternatives of anesthetic monitoring. **RESULTS:** We have found nine RCT and two systematic reviews published until April 2013 and conducted our own meta-analysis on seven trials. Two studies were excluded from the synthesis for not presenting the outcome of primary interest. Three RCT of moderate heterogeneity showed no difference in the occurrence of intraoperative awareness between the BIS group and the ETAC/ETAG/ETCO2 group. The quality of evidence was considered high in one study, moderate and low in the others (26,490 patients, I2 = 45.9%, RR = 1.28, 95% CI = 0.54 to 3.03, p = 0.57). Four clinical monitoring control group studies with no heterogeneity showed that the sensor BIS was more effective, requiring between 71 and 167 patients monitored for an event of intraoperative awareness avoided. The quality of evidence of the studies was considered high (7,779 patients, I2 = 0.0%, RR = 0.42, 95% CI = 0.27 to 0.65, p = 0, 0.0001). **CONCLUSIONS:** Clinical trials published until April 2013 showed favorable results in patient-oriented outcomes of BIS group when compared to clinical monitoring group but not to ETAC/ETAG/ETCO2 group.

PSY5

MORTALITY AND SURVIVAL IN INOPERABLE OR RESIDUAL/RECURRENT CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH): A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: CTEPH is a progressive and commonly fatal disease. A systematic literature review was conducted to synthesize evidence on mortality and survival in patients with inoperable CTEPH or residual/recurrent pulmonary hypertension (PH) after pulmonary endarterectomy (PEA). **METHODS:** Using specific search terms, we systematically searched for MEDLINE- and EMBASE-indexed studies on the epidemiology of CTEPH in various regions (including Western Europe, North America, New Zealand, or Australia) without temporal limits. Among these studies, we identified those that reported mortality and/or survival for patients with inoperable CTEPH or residual/recurrent PH post-PEA. These studies then underwent analytical narrative synthesis. **RESULTS:** In all, 71 articles met the criteria for acceptance into the review. Of these, 21 described mortality or survival in patients with inoperable CTEPH or residual/recurrent PH post-PEA. The proportion of patients with inoperable disease was 27%–41% in seven registries and retrospective studies in Europe. The proportion of patients who underwent PEA was 59%–69% in two Canadian studies and 10%–65% (median 50%) in 11 European studies. Among studies with ≥18 months of follow-up, mortality was higher in patients with inoperable CTEPH (13.4%–58%, with seven of 10 studies reporting mortality rates of 13.3%–21.4%) than among those with residual/recurrent PH post-PEA (7.4% after a mean follow-up of 50 months). Overall survival was lower among patients with inoperable CTEPH than among those with residual/recurrent PH post-PEA. Survival rates for inoperable CTEPH were 73%–93% at one year (10 studies), 41%–88% at three years (nine studies), and 53%–88% at five years (five studies). In contrast, patients with residual/recurrent PH post-PEA had five-year survival rates of 89.9%–100% (three studies). **CONCLUSIONS:** Inoperable CTEPH carries a particularly poor prognosis, with survival rates lower even than those for patients who have residual/recurrent PH following PEA.

PSY6

ANALYSES ADJUSTING FOR SELECTIVE CROSSOVER SHOW IMPROVED OVERALL SURVIVAL WITH DECITABINE COMPARED WITH TREATMENT CHOICE IN DACO-016 PHASE III TRIAL

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OBJECTIVES: Among patients with acute myeloid leukemia (AML), the DACO-016 randomized study showed reduction in mortality for DACOGEN®(decitabine, DAC) compared with treatment choice (TC): at primary analysis the Hazard Ratio (HR) was 0.85 (95% CI: 0.69- 1.04; stratified log-rank p=0.108). With two interim analyses, 2-sided alpha was adjusted to 0.0462. With one year additional follow-up the HR reached 0.82 (nominal p=0.037). These data, together with significant outcomes in secondary endpoints and a positive benefit-risk resulted in approval of DACOGEN in the EU, however not in the US. With the primary analysis only showing a strong trend, the French Haute Autorité de Santé negated a mortality benefit. Though prespecified, the log-rank test could be considered not optimal to assess the observed survival difference because of the non-proportional hazard nature of the survival curves. We applied the Wilcoxon test as a sensitivity analysis. **METHODS:** Patients (age ≥ 65 years, ineligible for chemotherapy) were randomized to DAC (N=242) or TC (N=243). For testing the observed treatment effect, Wilcoxon-test is considered more powerful in the context of non-proportional hazard curves compared to the log-rank test, as the former assigns more weight to earlier events. **RESULTS:** A total of 108 (44.4%) patients in the TC arm and 91 (37.6%) patients in the DAC arm selectively crossed over to subsequent disease modifying therapies at progression, which might impact the survival beyond the median with resultant converging curves (and disproportional hazards). The Wilcoxon-test stratified by baseline age, cytogenetic-risk and ECOG performance status showed a significant improvement in OS with DAC (7.7 [6.2; 9.2] months) versus TC (5.0 [4.3; 6.3] months) (p=0.0456). **CONCLUSIONS:** Wilcoxon-test indicated significant increase in survival for DAC vs TC in patients with AML compared to log-rank test at primary analysis.

SYSTEMIC DISORDERS/CONDITIONS – Cost Studies

PSY7

BUDGET IMPACT ANALYSIS OF DEFERASIROX IN THE TREATMENT OF NON TRANSFUSION DEPENDENT THALASSEMIA IN GREECE

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OBJECTIVES: Deferasirox is an oral iron chelator that has demonstrated efficacy in reducing excess liver iron concentration (LIC) in iron overloaded non-transfusion dependent thalassemia (NTDT) patients. This analysis estimated the budget impact of reimbursing deferasirox in Greece. **METHODS:** An open cohort budget impact model was developed from the Greek health care system perspective over 5 years. Comparators included deferoxamine, deferiprone, and combination therapy (deferoxamine plus deferiprone). NTDT prevalence, drug acquisition and administration costs were from Greece (2013 €). No discounting was applied. Deferasirox clinical inputs were derived from the THALASSA trial. Rate of reduction in LIC (decrease of 26%) was applied each year for deferasirox. This was assumed the same for all comparators. Patients remained on treatment until the 3 mg Fe/gr dw discontinuation threshold for LIC was reached. Treatment was reinitiated when LIC increased above 5 mg Fe/gr dw. Base case starting age was 10 years. Sensitivity analysis was performed on key model inputs. **RESULTS:** A total of 280 patients with NTDT were estimated to be treated with iron chelation per year. With no deferasirox, total drug acquisition and administration costs were € 3,545,406 and € 11,889,133, respectively. With the introduction of deferasirox, acquisition costs increased by 62% to € 5,738,323 and administration costs decreased by 58% to € 4,993,474. Total expenditure decreased by over 30% representing cost savings of € 4,702,742 over 5 years. Results were sensitive to acquisition costs, administration costs for deferoxamine, treatment efficacy and discontinuation threshold. **CONCLUSIONS:** Reimbursement of deferasirox in NTDT resulted in cost savings to the Greek health care system.

Avoidance of administration costs for infused treatments could offset the higher acquisition cost for deferasirox. Additional data is required to confirm efficacy of other treatments in patients with NTDT.

PSY8

THE BUDGET IMPACT OF QUTENZA® FOR THE TREATMENT OF NEUROPATHIC PAIN IN SWEDEN

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OBJECTIVES: Neuropathic pain (NP) is a common disorder which can be chronic, severe, and disabling and is associated with reductions in quality of life and considerable costs. Current first-line treatments for NP include tricyclic antidepressants and anti-convulsants. QUTENZA® is a cutaneous patch that allows rapid dermal delivery of capsaicin directly to the source of pain. The objective of this analysis is to estimate the burden of NP, current treatment costs and the budget impact of introducing QUTENZA® for the treatment of peripheral NP in non-diabetic adults in Sweden. **METHODS:** We constructed a budget impact calculator to estimate the impact of introducing QUTENZA® for 100 people in Sweden. Drug costs for each management strategy are annual costs, based on estimated market shares, and range from SEK 231 to SEK 5,806 (with SEK 3,909 for QUTENZA®). We assumed a 50% uptake of QUTENZA® and a 50% reduction in the use of concomitant medication in the model, based on evidence from real-world data. **RESULTS:** For a NP population of n=100, the cost of current prescribing was estimated at SEK 1.00 million. The cost of alternative prescribing including QUTENZA® was estimated at SEK 1.01 million. The annual cost of treating a patient with QUTENZA® was estimated as SEK 11,941. The estimated cumulative budget impact by year (for 100 patients, with the market share rising from 10% in Year 1 to 100% in Year 5) ranged from SEK 9,664 in Year 1 to SEK 67,949 in Year 5. **CONCLUSIONS:** The introduction of QUTENZA® results in a budget impact of SEK 67,949 for 100 patients over 5 years. This represents a minimal additional expenditure and could be considered good value for money given the added benefits for patients with NP in Sweden.

PSY9

PHARMACOECONOMIC ANALYSIS OF ANTI-INHIBITOR COAGULANT COMPLEX (AICC) IN THE TREATMENT OF INHIBITOR HEMOPHILIA

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OBJECTIVES: To identify the dominant scheme of inhibitor hemophilia bypassing agents therapy (comparing three regimens: Eptacog alfa monotherapy, combination therapy «Eptacog alfa + AICC» and «AICC + Eptacog alfa»). **METHODS:** Based on the crossover clinical research FENOC (Jan Astermark, Sharyne M., Donfield, 2007) the annual cost of treatment by bypassing agents in mild, moderate, severe and life-threatening bleeding is estimated. The analysis of the direct and indirect costs is conducted. Direct costs include the cost of bypassing agents therapy, the cost of emergency medical care, the cost of inpatient and outpatient treatment. Indirect costs include cost of patient's disability, GDP losses caused by mortality and disability, and sick-pay. Value of bypassing agents on demand therapy in three dosing schemes is identified: monotherapy Eptacog alfa (there is no alternative treatment), «Eptacog alfa + AICC» (after the first episode of bleeding no response patients to treatment from Eptacog alfa to AICC transferred) and «AICC + Eptacog alfa» (after the first episode of bleeding no response patients to treatment from AICC to Eptacog alfa transferred). **RESULTS:** Based on the clinical study FENOC, indicated that there is no significant difference in efficacy AICC and Eptacog alfa therapy in patients susceptible to this treatment. An analysis of the direct and indirect costs shows that the costs of the annual course of treatment of 142 patients in Russia are 66 mil EUR, 60,7 mil EUR and 53,1 mil EUR for treatments Eptacog alfa monotherapy, «Eptacog alfa + AICC» and «AICC + Eptacog alfa» schemes respectively. **CONCLUSIONS:** It is determined that the regimen «AICC + Eptacog alfa», will reduce reduces costs relative to the current treatment regimen for 12,9 mil EUR (19,54%) or provide additionally treat of 34 patients of this disease.

PSY10

POTENTIAL FINANCIAL IMPACT OF SUGAMMADEX IN ANAESTHETIC DEPARTMENTS: A BUDGET IMPACT ANALYSIS ON POTENTIALLY SHORT PROCEDURES REQUIRING NEUROMUSCOLAR BLOCKADE

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OBJECTIVES: To evaluate the economic impact on Italian NHS of using sugammadex within anaesthetic departments instead of neostigmine. **METHODS:** The number of procedures using neuromuscular blockings agents (NMBA) potentially eligible for sugammadex was elaborated by hospital discharge data available in Italy for the year 2010. Reduction in postoperative residual curarisation (PORC) rate and saved time allocated to extra procedures were taken from two recent meta-analyses. Costs considered in the analysis were drugs acquisition costs (sugammadex and neostigmine) and PORC management costs. **RESULTS:** Overall annual costs of sugammadex and neostigmine usage result about 34.5 and 31.6 Million Euro, respectively. Sugammadex prevents 99% of PORC episodes on 428,995 procedures; this is associated with savings of more than 30 Million Euro. Also the saved time in surgery procedures due to sugammadex results in an annual savings of 154,867 (36.1%) hours that could be used for further procedures. **CONCLUSIONS:** Sugammadex radically reduces PORC episodes during post-operative and it allows for shorter operating room occupation.

PSY11

THE BUDGET IMPACT ANALYSIS OF DEFERASIROX FOR THE TREATMENT OF IRON OVERLOAD DUE TO FREQUENT BLOOD TRANSFUSIONS IN CHILDREN AND ADOLESCENTS (AGE ≤18 YEARS)

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OBJECTIVES: The purpose of the budget impact analysis (BIA) was to estimate financial consequences of deferasirox (DSX) reimbursement within the health care treatment programme (HTP) on the budget of the National Health Fund (NHF) in Poland. **METHODS:** BIA was performed for a 2-year time horizon (July 2012 - June 2014) from the Polish public payer perspective. The target population qualified to the HTP programme were children and adolescents (age ≤18 years) with iron overload due to frequent blood transfusions. The population was estimated on the basis of medical expert opinion. Two scenarios were compared: the "existing scenario" – without reimbursement of DSX (only standard of care with deferoxamine (DFO) was available) and the "new scenario" – DSX reimbursed as part of HTP. In the analysis, only direct medical costs were included: costs of drugs and their administration, costs of monitoring and costs of blood transfusions. It was assumed that the cost of deferoxamine was included in the cost of hospitalization procedures related to chelation therapy. Due to the lack of available data on adverse events (AE) incidence during therapy with deferasirox or deferoxamine, the costs of AE's treatment were not considered. The calculations were performed in Microsoft Office Excel. **RESULTS:** NHF annual expenditures related to the introduction of deferasirox reimbursement will increase by PLN 454 thousand in the first year and by PLN 434 thousand in the second year of reimbursement compared with the "existing scenario." **CONCLUSIONS:** The positive reimbursement decision for DSX enables patients with iron overload access to safe and effective therapy. Deferasirox therapy will allow young patients to go back to normal functioning in their families and in society. The positive reimbursement decision will also contribute to improving the quality of life, self-esteem and emotional state of the patients.

PSY12

PHARMACOECONOMIC STUDY OF NUTRITION SUPPORT (NS) USAGE DURING INTENSIVE TREATMENT

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OBJECTIVES: To undertake a comparative analysis of 2 methodologies of intensive treatment (IT) , precisely: IT without NS and IT taking into account NS handling. **METHODS:** Pharmacoeconomic analysis "budget impact" was provided. Only direct costs were taken into account: expenses for drug therapy, hospitalization (intensive care unit and medical division) and late complications (pneumonia, sepsis, catheter and wound infection) treatment. Effectiveness data was taken from Russian clinical trial: Popov T.S., Shestopalov A.E., Tsvetkov D.S., Nechaev D.S., Kuz'min M.A. Nutrition Day in intensive care units of the Russian Federation. National association of parenteral and enteral nutrition – Moscow (Russia), 2011. Four types of NS were compared: IT without NS; IT + enteral nutrition (EN); IT + parenteral nutrition (PN) and IT + combined nutrition (CN). **RESULTS:** When carrying out comparative pharmacoeconomic study all calculations were made for 3 groups of patients depending on their health condition: lightly-severe, moderately severe and severe. According to the results of calculations transfer of patients from IT without NS to IT carrying out NS leads to reduction of total expenses, therefore economy of money for the state. Independent from patient health condition – the greatest economy of money arises when EN is used during IT. Further on degree of expressiveness of positive economic effect there is PN and the least NS economic type is CN. **CONCLUSIONS:** The results received during the study were analyzed and the rating of NS types, which were taking part in the research, from the point of view of their clinical efficiency and economic effectiveness for the state budget, was made.

PSY13

A BUDGET IMPACT MODEL FOR NOVOSEVEN FOR THE MANAGEMENT OF BLEEDING EPISODES IN PATIENTS WITH HAEMOPHILIA A TREATED WITH INHIBITORS

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OBJECTIVES: To demonstrate the economic impact of using NovoSeven compared to Feiba for the initial treatment of mild to moderate bleeding episodes in patients with haemophilia A with inhibitors. **METHODS:** A budget impact model was developed based on a previous economic evaluation to calculate the annual budget impact and the treatment cost per episode according to the different treatment strategies. The model presents the costs of the strategies to treat a mild to moderate bleeding episode with up to three lines of treatment, in which the impact parameters are the weight of the patient, the dose, the efficacy and the costs of medication and administration. Three treatment strategies were used: strategy 1: NovoSeven - NovoSeven - NovoSeven, strategy 2: Feiba - NovoSeven - NovoSeven and strategy 3: Feiba - Feiba - NovoSeven. Costs per episode and annual costs were calculated based on local input data on costs and resources and the perspective used was of the Spanish National Health Service (NHS). **RESULTS:** Total costs per patient for one bleeding episode were €10,253, €11,852 and €12,042 for strategies 1, 2 and 3, respectively. Lower total costs per patient with NovoSeven are due to a reduced need for further treatment and associated hospitalisation. Only using NovoSeven saves €23,985 compared to strategy 2 and €26,842 compared to strategy 3 annually. **CONCLUSIONS:** The use of NovoSeven in all three lines of treatment in patients with in haemophilia A compared to using Feiba in the first line of treatment and in the first and second line of treatment saves €1,599 and €1,789 respectively per bleeding episode. This is mainly due to reduced need for further treatment and associated hospitalisation with NovoSeven. Annual cost savings using only NovoSeven are the consequence of lower drug cost and higher treatment efficacy with NovoSeven.

PSY14

PHARMACOECONOMIC EVALUATION OF INTRAVENOUS FERRIC CARBOXYMALTOSE AND IRON SUCROSE IN CORRECTION OF PREOPERATIVE ANAEMIA IN PATIENTS UNDERGOING MAJOR ELECTIVE SURGERY

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OBJECTIVES: To assess the cost-effectiveness of ferric carboxymaltose (FCM) and iron sucrose (IS) in the correction of iron-deficiency anaemia (IDA) before elective major surgery in non-cardiac surgical patients and predict potential budget expenses for the day care services and blood transfusions. **METHODS:** The pharmacoeconomic model was developed based on the data from multicentre prospective study (E. Bisbe et al., 2011) on the efficacy of FCM and IS for correcting preoperative anaemia in patients undergoing major elective non-cardiac surgery. The cost-effectiveness of two intravenous iron formulations was measured as total costs of medicines and day care services per one patient attained iron replenishment or per one patient without IDA at the end of treatment. Budget impact analysis included expenses for the day care services and blood transfusion procedures during intraoperative and/or postoperative period. Sensitivity analysis was performed by including in the model of iron sucrose similars (ISSs). It was considered that treatment with ISSs requires dose increase up to 120-135% of dose of the original IS (E. Lee et al., 2013; J. Rottermbourg et al., 2010). **RESULTS:** The clinical efficacy of FCM was higher compared to that of IS, this was also reflected in better pharmacoeconomic profile of FCM. The CERs were 14,473.61 RUB and 15,222.83 RUB per one patient attained iron replenishment in the FCM and IS groups, respectively. Treatment with FCM was associated with 2.5-fold lower costs of day care services and 2.7-fold lower expenses for blood transfusion procedures. Additional expenses for the day care services were required for patients received ISSs due to increased frequency of injections; this was resulted in the highest CERs in the ISS group. **CONCLUSIONS:** The present study has demonstrated that administration of FCM is economically effective strategy to replenish body iron stores and correct IDA in surgical patients.

PSY15

COST ANALYSIS OF A FIBRIN SEALANT PATCH FOR MILD, MODERATE AND PROBLEMATIC SOFT TISSUE SURGICAL BLEEDING: A HOSPITAL PERSPECTIVE

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OBJECTIVES: Although there are several hemostats available, drawbacks include limitations with efficacy on first attempt and sub-optimal ease-of-use. Literature suggests that more efficacious hemostats may avert hospital resources and offset upfront acquisition costs. A study was conducted to estimate the cost impact of a novel fibrin sealant patch (i.e., EVARREST™) versus standard of care (SoC) in mild-moderate and problematic soft tissue surgical bleeding. **METHODS:** An economic model was developed to quantify 30-day cost impact of EVARREST from a U.S. hospital perspective. Key resources, collected from two trials, included quantity of initial treatment and re-treatment, operating time, hospitalization, transfusion risk, amount transfused, and ventilator utilization. SoC was composed of Surgicel (mild-moderate bleeding) or Surgicel (88%) and conventional methods (12%) (problematic bleeding). The primary analysis included resources clinically related to the significant hemostasis benefit of EVARREST vs. control (i.e., initial and re-treatment, operating time and transfusion). A secondary analysis included all resources collected. Published data on U.S. costs were applied to resource use. **RESULTS:** In problematic bleeding, the primary analysis predicted that EVARREST is cost-savings for the hospital vs. SoC (-$462 USD per patient) with robust one-way sensitivity results (range: -$199 to -$6,212 USD). In mild-moderate bleeding, EVARREST acquisition cost is partially offset with a cost impact of $507 USD per patient (sensitivity range: $175 to $851 USD). Secondary analyses predicted further resource reduction with EVARREST leading to cost-savings (-$5,096 USD per patient) or reduction in cost impact ($233 USD per patient) for problematic and mild-moderate bleeding respectively. **CONCLUSIONS:** This analysis suggests that the hospital cost impact of EVARREST depends on type of bleed. In problematic soft tissue bleeding, EVARREST may result in important cost savings for hospitals, in addition to meeting an important unmet need. Further study in additional populations may be required to confirm findings.

PSY16

COST ANALYSIS OF BYPASSING AGENT PROPHYLAXIS TREATMENT VERSUS ON-DEMAND THERAPY IN HEMOPHILIA A WITH INHIBITOR IN SPAIN

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OBJECTIVES: To estimate the treatment cost of prophylaxis and acute breakthrough bleeds with Activated Prothrombin Complex Concentrate (aPCC) versus on-demand therapy with recombinant Factor VIIa (rFVIIa) for severe hemophilia A (HA) with inhibitor patients, from the Spanish Healthcare System perspective. **METHODS:** A cost-analysis model was used to compare annual cost per patient of aPCC prophylaxis versus rFVIIa on-demand treatment. Cost estimation included prophylaxis pharmaceutical costs (aPCC), on-demand pharmaceutical treatment for bleedings, bleeding events management (excluding factor), surgeries and HA management. Prophylaxis regimen was 75.72IU/kg three times per week. Total dosage for each hemorrhagic event was 673.46µg/kg for rFVIIa and 233.13U/kg for aPCC, annual number of bleedings was 25 for on-demand therapy and 8 for prophylaxis, assuming 69% reduction due to prophylaxis. A baseline bleeding management cost (€2,971) was estimated based on resource use provided by an expert panel for four bleeding sites (joints [62.5%], muscle and soft tissue [28.6%], mucous membranes [3.6%] and other sites [5.4%]). Drug (ex-factory price with mandatory 7.5% rebate) and unitary costs (€, 2013) were obtained from local databases. **RESULTS:** Estimated annual treatment cost of prophylaxis with aPCC (€523,473) was lower than on-demand treatment with rFVIIa (€622,183). Based on the total agent consumption (789,109IU [aPCC] and 1,050,067µg [rFVIIa]) the pharmaceutical cost accounted for €496,350 for aPCC (14.6% on-demand bleedings and 85.4% prophylaxis) compared to €543,866 for rFVIIa (average bleeding cost of €9,062 [aPCC] and €21,556 [rFVIIa]). Yearly bleedings cost was €23,770 for aPCC versus €74,963 for rFVIIa. A baseline cost for HA management (€2,645) and an average cost of surgeries (€708/year) were estimated for both strategies. Results for sensitivity analyses showed cost-savings ranging from €22,525 to €996,384 of prophylaxis with aPCC vs. on-demand with rFVIIa. **CONCLUSIONS:** Three times/week aPCC prophylaxis could reduce 16% the total treatment cost of severe HA with inhibitor, saving up to €98,000/patient/year.

PSY17

RELATIONSHIP BETWEEN BODY MASS INDEX AND HEALTH CARE COSTS BY PLACE OF SERVICE IN EMPLOYED ADULTS

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OBJECTIVES: While previous studies have shown that overweight and obesity are associated with higher costs, less is known about health care costs by place of service (POS) at various levels of BMI. This study measures the impact of BMI as a continuous variable on health care cost at different places of service. POS categories include: pharmacy, doctor's office, inpatient hospital, outpatient hospital or clinic, emergency department, laboratory, and other. **METHODS:** Using 2003-2012 retrospective data from large employers throughout the United States, employees' BMI values were calculated using health risk appraisal data. All study employees were >=18, had >=12 months of health plan coverage after their index BMI screening date, and had no medical claims indicating pregnancy. Employees with BMI<18 (1st percentile) or BMI>47 (99thpercentile) were excluded. Generalized additive models on 12-month post-index POS costs produced estimates of the nonlinear relationship between BMI and cost after controlling for age, gender, marital status, race, salary, zip-code region and index year. **RESULTS:** This study included 71,633 eligible employees; 32.0% were female. The average BMI, age and annual salary were 27.3, 39.8 years and $81,382, respectively. Costs increased significantly with BMI in each POS (P<0.001). Total adjusted annual per-employee health care cost estimates at BMI values of 25, 30, 35, and 45 were $3043, $3932, $4357, and $7248, respectively. Cost estimates by POS at these BMI values were: Pharmacy ($706, $903, $1106, $1372), Inpatient ($398, $678, $643, $2440), Outpatient ($799, $1057, $1113, $1516), Office ($939, $1044, $1174, $1495), Emergency ($131, $159, $200, $186), Laboratory ($34, $38, $46, $43), and Other ($35, $53, $74, $196), respectively. **CONCLUSIONS:** Employees with higher BMI levels incurred more cost at each of the 7 places of service. Because of the high prevalence of overweight and obesity, these costs represent a significant burden for US employers.

PSY18

COHORT ANALYSIS ASSESSING HEALTH CARE COSTS ASSOCIATED WITH OBESITY AT VARIOUS PLACES OF SERVICE IN EMPLOYED ADULTS

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OBJECTIVES: This study determines the distribution of health care costs by place of service (POS; pharmacy, doctor's office, inpatient hospital, outpatient hospital or clinic, emergency department, laboratory, and other) among employees based upon body mass index (BMI). **METHODS:** Using 2003-2012 retrospective data from large employers throughout the US, employees' BMIs from health risk appraisal data defined three main cohorts (BMI<27 [normal weight], 27<=BMI<30 [overweight] and BMI>=30 [obese]). The 27<=BMI<30 cohort was further divided into 3 comorbidity subcohorts: those without diabetes, hypertension or dyslipidemia (NonT2DHtnDys), those with hypertension or dyslipidemia without diabetes (HtnDys), and those with diabetes with or without hypertension or dyslipidemia (T2D). All eligible employees were aged>=18, had >=12 months post-index health plan coverage, and had no pregnancy claims. Annual post-index costs were compared between cohorts and between subcohorts using two-part regression modeling, controlling for age, gender, marital status, race, salary, region, and index year. **RESULTS:** This study included 39,696 (BMI<27), 14,281 (27<=BMI<30), and 18,801 (BMI>=30) eligible employees, with total adjusted health care costs of $3,191, $3,695, and $4,844, respectively. Employees with higher BMI were significantly more likely to incur health care costs in every POS category. Obese employees (BMI>=30) had particularly high inpatient costs compared to other cohorts, averaging twice the cost of the BMI<27 cohort ($919 vs. $431, P<0.05). Total costs among subcohorts of 27<=BMI<30 were $2,863 (NonT2DHtnDys), $5,271 (HtnDys), and $7,594 (T2D). NonT2DHynDys employees had significantly lower health care cost than other subcohorts in every POS category. The T2D subcohort had significantly higher pharmacy, inpatient, doctor's office, laboratory and other health care costs when compared to HtnDys. **CONCLUSIONS:** Employees with higher BMI incurred higher average health care costs than other employees at all places of service. Comorbidities, particularly diabetes, exacerbate health care costs of overweight employees. This represents a significant economic burden for US employers given the high prevalence of overweight and obesity.

PSY19

HAEMOPHILIA A: ANNUAL COST COMPARISON BETWEEN FL-RFVIII AND BDD-RFVIII IN FRANCE: WE SHOULD COMPARE THE COST PER PATIENT INSTEAD OF THE PRICE PER UNIT

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OBJECTIVES: Hemophilia A is rare bleeding disorder where patients have defective or deficient levels of coagulation factor VIII (FVIII). Recombinant FVIII (rFVIII) are manufactured to treat the patients, either as a full-length rFVIII (FL-rFVIII) molecule replicating natural human FVIII or with the B-domain deleted (BDD-rFVIII). It has been suggested that Deletion of B domain had been implemented to improve production profitability. However, this deletion has been shown to induce increase factor consumption by 32.8% in the US (Epstein 2011) and also may increase the risk of developing inhibitors for previously treated patients (PTP) Hazard Ratio=10.8 (Aledort 2011). Both differences can have an important impact on patient health and on the national health care budget. **METHODS:** A Excel-based decision tree model had been developed to compare the overall cost to treat severe haemophilia A patients from a health care system perspective with the most used FL-rFVIII and

BDD-rFVIII in Europe. Clinical data are from the published literature. Pharmacy cost of rFVIII, immune tolerance induction (ITI) and bypassing agents for patients who developed inhibitors are considered from French health care perspective. **RESULTS:** Both products are listed and reimbursed at similar unit price whereas the overall cost to treat a patient with BDD-rFVIII is higher considering the increased consumption on prophylaxis and the risk of developing an inhibitor for PTPs. This may be translated into an increase cost of 36% over 1 year and 40% over 3 years when treating children and adult PTPs with prophylaxis. **CONCLUSIONS:** The cost study confirms the cost advantage of rFVIII (FL-rFVIII) as well as the need to compare the rFVIII based on the overall cost and not on the price per unit.

PSY20

COST OF ILLNESS OF NEUROPATHIC PAIN IN SPAIN IN 2012 FROM A SOCIETAL PERSPECTIVE

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OBJECTIVES: To quantify the total societal costs of Neuropathic Pain (NP) in Spain following a bottom-up prevalence approach. **METHODS:** The sample was drawn from the 2012 Adelphi NP Disease Specific Programme, a cross-sectional survey of 413 primary care physicians and specialists and their consulting patients across the EU5. Physicians completed patient record forms for 826 patients in Spain including patients' socio-demographic information, treatment history and resource utilization. Additionally, 577 patients voluntarily completed another questionnaire that included the Work Activity and Productivity Impairment Questionnaire (WPAI). Health-related costs were collected and adjusted to 2012 prices when needed. For professional caregivers' costs and work losses, Spanish average salaries were used. **RESULTS:** The 826 patients included accounted for a total of € 2,676,893.83, an average of € 3,240.79 per patient, with 72% (€2,350) of these being health related costs, including drugs (50%), consultations (11%), surgical (9%) and non-surgical (2%) procedures. Working losses related with patients' sick leave (as reported by doctors) accounted for 17% (€555) of the costs and professional caregiving added up to 10% of the total costs. The results were extrapolated to national prevalence figures of 2012 excluding patients assumed to be non-treated. The societal costs for 2012 were: health-related costs €514,583,543, work losses €119,417,964 and professional caregivers €72,204,921. Additionally, 91% of the caregivers were non-professional. 191 (33%) of the 577 patients completed the WPAI with an Overall Work Impairment score of 55%. Finally, 183 (33%) of the patients stated that NP prevented them from working at some point, with 26 patients stating this was "permanently". **CONCLUSIONS:** The economic impact associated with Neuropathic Pain (NP) implies substantial annual costs to the Spanish National Health Service of more than €500 Mio. and a large burden on patients' lives and their families. The results shown here suggest that an important part of the real cost is still hidden.

PSY21

EXPLORING THE BURDEN OF ILLNESS OF HEREDITARY ANGIOEDEMA IN THE UNITED KINGDOM

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OBJECTIVES: Hereditary angioedema (HAE) is a rare but potentially life-threatening condition with intermittent and unpredictable oedema affecting the larynx, abdomen and extremities. This study aims to define the burden of HAE in England and Scotland as published data are limited. **METHODS:** A comprehensive, cross-sectional, retrospective study of the burden of HAE (type I and II) in England and Scotland. Three data collection methods: 1) secondary care data identified using Hospital Episode Statistics based on D.84.1 diagnostic code (defects in complement system, C1-esterase inhibitor deficiency); 2) primary care data accessed through The Health Improvement Network (THIN) database using C-376-000 HAE diagnostic code. Both database analyses identified patients diagnosed ≤10 years and include all episodes ≤2years. Costs were calculated using most up-to-date best-matched HRG tariffs. 3) Primary research in five secondary care centres in England and Scotland collecting information on >100 patients (>18 years) via medical records ≤2years, matched with patient self-completion questionnaires and centre interviews. Selected centres represent different approaches to HAE management to ensure a national representative sample. **RESULTS:** Data collection from all three phases of the study is on-going. Early results from 1) indicate 1,174 HAE patients admitted to hospitals in England, for any reason, in the past two years. Mean length of stay, including day cases, was 2.8 days. The annual total cost of secondary care in England was £3,227,149, corresponding to per HAE patient cost of £2,749. **CONCLUSIONS:** This is the first comprehensive UK HAE cost of illness study, providing a comprehensive understanding from both NHS and patient perspectives. Important insight into patient demographics, pathway of care, treatment patterns, and any regional or sub-population differences in the standard of care will be provided, helping to raise disease awareness in the UK.

PSY22

ADRENAL INSUFFICIENCY: BURDEN OF DISEASE IN FRANCE IN 2011

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OBJECTIVES: Adrenal insufficiency (AI) is a rare disease caused by a deficiency in hormone synthesis by adrenal glands, due to either the destruction of the glands (primary AI: PAI) or hypothalamic / pituitary causes (secondary AI: SAI). Patients are treated with hormone replacement therapy, mainly hydrocortisone. Our aim was to assess the cost of AI management in France **METHODS:** We used data from the French National Health Insurance (Social security) on patients who benefited from a long duration disease status N°31 for their AI in 2011 (primary and secondary combined) on the one hand, and the results of a Delphi Panel survey on the other hand. This survey, involving 15 endocrinologists from academic hospitals, was designed to better understand the patients' pathway in the absence of guidelines. An epidemiological approach on the prevalence of the disease has led to a cost study using a "top-down" method. Sensitivity analyses were conducted on the following cost parameters: medical and drugs costs in primary care, costs of public and private hospitalizations - chosen according to their weight in the pathway described by the Delphi Panel. **RESULTS:** The social security paid a total of € 5,612,842 for 1377 AI patients in 2011. The annual cost per patient is therefore € 4,076, including 62% for primary care expenses, 29% for public hospital expenses and 9% for private hospital. The total population with AI is estimated between 26,000 and 30,000 patients, leading to a total cost ranging from € 106M and € 122M. A 1% reduction in hospital spending would generate a gain of € 430,000 to € 500,000 per year. **CONCLUSIONS:** Despite AI concerns few patients, significant costs are borne by Social Security. An increased compliance and a better management of symptoms such as fatigue could help optimizing this cost.

PSY23

ECONOMIC BURDEN OF PATIENTS WITH PAINFUL DIABETIC NEUROPATHY IN EUROPE: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: Painful diabetic neuropathy (PDN) is a complication of diabetes mellitus. The aim of this research was to describe the epidemiology and economic burden resulting from PDN in Europe. **METHODS:** A systematic literature review was performed according to a pre-defined search strategy and review criteria in Embase and PubMed from 2003 to 2012. Conference proceedings and Health Technology Assessment (HTA) organizations' websites were also searched from 2010 to 2012. **RESULTS:** In total, 23 original studies were identified that covered either epidemiology (n= 16) or economic burden (n=7) for PDN patients in Europe. 13 - 26% of European diabetes patients are reported to develop PDN. Health care costs per PDN patient were between €2,441 and €2,963 *per annum* in UK and Spanish studies, respectively. Inpatient care, medical visits and drug costs accounted for the majority of the total costs, although drug costs can vary widely depending on the choice of medication. Health care costs for PDN lead to a high total economic burden for European countries. Considering the identified prevalence data and cost estimates, the estimated total annual health care burden for the UK would be approximately €1.7 billion, from a payer perspective. In addition, PDN is significantly associated with disruptions in employment status and productivity loss, primarily driven by impairment while working (presenteeism), resulting in average European per-patient productivity losses of € 10,484 *per annum*. Pain severity highly influences economic outcomes: higher severity has been linked to significant increases in resource use, productivity losses and health care costs. **CONCLUSIONS:** The large number of PDN patients combined with the cost per patient results in a high economic burden of PDN for European countries. More severe pain results in increased resource use and costs for payers and society; therefore, more effective PDN treatments will lead to patient as well as economic benefits.

PSY24

COST OF OBESITY AND ECONOMIC VALUE OF OBESITY SURGERY FOR TURKEY (CEVOS-T)

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OBJECTIVES: Obesity and its comorbidities are among the primary challenges that health systems face globally. Obesity is rapidly becoming a problem in Turkey as well. Recent research has revealed that 30.3% of the population is obese(20.5% of males, 41% of females) of which 2.9% of the obese population is classified under the morbid obese category. The 2003 Burden of Disease Study also concluded that 26.006 deaths for males and 31.136 deaths for females could be averted by decreasing the ratio of obese population. **METHODS:** The objective of this study is to find out the economic impact of obesity with its possible economic benefits of obesity surgery for Turkey. **RESULTS:** Literature search and expert panel are the main methodologies used in the study. A comprehensive literature search was undertaken with key words in PubMEd to find out the extent of obesity and its comorbidities and treatment methods in Turkey. Cost of obesity for Turkey was calculated depending on the published literature. An expert panel questionnaire form was designed after the literature search aiming at finding the cost. The form was sent to the experts in advance and a panel discussion was undertaken to reach a consensus. After the consensus building phase the economic benefits of obesity surgery were estimated based on the price tariff declared by the Social Security Institution(SGK). **CONCLUSIONS:** Cost of obesity for Turkey was estimated as US$ 787.184.000 for 2012. It was the 1.05% of gross domestic product of Turkey. SGK pays US$ 1707 weighted average for obesity surgery. It was estimated that return of investment on obesity surgery can be possible after the third year of surgery. The study indicated that obesity has a great impact to Turkish economy. On the other hand, obesity surgery can have a positive impact with its economic benefits to Turkish health system.

PSY25

A SYSTEMATIC LITERATURE REVIEW ON THE EPIDEMIOLOGY AND ECONOMIC BURDEN OF ANAEMIA ASSOCIATED WITH CHRONIC KIDNEY DISEASE

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OBJECTIVES: The epidemiological and economic burden associated with anaemia in patients with chronic kidney disease (CKD) in Europe has not been explored recently using systematic literature review (SLR) methods. Therefore, an SLR was conducted to assess these topics. **METHODS:** A systematic search was conducted of MEDLINE- and EMBASE-indexed literature on anaemia in CKD from 2007 to 2012 for publications on epidemiology and economic burden. Data from included articles were abstracted into a pre-designed template and synthesised using qualitative methods. **RESULTS:** The review identified 19 studies reporting on epidemiology and nine on economic burden. The prevalence of anaemia among patients with CKD varied widely by setting, being generally lower in those from the general population and

primary care (range: 1.0%–9.4%) than in general hospitals (range: 5.8%–43.3%), and highest in specialist nephrology settings (range: 16.0%–97.6%). Also, prevalence rates increased with the CKD stage (1–2: 14.1%–27.9%; 3: 25.5%–91.1%; 4: 36.0%–85.5%; 5: 97.6%). The cost of managing anaemia per patient per year varied across studies from £2,616 (2006–2007 Great British Pounds; GBP) to £3,740 (2006 GBP) in the UK, to €5,617 in France (cost year not reported). One study reported that the overall cost of managing anaemia was highest in patients with CKD Stage 3 compared with other stages (3: £4,162,056 vs. 4–5: £243,288; 2006–2007 GBP). Another study reported higher costs per patient per annum for individuals with lower haemoglobin (Hb) levels (Hb >12 g/dL: €2,418; Hb <10 g/dL: €13,005; cost year not reported). Among patients with CKD, those with anaemia were more likely to be hospitalised (61% vs. 50% of those without anaemia). **CONCLUSIONS:** Anaemia is a highly prevalent condition in CKD across treatment settings in Europe, and the limited evidence available suggests it is associated with a substantial economic burden.

PSY26

MODELLING THE PREDICTIVE VALUE OF PAIN INTENSITY ON COSTS AND RESOURCES UTILIZATION IN PATIENTS WITH PERIPHERAL NEUROPATHIC PAIN

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OBJECTIVES: Peripheral neuropathic pain (PNP) implies a significant economic burden that results in major health care and indirect costs. The aim of the present analysis was modelling the association and predictive value of pain intensity on costs and resources utilization (health care and non-health resources) in patients with chronic PNP treated in routine clinical practice conditions in Spain. **METHODS:** Secondary economic analysis based on data from a multicenter, observational and prospective cost-of-illness study in patients with chronic PNP refractory to previous treatment. Data on resources utilization and pain intensity was collected at baseline and 12 weeks after starting a new treatment. Pain intensity was measured using the 0-100 mm Visual Analogue Scale (VAS) of the Short Form McGill Pain Questionnaire. Univariate and multivariate linear regression models were fitted to identify independent predictors of costs and health care and non-health care resources utilization. **RESULTS:** A total of 1703 patients were included in the current analysis. Pain intensity was an independent predictor of total costs ([Total costs(Euros)] = 35.6 x [VAS pain intensity] + 214.5; coefficient of determination [R^2]=0.19, p<0.001), direct costs ([Direct costs(Euros)] = 10.8 x [VAS pain intensity] + 257.7; R^2=0.06, p<0.001) and indirect costs ([Indirect costs(Euros)] = 24.8 x [VAS pain intensity] – 43.4; R^2=0.19, p<0.001) related to chronic PNP in the univariate analysis. Pain intensity remain significantly associated with total costs, direct costs and indirect costs after adjustment by other covariates in the multivariate analysis (p<0.001). The impact of pain intensity on health care and non-health care resources utilization accounted for such findings. **CONCLUSIONS:** Pain intensity predicts the health care and non-health care resources utilization, and costs related to chronic PNP. Management of patients with drugs associated with a higher reduction of pain intensity will have a greater impact on the economic burden of that condition.

PSY27

RESOURCE UTILIZATION AND COSTS ASSOCIATED WITH RITUXIMAB TREATMENT IN PATIENTS WITH PEMPHIGUS AND PEMPHIGOID: A COMPARISON OF 6 MONTHS BEFORE AND 6 MONTHS AFTER TREATMENT

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OBJECTIVES: Pemphigus and pemphigoid are a rare group of potentially fatal diseases, causing blistering on mucosal and epidermal surfaces. Long-term treatment with systemic corticosteroids and immunosuppressive agents such as intravenous immunoglobulin (IVIg) are usually required. Rituximab (RTX) is increasingly being used for autoimmune bullous dermatoses (AIBD) and has shown to be effective, however, in Canada, RTX is not approved for AIBD. Given the potential cost associated with the use of RTX, there is a need to quantify the issues around accessing it for AIBD patients. **METHODS:** Resources (e.g., treatment, lab costs, procedures, access to health care providers) associated with 89 AIBD patients were collected and quantified 6 months prior and 6 months post RTX initiation. Costs of adverse events secondary to standard treatment (e.g., steroid adverse effects such as diabetes, cataracts, osteoporosis etc) and costs of medications used to prevent steroid adverse effects (e.g., proton pump inhibitors, bisphosphonates) were not calculated. Unit costs (2013 $CAN) were applied to the resources. Overall cohort costs pre and post RTX, as well as cost per patient, were calculated. Cost drivers were identified. **RESULTS:** The overall cohort cost for 6 months pre-RTX was $3.7million (M), and 6 months post was $2.6M (30.3% decrease). IVIg was shown to be the main cost driver. 6 months pre-RTX, 157 months of IVIG was used ($3.6M) compared to 71 months ($1.6M) 6 months post. The cost associated with access to health care resources significantly reduced from $46,715 vs. $22,978, and fewer visits to the dermatologist were required (377 vs. 256 visits). A decrease was also observed in the cost of specialist consultations required ($5,807 vs. $3,234) and other treatment/medication use ($64,548 vs. $48,045). The cost per patient decreased ($41,497 vs. $28,923). **CONCLUSIONS:** RTX is effective in reducing the number of resources and costs associated with treatment of AIBD.

PSY28

HEALTH AND SOCIAL CARE RESOURCE USE BY INDIVIDUALS WITH FRAGILE X SYNDROME: RESULTS OF TWO DELPHI PANELS

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OBJECTIVES: To estimate health and social care resource use in treating individuals with Fragile X Syndrome (FXS) in Canada and the United Kingdom (UK). FXS is the most common inherited form of intellectual disability (ID) worldwide; however its impact on resource use is not well documented. **METHODS:** Delphi panels were formed to generate consensus-based estimates of resource use. Panelists from multiple disciplines were recruited (7 panelists in Canada, 6 in UK) and a questionnaire developed to obtain estimates from each panelist by 2 age groups, 2 severity levels and 24 service types for each of 9 items from the Aberrant Behavior Checklist (ABC) a proxy completed instrument to rate maladaptive behaviors of individuals with ID. A factor weight was estimated to differentiate costs by gender and a self-declared confidence score (1 – 5) was reported for each ABC item. Mean total service counts and coefficients of variation (CV) were calculated to assess variance between panelists and between rounds. Initial results were reviewed with panelists in a facilitated group discussion after which the questionnaire was repeated. Final data were based on the second round of estimation. **RESULTS:** Comprehensive resource data were collected for both countries. There was lower variance and higher confidence in both countries in round 2 compared to 1. Rounds 1 and 2 means (CV) for Canada were [6,723 (0.69) 8,575 (0.52)] and for UK were [6,953 (0.96) 6,023 (0.76)]. The average level of self-declared confidence increased from 2.6 to 3.3 in Canada and from 2.6 to 2.8 in the UK. **CONCLUSIONS:** The study generated comprehensive resource use data for treating individuals with FXS in Canada and the UK. Credible and validated estimates were generated through group discussion and refinement of initial estimates. The resulting data will be important in performing economic evaluations of treatments for patients with FXS.

PSY29

IMPACT OF BARIATRIC SURGERY ON OBESE PATIENTS MANAGEMENT AND RELATED COSTS: A FRENCH NATIONAL CLAIMS DATABASE ANALYSIS OVER THE PERIOD 2005 -2011

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OBJECTIVES: To gain an understanding of the impact of bariatric surgery on the current medical management of obese patients. **METHODS:** The EGB database is a 1/97 representative sample (around 600,000 individuals) of the national claims database covering the whole French population including outpatients and inpatient care. Adult patients treated for the first time over the period 01/01/2007 to 31/12/2009 by bariatric surgery were identified through related procedures and obesity ICD-10 codes. A cohort of patients was constituted with a 2-year follow-up before and after the index procedure date (T). Reimbursed medical consumption over this 4-year period was recorded and presence of co-morbidities was identified through ICD-10 codes, reimbursement of specific drugs or procedures. **RESULTS:** A total of 350 patients meeting the selection criteria were identified in the database with a mean age of 38.9 (+/- 11.3) years, 83.4% female and 69.7% had a BMI in the range 40-50. The distribution of patients according to bariatric procedure was gastric banding (62.6%), gastric by-pass (19.7%), sleeve gastrectomy (16.6%) and bilio-pancreatic diversion (1.1%). The annual per capita reimbursed health expenses evolved from 2.633€ (+/-3.124€) in Year (T-2), to 3.557€ (+/-3.380€) in Year (T-1), to 4.240€ (+/-3.840€) in Year (T+1) (excluding procedure cost) to 3.755€ (+/-5.037€) in Year (T+2). In 39% of patients those costs decreased between T-2 and T+2, (>5%) and the only two variables significantly explaining this decrease were the reduction of consumption for anti-Diabetes and/or anti-Hypertension drugs. Most items of medical consumption increased over the period pre and post procedure but started to decrease in Year T+2. **CONCLUSIONS:** The visits for preparing bariatric surgery were probably an opportunity for those patients to benefit from a general check-up which has generated extra short term medical consumption. Additional research with longer follow up could better capture the benefits of bariatric surgery on medical consumption.

PSY30

COST-CONSEQUENCE ANALYSIS OF A TREATMENT STRATEGY INCLUDING PONATINIB COMPARED TO A TREATMENT STRATEGY INCLUDING ONLY THE 2ND GENERATION TYROSINE KINASE INHIBITORS (2G TKIS), DASATINIB OR NILOTINIB, IN RESISTANT PATIENTS WITH PHILADELPHIA CHROMOSOME-POSITIVE (PH+) LEUKEMIA, IN ITALY

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OBJECTIVES: To assess treatment cost and duration (months) of major cytogenetic response (MCyR) using ponatinib in patients intolerant or resistant to 2G TKI, compared to treating with only 2G TKIs, in patients with Ph+ leukemia, in Italy. **METHODS:** A 3-year Markov model with 1-year cycles simulated patients with Ph+ leukemia to estimate outcomes in those eligible for ponatinib therapy, defined as 1) 2G TKI-resistant, 2) 2G TKI-intolerant if imatinib is not clinically appropriate, or 3) with T315I mutation. Eligible patients received treatment sequences including 2G TKIs and ponatinib in the ponatinib arm and 2G TKI only in the comparator arm. Patients without MCyR by 12 months were switched to the next therapy line until TKI options were exhausted, then to best supportive care. MCyR rates for 2G TKI or ponatinib were estimated from clinical trial data and expert opinion. Patients were assumed to accrue MCyR months until estimated treatment failure. Monthly treatment costs reflect approved EU dosing and list prices; cost of ponatinib was assumed equivalent to the US. **RESULTS:** We estimated 184, 280, and 360 ponatinib-eligible patients in years 1-3, respectively. Treating ponatinib-eligible Ph+ leukemia patients with 2G TKIs yielded a 3-year cost of €58.51 million and a total of 2,536 months in MCyR, at an average cost of €23,068/MCyR month. Using ponatinib in eligible patients cost €79.54 million and provided 5,649 months in MCyR, at an average cost of €14,079/MCyR month. **CONCLUSIONS:** The treatment strategy includ-

ing ponatinib provided more than double (2.2-fold) the MCyR months at 36% higher cost compared to the 2G TKI strategy. The average cost/MCyR month with ponatinib was lower than the average cost/MCyR month with 2G TKIs. While there are limitations with the methology and assumptions of the model, this analysis suggests treatment with ponatinib may provide good value for ponatinib-eligible Italian patients.

PSY31

EVALUATION OF THE COST-EFFECTIVENESS OF THE CAPSAICIN PATCH QUTENZATM FOR THE TREATMENT OF PERIPHERAL NEUROPATHIC PAIN IN THE UNITED KINGDOM

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OBJECTIVES: To estimate the cost-effectiveness of using the capsaicin patch QUTENZATM prior to use of more costly neuropathic pain medications for individuals with peripheral neuropathic pain (PnP). **METHODS:** A decision tree and Markov model was developed using inputs from a prospective, observational study. This study provided estimates of clinical efficacy, health utility and resource use. The model considered two treatment strategies: 1. a capsaicin patch followed by pregabalin and then a subsequent last-line therapy, and 2. no exposure to a capsaicin patch. A systematic review and meta-analysis were used to estimate the effectiveness of pregabalin. Response was defined as a ≥50% reduction in pain at week-8. Patients who responded were assumed to experience pain relief and increase in health-related quality of life until the resolution of pain (or death). Non-responders were assumed to switch therapy, and individual's that failed last-line therapy were assumed to experience baseline pain (unless resolution of pain or death). Costs were based on published sources. The primary outcome was the incremental cost-effectiveness ratio (ICER). The perspective was the UK National Health Service and personal social services. **RESULTS:** Key parameter estimates derived from the observational study were: the probability of response for capsaicin patch (29.5%), the mean number of patches per application (1.5), the mean time to retreatment (218 days), The baseline EQ-5D score was 0.370; response was associated with an increase in EQ-5D utility of 0.353 from baseline. The base-case ICER was £2,292 per quality-adjusted life-year (QALY). This varied by time horizon. Probabilistic sensitivity analysis suggested that over a lifetime horizon, a treatment strategy placing capsaicin patches before pregabalin had a 99.9% probability of being cost effective at a willingness-to-pay threshold of £20,000. **CONCLUSIONS:** The capsaicin patch used before pregabalin was a highly cost-effective treatment in the management of peripheral neuropathic pain.

PSY32

COST EFFECTIVENESS OF INDUCTION ANESTHETIC AGENTS

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OBJECTIVES: To evaluate the cost effectivenss of Thiopentone and Propofol for over night induction anesthesia in a tertiary care hospital. **METHODS:** A prospective observational study in which the patients scheduled for general anaesthesia were adminsitred EQ5D 5L(Qol question aire) after six hour and 24 hours of administering Induction Aneasthesia. Kuppuswamy scale was applied to asses the socioeconomic status along with the demographic detials **RESULTS:** The average of EQ5D5L scores for Propofal was 14.2 and for Thiopentone 16.0. The cost of the Propofol brand used in hospital were 250INR and 260INR. Thiopentone , only one brand was avialable costing 62 INR. The Propofol was the most commonly used induction anesthetic and it costs more than 4 times of Thipentone. The patients socioeconomic categorirzation based on Kuppuswmy Scale revealed nearly 50% of patients belonged to lower middle class and 35% middle class and rest of the patients to Upper class. Incremental cost effectivness ratio for Thiopentone agianst Propofol was found to be -110; **CONCLUSIONS:** The Propofol although expensive does not offer any advantage over the Thiopentone as for quality of life among patients who under went induction anethesia

PSY33

COST-EFFECTIVENESS ANALYSIS OF CYSTEAMINE IN THE TREATMENT OF PATIENTS WITH CYSTINOSIS – A RARE DISEASE

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OBJECTIVES: To perform a cost-effectiveness analysis (CEA) of cysteamine in the treatment of infantile cystinosis vs. control group consisting of patients who had been given only conservative and symptomatic treatment (CaST). **METHODS:** Markov model was developed in TreeAge Pro 2009. The model evaluated the costs and health outcomes of cysteamine treatment at a dose of 1.30 g/m^2/day compared with the use of CaST. The model distinguished two populations, depending on the time of initiation of the treatment (before the age of two – P1 and after the age of two – P2, which implies worse prognosis for the time of occurrence of end stage renal disease (ESRD)). The CEA was conducted from both a common payer perspective (a patient and a public payer) and a public payer perspective. The time horizon of the analysis covered the period from the age of one or four (depending on the start of cysteamine therapy) to fifty (currently, the oldest living patients with cystinosis reach the fifth decade of life). The main measures of the outcomes in the CEA were life-years gained (LYG) and life-years gained to the onset of ESRD. **RESULTS:** From the common payer perspective the cost per LYG was PLN 95,337 and PLN 192,272, respectively for the population P1 and P2. Cost of LYG to the onset of ESRD was PLN 33,317 and PLN 64,163, respectively for populations P1 and P2. The results obtained from the public payer perspective did not differ significantly from the results obtained from the common payer perspective. **CONCLUSIONS:** Cysteamine treatment of patients with cystinosis vs. therapy involving only CaST is more expensive, however produces better health outcomes. Regarding the acceptability threshold in Poland cysteamine therapy can be considered a cost-effective technology compared with CaST in patients who began treatment before the age of two.

PSY34

COST-EFFECTIVENESS OF SUGAMMADEX FOR ROUTINE REVERSAL OF NEUROMUSCULAR BLOCKADE, WITH EXTUBATION AT A TOF RATIO OF 0.9, IN ANAESTHETISED PATIENTS UNDERGOING ELECTIVE SURGERY IN ENGLAND AND WALES

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OBJECTIVES: To assess the cost-effectiveness of sugammadex compared with neostigmine + glycopyrrolate as a reversal agent for moderate and deep rocuronium or vecuronium-induced neuromuscular blockade (NMB) in the elective setting in England and Wales, when extubation occurs at a train-of-four (TOF) ratio of 0.9. **METHODS:** A decision tree comparing the cost-effectiveness of sugammadex versus neostigmine + glycopyrrolate when reversing moderate or deep NMB induced by commonly used neuromuscular blocking agents (NMBAs) (atracurium/rocuronium/vecuronium) was developed. Extubation was modelled to occur at a TOF ratio of 0.9, as may happen when using objective NMB monitoring to determine when to safely extubate. Time to recovery was used to calculate the cost of patients recovering in theatre based on both the average cost per minute of theatre time, and operating room (OR) staff costs per minute. Effectiveness was measured by the number of prolonged paralysis cases prevented by each treatment regimen. **RESULTS:** Reversal of moderate NMB: when considering average cost per minute of theatre time, results show that sugammadex strategies are dominant compared with all assessed comparators. When considering OR staff cost per minute, results show that rocuronium with sugammadex is dominant over all assessed comparators, with the exception of atracurium with neostigmine + glycopyrrolate (ICER< £100). Reversal of deep NMB: when considering either costing scenario, results show that sugammadex strategies are dominant over all assessed comparators, with the exception of atracurium with neostigmine + glycopyrrolate (ICER < £330). **CONCLUSIONS:** In clinical settings where extubation occurs at a TOF ratio of 0.9, and time savings may be realized for all OR staff, under both moderate and deep NMB scenarios in the elective surgery setting, sugammadex is either dominant or shows reasonable levels of cost-effectiveness (with low ICERs <£330 when not dominant against neostigmine+ glycopyrrolate), whilst also filling an unmet need for deep NMB reversal.

PSY35

COST-EFFECTIVENESS ANALYSIS OF A VACCINATION PROGRAMME FOR THE PREVENTION OF HERPES ZOSTER AND POST-HERPETIC NEURALGIA IN ADULTS AGED 50 AND OVER IN GERMANY

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OBJECTIVES: A vaccine is licensed in Europe for the prevention of Herpes Zoster (HZ) and postherpetic neuralgia (PHN) in adults aged ≥50 years. The objective of this study was to assess the cost-effectiveness of a vaccination programme in Germany in this population. **METHODS:** An existing European Markov Model was adapted to the German health care setting and cost-effectiveness outcomes were assessed from the statutory health insurance (SHI) and from the societal perspective. The Markov Model compares a HZ vaccination policy for adults aged ≥50 years with a no vaccination policy. Health states considered are healthy, HZ, PHN, healthy post-HZ and death. HZ and PHN states are further split by pain severity (mild, moderate or severe). Model outcomes include cost/HZ case avoided, cost/PHN case avoided and cost/quality-adjusted life year (QALY) gained. Additionally we assessed the number needed to vaccinate (NNV) to avoid one case of HZ or PHN. Input data were obtained from German data sources, international and German study results as well as published literature. Discounting was done in accordance to guidelines from the German Institute for Quality and Efficiency in Health Care (IQWiG). **RESULTS:** Preliminary results of the base-case analysis show incremental cost-effectiveness and cost-utility ratios (ICER) in amount of € 2,223 per HZ case avoided and € 22,923 per QALY gained from a payer perspective. In sensitivity analyses discount rates, vaccine prices and no hospitalization assumption showed a major impact on the results. **CONCLUSIONS:** Our cost-effectiveness analysis shows that a HZ vaccination policy for adults aged ≥50 years in Germany could provide public health and economic effects in the German health care system.

PSY36

THE POTENTIAL OF A REDUCTION IN THE RISK OF OPIOID-RELATED FRACTURES TO DRIVE THE COST-EFFECTIVNESS OF AN ANALGESIC

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OBJECTIVES: An increased risk for fractures has been observed in patients treated with opiates, possibly resulting from falls related to central nervous system effects, such as dizziness. Observational data suggest that the semisynthetic opioid, buprenorphine, may be associated with a lower fracture risk than some other opiates such as tramadol. Our objective was to perform a preliminary analysis to explore whether a buprenorphine-class drug has the potential to be cost-effective due to a reduced risk for fracture. **METHODS:** Decision-analytic modeling was used to project fracture-related outcomes and costs over 1 year. Quality-adjusted life-years (QALYs) and costs (in 2012 pounds sterling) were estimated from a health service perspective. Odds ratios for forearm, hip, and spine fractures, by drug, estimated from real-world hospital discharge data (Vestergaard et al., 2006), were applied to the risk for fracture in the general population.

Drug costs were based on the 10-µg per hour buprenorphine patch and the equivalent tramadol dose (2013 British National Formulary listings). Fracture costs were from a recent National Institute of Health and Care Excellence submission; utility weights were obtained from the literature. **RESULTS:** For a population of 100,000, the model predicted a reduction in the number of additional fractures (forearm, hip, or spine) associated with analgesic use from over 2,000 for patients treated with tramadol to under 20 for patients treated with buprenorphine. An estimated £5.5 million was saved and over 1,300 QALYs were gained. In sensitivity analysis, buprenorphine was dominant in most analyses and most sensitive to treatment duration. The cost-effectiveness estimate was below £20,000 per QALY in all scenarios. **CONCLUSIONS:** Our preliminary analysis suggests that buprenorphine has the potential to be dominant and cost-effective, compared with tramadol.

PSY37

COST-EFFECTIVENESS OF ENZYME REPLACEMENT THERAPY (ERT) WITH ALGLUCOSIDASE ALFA IN CLASSIC-INFANTILE PATIENTS WITH POMPE DISEASE

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OBJECTIVES: Infantile Pompe disease is a rare metabolic disease. Enzyme replacement therapy (ERT) has proven to have substantial effects on survival in infantile Pompe disease. However, costs of therapy are very high. This paper assesses the cost-effectiveness of ERT in infantile Pompe disease. **METHODS:** A patient simulation model was used to compare costs and effects of ERT with costs and effects of supportive therapy (ST). The model was filled with data on survival, quality of life and costs. For both arms of the model, data on survival were obtained from international literature. In addition, survival as observed among 20 infantile Dutch patients, who all received ERT, was used. Quality of life was assumed to be the same in both groups and was measured using the EQ-5D. Costs included the costs of ERT, which depend on a child's weight, and costs of health care use, informal care and infusions. A lifetime time horizon was used, with semi-annual time cycles. **RESULTS:** On average, ST receiving patients were modelled not to survive the first half year of life; whereas the life expectancy in the ERT patients was modelled to be almost 14 years. Lifetime incremental QALYs were 6.7. Incremental costs were estimated to be € 7.0 million, consisting for 95% of treatment costs. The incremental costs per QALY were estimated to be € 1.0 million. The incremental cost per life year gained was estimated to be € 0.5 million. **CONCLUSIONS:** In 2012, the Dutch health care insurance board advised the Minister of Health to reimburse enzyme replacement therapy in Pompe disease, despite its unfavorable ICER. Other factors, such as the rarity of the disease, equity considerations, and the relatively modest budget impact have probably played a role in this decision. These and other factors could be incorporated in a formal multi-criteria decision analyses.

PSY38

COST-EFFECTIVENESS AND COST-UTILITY ANALYSIS OF BELIMUMAB FOR THE TREATMENT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN PORTUGAL

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OBJECTIVES: To estimate the incremental cost-effectiveness (ICER) and cost-utility ratio (ICUR) of belimumab compared to standard care (SC) for the treatment of patients with Systemic Lupus Erythematosus (SLE) in Portugal. **METHODS:** A lifetime microsimulation model represented the complex and multidimensional course of SLE, based on long term data from a US cohort of SLE patients. The analysis was undertaken using a societal perspective with 5% discount rates for costs (direct and indirect costs), and effects [Life Years Gained (LYG) and QALY (Quality Adjusted Life Years)]. The model was calibrated with the phase III BLISS trials data, and UK utility values. The ICER and ICUR were estimated by comparison of SC *vs*SC with belimumab, with a lifetime analytic horizon. Belimumab non-responders were discontinued after 6 months and belimumab treatment was maximized at 3 years. **RESULTS:** The model demonstrated that adding belimumab to SC to treat SLE patients with high disease activity, positive anti-dsDNA antibodies, and low complement (C3, C4) levels, would result in a potential gain of 0.41 life-years, and 0.32 QALYs. Incremental costs were€ 8,400, resulting in an ICER of €20,649/LYG and ICUR of €25,917/QALY for the base case scenario. ICER and ICUR are insensitive to the follow-up treatment costs of SLE, and wastage of drug; moderately sensitive to duration of treatment, and waning time; and very sensitive to discount rates, and exclusion of indirect costs. The probabilistic sensitivity analysis reveals a cost-effectiveness probability of 59% for a €30,000/QALY threshold, and a median ICUR of €27,932/QALY (95% confidence interval: €14,215/QALY - €52,279/QALY). **CONCLUSIONS:** The analysis suggests that adding belimumab to SC for SLE patients with high disease activity, positive anti-dsDNA, and low complement levels, is cost-effective, presenting an ICER and ICUR below the commonly used threshold. This study is funded by GlaxoSmithKline, protocol #HO-13-13626

PSY39

THE COST OF PRODUCING A UNIT OF BLOOD IN HOSPITALS: A NATIONWIDE ECONOMIC ANALYSIS FOR THE CASE OF GREECE

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OBJECTIVES: To estimate the cost of producing a unit of blood from a NHS and societal perspective in Greece. **METHODS:** In line with the official guidelines, the cost of blood production accounted only for the resources expended for collection, processing, laboratory testing, storage, as well as the indirect donor's productivity loss. Hence, the cost associated to donor recruitment, pre-transfusion preparation, transfusion administration, follow up management of adverse events, and other long-term relevant costs were not taken into consideration. Two separate questionnaires were used to collect data regarding: personnel time, annual blood quantities collected, percentage of wastage, consumables utilization, institutional overheads, information technology expenditure, medical equipment utilized, nuclear acid tests, other laboratory tests and indirect costs. Data gather by 53 hospitals across the country. An economic model was build using also economic data collected by the National School of Public Health and the Ministry of Health. All data referred to the year 2012. **RESULTS:** The cost distribution was positively skewed (skewness:1.530). The unweighted mean cost of collecting a blood unit was estimated at €146.43 (*standard deviation*: +€28.18, *min/max*: €110.25-€240.84). In addition, the indirect cost of donors' loss of productivity was estimated at €33,70 (+€49,23). Major cost component appears to be the cost of personnel, which was estimated at €46.86 (+€24.86, €16.49-€132.59), accounting for 32.0% of the total direct cost. The average of blood unit wastage was estimated at 4.90%. There were not differences between the cost of producing a unit of blood in Athens compared with the rest of the country (Man-Whitney test, p-value: 0.341). **CONCLUSIONS:** This study indicates that the cost of producing a cost of blood isn't insignificant. These figures need to be complemented with those concerning the cost of transfusion to have a full picture of producing and using a cost of blood locally.

PSY40

BURDEN OF CYSTIC FIBROSIS IN THE RUSSIAN FEDERATION

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OBJECTIVES: The significance of cystic fibrosis associated with early disability, the need for long-term regular treatment and follow-up and is associated with high costs. Data reflecting the socio-economic burden of cystic fibrosis in Russia is low, which dictates the need for clinical and economic studies, for example – this study. **METHODS:** An assessment of the burden of cystic fibrosis with the use of tobramycin inhalation solution from different manufacturers and powder inhaled tobramycin (Tobi Podhaler) for the treatment of Pseudomonas infections in patients with cystic fibrosis. The study took into account only the direct medical costs of one patient based on standards of outpatient and inpatient care for patients with cystic fibrosis. **RESULTS:** The burden of cystic fibrosis with the use of tobramycin powder for inhalation Tobi Podhaler with the time horizon of 10 years is reduced faster than in similar groups of patients: the point of profitability is on the eighth year of treatment when compared with tobramycin-Gobbi and a 9-year - with Bramitobom, when the use of Tobi Podhaler requires less cost to 46,372 USD and 50,138, respectively. **CONCLUSIONS:** Additional costs are difficult to calculate due to the fact that tobramycin solution for inhalation requires compliance with "cold chain" at all stages of the life cycle of the product: transportation, storage at the distributor and at the pharmacy, storage at home. Thus, obtained data in controlled efficacy studies of tobramycin solution in actual practice, may be significantly lower.

PSY41

QUALITY OF LIFE BENEFITS AND COST IMPACT OF PROLONGED RELEASE OXYCODONE/NALOXONE VERSUS PROLONGED RELEASE OXYCODONE IN PATIENTS WITH MODERATE TO SEVERE PAIN AND OPIOID-INDUCED CONSTIPATION DESPITE THE USE OF 2 LAXATIVES: A UK COST UTILITY ANALYSIS

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OBJECTIVES: To evaluate the cost-effectiveness of prolonged release oxycodone/naloxone combination tablets [OXN; naloxone is added to counteract opioid-induced constipation (OIC)] in patients who are constipated despite the use of two laxatives, compared with prolonged release oxycodone (OXY) alone. **METHODS:** A model used data from one phase II randomised, controlled trial (RCT) in patients with moderate/severe cancer pain and a pooled analysis of two phase III RCT's in patients with moderate/severe non-cancer pain. A subgroup of patients with OIC who had failed on two or more laxatives at screening was applied in the analysis (n=178). The drug cost for pain therapy was combined with laxative costs and other resources to calculate the cost difference between OXN and OXY. Quality-adjusted life-year (QALY) gains were calculated by mapping Bowel Function Index scores to EQ-5D utility values. Deterministic sensitivity analyses were performed. The analysis was conducted from the perspective of the UK National Health Service (NHS). **RESULTS:** The incremental cost of OXN vs. OXY was £409.60 for the average treatment duration of 301 days. OXN gave an incremental QALY gain of 0.0524. The estimated incremental cost-effectiveness ratio (ICER) was £7,821.80 for OXN vs. OXY. The ICER remained below £30,000 for all sensitivity analyses, with OXN dominating OXY in some scenarios when higher constipation unit costs were applied. **CONCLUSIONS:** Patients treated with OXN experienced a quality of life gain, and OXN had an ICER considerably below thresholds normally regarded as cost-effective in the UK (£20,000 – 30,000/QALY). More research is required into the cost of treating OIC, with OXN dominating OXY (total cost saving to the NHS and quality of life benefit) in sensitivity on OIC unit costs. OXN is therefore estimated to be a cost-effective option for treating patients with moderate to severe pain and OIC, who are constipated despite the use of two laxatives.

PSY42

COST-EFFECTIVENESS OF PLERIXAFOR (PXF) FOR STEM CELL MOBILIZATION IN LYMPHOMA (NHL/HL) AND MULTIPLE MYELOMA (MM) PATIENTS IN POLAND

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OBJECTIVES: To assess cost-effectiveness of PXF, used in combination with G-CSF versus standard mobilization options used alone, to enhance mobilization of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation (auto-HCT). Target population, as defined by Polish opinion leaders, are patients with NHL/HL or MM whose cells mobilize poorly, i.e. predicted poor mobilizers (peripheral blood CD34+ cell count <10/mL) and proven poor mobilizers (failure of previous mobilizations). **METHODS:** PXF is an add-on therapy to currently reimbursed standard mobilization (SM) options: G-CSF or chemotherapy plus G-CSF. Two scenarios were compared: with and without PXF. Analysis was performed using a Markov decision model, developed in *TreeAge Pro 2013*. A probabilistic (Monte Carlo simulation) model with time-dependent transition probabilities included initial cycle, during which the individual undergoes mobilization and auto-HCT if cell collection is successful, and four mutually exclusive health states: progression-free survival (remission and durable remission – lymphomas only), further treatment after progression, palliative treatment/observation and death. A one-year Markov cycle length was used with half-cycle correction. Baseline cohort characteristics, disease progression and utility estimates were obtained from systematic literature review and questionnaire study among Polish clinical practitioners. The analysis was conducted from the Polish public payer, patients, and societal perspective, over a lifetime horizon. Discount rates were 5% (costs) and 3.5% (outcomes). **RESULTS:** The mean QALY gain were 7,378 (PXF) and 6,452 (SM). The mean costs were 188,404 PLN (€45,019) (PXF) and 157,073 PLN (€37,532) (SM). Base-case incremental cost-utility ratio (ICUR) in NHL/HL/MM population was 33,821 PLN/QALY (€8,082). Probability of PXF being cost-effective in Poland when compared to SM is 99,8% (current threshold of 105,801 PLN/QALY (€25,281)). **CONCLUSIONS:** Based on accepted cost/QALY threshold values in the Polish settings, PXF was proved to be cost-effective option for NHL/HL/MM patients with poor response to SM regimens.

PSY43

COST-UTILITY ANALYSIS (CUA) OF BELIMUMAB (BEL) IN THE TREATMENT OF ADULT PATIENTS WITH ACTIVE, AUTOANTIBODY-POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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OBJECTIVES: To estimate the cost-utility of BEL treatment of patients with SLE as an add-on therapy to intensive standard of care (SOC) vs. SOC in Poland. **METHODS:** The general population considered in the analysis were patients with SLE with significant disease activity, who met criteria of SLE diagnosis and were ineffectively treated with SOC. CUA was performed from the public payer perspective. The lifetime horizon was assumed. The decision model was developed in *MS Excel* and adjusted to Polish conditions. The calculations were performed using Monte Carlo microsimulation. The model included data from international clinical studies and Polish data on costs and resource utilization. Direct medical costs were included: costs of drugs, administration, diagnostic, monitoring and *costs related to disease activity*. Results were calculated for two patients populations: target population 1 (TP1) - patients with positive anti-dsDNA, low complement and ≥10 scores in SELENA-SLEDAI scale and target population 2 (TP2) - patients with positive anti-dsDNA, low complement, ≥6 scores in SELENA-SLEDAI scale and necessity of corticosteroids use. **RESULTS:** CUA results showed that BEL compared to SOC is more costly however, also more effective therapy. The ICUR was 113,986 PLN/QALY and 108,744 PLN/QALY, respectively for TP1 and TP2. Obtained results are placed slightly above the Polish acceptability threshold. Additional health effects related to BEL treatment instead of SOC were noticed both in LYG and QALY (0.432 and 0.4 LYG; 0.322 and 0.294 QALY, respectively for TP1 and TP2). Moreover, the model suggests lower frequency of cardiovascular events, and also pulmonary and renal complications in BEL arm. **CONCLUSIONS:** Since there is currently no effective treatment option of SLE in Poland, reimbursement of belimumab will give patients an access to a safe and effective therapy, which allows them to return to active life and career and also to improve their quality of life.

PSY44

COST-UTILITY ANALYSIS OF DEFERASIROX FOR THE TREATMENT OF IRON OVERLOAD DUE TO FREQUENT BLOOD TRANSFUSIONS IN THE CHILDREN AND ADOLESCENTS

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OBJECTIVES: To estimate the cost-utility of deferasirox (DSX) treatment of iron overload due to frequent blood transfusions in children and adolescents in Polish conditions. **METHODS:** Clinical effectiveness data were taken from previously performed systematic review of deferasirox for the treatment of pediatric patients (age ≤ 18 years) with iron overload due to frequent blood transfusions. The way of administration of chelation therapy (parenteral vs. oral) significantly affects patients' functionality and quality of life. Therefore it was decided to perform a cost-utility analysis. Analogous to other economic studies, it was assumed that patient survival was the same for both compared interventions: deferasirox and deferoxamine (DFO). In the analysis a simple decision model was developed. The calculations were performed using Monte Carlo microsimulation technique (100,000 trials). Only direct medical costs were included in the analysis: costs of drugs and their administration, costs of monitoring and costs of blood transfusions. The time horizon of the analysis was one-year period. Two perspectives were considered: a public payer (National Health Fund, NHF) and the patient and NHF perspective. The measure of effects was QALY (quality adjusted life years). **RESULTS:** The results showed that DSX compared to current standard treatment of iron overload due to frequent blood transfusions (DFO) in the children and adolescents is more costly however also more effective therapy from both considered perspectives. The ICUR (incremental cost-utility ratio) of replacing DFO by DSX was 26,180 PN/QALY from NHF perspective. The results from both patient and NHF perspective was similar. **CONCLUSIONS:** With reference to the acceptability threshold in Poland the oral chelation therapy in the population of children and adolescents with iron overload due to frequent blood transfusions with deferasirox is cost effective intervention when compared with deferoxamine.

PSY45

COST-EFFECTIVENESS OF SAPROPTERIN VERSUS PHENYLALANINE FREE DIET IN PATIENTS WITH PHENYLKETONURIA IN EGYPT

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OBJECTIVES: Phenylketonuria (PKU) is an orphan disease with incidence rate 1:5000 in Egypt. Cost-effectiveness of Sapropterin versus Phenylalanine (PHE) free diet in PKU patients from the insurer perspective was evaluated over a time horizon of 10 years. **METHODS:** A cohort Markov chain model with six health states: healthy, mild PKU, controlled mild PKU, classical PKU, controlled classical PKU and death was identified based on the process of the disease. The length of a cycle was set at one year. The transition probabilities were derived from updated, previously published studies in Egyptian patients with PKU. Relative risk of Sapropterin and utilities were derived using international published sources. Direct Medical costs were obtained from the Ministry of Health mandatory Tarrif in Egypt. All costs and effects were discounted at 3.5% annually. All costs were reported in Egyptian pounds of the financial year 2013. Deterministic sensitivity analysis was conducted. **RESULTS:** Total costs for Sapropterin and PHE free diet were 304.1687 EGP and 188.6498 EGP respectively. QALYs for Sapropterin and PHE free diet were 0.00566 and 0.00547 respectively. The incremental cost-effectiveness ratio (ICER) for Sapropterin versus PHE free diet was 602,933 EGP/QALY. Sapropterin is not cost effective because it is more than 3 times GDP/capita in Egypt (57,566 EGP). The ICER was most sensitive to the utility of the states 'classical PKU' and 'controlled classical PKU'. **CONCLUSIONS:** World Health Organization recommends that interventions that cost more than 3 times GDP/capita for one Disability Adjusted Life Year (DALY) avoided should not be reimbursed. Despite the difference between DALY and QALY, one can assume they are similar to be able to put a value on the outcome. Sapropterin doesn't represent a good value for money compared to PHE free diet in the Egyptian PKU patients.

PSY46

A COST-UTILITY ANALYSIS OF LIGHTERLIFE TOTAL AS A TREATMENT FOR OBESITY IN THE UNITED KINGDOM

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OBJECTIVES: LighterLife Total (LLT) is a weight loss programme for the obese (BMI ≥30kg/m2) combining a very low calorie diet (VLCD) with weekly support groups for behaviour modification. This study evaluated the cost-effectiveness of LLT compared with dietary and surgical interventions. This is the first study assessing the cost-effectiveness of a VLCD. **METHODS:** A cohort model was developed to assess the reduction in BMI in the first 12 months following intervention with LLT, gastric banding, gastric bypass, Weight Watchers, Counterweight, Slimming World and no treatment, and the subsequent yearly BMI increase. Published all cause-mortality was applied by age and BMI. Co-morbidity prevalence (diabetes, colorectal cancer, CHD) was applied by BMI. Costs were applied for each intervention and for co-morbidities, from a UK health care perspective. Utilities were calculated by BMI with an additional decrement for co-morbidities. A 10 year time horizon was used. Analyses were run for two subgroups: BMI 30-40 in and BMI >40. **RESULTS:** BMI 30-40: compared against no treatment, Counterweight, Weight Watchers and Slimming World, LLT was associated with higher costs, but also greater QALYs and was cost-effective against all, with incremental cost-effectiveness ratios of £14,937, £16,004, £16,182, and £19,840, respectively. BMI >40: compared against no treatment LLT incurred higher costs, but also greater QALYs and was cost-effective (ICER = £5,349). LLT was less effective than banding and bypass. The budget impact of uptake of LLT across the UK was assessed for both BMI 30-40 and BMI >40 groups. **CONCLUSIONS:** BMI 30-40: LLT was more costly than dietary interventions, but lead to increased QALYs and was estimated to be cost-effective. BMI >40: LLT resulted in a lower initial BMI reduction than gastric banding and bypass. LLT was estimated to be cost-effective against no treatment in both groups.

PSY47

FULL COST OF PLASMA FROM VOLUNTARY NON REMUNERATED DONORS IN ITALY

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OBJECTIVES: In Italy, within the legal mandate to pursue national self-sufficiency of secondary blood products, the Regions are starting to organize trade to offset need/availability unbalances. Therefore the determination of the full cost to the Regions of plasma collection and handling is needed. **METHODS:** Plasma is obtained from voluntary, non-remunerated donors either from full blood or from apheresis, and is collected either directly in facilities of the Regional Health Services, or indirectly through the net of donors' associations before being delivered to the transformation industry for processing. Amount and costs of materials and activities needed for collecting, producing, validating, and distributing plasma were obtained from the transfusional medicine department of the Verona province, Veneto Region. Attributable overhead expenses are assumed at 15% of direct cost. When plasma is collected as part of the whole blood or from multicomponent apheresis, common costs are attributed basing on the commercial value of single components, taken as proxy of the willingness-to-pay for them. In an alternative scenario, only product-specific costs are attributed to plasma recovered from whole blood donations, for which the driving need is the supply of red blood cells. **RESULTS:** Total cost per liter of plasma sent for processing is estimated in 114 and 286 euros, respectively, for collection from whole blood and apheresis. Given the current mix of plasma origin, the weighed mean cost of plasma to the Regions before processing charges is estimated in 157 €. When plasma recovered from whole blood donations is considered by-product, its cost per liter sent to industry is estimated in 27 €, and the corresponding weighed mean cost in 92 €. **CONCLUSIONS:** The Italian donor-based system, in addition to

its ethical and social values, supplies plasma at a lower or comparable cost than commercially available.

PSY48

INDIRECT COSTS OF SYSTEMIC LUPUS ERYTHEMATOSUS-RELATED ABSENTEEISM IN POLAND: AN ANALYSIS BASED ON SOCIAL INSURANCE INSTITUTION DATA

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OBJECTIVES: To estimate indirect costs of systemic lupus erythematosus (SLE) in Poland, based on absenteeism in the workplace data derived from Department of Statistics of the Social Insurance Institution (ZUS). **METHODS:** Available insurance information consisted of data on: (1) sick leaves, (2) short-term inability to work - on the basis of decisions authorizing rehabilitation services (3) long-term inability to work – on the basis of medical certificates awarded because of incapacity for work. To calculate indirect costs we used three parallel alterations of the human capital approach (HCA) method - based on: the average monthly gross earnings, Gross Domestic Product (GDP) per capita or gross value added per 1 employee (adjusted by a factor of marginal productivity of labor). **RESULTS:** In 2010, in patients with SLE in Poland, sick leaves, short-term and long-term inability to work were responsible for: 1897, 596 and 27 012 months of absenteeism, in 1600, 112 and 2481 persons, respectively. The total number of 2459 years of lost productivity corresponded to indirect costs of: 100,421,579 PLN, 97,215,041 PLN or 161,743,804 PLN, based on average earnings, GDP per capita or adjusted gross value added per employee, respectively. **CONCLUSIONS:** Two of the three approaches, in addition - the most frequently mentioned in the literature, indicated the indirect costs of systemic lupus erythematosus in Poland at around 100 million PLN per year. Our estimates of indirect costs may be undervalued because it did not include the cost of lost productivity due to premature mortality in the course of SLE, and the costs associated with a reduction in the efficiency of the work done despite of the disease (preseenteism).

PSY49

CHARACTERIZING DISEASE BURDEN IN AN ULTRA-RARE DISEASE IN THE UNITED STATES: TRANSTHYRETIN (TTR) AMYLOIDOSIS PATIENTS & CAREGIVERS

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OBJECTIVES: TTR amyloidosis, a progressive, degenerative ultra-rare genetic disease, can cause familial amyloid polyneuropathy (TTR-FAP) and cardiomyopathy (TTR-CM), requiring substantial caregiver support. This study evaluated the burden of illness on patients' and caregivers' work productivity, health care resource use (HCRU), and health-related quality of life (HRQoL). **METHODS:** An online survey including the Work Productivity & Activity Impairment (WPAI) questionnaire, EQ-5D, & HCRU questions recruited TTR-FAP and TTR-CM patients and caregivers through two U.S.-based patient advocacy groups. **RESULTS:** Thirty-three TTR patients (26 males) and 18 caregivers (7 males) completed the survey. Most were aged over 60; mean disease duration was approximately 6 years (patients) or 5 years (caregivers with disease). Most patients and caregivers had a college degree. Generally caregivers (77.8%) were the primary caregiver for their patient; 61.1% also had amyloidosis. Unemployment was high in patients with TTR-FAP (42.9%), TTR-CM (60.0%), both TTR-FAP/CM (71.4%); only 33.3% of caregivers reported working part/full-time. Employment was highest for TTR-FAP patients (n=10), yet 11.8% missed work, 32.2% were impaired at work and 38.5% reported overall work impairment due to TTR. Liver transplant, the primary treatment option, occurred in 42.4% patients and 18.2% caregivers with disease. A majority of patients reported outpatient visits to health care providers in the past 3 months for disease: 85.7% TTR-FAP, 100% TTR-CM, and 85.7% for TTR-FAP/CM. Hospitalization rates ranged from 14.3-30.0% across all patient groups, with 14.3-23.8% for emergency visits. EQ-5D Index scores for patients were 0.80 (SD=0.14) with transplant, and 0.68 (SD=0.16) without transplant. Caregivers with disease and transplant had lower EQ-5D Index scores (M=0.14, SD=0.35) than those without transplant (M=0.41, SD=0.32). The pattern was similar for EQ-5D VAS results for patient and caregiver groups. **CONCLUSIONS:** TTR amyloidosis is associated with substantial disruption in employment rates, work productivity, high levels of resource use, and poor HRQoL for patients and caregivers.

PSY50

RESOURCE CONSUMPTION EVALUATION ASSOCIATED WITH RITUXIMAB ADMINISTRATION IN PORTUGAL

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OBJECTIVES: Determine the costs associated with rituximab intravenous (iv) preparation and administration in follicular non-Hodgkin lymphoma (NHL) and estimate the difference *versus* rituximab subcutaneous (sc) formulation, considering material resources (MR) consumption and health care professionals (HCP) time spent in each procedure. Patient's and chair time savings in hospital Day Care Unit (DCU) were also estimated. **METHODS:** Rituximab iv data was collected, between November 2012 and January 2013, through face to face interviews with pharmacists and DCU nurses responsible for the preparation and administration in each hospital. The HCP time cost was calculated by multiplying their income per hour by the average time spent on each procedure; MR costs were determined based in official databases or in "table values" provided by the manufacturers. Rituximab sc administration time was based in the respective pivotal clinical trial - SABRINA (BO22334). **RESULTS:** Ten hospitals from mainland Portugal were included, with a weekly average of 7 NHL patients treated with rituximab iv. The HCP average overall active time spent with rituximab iv preparation and administration, per treatment cycle, was about 89 minutes *versus* 16 minutes estimated for sc. An average overall cost reduction of 93% was estimated with sc *versus* iv (3€ *versus* 45€, respectively). DCU chair time capacity could be increased by 3 and 7 fold if one considers combination or maintenance therapy, respectively, with rituximab sc *versus* iv, due to SC much faster administration. Rituximab sc reduces the overall time patients spend in an infusion chair by 95% (7 min with sc *vs.*143 min with iv). **CONCLUSIONS:** Rituximab sc formulation potentially offers significant resource (material and HCP time) savings, improves hospital organization and provides clear benefits for patients regarding time saved and administration convenience. Ultimately, rituximab sc increases hospital efficiency that's critical in the current economic climate.

SYSTEMIC DISORDERS/CONDITIONS – Patient-Reported Outcomes & Patient Preference Studies

PSY51

THE ASSOCIATION BETWEEN SEVERITY OF 'AVERAGE' PAIN (NPRS) AND THE EQ-5D INDEX IN PATIENTS WITH NEUROPATHIC PAIN

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OBJECTIVES: Pain is an important driver of health-related utility. Our purpose was to characterise the association between pain severity and the EQ-5D index. **METHODS:** Paired values for the Numerical Pain Rating Scale (NPRS) average pain score (previous 24 hours) and the EQ-5D index were available from a prospective, non-interventional study of people with neuropathic pain treated with an 8% capsaicin patch (Qutenza™). The NPRS records pain on an integer scale between 0 and 10 units, representing no pain and worst imaginable pain, respectively. The EQ-5D index is derived from impairment level (none/moderate/severe) across five domains (Mobility, Self-care, Usual activities, Pain & discomfort, Anxiety & depression), and values health-related utility on a scale of 1 to 0, meaning perfect health and death, respectively. Generalized linear mixed models with a normal probability distribution, identity link function, and a first-order autoregressive covariance structure were tested to determine the relationship between EQ-5D index score (scale) and NPRS average 24 hour pain score (ordinal). **RESULTS:** For the purposes of this preliminary analysis, 170 patients with NP contributed 353 combined observations from baseline observation and follow-up assessments at week-8 and week-12. The GLMM model that best fitted the data (smallest Information criterion) had one random effect (subject + intercept) and one fixed effect (NPRS + intercept). The fixed-effects coefficients were: (Intercept) 0.728 + (NPRS1: β 0.000; 95%CI -0.0186, 0.186) + (NPRS2: -0.045;-0.205,0.116) + (NPRS3: -0.075;-0.227,0.078) + (NPRS4: -0.207;-0.364,-0.049) + (NPRS5: -0.181;-0.338,-0.024) + (NPRS6: -0.315;-0.471,-0.159) + (NPRS7: -0.323;-0.478,-0.167) + (NPRS8: -0.458;-0.618,-0.299) + (NPRS9: -0.638;-0.825,-0.451) + (NPRS10: -0.740; -0.927,-0.553). Predicted utility was highly correlated (R^2=0.753) with observed utility. Mean squared error for predicted utility was 0.033 (sd 0.052). **CONCLUSIONS:** Neuropathic pain was highly correlated with utility with a difference of around 0.8 utility units across the NPRS range. All domains of the EQ-5D differed across the NPRS.

PSY52

MEASURING PROS THAT MATTER TO BARIATRIC AND BODY CONTOURING SURGERY: THE BODY-Q

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OBJECTIVES: Health care payers are interested in funding bariatric surgery because it resolves a range of obesity-related health problems. However, following weight loss, many patients are left with unsightly excesses of skin and require body-contouring surgery. Our team has developed a new PRO instrument (i.e., the BODY-Q) to measure satisfaction and quality of life of bariatric and body-contouring surgery patients. Unlike existing PRO instruments, the BODY-Q is composed of scales that measure appearance-related concerns, which is an important reason why patients seek treatment. The BODY-Q also stands apart as it the only PRO instrument designed to measure change in patients concerns throughout the entire weight loss journey. **METHODS:** We followed international guidelines for the development of a PRO instrument. This abstract presents Phase I results, i.e., qualitative phase. Patient stories were used to develop a conceptual framework covering the key concerns of patients, and to develop a set of preliminary items. Items were grouped into clinically meaningful scales and instructions and four-point response options were developed. The scales were refined by obtaining feedback from a sample of surgical experts and patients. **RESULTS:** From 59 patient interviews, we developed a conceptual framework. Over 3,500 preliminary items were developed and used to inform the following 17 independently functioning scales: 1) appearance scales measuring the body, abdomen, upper arms, buttocks, inner thighs, hip and outer thighs, skin and scars; 2) quality of life scales measuring body image, sexual, psychological and social wellbeing, physical function and symptoms; and 3) process of care scales measuring satisfaction with information, doctor and office staff. **CONCLUSIONS:** Phase II involves a multicentered field-test in Canada and the USA. Rasch Measurement Theory analysis will be used to determine which items to retain in each scale based on their performance against a standard set of psychometric criteria.

PSY53

THE USE OF PREFERENCE BASED MEASURES IN HAEMOPHILIA: IS THE CURRENT EVIDENCE BASE USEFUL FOR EVIDENCE BASED DECISION MAKING?

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OBJECTIVES: To identify and evaluate the published evidence base on the use of preference based measures for assessing haemophilia related outcomes, and to discuss their limitations and gaps for evidence based decision making. **METHODS:** A systematic review was carried out for 25 year time period 1988 to 2013 to investigate preference based evaluations of treatments and/or outcomes related to haemophilia. The search terms included:utility, QALY, standard gamble, time-trade-off, contingent valuation, conjoint analysis, and discrete choice. **RESULTS:** The search identified 22 original peer reviewed articles, covering a range of countries and treatments. There were 7 cost-utility analyses, and 7 studies reporting use of the EQ 5D to determine utility values for haemophilia health states. Two studies, both from Canada, were vignette type studies that directly assessed utilities for treatment related health states. The EQ 5D studies produced reasonably consistent utilities, whereas the vignette studies produced variable results. Six studies were conjoint analysis and/or willingness to pay studies and focused on the value of attributes of new treatments. As is typical of studies in rare diseases, there were limitations in all studies related mainly to small sample sizes, uncontrolled designs and potentially confounding factors. The main evidence gaps were a lack of preference/utility data for caregivers, or the direct impact of bleeding on utilities, and only one study used a generic measure other than the EQ 5D (the SF-6D) to generate utilities for haemophilia health states. **CONCLUSIONS:** Given that haemophilia is a rare condition, there is a reasonably large evidence base of preference based studies for potential use in evidence based decision making. However, the limitations and gaps in the studies identified mean that there are still limitations in the evidence base to support a comprehensive assessment of the value of new interventions for haemophilia.

PSY54

PATIENTS AT THE CENTER OF REGULATORY DECISIONS: USING STATED-PREFERENCE DATA TO HELP REGULATORS ANSWER DIFFICULT QUESTIONS

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OBJECTIVES: In collaboration with FDA's Center for Devices and Radiological Health (CDRH), we developed and administered a best-practice discrete-choice experiment (DCE) survey to elicit preferences for outcomes associated with using weight-loss devices to demonstrate how DCE data can help determine meaningful benefits for regulatory decisions involving serious side-effect risks. **METHODS:** An online DCE questionnaire was administered to adult residents of the United States who reported having or having had a body mass index (BMI) of at least 30 kg/m^2. Respondents evaluated constructed hypothetical weight-loss devices with different features identified with the help of clinicians at CDRH. Weight-loss devices were defined in terms of device effectiveness, device-related risks of side effects, surgery requirements for implantation, and diet restrictions. An efficient experimental design ensured that device profiles provided the necessary statistical information to identify the choice-model parameters. Random-parameter choice models produced preference weights indicating the strength of preference for device features. These weights were used to calculate the maximum acceptable risk of dying or minimum required weight loss associated with various device profiles. **RESULTS:** A total of 540 respondents completed the online survey. Results from the study show that respondents had well-defined, plausible preferences for different outcomes associated with weight-loss devices. Internal validity tests, including a scope test of sensitivity to absolute risk levels, indicated the data are of high quality. Preference results were used to construct an Excel-based tool that calculates the necessary benefits to offset the device-related risks with confidence intervals for any device that can be described by features included in the study design. **CONCLUSIONS:** Results confirm the feasibility of using DCE methods to evaluate patients' tolerance for weight-loss device risks, as well as the feasibility of constructing a policy-relevant decision aid that makes this information accessible to regulators.

PSY55

HEALTH RELATED QUALITY OF LIFE BY LINE OF THERAPY IN IMATINIB-RESISTANT OR IMATINIB-INTOLERANT PATIENTS WITH CHRONIC MYELOID LEUKEMIA TREATED WITH BOSUTINIB MEASURED BY EQ-5D

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OBJECTIVES: Bosutinib a dual Src/Abl tyrosine kinase inhibitor (TKI) demonstrated efficacy in a phase 1/2 study of patients with relapsed/refractory Chronic Myeloid Leukemia (CML). Health utilities were reported in the imatinib IRIS study, but there is limited information from relapsed/refractory CML patients. The objective was to evaluate the effect of bosutinib on health utilities in patients with CML after failure with imatinib. **METHODS:** Evaluation of patient HRQoL was an exploratory objective in the clinical trial measured using the EQ-5D, which consists of 5-items: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each item ranges from 1 ("no problems") to 3 ("extreme problems"). The EQ-5D was completed at weeks 4, 8, 12 and every 12 weeks thereafter, as well as treatment completion and scored according to the UK tariff. **RESULTS:** Of the N=570 patients included in the trial, 288 were second line chronic phase (CP 2L) CML, 118 were third line CP patients (3L), 76 were accelerated phase (AP) and 64 blast phase (BP). For 2L patients, the mean utility score at baseline was 0.83 (SD 0.21), and was maintained throughout the course of the study demonstrating a significant improvement at week 36 (mean change from baseline 0.04, p=0.01). For 3L patients, the mean utility at baseline was 0.80 (SD 0.22), and maintained throughout the study. There were no statistically significant differences from baseline through week 36 in health utility in 3L patients. The mean utility at baseline for advanced patients was 0.78 (SD 0.28) for AP and 0.66 (SD 0.30) for BP patients and was maintained throughout the study. **CONCLUSIONS:** These data suggest that relapsed/refractory CML patients treated with bosutinib maintain their quality of life throughout the trial regardless of the line of treatment or phase of disease. These results highlight the value of capturing patient HRQoL in CML treatment.

PSY56

A SYSTEMATIC REVIEW ON THE EFFECT OF BEHAVIORAL VERSUS SURGICAL INTERVENTION ON OBESE PATIENTS' PSYCHOLOGICAL WELL-BEING

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OBJECTIVES: Approximately 400 million people worldwide are considered obese as defined by the World Health Organization. In Europe, 15.5% of adults have a body mass index of ≥30 kg/m^2. Diabetes, heart disease, and stroke, are among the most common obesity-related comorbidities. Furthermore, obesity has also been found to cause depression and emotional distress, negatively affecting the quality of life of obese patients. With obesity at the forefront of many social and health care dialogues, treatment guidelines currently suggest exercise (often linked with changes in diet) or weight loss surgery to effectively treat obesity. This review seeks to understand which of these two types of interventions, exercise or surgical, have a greater impact on obese patients' emotional and psychological well-being. **METHODS:** A systematic review of peer-reviewed literature was conducted to identify RCTs and observational studies that measure any type of emotional or psychological change in patients who underwent either of the interventions of interest for weight loss: exercise or weight loss surgery. Embase and Medline databases were searched for articles published from 2004 to 2013. Search terms were used to identify studies that assessed psychological well-being of obese patients who either exercised or underwent weight loss surgery. **RESULTS:** The search identified 40 studies, of which 11 measured relevant interventions and measures of psychological well-being. Of those, 9 investigated patients undergoing bariatric surgery, while only 2 explored exercise interventions. All of the studies indicated improvements in patients' emotional health, except for 1 bariatric surgery study, where patients were shown to have no change in symptoms after weight loss plateaued. **CONCLUSIONS:** While both interventions, when they lead to weight loss, seem to result in improvements in patients' psychological well-being, there is limited data to conclude whether one intervention is more effective in improving psychological well-being. Further study is needed, especially for exercise interventions.

PSY57

OBESITY TRENDS 2006-2012 IN THE UNITED STATES: RESULTS FROM THE NATIONAL HEALTH AND WELLNESS SURVEY

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OBJECTIVES: According to the Centers for Disease Control and Prevention, there were dramatic increases in the obesity rates in the US since 1980s which reached a plateau after 2003[1]. The objectives of this study were to examine obesity trends across US adults from 2006-2012 by various gender/age groups and changes in activity impairment. **METHODS:** Results were from the US National Health and Wellness Survey, a nationally representative, online survey. Respondents were age ≥ 18 years, and results were weighted/projected to reflect the gender, age, and race/ethnic proportions, as determined by the Current Population Survey (US Census Bureau). This analysis focused on adults age ≥ 20 by BMI Class 1 (BMI>=30 & <35 kg/m^2), Class 2 (BMI>=35 & <40 kg/m^2), and Class 3 (BMI>=40 kg/m^2). Activity impairment was assessed from the Work Productivity and Activity Impairment Questionnaire. **RESULTS:** The proportions of adults age 20+ with Class 1, Class 2 and Class 3 obesity levels have slowly declined from 2006 to 2012 (Class 1: 19.3% in 2006 to 18.4% in 2012; Class 2: 9.2% in 2006 to 8.2% in 2012; Class 3: 7.3% in 2006 to 6.7% in 2012). This is consistent across most age/gender subgroups, except in the group of men age 60+, which showed increases of Class 2 (7.5% to 8.2%) and Class 3 obesity (3.7% to 4.6%); Activity impairment declined along with the decline of obesity prevalence (men and women), though women reported greater impairment than men in the corresponding BMI Class. **CONCLUSIONS:** The data suggested a slight decline in obesity prevalence and improvement in activity function in the US population recently. However, obesity remains a pandemic with tremendous health and economic burden and calls for continuous effort in education, prevention and management. References 1 Centers for Disease Control and Prevention. Referenced June 11, 2013. http://www.cdc.gov/obesity/data/facts.html

PSY58

THE IMPACT OF INCREASING PAIN SEVERITY ON IMPAIRMENT OF REGULAR DAILY ACTIVITIES

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OBJECTIVES: To evaluate to what extent pain severity was associated with impairment of regular daily activities other than paid work. **METHODS:** Study data originated from a prospective, non-interventional study of people with NP treated with the capsaicin patch QUTENZA™. Repeated observations from baseline- and 12-week follow-up assessments for the Numerical Pain Rating Scale (NPRS) 'average pain in the last 24 hours' score, and the Activity Impairment (AI) score from the Work Productivity Activity Index (WPAI-NP) were analysed. The NPRS subjectively records pain on a scale between 0 (no pain) and 10 (worst imaginable pain). The WPAI-NP Activity Impairment Index measured the extent to which NP affected regular daily activities from 0% (no effect) to 100% (complete prevention). Generalized linear mixed models (GLMM; SPSS v20), with a normal probability distribution, identity link function, and a first-order autoregressive covariance structure were tested to determine the relationship between WPAI-NP-AI (scale) and NPRS (ordinal). **RESULTS:** A total of 171 patients with NP contributed 253 combined observations from baseline and week 12 follow-up assessment. Mean age at baseline was 59.4 years (sd 14.9) and 44% of subjects were male. The GLMM model that best fitted the data (smallest information criterion) had one random effect (subject+intercept) and two fixed effects (Sex+NPRS+intercept). The significant (p<0.05) fixed-effects coefficients were: (Intercept) 14.2+(Male: β -7.0; 95%CI -13.5,-0.5)+(NPRS3: 24.4;9.0,39.8)+(NPRS4:9.4;13.5,45.3)+(NPRS5:36.5;21.2,51.8)+(NP

RS6:43.7;28.5,60.0)+(NPRS7: 46.3;31.1,61.5)+(NPRS8: 58.5;42.6,74.4)+(NPRS9:2.0;44.2, 79.8)+(NPRS10:72.2;54.7,89.7). The estimated marginal mean WPAI-NP-AI increased linearly from 10.1% at NPRS 0 to 84.8% at NPRS 10. Predicted WPAI-NP-AI was highly correlated with observed values (R-squared=0.889); mean absolute error (predicted-observed) was 9.6 (sd 6.9). **CONCLUSIONS:** In people with chronic NP, increasing pain severity was associated with a linear increase in impairment of regular daily activities other than paid work. Interventions that reduce pain are likely to improve functioning.

PSY59

HEALTH-RELATED QUALITY OF LIFE IN BRAZILIAN OBESE PATIENTS SUBMITTED TO BARIATRIC SURGERY: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: Bariatric surgery is the best long-term treatment for morbid obesity with clinical improves, like reductions in blood pressure, glucose and lipids levels. However postoperative complications and psychosocial issues may impact quality of life (QoL). This study aims to assess health-related quality of life (HRQoL) in Brazilian obese patients submitted to bariatric surgery. **METHODS:** A systematic review was conducted by April 2013 through Cochrane Collaboration, Medline, EMBASE, and Lilacs databases. Studies that described QoL in Brazilian obese patients were included in this review. Bariatric Analysis and Reporting Outcome System (BAROS), Moorehead-Ardelt quality of life questionnaire II (M-A-QoLQII), Abbreviated WHOQoL questionnaire and Short Form-6D (SF-6D) were used to evaluate the behavior of patients who underwent bariatric surgery in relation to QoL domains. **RESULTS:** Seven studies met eligibility criteria. In all studies, individuals presented body mass index (BMI) $\geq$ 40kg/m^2 or $\geq$ 35 kg/m^2 associated with comorbidities. Patients reported their self-esteem (SE), physical activity (PA), social relations (SR), disposition to work (DW) and sexual activity (SA), after bariatric surgery. According to the M-A-QoLQII, three studies showed HRQoL improvement in 28.9%, 39.5%, 28.4%, 30% and 25.6% of patients for SE, PA, SR, DW and SA, respectively. And 68.9%, 50.6%, 53.1%, 52.2%, 45.6% of patients guaranteed greatly improved regarding those parameters, respectively. After weight loss, bariatric surgery was effective to improve QoL in PA domain. Besides, when compared to patients submitted to medical treatment, patients who underwent surgical procedure presented an improvement of 93% in HRQoL, contrasting with 65.4% of the medical cohort ($p<0.001$). Only one study measured QoL before and after bariatric surgery: SF-36 domains and M-A-QoLQII showed that post-surgery results were invariably better than pre-surgery ones ($p<0.001$ for all domains). **CONCLUSIONS:** The present review demonstrated the potential QoL improvements in Brazilian patients after bariatric surgery, in addition to clinical benefits.

PSY60

STUDY OF QUALITY OF LIFE AND COSTS FOR CML PATIENTS IN BULGARIA

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OBJECTIVES: To analyze the cost of therapy for patients with chronic myeloid leukemia (CML) and their quality of life. **METHODS:** It is retrospective as regard to cost and prospective as regard to quality of life analysis. Five university hospitals in four major cities treating all 320 CML-patients are included for the period 2011-2012. Information is collected from the patients' records about the health care resources used as medicines for CML, additional therapy, hospitalizations and physicians visits. The assessment of health related quality of life is conducted with validated for the country SF-36 questionnaire. **RESULTS:** A total of 164 (51.2%) men and 156 (48.75%) women, average age 53.96±15.41 were observed. The average CML pharmacotherapy monthly cost is 5976.4 BGN, the average total pharmacotherapy cost for additional diseases is 566.27 BGN and the average additional costs for physicians' visits and hospitalization is equal to 1504.69 BGN. The most expensive CML therapy is with Dasatinib 7771.20 BGN and the cheapest is Imatinib therapy equal to 5245.15 BGN. The most common additional diseases are cardiovascular (68%), followed by endocrine (29%). There is significant correlation between overall assessment for quality of life and average total additional costs – the higher assessment for QoL, the lower costs for hospitalization and visits. With the significantly highest score is the scale Bodily pain, followed by Physical functioning, and the lowest are Vitality, energy or fatigue and Role limitation. In most of patients on Imatinib (77.9%) are recorded good hematological responses and 66.7% are with major molecular response. **CONCLUSIONS:** CML is a disease consuming significant health care resources especially for major pharmacotherapy with TKIs. Infrequent physicians' visits and rarer hospitalizations generate higher assessment of quality of life.

PSY61

TREATMENT SATISFACTION AND ITS ASSOCIATION WITH HEALTH OUTCOMES IN PATIENTS WITH NEUROPATHIC PAIN

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OBJECTIVES: Neuropathic pain (NP) is a chronic progressive disease which is hard to control. This analysis investigates patients' satisfaction with pain therapy and its relationship with pain severity and health related quality of life (HRQoL). **METHODS:** Data were drawn from the 2012 Adelphi NP Disease Specific Programme, a cross-sectional study involving 413 primary care physicians and specialists across Europe. Physicians provided detailed records for 3956 NP patients, of which 1568 patients voluntarily completed EQ-5D and Brief Pain Inventory questionnaires. HRQoL was measured via the EQ-5D, satisfaction via a three-option question answered by the patient, and pain via the Brief Pain Inventory (BPI) interference score. Boxplot analyses were used to compare outcomes across satisfaction groups. **RESULTS:** Only 64 (4.08%) were satisfied with their treatment, and 1504 (95.92%) not satisfied. A positive relationship was observed between satisfaction and HRQoL, with the most satisfied group recording a 31.62% higher EQ-5D score (mean 0.75 vs. 0.57, $p<0.01$) relative to the next most-satisfied group. A negative relationship was observed between satisfaction and pain, with the most satisfied patient group scoring 30.89% lower pain scores (mean 3.40 vs. 4.91, $p<0.01$). **CONCLUSIONS:** Most neuropathic pain patients are not satisfied with their current pain therapy. This analysis suggests a negative relationship between treatment satisfaction and reported pain severity as well as a clear positive relationship between treatment satisfaction and health related quality of life. The results highlight the need for a more targeted treatment of neuropathic pain patients.

PSY62

PROFILE OF BACK PAIN SUFFERERS ACROSS 5EU COUNTRIES

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OBJECTIVES: According to the Pain in Europe Study, about one in five EU adults have chronic pain. Back pain / lower back pain is among the most commonly cited location of pain.[1] Additionally, research has suggested that pain has a negative impact on sufferer mental health, employment, sleep and personal relationships.[2] This analysis profiles and compares adults experiencing back pain to adults without pain across 5EU. **METHODS:** Results were taken from the 2011 5EU National Health and Wellness Survey, a nationally representative, self-administered survey. Respondents were adults age 18 and over from France, Germany, Italy, Spain and UK. This analysis focuses on adults diagnosed with back pain or experienced pain as a result of back problem in the past month- ("patients with back pain"). Quality of life was measured using the SF12v2 scale. Activity impairment was measured using the Work Productivity and Activity Impairment scale. **RESULTS:** Out of the total sample of n=57,512, ~10% (n=5,984) have back pain. Relative to adults without pain, back pain sufferers are older on average (48.9 vs. 46.3), more likely to be women (57% vs. 48%), and obese (27% vs. 16%). Their overall mental and physical quality of life scores are significantly lower (43.2 vs. 47.9, $p < 0.001$ and 40.3 vs. 50.9, $p < 0.001$). In addition, back pain sufferers are exhibited more work impairment (absenteeism and presenteeism) and activity impairment, and utilized health care resources to a greater extent than non-sufferers (i.e., greater physician visits, hospitalization, and ER). All these results are notably higher among back pain patients treated with a prescription. **CONCLUSIONS:** Considering the prevalence of back pain among adults, the level of work impairment and quality of life limitations impacts a substantial portion of adults in the 5EU population. Improvements in treatment of back pain are needed to reduce this burden.

PSY63

EVALUATING WILLINGNESS-TO-PAY THRESHOLD FOR SUGAMMADEX REVERSAL OF ROCURONIUM-INDUCED NEUROMUSCULAR BLOCKADE: A CONTINGENT VALUATION SURVEY

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OBJECTIVES: Reversal of the residual effect of rocuronium or vecuronium by neostigmine may be slow and associated with side-effects. Sugammadex, a selective relaxant binding agent, encapsulates rocuronium to provide for a rapid reversal of residual neuromuscular blockade. Also, postoperative residual neuromuscular block can reduce delay of awakening, recovery, and dissatisfaction of patient. The aim of this study is to evaluate the willingness-to-pay (WTP) of sugammadex for effectiveness and safety using a contingent valuation method. **METHODS:** A total of 505 adult general population and 60 experts (anesthesiologist and surgeon) participated in a face-to-face survey. The respondents were surveyed separately each scenario of moderate and deep blocks for surgery. The scenario was designed to provide information concerning reversal time on neuromuscular block, adverse reaction of PRNB, and quality of surgery or recovery. The out-of-pocket WTP for sugammadex was utilized open answer. **RESULTS:** In general population, WTP values for sugammadex were 81,768 Korean won (KRW) in moderate block and 128,622 KRW in deep block. The same sample answered 89,017 KRW and 141,536 KRW for WTP for their family members in moderate block and deep block, respectively. Experts were estimated the WTP of 99,417 KRW in moderate block and 153,250 KRW in deep block. For patients, experts suggested that 82,517 KRW and 132,517 KRW were appropriate WTP. The WTP was statistically significantly higher in the general population who had been taken operation and older than their counterparts. **CONCLUSIONS:** The WTP for sugammadex was ranged the 81,768 to 99,417 KRW in moderate block, and the 128,622 to 153,250 KRW in deep block. The WTP of general population for their family members was higher than the WTP for their own, and the expert's WTP was higher than their patients.

SYSTEMIC DISORDERS/CONDITIONS – Health Care Use & Policy Studies

PSY64

LIKELIHOOD OF USE AND PERCEPTION TOWARDS BIOSIMILARS IN RHEUMATOID ARTHRITIS ARENA: SURVEY OF RHEUMATOLOGISTS IN EUROPEAN UNION, BRAZIL, JAPAN AND CHINA

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OBJECTIVES: To assess rheumatologist perception towards biosimilars and the likelihood of use of biosimilars to manage RA patients in the EU, Brazil, Japan and China. **METHODS:** A multi-country cross-sectional survey was conducted in top-5 EU countries (UK/Germany/Spain/France/Italy), Brazil, Japan and China in April/May 2013 using an online physician panel in the respective geographies; rheumatologists were randomly selected for survey participation to be geographically representative in select countries/regions. Surveys assessed the rheumatologist perceptions of biosimilars in terms of factors that would prevent them from using

biosimilars among their biologic-eligible RA patients, and their likelihood of use of biosimilars. Descriptive statistics are reported. **RESULTS:** A total of 173 rheumatologists participated in the survey. Years of experience practicing rheumatology was: <=1yr:0%, 2-5yrs:6%, 6-10yrs:17%, 11-20yrs:42%, >20yrs:32%. Geographic distribution of rheumatologists was: 5EU-58%, Brazil-23%, Japan-11% and China-9%. Mean RA patient-volume/year was 291 (5EU-329, Brazil-259, Japan-232 and China-189). Overall, 47% of rheumatologists reported that they would prescribe a biosimilar to their eligible RA patients "definitely or highly likely" (5EU:58%, Brazil:21%, Japan:47%, China:47%); 51% of rheumatologists reported that they would try using biosimilars for 1-2 yrs among a small group of patients in their practice before starting to use it in a majority of biologic-eligible RA patients in their practice (5EU:60%, Brazil:33%, Japan:42%, China:47%). The top-5 factors that would prevent them from using biosimilars were diverse across the countries (Overall/5EU/Brazil/Japan/China): Doubts in similarity to original molecule 60%/63%/67%/47%/33%), inadequate safety/efficacy profile/data (53%/51%/51%/58%/60%), lack of long-term data (46%/51%/41%/32%/40%), lack of national guidelines recommending the use of biosimilars (37%/39%/31%/32%/47%) and lack of data from local country/market (31%/23%/41%/42%/47%). **CONCLUSIONS:** Across markets, over half of the rheumatologists expressed concerns/reservations towards prescribing biosimilars to their eligible RA patients. While payer organizations look to biosimilars to contain costs and make medicines more affordable to RA patients in need, potential barriers to biosimilar adoption may exist.

PSY65

BARRIERS TO BIOLOGIC THERAPY USE FOR AUTOIMMUNE DISORDERS IN EMERGING MARKETS

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OBJECTIVES: Biologic therapy is increasingly used to treat autoimmune disorders in developed markets, but usage is still low in emerging markets. This analysis was conducted to identify factors associated with current use of biologic medication among patients with autoimmune disorders in emerging markets. **METHODS:** Data were from the Brazil, China, and Russia National Health and Wellness Surveys, cross-sectional surveys representative of the total adult population (Brazil) or urban adult population (China and Russia) in each country, conducted in 2011 and 2012. Respondents self-reporting physician diagnosis of ankylosing spondylitis, Crohn's disease, psoriasis, psoriatic arthritis, rheumatoid arthritis, or ulcerative colitis and using a prescription medication (Rx) for at least one of those conditions were included; patients with missing data for any covariate were excluded. Binomial logistic regression included the following predictors: age, sex, country, income, Charlson Comorbidity Index (CCI), body mass index (BMI), monthly out of pocket (OOP) costs for Rxs, fear of needles, condition severity, length of diagnosis, and type of treating physician. **RESULTS:** Of 1,507 respondents included in the analysis, 300 (19.9%) were using a biologic. Of those, 82.0% (n=246) were in China. Relative to China, patients were less likely to use biologics in Brazil (OR 0.21; 95% CI: 0.13, 0.36) and Russia (OR: 0.29, 95% CI: 0.18, 0.46; ps<0.001). Higher CCI was associated with use of biologics (OR: 1.18, 95% CI: 1.10, 1.26; p<0.001), as were higher OOP costs (OR: 2.37, 95% CI: 1.04, 5.42; p<0.05) compared to no OOP costs. Fear of needles was positively associated with biologic use (OR: 1.57, 95% CI: 1.18, 2.09; p<0.01). No other covariates were significant. **CONCLUSIONS:** Country was by the strongest predictor of biologic use in patients with autoimmune conditions in emerging markets, but higher costs and more comorbidities were associated with biologic use across emerging markets.

PSY66

DISEASE STATUS, TREATMENTS AND OUTCOMES OF PATIENTS WITH ANKYLOSING SPONDYLITIS RECEIVING THEIR FIRST BIOLOGIC IN THE UNITED STATES AND EUROPEAN UNION

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OBJECTIVES: To compare the disease status, treatments and outcomes of patients with AS receiving their first biologic in UK, Germany, France, Italy and Spain (5EU) with the US. **METHODS:** A multi-country multi-center medical chart-review study of AS patients was conducted between October-December 2012 among physicians (rheumatologists: 5EU: 97%, US: 99%) in hospitals and private practices to collect de-identified data on AS patients who were recently treated with a biologic as part of usual care. Physicians were screened for duration of practice and patient volume and recruited from a large panel to be geographically representative in each country. Eligible AS patient charts (>2) were randomly selected from a sample of prospective patients visiting each center/practice during the screening period. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status/outcomes. **RESULTS:** Seven hundred and ninety seven eligible AS patient charts (5EU:613, US: 184) were abstracted; 701 (5EU:549, US: 152) patients were on their first biologic (mean-age: 5EU:42.5yrs/US:42.4yrs; female: 5EU:16.2%/US:17.1%). Time-to-1st biologic from diagnosis (5EU:55.3months/US:46.8months) and time-on-current biologic (5EU:31.7months/US:44.3months) differed between regions. Top-2 biologic treatments observed were – adalimumab (5EU:43%/US:35%) and etanercept (5EU:30%/US:41%). Among the top-3 reasons for biologic treatment initiation, 'mechanism of action' & 'improve signs/symptoms' were observed in both 5EU and US, whereas 'positive personal experience' (5EU) and 'prevention of structural damage' (US) were also observed. Key lab measures documented were: ESR (5EU:17.4mm/h, US:20.9mm/h) and CRP (5EU:8.8mg/dl, US:2.7mg/dl). Current disease severity per physician-judgment (mild:moderate:severe) was: 5EU-63%:32%:6%, US-62%:34%:5%. Among patients with available data, current HAQ (5EU:1.3, US:0.8), BASDAI (5EU:2.9, US:3.4), VAS provider score (5EU:2.9, US:2.5), VAS patient score (5EU:3.0, US:2.7), Swollen Joint Count (5EU:1.3, US:0.5), and Tender Joint Count (5EU:2.0, US:0.9) differed across regions. **CONCLUSIONS:** Among AS patients receiving their first biologic, disease severity differed between 5EU and US, with patients in 5EU with relatively higher burden and poorer outcomes.

PSY67

VARIATIONS IN TREATMENT PATTERNS AND DISEASE SEVERITY AMONG PATIENTS WITH PSORIASIS RECEIVING THEIR FIRST BIOLOGIC IN EUROPEAN UNION

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OBJECTIVES: To assess the treatment patterns and current disease severity of patients with PsO receiving their first biologic in 5EU, namely, UK, Germany (DE), France (FR), Italy (IT) and Spain (SP). **METHODS:** A multi-country multi-center medical chart-review study of PsO patients was conducted among dermatologists in hospitals/private practices to collect de-identified data on patients who were recently treated with a biologic as part of usual care. Physicians were screened for practice-duration (3-30 yrs) and patient-volume (incl.>2PsO biologic patients/month) and recruited from a large panel to be geographically representative in each country. Physicians abstracted charts of next five consecutive biologic patients within each center/practice. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease severity. Results from patients on first biologic treatment were analyzed. **RESULTS:** In 4Q2012, 225 physicians abstracted 924 eligible PsO patient charts; 690 (75%) were on their first biologic (mean-age:46.9yrs, female:36%). Geographic distribution-UK:18%, DE:21%, FR:19%, IT:21%, SP:21%. Time-to-1st biologic from diagnosis (months)/time-on-current biologic (months) varied- UK:140/17, DE:119/10, FR:138/15, IT:103/18, SP:127/17. Top-4 first-line biologic treatments observed were etanercept, adalimumab, infliximab and ustekinumab. Treatment experience prior to first biologic varied dramatically (not mutually exclusive): Immunomodulators-UK:92%,DE:51%,FR:68%,IT:73%,SP:76%; phototherapy-UK:55%,DE:71%,FR:59%,IT:32%,SP:37%; topicals-UK:41%,DE:69%,FR:46%,IT:43%,SP:39%; retinoids-UK:29%,DE:30%,FR:34%,IT:42%,SP:40%; fumerates-UK:13%,DE:69%,FR:0%,IT:1%,SP:0%; corticosteroids-UK:2%,DE:32%,FR:10%,IT:14%,SP:10%; Average # of flares in the past yr were: UK-1.0,DE-1.3,FR-1.1,IT-1.0,SP-1.6. Mean current PASI scores were: UK-8,DE-20,FR-12,IT-18,SP-11. Current disease severity per physician judgment was (remission/mild/moderate/severe): UK-45%/25%/20%/10%, DE-26%/19%/21%/35%, FR-42%/34%/15%/9%, IT-39%/19%/31%/11%, SP-44%/29%/26%/2%. Mean number of treatments prior to first biologic varied by current disease severity (remission/mild/moderate/severe): UK-2.7/3.1/2.6/3.1, DE-3.0/3.7/2.7/4.1, FR-2.2/2.6/2.2/2.4, IT-2.2/2.2/2.3/2.1, SP:2.4/2.2/2.3/2.3. **CONCLUSIONS:** Among PsO patients receiving their first biologic, treatment patterns and disease severity varied across 5EU, with patients in Germany disproportionately experiencing higher disease burden. Factors influencing the observed variations in care and optimal therapeutic approaches (including treatment sequencing) aligned with clinical guidelines to decrease patient disease burden warrants scrutiny.

PSY68

PHARMACOTHERAPY COSTS OF MULTIPLE MYELOMA IN THE CZECH REPUBLIC: A RETROSPECTIVE ANALYSIS

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OBJECTIVES: In the Czech Republic there are three modern molecules available for the treatment of multiple myeloma: bortezomib, thalidomide and lenalidomide. In order to better understand this evolving specific market, analysis of consumption trends has been conducted with emphasis on the molecules' mutual influence. **METHODS:** Time-consumption curves of bortezomib, lenalidomide and thalidomide since 2009, based on the economic data of the General Health Insurance Company of the Czech Republic, were analyzed. While there was reimbursement for thalidomide in the first line treatment and bortezomib in the second line in 2009, we focused on and evaluated the impact of the launch of lenalidomide in 2009 (as a second line treatment). We also investigated the extension of reimbursement of bortezomib for the use in the first line in 2010. **RESULTS:** The introduction of lenalidomide (2009) led to a rapid decline in thalidomide consumption within the next year, in contrast to bortezomib, the consumption of which appeared unaffected. Furthermore, also the consumption of thalidomide decreased profoundly following the extension of reimbursement conditions of bortezomib (2010). The overall relative reduction in thalidomide consumption observed within the two years between 2009 and 2011 was 70%. **CONCLUSIONS:** The presented retrospective analysis shows that the impact of myeloma treatment on payers' financial budgets has increased nearly 3-times in the last four years. The extension of reimbursement of bortezomib had a clear impact on the consumption of thalidomide, which was its supposed comparator in the first line therapy. However, it appears that even though the introduction of lenalidomide did also significantly affect the consumption of thalidomid, it had no apparent impact on the use of bortezomib.

PSY70

APPETITE SUPPRESSANTS: A DRUG UTILISATION STUDY

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OBJECTIVES: To determine the prescribing and cost of appetite suppressants in a defined private sector patient population, as well as the prescribing of other medicines to the patient sample. **METHODS:** A retrospective drug utilisation study was conducted on a medical insurance claims database in South Africa for 2010 and 2011. No clinical information was available in the database. **RESULTS:** In 2010, 37 patients (86.49% females) were prescribed 44 appetite suppressants at a total cost of R9813.39, of which 75.0% were for phentermine. The average age of patients was 40.95 (SD=12.37) years. In 2011, 27 patients (77.78% females) received 42 prescriptions for appetite suppressants at a total cost of R9967.73. The average age of patients was 40.04 years (SD=10.41) (females: 37.95 (SD=7.76) years; males 47.33 (SD=10.52) years). Most products (80.95%) were for phentermine, followed by d-norpseudoephedrine (14.29%) and diethylpropion (4.76). Prescribing patterns in 2010 and 2011 were similar. Appetite suppressants are strictly regulated in South Africa.

In 2011, a total of 630 products (all therapeutic classes) were prescribed. The most often other prescribed classes in 2011 were gastrointestinal tract products (14.60%), cardiovascular agents (11.11%) and antimicrobial products (9.52%). The most frequently prescribed subclasses were HMG-CoA reductase inhibitors (statins), analgesic combinations, non-selective COX-inhibitors and selective serotonin re-uptake inhibitors. The total amount claimed from the medical insurance scheme for all the products was R73013.71, however, only R37553.24 was paid out. Appetite suppressants were excluded from patients' medical insurance benefits. **CONCLUSIONS:** A limited number of strictly regulated appetite suppressants were prescribed. Appetite suppressants that patients can buy over-the-counter were not included in this study. Pseudoephedrine has recently been rescheduled to be more strictly controlled due to its abuse potential. Further consumer studies on appetite suppressants which include clinical information will provide a useful insight into the role of these products in weight loss efforts.

PSY71

ANALYSIS OF THE REIMBURSED PSORIASIS MARKET IN HUNGARY BETWEEN 2007 AND 2011

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OBJECTIVES: Psoriasis is a chronic skin disease of scaling and inflammation, typically characterized by erythematous papules and plaques with a silver scale. In Hungary, approximately 150.000 – 200.000 people are affected. We sought to evaluate the available reimbursed psoriasis treatment options, the economic impact of the disease, and in general we attempted to see beyond the market trends and patients characteristics observed in the analysed dataset. **METHODS:** Data were derived from the nationwide dataset of the Hungarian National Health Insurance Fund Administration, the single health care financing agency of Hungary. Data were evaluated according to sex, age, geographical region, type of care and specialty of the prescribing physician. The analysis covers data of all reimbursed pharmaceuticals and other medical services between 1 January 2007 and 31 December 2011. **RESULTS:** The median age was between 51 and 55 years. A bimodal age of onset has been recognised in several large studies, but in this patient cohort people between the ages of 30 and 69 were overrepresented. We found no significant deviation between counties, but there is a clear seasonality in the data. During each year of the analysed period the number of patients who redeemed at least one reimbursed drug fell short compared to the prevalence based estimates. At any given time close to 80% of the patients did not receive any reimbursed treatment and the number of sold packages continuously decreased over the 5-year period. The introduction of biologic treatments also significantly affected the market. **CONCLUSIONS:** To our knowledge, no systematic empirical research exists addressing the question of how psoriasis market changed over the time in Hungary. The data suggest relatively poor adherence to treatment regimens frequently seen and documented in other studies as well.

PSY72

UTILIZATION PATTERNS FOR TREATMENT WITH STRONG OPIOIDS FOR CHRONIC BACK PAIN IN GERMANY

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OBJECTIVES: Although opioids are a well-accepted and effective method for pain management, it is still a challenge for physicians to find adequate treatment schemes in non-malignant pain. Inadequate treatment might impact quality of life and induce social and psychological problems. Aim of this survey was to describe treatment patterns of chronic back pain (CBP) in Germany. **METHODS:** In a cross-sectional, non-interventional survey n=4,283 German physicians were asked to report experiences with strong opioids in CBP. Statistical analysis was performed to analyze relationships between strong opioids and potential side effects. **RESULTS:** The majority of physicians (54.4%) at least partly accept strong opioid therapy in CBP noting treatment benefits in 69.6%. Most prescribed therapies are non-opioids like NSAIDs/COX-2 (55.1%) and physiotherapy (47.7%). 22.7% of all CBP receive strong opioids (26.0% fentanyl, 19.9% oxycodone/naloxone, 17.8% oxycodone, 13.9% hydromorphone, 13.8% burprenorphine, 13.7% morphine, 7.3% tapentadol, 1.8% L-methadone). 16.5% are treated in monotherapy, 23.6% with multimodal treatment. 67.5% show a reduction in pain intensity ≥50%. 25.8% need strong opioids for longer than 12 months. 26.2% need an increased dosage. Furthermore, 20.2% of patients experience a decrease in efficacy, which leads to opioid rotation (15.1%). 23.4% have persistent side effects (25.3% never, 46.4% temporary) wherefore 16.1% switch and 15.2% withdraw the treatment. Most side effects are observed near start of therapy, with constipation being the most common and resistant side effect (49.1%). After treatment discontinuation, pain status is considerable worsened in 34.3%. Correlation analysis shows that morphine has the highest probability of side effects when compared to oxycodone and oxycodone/naloxone. **CONCLUSIONS:** Although physicians see the medical need, CBP patients seem not to be overly treated with strong opioids. Obviously, morphine is not the treatment of first choice. Treatments chosen strongly depend on physician specialty. As anticipated, constipation is the most common and resistant side effect.

PSY73

VARIABILITY OF CLINICAL PRACTICE FOR BARIATRIC SURGERY IN SPAIN

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OBJECTIVES: Geographical variations in medical practice are expected to be small when the evidence about a particular technology is abundant. This would be the case of bariatric surgery (BS), which has been demonstrated to be an effective intervention to promote weight-loss in patients with indications for this procedure (PWI). Moreover, BS has recently proven to be cost-effective and drive long-term savings, compared to a "do-nothing" intervention, for the Spanish National Health System. The objective of this research is to analyze the differences in adoption of BS among the different Spanish Autonomous Communities (Regions). **METHODS:** Ecologic design. A retrospective analysis of the Spanish 2011 Health System Survey was conducted to estimate the prevalence of adult PWI for BS in each Region. The results were therefore extrapolated to the total regional adult population reported by the National Institute of Statistics for 2011. The total number of bariatric surgeries by Regions during 2011were retrieved from the database of the National Health Ministry (ICD-9-CM: 44.31, 44.39, 44.38, 44.95 and 44.69) **RESULTS:** Variation in the annual provision of BS was large, ranging from 0.81% of patients with indication for Murcia, to 0.11% in Navarra. For the rest of Regions, the percentage of PWI operated in 2011 was: Madrid=0.62%; Castilla y León=0.60%; Aragón=0.35%; Cataluña=0.33%; Pais Vasco=0.32%; Com. Valenciana=0.30%; Cantabria=0.30%; Canarias=0.30%; Extremadura=0.23%; Galicia=0.22%; Asturias=0.19%; Andalucía=0.18%; Castilla La Mancha=0.15%; Baleares=0.14% and La Rioja=0.13%. **CONCLUSIONS:** These results raise the hypothesis that living in a certain Region may strongly affect the probability of a PWI receiving BS. In such case, this variability should be tackled, particularly in a country where most patients are supposed to have access to this treatment without any copayment. Further research with more accurate estimations and multilevel analysis models would be desirable to confirm these results.

PSY74

PIVOTAL STUDIES OF ORPHAN MEDICINAL PRODUCTS – AN ANALYSIS OF QUALITY OF CLINICAL EVIDENCE

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OBJECTIVES: Recent debate on the long-term effectiveness of some orphan medicinal products (OMPs) led us to question whether the initial standards for clinical evidence for OMPs, set by EMA at the time of marketing authorization, are too low. Therefore, the aim of this study was to quantitatively evaluate the characteristics and quality of clinical evidence that is presented for OMPs to obtain marketing authorization in Europe. **METHODS:** We quantitatively assessed the characteristics and quality of clinical evidence of the pivotal studies of 64 OMPs as described in the European Public Assessment Report and/or the Scientific Discussion document prepared by the Committee for Human Medicinal Products of the EMA using a new and validated instrument. **RESULTS:** The 64 OMPs were altogether authorized for 78 orphan indications, for which 117 studies were identified as 'pivotal' or 'main' studies. In approximately two thirds of the studies, the allocation was randomized (64.8%) and a control arm was used (68.5%). Half of the studies applied some type of blinding. Only a minority (26.9%) of the studies included a Quality-of-Life (QoL) related endpoint, of which a third claim an improvement in QoL. Upon analyzing the quality of reporting, we found that some aspects (i.e. the endpoints, the sampling criteria, and the interventions) are well described, whereas other items (i.e. a description of the patients and of potential biases) are not reported for all studies. **CONCLUSIONS:** In conclusion, the pivotal studies that are the basis for marketing authorization of OMPs are a cause for concern, as they exhibit methodological flaws. Additionally, there are shortcomings in the reporting of those studies that complicate the interpretation. A more demanding regulatory process for OMPs is needed to guide evidence-based clinical decision-making.

PSY75

HOW TO DETERMINE SIZE OF PATIENT POPULATION WHEN THE RIGHT DATA ISN'T THERE?

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OBJECTIVES: As costs of health care continue to rise, payers need to quantify the potential patient population for a new treatment. In the case of a novel treatment for intractable pain that would be for end of life cancer patients, it was necessary to consider alternative methods for calculating the potential patient population size. This study determined different approaches for identifying patient subpopulations in cancer for 'end-of-life' pain therapies **METHODS:** PAREXEL conducted a literature search on the number of cancer pain patients with intractable pain. Data was found on cancer patients with pain but not those at the end of their lives with intractable pain. Alternative measures were considered, and cancer mortality data was identified as a surrogate for end of life cancer patients. The WHO's guidelines on cancer pain estimate that 10 to 25% of cancer pain patients have intractable pain. Based on such surrogate measures, we were able to determine an estimated number of cancer patients with intractable pain at the end of their lives. **RESULTS:** Prior to this study, the target patient population was estimated to be 156,000 in the US and an equivalent number in Germany, UK, Spain and France. However, based on the surrogate measures, the results were much lower: 30,000 in the US and 31,000 in the 4 EU countries. These numbers were validated by interviewing 22 pain clinicians in the US and EU and 23 payers in the US and EU. **CONCLUSIONS:** By providing payers with accurate estimates of potential patient populations they will be better able to determine the cost implications of covering novel treatments. Given that the care provided to patients at the end of their lives is usually significantly higher than at any other time, treatments for end of life care have economic implications for payers.

PSY76

COST-MINIMIZATION OF MABTHERA INTRAVENOUS VERSUS SUBCUTANEOUS ADMINISTRATION

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OBJECTIVES: To identify and compare all costs related to preparing and administrating MabThera for the intravenous and subcutaneous formulations in Dutch hematological patients. The a priori notion is that the costs of subcutaneous MabThera

injections are lower compared to intravenous infusion due to potential lower time investments, shorter pharmacy preparation time, less patient chair time and less spillage. **METHODS:** We use a prospective, observational, bottom up, micro-costing approach aiming at the inclusion of 50 patients with hematological disease. Primary cost outcomes comprise the labor costs for nurses and pharmacists/pharmacy technicians, materials, hourly daycare costs and drug spillage costs. Exact timings are measured using stopwatches, dosing and spillage is measured using registered MabThera volumes in the Hospital Pharmacies' registrations and materials are exactly numbered and labeled. List prices are used for materials and MabThera costs, hourly nurse and pharmacy time is costed according to salaries, and day-care is costed using the Dutch guideline for costing research in health care. Anticipating positive outcomes of the currently ongoing non-inferiority study, efficacy of MabThera along both administration routes was implicitly assumed similar; additionally parity pricing is assumed. **RESULTS:** Interim results based on 24 patients included so far indicate that extra costs of intravenous infusion over subcutaneous injections are on average €175 per administration. This difference is primarily constituted by €100 lower daycare costs related to shorter chair time for subcutaneous as compared to intravenous administration. **CONCLUSIONS:** Our interim cost-minimization analysis suggests that subcutaneous injection of MabThera involves lower administration costs than intravenous infusion. With similar efficacy assumed, cost savings can be achieved at no expense of health, by including subcutaneous MabThera injections in the Dutch reimbursement system. Notably, over a full course of administrations (8 cycli) cost savings may easily surpass €1000 per patient per year.

PSY77

IS IT WORTH HAVING ORPHAN DRUG STATUS IN GERMANY POST-AMNOG?

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OBJECTIVES: To review the assessments of benefit for orphan drugs within the early benefit assessment process after implementation of AMNOG in Germany. **METHODS:** Secondary research was used in this study. **RESULTS:** In contrast to other pharmaceuticals, by law, the benefit of orphan drugs (ODs) is proven by market authorization. No assessment vs. an appropriate comparator as defined by G-BA will be conducted, provided the revenue is less than 50 mio. EUR based on pharmacy retail prices including VAT over the past twelve months. IQWiG only assesses the accuracy of the number of patients and the therapy costs stated in the value dossier, while GB-A defines the extent of the benefit based on the Phase III data submitted with the abbreviated dossier. Seven ODs have been assessed by G-BA since implementation of AMNOG in 2011. Only one OD has received considerable benefit status in one patient subgroup, whilst two ODs have been classified as not quantifiable, and the other ODs assessed so far have been granted only a minor benefit. Prices have been negotiated for only 2 ODs so far: For Pirfenidon, with an unquantifiable benefit, a rebate of 11% was applied, while Tafamidis, with a minor benefit, received a rebate of 24.5%. **CONCLUSIONS:** There is a clear benefit for ODs (with annual sales of less than 50 mio EUR) in terms of reduced administrative burden and costs associated with the abbreviated value dossier submission. Furthermore, the OD status and the absence of a comparative added benefit assessment warrant a benefit score, whereas 60% of the non-orphan pharmaceuticals failed to prove an additional benefit vs. the defined comparator. As only two orphan drugs have completed price negotiations, it is very difficult to estimate, whether OD status will have a positive impact on future pricing opportunities after AMNOG.

PSY78

COST-EFFECTIVENESS OF SCHOOL-BASED HEALTH PROMOTION IN CANADA: A LIFE-COURSE MODELING APPROACH

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OBJECTIVES: The Alberta Project Promoting active Living and healthy Eating (APPLE) Schools has been recognized as a "best practice in preventing childhood obesity. To inform decision making on the expansion and resource allocation for such school-based program like the APPLE Schools, we evaluated its cost-effectiveness and return-on-investment following a life-course approach. **METHODS:** We developed a state transition model to represent the life-time progression of weight status of three groups of children who were obese, overweight or normal weight at 11 years. The model quantified impacts of the intervention in terms of prevented excess weight cases, improved quality-adjusted life years (QALY), and avoided health care costs. Both costs and QALYs were estimated to their present value using 3% discount rate. **RESULTS:** The incremental cost-effectiveness ratio (ICER) of the APPLE Schools program was CA$ 15,833 per 1 QALY gained, and CA$ 24,359 or 11,047 per 1 obese or overweight case prevented in adult population. Every 1,000 children intervened; the program costs CA$190,000, and the estimated saving in the health care costs is about CA$ 2.3 million, that is equivalent to a benefit-cost ratio of 13:1. The sensitivity analyses showed that the incremental cost-effectiveness of the APPLE Schools program was robust against variations of program costs and model parameters. **CONCLUSIONS:** The APPLE Schools program is a cost-effective intervention for obesity prevention, and promises substantial return on investment. Expanding the coverage and allocating resources towards school-based programs is central to the fight against obesity epidemic in Canada.

PSY79

PAYER ASSESSMENT AND REIMBURSEMENT POLICY FOR RARE DISEASES: A REVIEW OF THE LITERATURE

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OBJECTIVES: To review the published literature to identify: a) the most frequently cited challenges relating to payer assessment and reimbursement of rare disease treatments (including orphan drugs), and b) to review author recommendations to improve the assessment of these treatments. **METHODS:** A systematic literature review of Medline and EMBASE databases was conducted for the period 2000 - 2013. The search sought to identify papers on the topic of assessment and reimbursement policy for rare diseases. Health policy studies, commentaries, and review articles were included. Clinical or economic studies of specific drugs or diseases were excluded. Information was extracted on assessment and reimbursement challenges and author recommendations for addressing these issues. **RESULTS:** The literature review identified 726 papers; 49 met the inclusion criteria. The most frequently identified issues included multiplicity of orphan indications (34/49), high per-patient cost (32/49), and the difficulty in undertaking robust clinical and economic evaluations given limited evidence (32/49). Several authors commented on limitations of current health technology appraisal processes. The issue of equity and societal preference for funding rare diseases was highlighted in almost half of the papers (22/49). Lack of availability of alternative treatments was also considered an important factor. Suggestions for improvements to the assessment and reimbursement process included: greater use of registries (22/49), adjustment to preference weights used in cost effectiveness analysis (19/49) and conditional reimbursement and risk-sharing-schemes (12/49). Some authors advocated alternative pathways for assessing rare disease treatments including a specific approach utilising multi-criteria decision analysis. **CONCLUSIONS:** The debate on payer policy in rare diseases has grown in the last 5 years as concerns have increased about patient access to new medicines. While there is some consistency in the literature, there is as yet little consensus on how policy should be changed to address these issues.

PSY80

A SYSTEMATIC REVIEW OF THE EFFECTIVENESS OF TAXES IN PREVENTING OBESITY TRENDS

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OBJECTIVES: Obesity prevalence is increasing worldwide, a worrying trend as it relates to many diseases and imposes significant direct and indirect health care costs. The purpose of the present study was to assess the impact of taxation policies upon the consumption of Sugar Sweetened Beverages (SSBs) and High in Fat Sugar and Salt (HFSS) foods and ultimately caloric intake and weight outcomes. **METHODS:** The review identified relevant papers from web-based searches in comprehensive databases such as: Pubmed, Web-of-Science, Cochrane Library, Ag Econ, Econlit and National Agricultural library. Searching was conducted with all potential combinations of various relevant for the purposes of the study financial, nutritional, and outcome terms. Thereafter, abstracts were reviewed and studies were selected based on predefined criteria. The search included studies published from 1990 up to February of 2013 in English language. The characteristics and the results of the selected studies were extracted in a special form and consequently were reviewed and synthesized, based on the methodological design. **RESULTS:** A total of fifty five studies were finally included in the review. Several different types of studies showed a reduction in purchases and consumption of SSBs or HFSS foods when prices increase due or not due to taxation, but the subsequent effect upon total caloric intake was much smaller. A few studies which report weight outcomes, indicate that they are either insignificant or very small in magnitude to cause any public health improvements. **CONCLUSIONS:** The effectiveness of taxation policies to curb obesity levels is doubtful and the desired objectives not easily attainable, mainly because of the complex nature of consumer behavior and the impact of substitution effects, for which there is limited evidence to date. There is need to investigate in more depth the potential underlying mechanisms and the links between price increase policies, obesity and public health outcomes.

PSY81

MANAGED ENTRY AGREEMENTS AND ORPHAN DRUGS: A EUROPEAN COMPARATIVE STUDY (2006-2012)

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OBJECTIVES: To identify, describe and classify managed entry agreements (MEAs) applied to orphan drugs by national payers and to analyse their practice in Europe. **METHODS:** To identify and describe MEAs, national HTA and reimbursement decisions on orphan drugs across seven European countries were reviewed and their main characteristics extracted. To fill data gaps and validate the accuracy of the extraction, collaboration was sought from national payers. To classify MEAs, a bespoke taxonomy was implemented. Identified MEAs were analysed and compared by focusing on five key themes, namely by describing the MEAs in relation to: drug targets and therapeutic classes, geographical spread, type of MEA applied, declared rationale for setting-up of MEAs, and evolution over time. **RESULTS:** Forty-two MEAs for 26 orphan drugs, implemented between 2006 and 2012 and representing a variety of MEA designs, were identified. Italy was the country with the highest number of schemes (n=15), followed by The Netherlands (n=10), England and Wales (n=8), Sweden (n=5) and Belgium (n=4). No MEA was identified for France and Germany due to data unavailability. Antineoplastic agents were the primary targets of MEAs. 55% of the identified MEAs were performance-based risk-sharing arrangements; the other 45% were financial-based. Nine of these 26 orphan drugs were subject to MEAs in two or three different countries, resulting in 24 MEAs. A total of 60% of identified MEAs focused on conditions whose prevalence is inferior to 1 per 10,000. **CONCLUSIONS:** This study confirmed that a variety of MEAs were increasingly used by European payers to manage aspects of uncertainty associated with the introduction of orphan drugs in the health care system, and which may be of a clinical, utilisation, or budgetary nature. It remains unclear whether differences in the use of MEAs reflect differences in how 'uncertainty' and 'value' are perceived across health care systems.

RESEARCH POSTER PRESENTATIONS – SESSION II
DISEASE-SPECIFIC STUDIES

CANCER – CLINICAL OUTCOMES STUDIES

PCN1
A LITERATURE REVIEW ON THE HUMANISTIC AND ECONOMIC BURDEN OF MINERALOCORTICOID EXCESS SYNDROME
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OBJECTIVES: Notable side effects of abiraterone for advanced prostate cancer are oedema, hypertension, and hypokalemia, constituting a mineralocorticoid excess syndrome (MES). Although abiraterone is co-administered with prednisone to minimise MES symptoms, they remain a burden requiring concomitant therapies to manage each toxicity and/or treatment with costly mineralocorticoid receptor antagonists. A literature review was conducted to assess the impact of MES symptoms on health-related quality of life (HRQoL) and health care costs in patients across a number of disease areas. **METHODS:** Outside prostate cancer, MES is a broad syndrome which is best characterised as bilateral primary aldosteronism (PA). Electronic databases were searched for data on the economic and humanistic burden of MES (or its symptoms in combination) and/or PA. **RESULTS:** Even though no studies were identified in a specific prostate cancer population, nine studies found humanistic burden and three of the economic burden related to MES (PA) in the literature. Patients with MES (PA) had significantly impaired HRQoL (measured by SF36 and SF12) compared with the general population, especially on physical domains, general health perceptions, and vitality. Patients also exhibited greater levels of anxiety, depression and somatization. Use of mineralocorticoid receptor antagonists was associated with reduced HRQoL. Despite sparse direct economic data on MES, hypertension and oedema were associated with increased health care resources and costs. Chronic oedema was additionally associated with hospitalisation and lost productivity. **CONCLUSIONS:** MES symptoms can significantly impair HRQoL and may increase resource use. The impact of these symptoms in an advanced prostate cancer population is likely to be exacerbated, as many of these elderly patients already have serious co-morbidities. Further research is required to determine the incidence and severity of MES in patients receiving abiraterone in actual clinical practice and the impact these symptoms have on health care resource use and the well-being of patients with prostate cancer.

PCN2
BISPHOSPHONATES-ASSOCIATED OSTEONECROSIS OF JAW IN CANCER PATIENTS: A META-ANALYSIS
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OBJECTIVES: This meta-analysis aims to assess the incidence of osteonecrosis of the jaw(ONJ)associated with bisphosphonates in cancer patients. **METHODS:** The published literature was systematically searched and reviewed using MEDLINE and the Cochrane Central Register of Controlled Trials on 30 April 2013. Any randomized controlled trial assessing the role of bisphosphonates in cancer patients and clearly mentioned the event of ONJ were eligible for inclusion. Studies that included specific risk estimates were pooled using a random-effects model. The quality of these studies were assessed with RevMan statistical software (version 5.0). **RESULTS:** Eight of 21 randomized controlled clinical trials were included. Thirteen studies were excluded due to no cases of osteonecrosis of jaw were reported. A total of 13,399 patients were collected in eight studies, 6686 patients were assigned to bisphosphonates group and 6713 were assigned to control group. Twenty-eight cases (28/6686,0.42%) of ONJ were reported in bisphosphonates group. No patient was reported in control group. Risk ratio was used to estimate the risk of osteonecrosis of the jaw associated with bisphosphonate. Pooled results showed very lower risk of ONJ associated with bisphosphonates 5.61 (95% CI: 1.90, 16.52). No heterogeneity was found in our study. **CONCLUSIONS:** Although the risk ratio of ONJ associated with the use of bisphosphonates is low in our study, we still need to suggest physicians to make a particular concern on using bisphosphonates in cancer patients. We suggest that a large and well design of risk of ONJ as primary endpoint, prospective multi-center studies should be conducted in the future.

PCN3
SKELETAL-RELATED EVENTS HAVE A SIGNIFICANT IMPACT ON HEALTH-RELATED QUALITY OF LIFE IN MEN WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER (MCRPC) FOLLOWING DOCETAXEL THERAPY FAILURE
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OBJECTIVES: Patients with mCRPC are at risk of experiencing skeletal-related events (SREs), defined as pathologic fracture, spinal cord compression, and the need for radiotherapy or surgery to bone. We examined the immediate impact of an SRE on patients' HRQoL. **METHODS:** Data were obtained from the AFFIRM study, a phase 3 trial of enzalutamide vs. placebo in patients with mCRPC. Only patients experiencing any type of SRE were included in the analysis (*n=284*). For patients with multiple SREs, only the first event was used. HRQoL was assessed at baseline and at fixed intervals throughout the study until treatment discontinuation using the FACT-P (Functional Assessment of Cancer Therapy–Prostate) instrument. We used linear mixed-effects models to model each patient's longitudinal trajectory of FACT-P outcomes before the first SRE and to estimate how far the post-SRE value of HRQoL deviated from that trajectory. **RESULTS:** SREs were associated with a deterioration of HRQoL with an adjusted mean change of -6.93 (95% CI: [-9.92; -3.95]) of the FACT-P total score for any SRE. The largest impact was observed in subjects with spinal cord compression, which induced a mean decrease in the FACT-P total score of -9.68 (95% CI: [-16.10; -3.27]); pathological bone fractures and radiation or surgery to bone determined changes in FACT-P total score of -7.61 (95% CI: [-16.79; 1.56]) and -6.68 (95% CI: [-10.25; -3.11]), respectively. The standardized effect size was moderate (any SRE: -0.32; spinal cord compression: -0.49; pathological bone fracture: -0.35; radiation or surgery to bone: -0.30). **CONCLUSIONS:** Consistent with previous analyses in metastatic prostate cancer [Weinfurt K.P., et al. Annals of Oncology 2005;16: 579–584], our findings demonstrate that SREs lead to significant functional declines in patients' daily lives. Therefore, any therapy reducing or delaying the occurrence of SREs should also reduce the effects of SREs on HRQOL.

PCN4
CAN ADMINISTRATIVE DATA PREDICT CHEMOTHERAPY ADVERSE EVENTS?
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OBJECTIVES: The rates of adverse events (AEs) are an important component of chemotherapy cost effectiveness. However, AE rates in clinical practice are difficult to obtain. This study aimed to determine whether Australian administrative data could identify the incidence of selected chemotherapy AEs. **METHODS:** The Elements of Care study (EoC) was a prospective cohort of individuals in New South Wales undergoing chemotherapy for breast, colorectal or lung cancer. Primary data, including AEs experienced, was collected through questionnaires and medical record review. Linked administrative data of prescriptions and medical services for each participant were available from the Pharmaceutical Benefits Scheme (PBS) and Medicare Benefits Schedule (MBS). This data was used to identify if an individual was treated for one of the selected AEs (diarrhoea, vomiting, anaemia and neutropenia) in the three days after a chemotherapy dose. These proxy-identified AE rates were compared with the self-reported AE rates using 2x2 contingency tables, with significance of any differences calculated using odds ratios and chi-square statistics. **RESULTS:** There were 482 individuals in EoC. The proxy identified much lower rates of AEs than were self-reported, capturing 30% of self-reported cases of nausea and vomiting, 1.3% of self-reported diarrhoea, and less than 1% of self-reported anaemia and neutropenia. Additional analyses did not identify a pattern in the grade of AEs or type of treatment received that the proxy was more likely to identify. **CONCLUSIONS:** Overall there was poor concordance between the two measures of AE rates. This may be due to low treatment rates for AEs, poor capturing of AE treatments by the proxy, or over-reporting of adverse event by participants. Regardless, it would appear that administrative data such as the MBS and PBS are not suitable for estimating the incidence of AEs in clinical practice, and bottom up data collection techniques such as EoC are essential.

PCN5
EVALUATION OF THE BURDEN OF ILLNESS OF SKIN CANCER AMONG VETERAN PATIENTS UNITED STATES
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OBJECTIVES: To evaluate the burden of skin cancer among U.S. veteran patients. **METHODS:** Patients diagnosed with skin cancer were identified (International Classification of Disease 9th Revision Clinical Modification [ICD-9-CM] diagnosis code 232.xx) using the Veterans Health Administration (VHA) Medical SAS datasets from October 1, 2009 to September 30, 2011. The first diagnosis date was defined as the index date. A comparison group of patients without skin cancer of the same age, region, gender and index year were identified and matched on baseline Charlson Comorbidity Index with a randomly chosen index date to minimize selection bias. Patients in both groups were required to be at least 18 years old and have 1 year continuous health plan enrollment pre- and post-index date. Follow-up health care costs and utilizations were compared between the two groups after using 1:1 propensity score matching adjusting baseline characteristics. **RESULTS:** A total of 12,504 patients were identified for the skin cancer and comparison cohorts. After 1:1 propensity score matching, each group included 4,400 patients with well-balanced baseline demographic and clinical characteristics. Patients diagnosed with skin cancer had higher percentages of inpatient (5.75% vs. 2.64%, p<0.01), emergency room (11.89% vs. 6.50%, p<0.01), physician office (99.95% vs. 66.70%, p<0.01), outpatient (99.95% vs. 67.41%, p<0.01), and pharmacy visits (91.89% vs. 71.30%, p<0.01). Patients in the skin cancer cohort also incurred higher expenditures in inpatient ($1,494 vs. $555, p<0.01), emergency room ($108 vs. $60, p<0.01), physician office ($4,486 vs. $1,480, p<0.01), outpatient ($4,780 vs. $1,639) and pharmacy visits ($707 vs. $429, p<0.01) than patients in the comparison group. **CONCLUSIONS:** Study results suggest that cancer patients diagnosed with skin cancer incurred significantly higher costs and health care resources compared to patients without.

PCN6
EVALUATION OF THE BURDEN OF ILLNESS OF COLORECTAL CANCER AMONG VETERAN PATIENTS IN THE UNITED STATES
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OBJECTIVES: To examine the economic burden and health care utilizations of colorectal cancer patients in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration Medical SAS datasets (01OCT2008-30SEP2012). Patients (≥18 years of age) diagnosed with colorectal cancer (International Classification of Disease 9th Revision Clinical Modification ICD-9-CM codes 153.xx, 154.xx) were identified. The first diagnosis date was designated as the index date. A comparator group was created by categorizing patients without colorectal cancer but of the same age, region, gender and index year, and matching them by baseline Charlson Comorbidity Index. The index date for the comparison group was selected randomly to minimize selection bias. Continuous medical and pharmacy benefits for 1 year pre- and 1 year post-index date were required. One-to-one propensity score matching (PSM) was used to compare the health care costs and utilizations during the follow-up period between

the colorectal cancer and comparison groups, adjusted for baseline demographic and clinical characteristics. **RESULTS:** A total of 75,208 patients were identified for the colorectal cancer and comparison cohorts. After 1:1 PSM, 24,053 patients were matched from each group, and the baseline characteristics were proportionate. Patients diagnosed with colorectal cancer had more health care utilization including inpatient (20.40% vs. 2.61%, p<0.01), emergency room (ER) (15.32% vs. 6.06%, p<0.01), outpatient (99.60% vs. 64.31%, p<0.01) and pharmacy visits (88.30% vs. 66.20%, p<0.01). The higher health care utilization resulted in increased health care costs, including high inpatient ($9,867 vs. $795, p<0.01), ER ($158 vs. $61, p<0.01), outpatient ($5,020 vs. $1,585, p<0.01), pharmacy ($1,345 vs. $523, p<0.01) and total costs ($16,232 vs. $2,903, p<0.01) for patients diagnosed with colorectal cancer compared to patients in the comparison group. **CONCLUSIONS:** Veteran patients diagnosed with colorectal cancer incurred significantly higher health care utilization and costs over a 1-year period compared to patients without colorectal cancer.

PCN7

EVOLUTION OF MOLECULAR DIAGNOSTIC TEST USAGE IN SOLID TUMOURS IN WESTERN EUROPE: AMBITION STUDY (ANALYSIS OF MOLECULAR BIOMARKER TESTS IN ONCOLOGY)

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OBJECTIVES: The development of targeted therapies has changed the paradigm of cancer management necessitating the use of robust biomarkers to identify eligible patients. This study aims to evaluate trends in molecular diagnostic test (MDT) uptake across various solid tumors. **METHODS:** This study used IMS Oncology Analyzer™, a patient database collected through a quarterly physician panel survey. This database provides comprehensive insight into cancer care. Selected patients were at advanced/metastatic stages and diagnosed with breast (BC), stomach (SC), non-small cell lung cancer (NSCLC) or colorectal cancer (CRC) and receiving chemotherapy. MDT uptake was analyzed from time 0 (year of the European Medicines Agency –EMA– approval of the associated targeted therapy) until 2012. The analysis was done on 5 EU countries (France, Germany, Italy, Spain and UK). **RESULTS:** Trastuzumab was approved in HER2+ BC by the EMA in 2000 and had a line extension in 2004. In metastatic BC, the proportion of HER2-tested patients in 2004 was 60% (787/1,320) versus 94% (1,351/1,430) in 2012. Following further approval in 2010 for use in HER2+ advanced SC, HER2-testing grew from 17% (176/1,015) to 50% (501/993) between 2010 and 2012 in this population. In the year that Gefitinib gained EMA approval in EGFR+ NSCLC (2009), 8% of advanced NSCLC patients (280/3,465) were EGFR-tested. This proportion increased to 56% (2,092/3,708) in 2012. Panitumumab and Cetuximab obtained EMA approval for KRAS-wild type CRC in 2007 and 2008 respectively. In 2009, 42% (1,183/2,843) of metastatic CRC patients were K-RAS-tested and 62% (1,782/2,873) in 2012. **CONCLUSIONS:** The use of MDTs has become increasingly important in oncology as more targeted therapies are launched. While consistent growth in testing is established, differences exist in the delay to achieving routine testing of patients. Further observation of MDT usage is required, considering national health guidelines, to better understand movement towards personalized cancer management.

PCN8

A LESSON LEARNT FROM AVASTIN®: - BEVACIZUMAB INDUCED HYPERTENSION AS A PREDICTIVE BIOMARKER OF PATIENT RESPONSE IN OVERCOMING REGULATORY AND HEALTH TECHNOLOGY ASSESSMENT (HTA) HURDLES

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BACKGROUND: The high cost of VEGF-targeted anti-angiogenic therapies within a financially strained health-system, makes reimbursement decisions a potentially limiting factor for new compounds. Failure to demonstrate adequate clinical benefit and cost-effectiveness in HER-2 negative metastatic breast cancer resulted in significant regulatory and health technology assessment (HTA) challenges. There is increasing expectation for new drugs to have companion diagnostics that identify likely patient responders, with growing support for using biomarkers to inform treatment decisions **OBJECTIVES:** The purpose of this study was to critically examine published literature on trials incorporating biomarkers related to VEGF inhibition across different cancer indications, to explore their value as predictive, prognostic, pharmacological or surrogate response biomarkers **METHODS:** A search with a strict set of inclusion criteria was used to review the current literature. Information was gathered for 13 biomarkers that have been explored for anti-VEGF therapy and a database was compiled housing raw experimental data for comparison. Each biomarker was critically evaluated and ranked accordingly, to validate their potential as predictive, prognostic, pharmacodynamic and surrogate endpoint markers for bevacizumab-based therapies, with consideration for likely regulatory, clinical and payer acceptance. **RESULTS:** A total of 222 published studies were incorporated into the analysis. Plasma VEGF-A, PlGF and soluble VEGFR-1/VEGFR-2 demonstrated value as pharmacodynamic biomarkers with limited prognostic value. CECs and CA19-9 showed prognostic and predictive value under restricted indications. Blood pressure demonstrated superiority in its ability to predict response to bevacizumab. **CONCLUSIONS:** The evidence suggests the incorporation of biomarkers in clinical trial design must be tailored to the drug and the cancer indication to which the therapy is applied. The potential for blood pressure as a biomarker of response to bevacizumab has been highlighted. Bevacizumab-induced hypertension should therefore be considered as a key candidate for future biomarker-driven trials, increasing the likelihood of test-treatment acceptance by key regulatory and HTA stakeholders.

PCN9

PREGNANCY AFTER BREAST CANCER IN 2000-2002 AND 2010-2012: A RETROSPECTIVE DATABASE ANALYSIS

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OBJECTIVES: Women of childbearing age with a diagnosis of breast cancer often want to conceive a child after treatment. Some reports found that pregnancy does not increase the risk of cancer recurrence after successful treatment. These reports and positive changes in the survival rates of breast cancer patients can impact the decisions of patients and physicians. The goal of this study was to estimate the number of women who survived breast cancer and subsequently became pregnant and to determine the time between the cancer diagnosis and pregnancy in the time periods between 2000-2002 and 2010-2012, respectively. **METHODS:** This retrospective study analysed longitudinal routine care data collected by gynaecologists in Germany (IMS® Disease Analyzer). Data from women aged 20-45 with a pregnancy within 10 years after the first breast cancer diagnosis from 102 gynaecological practices in Germany (Disease Analyzer database; 01/1992 to 12/2012) were analysed. **RESULTS:** In the time period 2000-2002, 65 (projected to national level: 4615) women became pregnant after a breast cancer diagnosis; this number increased to 114 (projected to national level: 8094) between 2010-2012. The mean age did not significantly change between 2000-2002 and 2010-2012 (33.8 (SD: 6.0) and 34.2 years (SD: 6.1)). The time between the first breast cancer diagnosis and pregnancy identification was 896 days (SD: 690) in 2000-2012 and 552 days (SD: 696) in 2010-2012 (p<0.01). **CONCLUSIONS:** This retrospective analysis showed that the number of pregnancies following breast cancer diagnosis has significantly increased in the last 10 years. More over, the time to pregnancy has become significantly shorter. This is indicative of the positive and hopeful developments for young women affected by breast cancer. Further studies on this important research topic are necessary.

PCN10

EVALUATION OF VARIABLE RELEVANCE AND ACCESSIBILITY TO SUPPORT PERSONALIZED MEDICINE IN BREAST CANCER

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OBJECTIVES: About 1 in 8 U.S. women will develop invasive breast cancer during their lifetime. Response to treatment varies among women depending on several factors. This work identified and prioritized the essential variables to implement personalized cancer treatment, and determined the feasibility of obtaining these variables from available data sources toward a real time clinical decision aid. **METHODS:** A focus group of 10 breast cancer clinicians was conducted to determine possible variables for inclusion into the clinical dashboard. An electronic 3-categorical scale (must have, would like to have, unnecessary) survey was conducted among a broader group of breast cancer clinicians. Variables were classified by category and mention frequency (Mode). The accessibility of these variables from two separate cancer care databases was evaluated by data querying, text search and electronic chart review and categorized as available, difficult to access, or unavailable. **RESULTS:** Ten clinicians identified 67 possible variables for inclusion into the dashboard. According to the broader electronic survey 25 clinicians determined 39 "must have" variables with 9 patient specific variables (e.g. age at diagnosis, comorbidities, hormone replacement use, cancer history); 13 tumor specific variables (e.g. clinical stage at diagnosis, histologic grade, laterality) and 17 timeline related variables (e.g. date and type of surgery, chemo/endocrine/targeted therapies received by date, chemotherapy regimen and cycle information, overall survival). 34 of identified "must have" variables were accessible from at least one of available databases. Of the relevant variables five may be difficult to access, including BRCA testing and status, performance status, date and site of recurrence, disease free survival and treatment delay. **CONCLUSIONS:** Breast cancer clinicians identified 39 essential variables, the majority of which can be obtained from currently available databases and then uploaded into a clinical dashboard to support personalized medicine at the point of care for patients with breast cancer.

PCN11

AN INDIRECT TREATMENT COMPARISON OF THE EFFICACY OF EVEROLIMUS (AFINITOR®) AND FULVESTRANT FOR THE TREATMENT OF HORMONE RECEPTOR POSITIVE (HR+) HER2 NEGATIVE (HER2–) ADVANCED OR METASTATIC BREAST CANCER

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OBJECTIVES: To indirectly compare the efficacy (progression free survival (PFS)/time to progression (TTP) and overall survival (OS) of everolimus plus exemestane (EVE+EXE) with fulvestrant in patients with hormone receptor positive, HER2 negative advanced or metastatic breast cancer. **METHODS:** A systematic search of the Cochrane Library and other resources was undertaken to identify reviews and clinical trials reporting interventions for metastatic breast cancer that would allow an indirect comparison of fulvestrant and EVE+EXE. A Bayesian fixed effect model was used with exemestane adopted as the base treatment for the model because it provided the most information in the network. The basic parameters of the model are the log hazard ratios with respect to exemestane for PFS/TTP and OS from the included studies. In the absence of full networks for TTP/PFS, these outcomes were assumed to be the same measure in a disease with short survival times. **RESULTS:** Six trials contributed to a network for PFS/TTP and five to a network for OS. Because the comparator treatment was used as the base treatment, a HR > 1 indicates that the comparator is less effective than everolimus. For PFS/TTP, EVE+EXE performed better than fulvestrant 250mg (HR 2.13 Credible interval (CI):1.72 to 2.63) and 500mg (HR 1.69 CI: 1.30 to 2.22). This difference was statistically significant. For OS, EVE+EXE performed better than fulvestrant 250mg (HR 1.36 CI: 0.95 to 1.97) and 500mg (HR 1.15 CI: 0.76 to 1.75) but the difference was not statistically significant. A complete statistical assessment of heterogeneity for PFS/TTP and OS was not possible because of data limitations. **CONCLUSIONS:** EVE+EXE confers better PFS/TTP benefit in HR+ HER2-ve metastatic breast cancer when indirectly compared with fulvestrant 250mg

or 500mg. The indirect analysis did not show a statistically significant difference in OS between everolimus compared with fulvestrant.

PCN12

SMALL MOLECULE TARGETED THERAPIES FOR THE SECOND LINE TREATMENT OF METASTATIC RENAL CELL CARCINOMA (MRCC): A SYSTEMATIC REVIEW AND INDIRECT COMPARISON OF SAFETY AND EFFICACY

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OBJECTIVES: Patients with mRCC and a good performance status typically receive an anti-VEGFR TKI (sunitinib or pazopanib) as initial therapy. Upon disease progression or intolerance, there are four orally-administered agents approved in the 2nd - line setting (including cytokine-refractory). However, head to head comparative trial data are limited. In the absence of such data, mixed treatment comparison (MTC) models are a widely accepted statistical method for generating comparative effectiveness information. In this study, an indirect comparison on the safety and efficacy was undertaken between axitinib, sorafenib, pazopanib and everolimus for 2nd - line therapy in advanced RCC. **METHODS:** A systematic review of major databases was conducted from January 2005 to June 2013 for randomized controlled trials evaluating at least one of the four agents in 2nd- line mRCC. Bayesian MTC models were fitted to assess comparative effectiveness based on multiple endpoints: tumour response, progression free survival (PFS), grade III/IV toxicities such as diarrhea, fatigue, hand foot skin reaction, rash and stomatitis as well as treatment discontinuations. **RESULTS:** A total of four randomized trials meeting the inclusion criteria were appropriate for the statistical pooling exercise. All four agents seem able to induce tumour shrinkage and provide patients with a clinically meaningful PFS benefit. Axitinib was superior to pazopanib (HR = 0.64; 95%CrI: 0.42 to 0.96) and sorafenib (HR = 0.70; 95%CrI: 0.57 to 0.87) in terms of PFS. However, patients receiving axitinib would be at an elevated risk for fatigue and to a lesser extent, stomatitis. **CONCLUSIONS:** Keeping in the mind the caveats associated with cross-trial comparisons, axitinib appears to provide superior PFS benefits relative to pazopanib and sorafenib. However, this is at a cost of a higher frequency of some dose-limiting toxicities. Everolimus, an mTor inhibitor, is mechanistically distinct from the other agents evaluated and would be a useful option post anti-VEGFR TKI failure.

PCN13

TARGETED THERAPY IN TRIPLE-NEGATIVE METASTATIC BREAST CANCER (TNBC) - A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: To perform a systematic review and meta-analysis of all randomized controlled trials comparing the efficacy of targeted therapy to conventional CT in patients with metastatic Triple-Negative Breast Cancer (TNBC). **METHODS:** Several databases were searched, including MEDLINE, EMBASE, LILACS, and CENTRAL. The primary endpoint was progression-free survival (PFS). We performed a meta-analysis (MA) of the published data. The results were expressed as Hazard Ratio (HR) or Risk Ratio (RR), with their corresponding 95% confidence intervals (CI 95%). **RESULTS:** The final analysis included 12 trials comprising 2,054 patients with TNBC. It was evidenced studies with conventional CT plus targeted therapy including bevacizumab (Bev), sorafenib (Sor), cetuximab and iniparib. The PFS was higher in patients who received Bev plus CT compared to CT alone in previously untreated patients with TNBC (fixed effect: HR=0.62; CI 95%=0.51-0.75; p<0.00001). The PFS was also higher in one study with Bev plus CT in previously treated patients (fixed effect: HR=0.49; CI 95%=0.33-0.74; p=0.0006). Sor plus CT was available in first-line and second-line. The PFS was higher in the group with Sor versus CT alone (fixed effect: HR=0.69; CI 95%=0.49-0.98; p=0.04) and iniparib plus CT (fixed effect: HR=0.75; CI 95%=0.62-0.90; p=0.002). **CONCLUSIONS:** Bev, Sor and iniparib, when associated with the conventional CT, demonstrated gains in the PFS of patients with TNBC.

PCN14

ABIRATERONE AND ENZALUTAMIDE FOR THE TREATMENT OF METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) POST CHEMOTHERAPY: AN INDIRECT COMPARISON AND BUDGET IMPACT ANALYSIS

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OBJECTIVES: Abiraterone and enzalutamide are two new treatment options for patients with mCRPC after docetaxel-based chemotherapy. This study aims to understand the relative clinical and economic value of these therapies. **METHODS:** Two pivotal clinical trials were conducted to evaluate abiraterone and enzalutamide in post-docetaxel treatment of mCRPC: Study COU-AA-301 for abiraterone and the AFFIRM trial for enzalutamide. The PICO (population, intervention, comparison, and outcomes) construct was employed to assess the comparability of the trials, followed by an indirect treatment comparison (ITC) using the Bucher method and a mix treatment comparison using Bayesian statistics. An economic evaluation was performed based on the ITC results. **RESULTS:** Several key differences were identified between the COU-AA-301 and AFFIRM trials. First, the studies used different comparators. Abiraterone plus prednisone was compared with prednisone alone, while enzalutamide was compared with placebo. Second, the endpoints rPFS, PSA progression, and PSA response were defined differently between trials, and thus were not included in the analysis. To address the difference in comparators, the ITC was performed using data from COU-AA-301 and subjects receiving corticosteroids concurrently in the AFFIRM trial. OS was significantly improved with both abiraterone and enzalutamide (3.9 and 3.2 months respectively). The ITC results were HR = 0.949 (95% CI: 0.712-1.26) for abiraterone versus enzalutamide using the Bucher method, and HR = 0.948 (95% CI: 0.711-1.26) using the Bayesian method. Using the US price for abiraterone and enzalutamide (approved in the US only), and assuming 25% of patients received therapy following docetaxel, cost savings from using abiraterone would be >$10K/patient/year or $49.0M/year nationally. **CONCLUSIONS:** Differences in study design should be addressed when conducting an ITC. The evidence from this ITC shows that abiraterone and enzalutamide have similar efficacy in OS in mCRPC post chemotherapy. However, abiraterone is cost saving compared to enzalutamide in this analysis.

PCN15

DIFFERENCES IN MEDICAL COST AND SURVIVAL BETWEEN TRIAL AND NON-TRIAL PATIENTS WITH ACUTE MYELOID LEUKAEMIA – A UK POPULATION-BASED PROPENSITY ANALYSIS

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OBJECTIVES: Information about acute myeloid leukaemia (AML), including the costs of treatment and survival-estimates, are usually derived from clinical trial data. However, it is not known whether this information is generalizable to non-trial patients. This study was carried out to evaluate the differences in medical costs and survival between trial and non-trial patients with AML; and hence assess the external validity of trial data to the general patient population. **METHODS:** The Haematological Malignancy Research Network (HMRN, www.hmrn.org) is an established population-based patient cohort that registers around 2000 newly diagnosed patients each year. All adults (≥18) newly diagnosed with AML between September 2004 and August 2007 and treated with induction intent were included. Patients were followed until August 2012, and the comparative outcomes were medical costs and survival. Standard statistical analyses were used to measure unadjusted difference in outcomes, and propensity score analyses were applied to measure differences by adjusting for baseline imbalance in pre-treatment characteristics between trial and non-trial patients. **RESULTS:** Overall, 173 patients treated with induction intent were included, of which 106 were trial and 67 non-trial. Trial participation was associated with younger age, fewer comorbidities, better prognosis, and being treated at teaching hospitals. Before controlling for patients' characteristics, trial patients had better survival and incurred higher costs (p<.0001 for both). After controlling for patients' characteristics by carrying out propensity score analyses, these differences remained significant in both survival (median survival 28.7 vs. 8 months; p<.0001) and medical costs (mean costs £84,497 vs. £49,624; p<.0001). **CONCLUSIONS:** For AML patients treated with induction intent, significant differences were observed in treatment costs and survival according to trial status, both before and after controlling for patients' pre-treatment characteristics. Data generated solely from clinical trials may therefore not be generalizable to non-trial patients and should be treated with some caution when used to facilitate decision-making.

PCN16

THE EFFECT OF POSITIVE MARGINS ON OUTCOMES IN BREAST CANCER

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OBJECTIVES: To review the data available on excision margins following breast-conserving therapy (BCT), focusing on definitions of positive and clear margins, percentage of operations resulting in positive margins, the effect of positive margins on future treatment, and the relationship between positive margins and disease-free and overall survival. **METHODS:** Targeted searches of PubMed were conducted using a predefined search strategy. Data from robust systematic reviews and/or meta-analyses were given priority. **RESULTS:** Definitions of positive and negative margins are variable, but typically a clear margin of 2 mm is considered acceptable. Most studies indicate positive margins in 20%-40% of patients after wide local excision. Guidelines recommend that patients with positive margins after BCT undergo repeat surgery, and in surveys, most physicians said they would recommend re-excision when there is tumour within 1 mm of the margin. In the identified studies, 20%-30% of patients underwent re-excision and approximately 2% had multiple re-excisions (two or more); 10%-15% of patients who initially had lumpectomy later had a mastectomy. There is a significant association between margin status and local recurrence (in a recent meta-analysis, the odds ratio was 2.42 for positive vs. negative margin status; 95% confidence interval, 1.94-3.02; P<0.001). However, among patients with a clear margin, width is not clearly related to risk of local recurrence. Four studies that assessed the effect of margin status on overall or disease-specific survival were identified, three reported a significant association (e.g., cause-specific survival at 12 years significantly associated with margin status, P<0.001). **CONCLUSIONS:** Definition of adequate margins remains controversial. None-the-less, final margin status is a key prognostic factor following BCT. The data identified suggest that an intervention that reduces the rates of positive margins during BCT may have the potential to improve outcomes and reduce the burden on patients and health care providers.

PCN17

A MIXED TREATMENT COMPARISON (MTC) TO COMPARE PROGRESSION FREE SURVIVAL (PFS) ASSOCIATED WITH DIFFERENT CHEMOTHERAPY REGIMENS FOR PLATINUM-SENSITIVE OR PARTIALLY PLATINUM-SENSITIVE RECURRENT ADVANCED OVARIAN CANCER

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OBJECTIVES: This research was conducted during a review of the manufacturer's submission (MS) to the NICE Single Technology Appraisal programme for bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor. Bevacizumab in combination with gemcitabine/carboplatin has recently been licensed for use in patients with platinum-sensitive or partially platinum-sensitive recurrent advanced ovarian cancer. This research compared this new triple therapy with treatments used in clinical practice in the UK: platinum monotherapy, gemcitabine/carboplatin, paclitaxel/carboplatin, pegylated liposomal doxorubicin hydrochloride (PLDH)/carboplatin. **METHODS:** Randomised controlled trials (RCTs) for inclusion were identified using the MS for bevacizumab. RCTs were assessed for comparability based on patient population, disease severity, platinum sensitivity, and treatments received. An MTC was conducted using a Bayesian Markov chain Monte Carlo simulation.

Fixed and random effects models were explored with results reported for the best fitting model. Hazard ratio (HR) was chosen as the summary statistic. **RESULTS:** The network of 6 RCTs formed a linear series of "steps", which facilitated comparison of all chemotherapy regimens of interest. The fixed effects model was the best-fitting model. There was reasonable agreement between the number of unconstrained data points, residual deviance and pair-wise results, suggesting a coherent network. Using bevacizumab/gemcitabine/carboplatin as the baseline, the results for PFS for the other chemotherapy regimens were: platinum monotherapy (HR 2.92, 95% Credible Interval [CrI]: 2.10 to 3.96), gemcitabine/carboplatin (HR 2.09, 95% CrI: 1.65 to 2.60), paclitaxel/carboplatin (HR 2.16, 95% CrI: 1.50 to 3.01), PLDH/carboplatin (HR 1.77, 95% CrI: 1.20 to 2.51); where a HR>1 favours bevacizumab/gemcitabine/carboplatin and a HR<1 favours the comparator. **CONCLUSIONS:** This research suggests bevacizumab in combination with gemcitabine/carboplatin may offer significantly longer PFS compared with other chemotherapy options available in the UK.

PCN18

EFFICACY OF BRENTUXIMAB VEDOTIN AND OTHER TREATMENTS IN PATIENTS WITH RELAPSED OR REFRACTORY (RR) SYSTEMIC ANAPLASTIC LARGE-CELL LYMPHOMA (SALCL): A SYSTEMATIC REVIEW

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OBJECTIVES: Brentuximab vedotin (ADCETRIS®), a CD30-targeted antibody-drug conjugate, has conditional approval in Europe for the treatment of adult patients with RR sALCL. This systematic review summarized the efficacy of other treatments for RR ALCL, for comparison with brentuximab vedotin. **METHODS:** A systematic literature review identified studies published between 1993 and February 2013 reporting efficacy of treatments in adult patients with RR ALCL, or more generally with RR peripheral T-cell lymphoma (PTCL) including ≥1 ALCL patient. Five databases were included: EMBASE, MEDLINE, and the WHO ICTRP; reviews published since 2011 were also searched manually for additional studies. English publications reporting complete remission/response (CR) rate and/or 2-year overall survival (OS) in RR ALCL/PTCL populations were included. Publications of principal treatment with bone marrow transplantation or radiotherapy were excluded. CR rates and 2-year OS, from the identified studies and from the brentuximab vedotin single-arm phase 2 trial in sALCL (SG035-0004), were summarized. **RESULTS:** Of 1653 publications screened, 12 studies were eligible for inclusion; all were phase 1 or 2 or unspecified prospective non-randomized studies. For these studies, the CR rates were 0–28% in RR PTCL patients (n=4–130 PTCL; median age 36–69 years; n=1–41 ALCL), and for the 6 studies that also reported CR outcomes in the subset of RR ALCL patients (n=13–130 PTCL; median age 47–69 years; n=2–41 ALCL), the CR rates were 0–33% in RR ALCL patients. For RR ALCL patients treated with brentuximab vedotin in SG035-0004 (n=58 sALCL; median age 52 years) the CR rate was 59%. The 2-year OS ranged from 7–33% in the 5 identified studies that reported OS, compared with 63% with brentuximab vedotin in SG035-0004. **CONCLUSIONS:** The CR rate and 2-year OS for brentuximab vedotin in RR sALCL appear to exceed that of other therapies in RR ALCL/PTCL.

PCN19

A COMMUNITY-BASED, CASE-CONTROL STUDY EVALUATING MORTALITY REDUCTION FROM GASTRIC CANCER BY ENDOSCOPIC SCREENING IN JAPAN

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OBJECTIVES: Although gastric cancer has decreased in the last three decades, it is still the second leading cause of cancer death worldwide. In Asian countries, the burden of gastric cancer has remained, and screening is still expected to prevent gastric cancer death. In order to evaluate reduction of mortality from gastric cancer by endoscopic screening, a community-based, case-control study was conducted in Japan. **METHODS:** Case subjects were defined as persons who had died of gastric cancer between 2003 and 2006 in four cities, Tottori Prefecture, and between 2006 and 2010 in Niigata City, Japan. Up to six control subjects were matched by sex, birth year (±3 years), and residence of each corresponding case from population lists in the study areas. Controls were required to be disease-free at the time when the case was diagnosed gastric cancer. The odds ratios were calculated for those who had ever participated in endoscopic screening or radiographic screening before the reference date when the case was diagnosed gastric cancer, compared with persons who had never participated in any screening. Conditional logistic-regression models for matched sets were used to estimate the odds ratios and 95% confidence intervals. **RESULTS:** There were 288 males and 122 females for case subjects, with 2,292 matched control subjects. Compared with those who had never been screened before the date of diagnosis of gastric cancer in cases, the odds ratios within 48 months from the diagnosis date were 0.703 (95% confidence interval :0.497-0.996) for endoscopic screening and 0.860 (95% confidence interval :0.631-1.171) for radiographic screening. **CONCLUSIONS:** The result suggests a 30% reduction from gastric cancer mortality by endoscopic screening compared to no screening within 48 months before the diagnosis date of gastric cancer.

PCN20

BENEFIT OF ADDING PANITUMUMAB TO FOLFOX4 IN PATIENTS WITH KRAS/NRAS WILD-TYPE (WT) METASTATIC COLORECTAL CANCER (MCRC): A NUMBER-NEEDED-TO-TREAT (NNT) ANALYSIS

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OBJECTIVES: To calculate NNTs for panitumumab+FOLFOX4 vs FOLFOX4 alone (PRIME study) to achieve one objective response (OR rate [ORR] analysis) or prevent one disease progression (PFS analysis) or death (OS analysis) at 6/12 or 12/24 months. **METHODS:** In PRIME, 1183 patients with previously untreated mCRC were randomised. Using data from an exploratory analysis conducted when 80% of patients had died, NNTs (Bender. Encyclopedia of Biostatistics, Second Edition; Volume 6, pp3752-61) were retrospectively calculated in patients with *KRAS/NRAS* WT (n=505; exons 2-4 assessed) mCRC overall and in the ECOG performance score 0/1 (n=473) subgroup. ORR and PFS events were defined using RECIST. **RESULTS:** In the overall *KRAS/NRAS* WT population, 59.3% vs 45.6% of patients receiving panitumumab+FOLFOX4 vs FOLFOX4 alone, respectively, achieved an OR; NNT(95% CI) in the ORR analysis was 7.3(4.5-19.9). In the ECOG 0/1 subgroup, 61.3% vs 46.4% of those receiving panitumumab+FOLFOX4 vs FOLFOX4 alone, respectively, had an OR; the NNT(95% CI) was 6.7(4.2-16.5). For the PFS overall population analysis, the HR(95% CI) was 0.74(0.62-0.90); HR(95% CI) for the ECOG 0/1 subgroup was 0.72(0.59-0.88). NNTs(95% CI) in the overall population at 6 and 12 months were 12.8(8.3-34.1) and 9.2(5.7-25.9), respectively; corresponding values for the ECOG 0/1 subgroup were 11.9(7.9-27.8) and 8.4(5.3-20.8). For the OS overall population analysis, the HR(95% CI) was 0.76(0.63-0.93); HR(95% CI) for the ECOG 0/1 subgroup was 0.74(0.60-0.90). NNTs(95% CI) in the overall population at 12 and 24 months were 16.8(10.4-57.1) and 10.4(6.2-37.1), respectively; corresponding values for the ECOG 0/1 subgroup were 16.0(10.3-44.1) and 9.4(5.9-27.2). **CONCLUSIONS:** In these analyses NNTs for PFS, OS and particularly ORR were low, reflecting the high therapeutic benefit of adding panitumumab to FOLFOX4 in patients with *KRAS/NRAS* WT mCRC. Limitation by ECOG score 0/1 further lowered NNTs for PFS and OS.

PCN21

INDIRECT COMPARISON ANALYSIS TO EVALUATE THE CLINICAL EFFECTIVENESS OF TRASTUZUMAB EMTANSINE (T-DM1) VERSUS OTHER TREATMENTS FOR HER2-POSITIVE METASTATIC BREAST CANCER (MBC)

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OBJECTIVES: T-DM1, an antibody-drug conjugate which combines the antitumor properties of trastuzumab (H) with the cytotoxic agent DM1, is approved for the treatment of patients with MBC previously treated with trastuzumab+taxane. We compared the clinical effectiveness of T-DM1 versus all available therapies used in the treatment of unresectable HER2-positive locally advanced breast cancer (LABC) or MBC. **METHODS:** This systematic review (SR) and indirect treatment comparison (ITC) included all published data between January 1, 1998 and December 20, 2012. Studies were chosen in accordance with conventional methods for performing and reporting SRs and ITCs (i.e., Cochrane Handbook for SRs, PRISMA, ISPOR guidelines, and major HTA agencies). Eligible trials were controlled trials of treatments for unresectable HER2-positive LABC or MBC that had progressed after treatment with combination of trastuzumab+taxane in the adjuvant or MBC setting. Progression had to have occurred after the most recent treatment for LABC or MBC or within 6 months after treatment for early-stage disease. **RESULTS:** Seven RCTs and two non-randomized controlled trials (n-RCTs) met the inclusion criteria. Of the seven RCTs, five had a common comparator, being eligible for the ITC. The other two RCTs and two n-RCTs did not have a common comparator and were thus not included in the ITC. T-DM1 was the only treatment to demonstrate statistically significantly longer overall survival (OS) and progression-free survival (PFS) when directly compared to capecitabine+lapatinib, and when indirectly compared to capecitabine+trastuzumab (PFS HR [95% CI]: 0.53 [0.32, 0.86], p=0.01; OS HR [95% CI]: 0.56 [0.35, 0.91]; p=0.01) and capecitabine monotherapy (PFS HR [95% CI]: 0.36 [0.25, 0.51]; p<0.0001); OS (HR [95% CI]: 0.53 (0.39, 0.72); p=0.0009). **CONCLUSIONS:** In this ITC, T-DM1 was associated with longer OS and PFS versus capecitabine+trastuzumab and capecitabine monotherapy in patients with HER2-positive LABC or MBC with disease progression after treatment with trastuzumab+taxane.

PCN22

SECOND-LINE TREATMENT OF METASTATIC COLORECTAL CANCER (MCRC): A SYSTEMATIC LITERATURE REVIEW (SLR) AND FEASIBILITY ASSESSMENT OF CONDUCTING INDIRECT TREATMENT COMPARISON (ITC) ANALYSIS

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OBJECTIVES: To investigate the efficacy and safety of second-line chemotherapy in mCRC and to determine the feasibility of relative efficacy between treatments using indirect or mixed treatment comparisons. **METHODS:** An SLR on randomized trials published from 1992–2012 was performed. EMBASE, PubMed, CENTRAL databases were consulted. Manual searches (including ASCO and ESMO abstracts) were also conducted. Eligible studies evaluated second-line clinical efficacy and safety endpoints in mCRC. **RESULTS:** Twenty-seven trials with patients enrolled ranging from n=33–1,226 were identified. Patients were markedly diverse in terms of ECOG, EGFR, or *KRAS* status, and prior treatment exposures: oxaliplatin (k=9), irinotecan +/- 5-FU (k=5), bevacizumab (k=7), and 5-FU (k=22). On-study treatments and comparators were also diverse: FOLFIRI alone (t=6) or with panitumumab (t=2) or aflibercept (t=1); FOLFOX4 alone (t=6) or with bevacizumab (t=1); bevacizumab alone (t=1) or with chemotherapy (t=2); irinotecan alone (t=19) or with FOLFOX4 (t=2) or cetuximab (t=1); and miscellaneous other regimens (t=19). Study methodologies varied in analysis populations (ITT [k=24] vs. per protocol or not reported [k=3]), primary efficacy outcomes (OS, PFS, and/or tumor response, as variably measured), follow-up durations, and timing of outcomes measurements. Preliminary network diagrams to assess feasibility of meta-analyses for ITC revealed only a single study for each treatment comparison of interest. Assumptions of comparability of apparently diverse patients, past and current treatment regimens, and comparator arms would be necessary to pool treatment groups for meta-analysis of treatment effectiveness across studies and hence, is not feasible. Given the lack of SOC treatments used in many trials, introducing such assumptions will compromise the evidence-based criteria for quantitative clinical data syntheses for indirect or mixed treatment

comparisons. **CONCLUSIONS:** Current standards around second-line treatment of mCRC have evolved over time. The substantial clinical, methodological, and statistical heterogeneity in the available data prevents evidence-based quantitative comparisons of treatment outcomes at this time.

PCN23

COMPARISON BETWEEN EVEROLIMUS (AFINITOR®) AND CHEMOTHERAPY AGENTS (CAPECITABINE, DOCETAXEL AND DOXORUBICIN) FOR THE TREATMENT OF HORMONE RECEPTOR POSITIVE (HR+) HER2 NEGATIVE (HER2–) ADVANCED OR METASTATIC BREAST CANCER

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OBJECTIVES: This study compares everolimus (EVE) versus the most commonly used chemotherapy agents in UK clinical practice (capecitabine [CAPE], docetaxel [DOC] and doxorubicin [DOX]) in patients with hormone receptor positive, HER2 negative advanced or metastatic breast cancer with the purpose of determining the effect of everolimus versus chemotherapy through the derivation of hazard ratios (HR). **METHODS:** A systematic review of the literature was performed to find evidence that could link EVE with chemotherapy (CAPE, DOC and DOX) in terms of progression-free survival (PFS) and overall survival (OS). No head-to-head trials comparing EVE versus chemotherapy were found, the only study that linked hormonal therapy with chemotherapy for treatment of metastatic breast cancer was Wilcken *et al.* (2003). Wilcken *et al.* identified three studies which compared OS for tamoxifen versus chemotherapy. None of the studies identified in the systematic review reported PFS. The link between EVE versus chemotherapy through Wilcken *et al.*(2003) was established via tamoxifen (using Bucher methods), so it was assumed that PFS for chemotherapy would be the same as PFS for everolimus versus tamoxifen (TAM) from the TAMRAD trial. **RESULTS:** HR for everolimus versus tamoxifen for PFS from the TAMRAD trial is 0.54. For OS, Wilcken et al. derived a HR for chemotherapy versus tamoxifen of 0.94. To calculate the HR for OS for everolimus vs tamoxifen the inverse was applied to the OS HR from the TAMRAD trial (0.45), hence (1/0.45)=2.22. The HR for OS for everolimus versus chemotherapy is therefore (0.94x2.22)=2.09. Because a class effect was assumed for the three chemotherapy agents, these HRs were applied to capecitabine, docetaxel and doxorubicin equally. **CONCLUSIONS:** Compared with the most commonly used chemotherapy agents in UK clinical practice (CAPE, DOC and DOX), everolimus has a lower risk of death as demonstrated by the HRs derived.

PCN24

TREATMENTS FOR EGFR MUTATION POSITIVE NSCLC – A NETWORK META-ANALYSIS

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OBJECTIVES: Lung cancer is the most common cause of cancer-related deaths world-wide. Afatinib is a novel, potent, irreversible ErbB family blocker. In EGFR mutation-positive locally advanced and metastatic non-small cell lung cancer, afatinib shows superior effectiveness as a 1st-line treatment compared to standard-of-care chemotherapy. To date, no head-to-head trial results exist to compare the efficacy of afatinib to reversible EGFR TKIs, gefitinib or erlotinib. The analyses presented here attempt to fill this gap by means of a network meta-analysis (NMA). **METHODS:** A systematic literature review (2002-2012) identified the best available evidence. Results from afatinib's pivotal trials (LUX-Lung 3, LUX-Lung 6) were added. A NMA following a Bayesian approach (in WinBUGS) was applied to estimate the relative treatment effects between afatinib, gefitinib and erlotinib. Outcomes of interest were progression free survival (PFS) and overall survival (OS). For PFS, results by investigator review were considered as not in all trials PFS was assessed independently. Versus erlotinib, afatinib's results in the two most common EGFR mutations studied in erlotinib trials were considered. Sensitivity analyses were performed to confirm the robustness of results. **RESULTS:** Twenty studies, including LUX-Lung 3 and LUX-Lung 6, were included; 19 reported OS, 14 reported PFS. Results from random effects models are reported. All comparisons versus reversible TKIs favoured afatinib, although in most analyses the upper credible interval limit exceeded 1. The estimated probability of afatinib being best regarding PFS in all mutations was 80% compared to 17% for erlotinib and 3% for gefitinib, and was 43% regarding OS compared to 13% for gefitinib and 3% for erlotinib. **CONCLUSIONS:** Afatinib consistently showed superior efficacy versus chemotherapy in the pivotal trials. In the absence of head-to-head trial results versus reversible TKIs, the NMA results suggest also potential superiority of afatinib for both PFS and OS when compared to erlotinib and gefitinib.

PCN25

QUALITY INDICATORS OF THE FOURTH SCREENING ROUND (2008-2009) OF THE HUNGARIAN ORGANIZED, NATIONWIDE BREAST CANCER SCREENING PROGRAMME

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OBJECTIVES: Organized, nationwide screening for breast cancer with mammography started in Hungary in January 2002. Women in the age group 45-65 years are the target population and 2 years screening interval is applied. The aim of this study is to evaluate the quality indicators of the 4th screening round (2008-2009). **METHODS:** The data derive from the financial database of the National Health Insurance Fund Administration (NHIFA) covering the period of 2008-2009. We calculated the following indicators: recall rate of women who underwent mammography examinations, attendance of re-called women, proportion of women referred to surgery, proportion of women who underwent surgery compared to referred women, proportion of benign and malignant cases. **RESULTS:** In 2008-2009 there were 477904 screening mammography examinations in Hungary. 5.15 % of participating women were re-called. The attendance of re-called women was 92.25 %. Altogether 2092 women (9.7 %) were referred for breast surgery but only 1485 women (71.0 %) underwent surgery. Histological examination confirmed 281 benign (18.9 %) and 1204 malignant (81.1 %) cases. **CONCLUSIONS:** The quality indicators of the Hungarian organized mammography screening program met the recommendations of international professional guidelines. However, in addition to current indicators, new ones should be introduced in order to provide a more comprehensive monitoring of the program.

PCN26

THE ATTENDANCE OF THE FOURTH SCREENING ROUND (2008-2009) OF THE HUNGARIAN ORGANIZED, NATIONWIDE BREAST CANCER SCREENING PROGRAM

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OBJECTIVES: Organized, nationwide screening for breast cancer with mammography started in Hungary in January 2002. Women in the age group 45-65 years are the target population and 2 years screening interval is applied. The aim of this study is to analyze the attendance rate of the 4th screening round (2008-2009). **METHODS:** The data derive from the financial database of the National Health Insurance Fund Administration (NHIFA) covering the period of 2008-2009. We calculated two attendance indicators. The up-take of the program means the percentage of women aged 45-65 who, having been sent an invitation for screening, attend a screening unit and undergo mammography in response to that invitation. We defined coverage as the ratio of women in the age group 45-65 years having either a screening mammography or a diagnostic mammography. **RESULTS:** In 2008-2009 there were 477904 screening mammography cases and 1204893 diagnostic mammography examinations in Hungary. We found 49.4 % and 41.5 % up-take in 2008 and 2009 respectively; and 45.0 % combined rate for 2008/2009. The screening coverage was 31.2 % and the diagnostic coverage was 20.4 %, while the total coverage (screening and diagnostic) was 50.1 %. **CONCLUSIONS:** The attendance of the Hungarian organized breast cancer screening program – compared to the previous period before the implementation of the organized screening program – is promising, although to achieve the expected results in mortality decrease a further improvement of both the uptake and coverage is necessary.

PCN27

RACIAL DISPARITIES IN DIFFUSION, COMPARATIVE MORBIDITY, AND DISEASE CONTROL OF INTENSITY-MODULATED RADIATION THERAPY COMPARED TO CONFORMAL RADIATION THERAPY FOR LOCALIZED PROSTATE CANCER

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OBJECTIVES: Recent advances in prostate cancer radiation therapy (RT) technology have led to the development of costlier treatments such as intensity-modulated radiation therapy (IMRT) compared to the prior standard, conventional radiation therapy (CRT). This study examines the two treatment modalities to determine if racial disparities in morbidity and disease control may be explained by differential use of IMRT versus CRT. **METHODS:** A population-based study was conducted using Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data from 2000 through 2009 for patients with non-metastatic prostate cancer. Adjusted Cox Proportional Hazards models were conducted, adjusting for demographic and clinical characteristics. Results are presented as (Adjusted Hazard Ratio [95% Confidence Interval]). In subjects without prior morbidity at RT, the rate of recurrence, hip fracture, erectile dysfunction, disorders related to gastrointestinal, and urinary (incontinence and non-incontinence) morbidity were compared by race with IMRT as the referent group. **RESULTS:** Approximately 10,976 men [524 African-American (AA) CRT; 423 AA IMRT; 4,746 Caucasian CRT; 5,283 Caucasian IMRT] met study eligibility. Diffusion of IMRT was slower among AA compared to Caucasians ($p<0.001$). Caucasians receiving CRT were at a greater risk for hip fracture [1.29; (1.16, 1.43)], cancer recurrence [1.13; (1.04, 1.23)], or urinary incontinence [1.09; (1.01, 1.19)] than those receiving IMRT. No estimates comparing AA CRT recipients to AA IMRT recipients reached statistical significance, though cancer recurrence, erectile dysfunction, and gastrointestinal morbidity rates were greater for CRT subjects **CONCLUSIONS:** There were no statistically significant racial disparities in morbidity and disease control related to differential use of IMRT versus CRT. However, diffusion of IMRT was significantly slower among AA. Future research should include more years of follow-up data and a larger sample of AA in order to understand whether measured differences in treatment diffusion achieve clinical significance sufficient to explain a portion of the racial disparity in prostate cancer mortality.

PCN28

OFF-LABEL TRASTUZUMAB USAGE IN BREAST CANCER PATIENT IN TURKEY

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OBJECTIVES: Off-label use of medications is extremely common especially in oncology. The aim of this study is to help update the guidelines and determine pharmaceuticals and off-label indications in breast cancer. **METHODS:** This study involved patients (n=1317) with metastatic breast cancer with tumors that were defined as human epidermal growth factor receptor 2, ErbB-2 positive who received trastuzumab or other medicine application off-label usage in Turkey. During this period using trastuzumab was licenced only for 9 weeks, not for 52 weeks in Turkey. A computer search was performed using the TITCK's (Turkish Drug and Medical Devices Institution) database. The patient base was searched for off-label medicine applications between 1 June 2008 to 1 June 2010. **RESULTS:** The average age were 49.02 ± 10.46. Overall, 85 % of applications were approved in generally 8 or 9 weeks period. It was found that the Marmara Region had the highest application percentage (33.26 %) and then the Central Anatolia Region (27.9 %). Evaluated on the base of cities Istanbul, Ankara and Izmir had the most applications with 29.6 %, 19.2 % and 15.7 % respectively. University hospitals were created the most of the applications (81.1%), other applicaitons were from education & research hospitals (10.2 %) and private hospitals (5.9 %). Off-label drug usage in breast cancer medication, physicians were preferred trastuzumab, trastuzumab+vinoralbin and lapatinib. **CONCLUSIONS:** Trastuzumab had the highest percentage in all off-label medicine applications for breast cancer usage. On the other hand, 85 % of all trastuzumab off-label usage applications were approved. The reason of 15 % of trastuzumab applications is needed to be investigated further.

PCN29

ASSESSMENT OF PATIENT POPULATION WITH NSCLC BY STAGE, ECOG-PS, EGFR MUTATION STATUS AND LINE OF THERAPY IN GERMANY

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OBJECTIVES: To assess the patient population with advanced non-small cell lung cancer (NSCLC) with EGFR (epidermal growth factor receptor) positive mutation in Germany who are eligible for tyrosine-kinase inhibitor (TKI) therapy. An accurate assessment of the relevant patient population provides the basis for budget impact analyses in health technology assessments. **METHODS:** A systematic literature review was conducted. In addition, data from various cancer registries, cohort studies and surveillance studies were analyzed and compared with the findings in the literature. **RESULTS:** In a first step the proportion of patients with NSCLC was determined. Data was further differentiated by histologic subgroup (adenocarcinoma, large-cell carcinoma, squamous carcinoma and other carcinoma). The analysis revealed that the proportion of adenocarcinoma among the group of NSCLC has increased in Germany, especially among women from about 40% in 2000 to over 58% in 2009, in men from 28% to almost 40%, respectively. The proportion of patients with locally advanced or metastatic NSCLC (stage IIIb/IV) ranged between 51%-70%. The proportion of patients harbouring an EGFR mutation ranged between 5%-17%, differing by histologic subgroup, with the highest EGFR mutation rates (9%-26%) in patients with adenocarcinoma. The distribution of patients by ECOG (Eastern Cooperative Oncology Group) Performance Status (PS) showed that at diagnosis 63%-92% had an ECOG-PS 0-1. On average, first line therapy was received by over 80% of patients, while only 52%-65% underwent second line therapy and third line therapy was received by 15%-25% only. **CONCLUSIONS:** By analyzing all available data it is possible to provide good estimates of the relevant patient population. Although significant advances have been made in reporting and data collection for relevant patient subgroups related to NSCLC, there still is a large lack of representative data on a national level in Germany.

PCN30

ESTIMATING PREVALENCE OF PROSTATE CANCER CLINICAL STATES USING A DYNAMIC PATIENT PROGRESSION MODEL

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OBJECTIVES: Prostate cancer (PC) is the most common solid neoplasm in Europe. Accurate estimates of prevalence and patient flow through PC states are necessary to analyse disease burden and the health economic impact of novel therapies. This study presents a dynamic patient progression model (PM) estimating the population size of 13 PC clinical states across 8 European countries (EU8; Belgium, France, Germany, Italy, The Netherlands, Spain, Sweden, and UK). **METHODS:** A dynamic PM was developed using a 27-year time horizon to estimate the prevalence and progression of PC from diagnosis through possible death, using a sequence of 13 Markov clinical states (5 non-metastatic and 8 metastatic). Incidence data were taken from local country registries from 1993 to 2012, and a simple growth model was used to forecast incidence rates to 2020 and beyond. PM flow structure, probabilities of prevalence, progression, and mortality per clinical state were determined using a Delphi panel of PC experts from the EU8 countries and based on published literature and local research. **RESULTS:** A consensus of expert opinion was reached on the clinical states and flow rates of patients with PC in Europe. This resulted in a refined PM with new clinical states that represent the current treatment paradigm for PC. The PM also estimated growth in prevalence and mortality of future PC patient populations across 13 different clinical states of PC from 2012 to 2020. Five-year prevalence rates from the PM were in agreement with those from the GLOBOCAN 2008 project. **CONCLUSIONS:** The PM obtained by consensus of expert opinions provided patient prevalence and mortality estimates for 13 distinct PC clinical states. The PM and patient flow rates provide a representative simulation of the local environment, which can be used to assess PC disease burden, health economic impact, and cost of PC care in the EU.

PCN31

THERAPY SEQUENCES IN MULTIPLE MYELOMA – A CLINICAL MODEL STUDY IN REGARDS OF A GERMAN COST CONTEXT

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OBJECTIVES: With a vast number of possible treatment options for Multiple Myeloma patients, it is unclear in which combination and sequencing compounds should be used to achieve prolonged overall survival. This question cannot be timely answered with an RCT, a health economic model (1) was used to approximate for OS and adopted for a German cost setting. **METHODS:** Using a combination of meta-analysis and -regression, the possible overall survival of different therapy sequences is approximated in a Markov model. Data source for this model is a systematic literature research covering 2008-2012, identifying a total of 68 studies and 11.115 patients in Multiple Myeloma. From each study treatment arm, response per therapy and therapy line was extracted. Subsequently, a regression analysis was used to specifically determine the "time to next treatment (TTNT)". TTNT is used in our model study to reflect the positive correlation of response to therapy and disease progression, which has shown to be highly related (2-5). Using TTNT, the model can now demonstrate which sequence of therapies in 1st, 2nd and 3rd line will total to a possible OS of a patient. **RESULTS:** We analyzed 13 sequences from over 200 theoretical combinations, based on their German approval. Early usage of new compounds results in a prolongation of overall survival of at least 6 months, compared to the standard therapy with melphalan/prednisone (6), with minimal possible OS between 3.98 and 5.06 years. Cost data from Germany were included to amount costs of therapy for a complete sequence. For the sequences presented, costs range between 69.000 and 135.000 €. The majority of those costs accrue from drugs, not from other resources. **CONCLUSIONS:** An important topic of modeling approaches is to show both internal and external validity, which is both needed to validate the prognoses. The external validation is currently undertaken using data from cancer registries and non-interventional studies.

PCN32

THE ESTIMATED SURVIVAL OF PATIENTS WITH DOUBLE REFRACTORY CHRONIC LYMPHOCYTIC LEUKAEMIA; A REANALYSIS OF NICE TA202 USING BAYESIAN METHODOLOGY TO MODEL OBSERVED DATA

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OBJECTIVES: Standard therapy for chronic lymphocytic leukaemia (CLL) is fludarabine, followed by alemtuzumab. Patients resistant to both treatments (double refractory (DR)-CLL) receive best supportive care (BSC). Ofatumumab is licensed for the treatment of DR-CLL, but was not recommended by the National Institute for Health and Care Excellence (NICE technology appraisal 202 (TA202)). There is little clinical data for BSC in DR-CLL. TA202 identified a single-arm study of ofatumumab and an observational study of BSC. Survival for BSC in TA202 was modelled by fitting a Weibull distribution to data for ofatumumab non-responders. The effects of ofatumumab were estimated by assuming a proportional hazards model. The objective of this study was to investigate the potential sources of survival data for BSC, and the impact of the choice of survival distributions used in TA202 on the cost-effectiveness of ofatumumab. **METHODS:** Individual patient-level data was reconstructed from Kaplan-Meier curves using a published algorithm. Plausible survivor functions were fitted to the data using Markov chain Monte-Carlo simulation. Goodness-of-fit to the observed data was assessed using deviance information criterion and the clinical plausibility of extrapolations using subjective opinion. The cost-effectiveness model from TA202 was reproduced including alternative survival data. **RESULTS:** A Weibull distribution provided the best fit to the data and was most clinically plausible. If proportional hazards were assumed (as in TA202) the incremental cost-effectiveness ratio (ICER, incremental cost per life year gained) was £52,400, similar to £49,252 reported in TA202. Relaxing the assumption of proportional hazards increased the ICER to £85,618. **CONCLUSIONS:** The best fitting and most clinically plausible model was a Weibull distribution, giving results consistent with TA202; however both the use of a subgroup of a single arm trial and of data from multiple studies has a high level of uncertainty. Relaxing the assumption of proportional hazards increased the ICER.

PCN33

AFLIBERCEPT + FOLFIRI (AF) VERSUS. PLACEBO + FOLFIRI (PF) IN METASTATIC COLORECTAL CANCER (MCRC): MEAN OVERALL SURVIVAL (OS) IN A "BETTER RESPONDERS" PATIENT POPULATION OF THE VELOUR TRIAL

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OBJECTIVES: The VELOUR trial demonstrated significant survival benefit for aflibercept plus FOLFIRI (5-fluorouracil-leuocovorin-irinotecan) versus FOLFIRI alone in mCRC patients previously treated with oxaliplatin. Multivariate analysis identified a subset of "better responder" patients who derive sustained benefit with AF, which includes patients who did not experience an early relapse directly from adjuvant setting (10% of patients included in VELOUR) and with either ECOG PS0 or (PS1 and ≤1 metastatic site). Median OS was significantly improved in AF arm: 16.2 versus 13.1 months for PF (adjusted HR = 0.73 [95% CI: 0.61–0.86]). Mean survival estimation can render a more meaningful estimate for long-term benefit of interventions and can be effectively applied to clinical and economic decision support. Our objective was to derive mean OS for the "better responders" subgroup in VELOUR. **METHODS:** As survival probability at the end of the follow-up period was 21% in AF vs 8% in PF, mean OS was estimated by extrapolating the KM curve using a survival function over a 15-year period. Five standard parametric distributions were tested: exponential, Weibull, lognormal, loglogistic and Gompertz. Goodness-of-fit of distributions was evaluated by Akaike's Information Criteria (AIC), Bayesian Information Criteria (BIC) and graphical methods. **RESULTS:** Of the 1226 patients enrolled in VELOUR, 404

(66.0%) AF patients and 406 (66.1%) PF patients were classified in "better responders" subgroup. Lognormal and loglogistic distributions were the 2 distributions providing the best fit to the observed OS data, with very similar and good fit. Mean OS over 15-years using loglogistic distribution was 24.8 vs. 18.6 months for AF and PF, respectively. **CONCLUSIONS:** Post-hoc analysis suggested that the "better responders" subgroup of patients within VELOUR derived enhanced survival benefit with the AF combination. The results highlight the therapeutic benefit of AF in clinically relevant patient subpopulations.

PCN34
FACTORS DRIVING INEQUALITY IN PROSTATE CANCER SURVIVAL: A POPULATION BASED STUDY
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OBJECTIVES: As cancer control strategies have become more successful, issues around survivorship have become increasingly important to researchers and policy makers. The aim of this study was to examine the role of a range of clinical and socio-demographic variables in explaining variations in survival after prostate cancer diagnosis, paying particular attention to the role of health care provider(s) (i.e. private vs. public) and socio-economic status. **METHODS:** Data were extracted from the National Cancer Registry Ireland, for patients diagnosed with prostate cancer from 1998-2009 (N=26,183). A series of multivariate Cox and logistic regression models were used to examine the role of health care provider and socio-economic status (area-based deprivation) on survival, controlling for age, stage, Gleason grade, marital status and region. Survival was based on all-cause mortality. **RESULTS:** Individuals who were treated in a private care setting were more likely to have survived than those who had not, when other factors were controlled for. A socio-economic gradient was evident with respect to marital status, region of residence, clinical stage and Gleason grade. The effect of socio-economic status was modified by health care provider, such that risk of death was higher in those of lower socio-economic status for men treated by public, but not private, providers. **CONCLUSIONS:** The role of health care provider (a proxy for voluntary private insurance) and socio-economic status in survival of men with prostate cancer may give rise to equity concerns regarding the operation of the Irish health care system and warrants further investigation.

PCN35
CONDITIONAL SURVIVAL (CS) PROBABILITIES FOR ADVANCED MELANOMA PATIENTS TREATED WITH IPILIMUMAB: MODEL BASED ANALYSIS
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OBJECTIVES: There are few treatments available for advanced melanoma and survival rates are low. While the incidence of the disease continues to rise, only two new treatments have come to the market recently: ipilimumab and vemurafenib. Ipilimumab is indicated in Europe for the treatment of advanced melanoma in adults who have received prior therapy. Ipilimumab has demonstrated a statistically significant improvement in overall survival in 2 Phase III RCTs. Prolonged survival (>2 years in some patients) has been shown (MDX020 & 024). **METHODS:** Data from the MDX010-20 trial, which was conducted in previously treated patients with a maximum follow up duration of 55 months, was used to develop an economic model for health technology assessment in England & Wales. This model has been used to predict the conditional survival (CS) of patients treated with ipilimumab (based on both ipilimumab containing arms) compared to gp100 – the active control. The model used patient level Kaplan–Meier data for the first 18 months, parametric curves fitted to the patient level data from 18 months to 5 years, and published AJCC registry data beyond 5 years. **RESULTS:** The curves were a good fit to the MDX010-20 trial data (MAE 0.003) and consistent with published Phase II data (which provides a longer time horizon). Given an ipilimumab patient has survived 2 years, the modelled probability of being alive at 5 years is 67% (49%,79%) (gp100: 15% [9%,21%]) and at 10 years is 54% (39%, 63%) (gp100: 2% [1%,3%]). **CONCLUSIONS:** The model shows that a substantial proportion of patients treated with ipilimumab surviving to 2 years are likely to have sustained survival benefits: more than 50% of ipilimumab patients surviving to 2 years are alive at 10 years, with 29% remaining alive at 20 years. This level of sustained survival is not shown by gp100 patients.

PCN36
ESTIMATING AND MODELING LONG TERM SURVIVAL IN LUNG CANCER USING MIXTURE PARAMETRIC MODELS
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OBJECTIVES: To ascertain the existence of several populations regarding overall survival (OS) in patients with advanced non-small-cell lung cancer (NSCLC). **METHODS:** Data of OS from the Cuban National Cancer Registry (CNCR) and from Cuban multicentre trials of immunotherapy were analysed with a lognormal mixed model assuming 1 to 6 underlying populations. The Bayesian Information Criterion (BIC) was used to select the best model fitted to the data in all cases. **RESULTS:** The CNCR provided data for 31133 patients diagnosed with lung cancer since January 1998 until December 2008. Of those, 7286 patients presented stages IIIb-IV of NSCLC at diagnosis and were selected for analysis. The immunotherapy Cuban trials provided data for more than 750 patients enrolled in 8 trials conducted since 1997 until 2010. The mixed model applied to CNCR data separated 4 populations: very high risk (OS mean time = 0.62 months, 23% of the sample); high risk (OS mean time = 3.1 months, 34%); medium risk (OS mean time = 9.2 months, 35%); and low risk (OS mean time = 29.1 months, 8%). Results for clinical trials separated 2 populations for controls and 3 populations for the immunotherapy groups. For controls a population of medium risk (OS mean time = 11.6 months, 61%) and other of low risk were obtained (OS mean time = 31.7 months, 38%). For NSCLC patients with immunotherapy a population of medium risk (OS mean time = 11.2 months, 55%); a population of low risk (OS mean time = 23.8 months, 33%); and another of very low risk or long-term survival were obtained (OS mean time = 55.5 months, 12%). **CONCLUSIONS:** Our analyses support the existence of several populations regarding OS among advanced stage lung cancer.

PCN37
SURVIVAL ANALYSIS USED IN COMPANY SUBMISSIONS TO THE NATIONAL CENTRE FOR PHARMACOECONOMICS, IRELAND
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OBJECTIVES: Many company submissions received by Health Technology Assessment (HTA) Agencies evaluate the cost effectiveness of interventions which impact on survival. An accurate estimate of the survival benefit is required to calculate a reliable estimate of cost effectiveness. Generally the relevant trial data is immature and must be extrapolated. Many extrapolation models are available. Model choice is critical; different models can lead to different cost effectiveness results. The objectives were to review the methods/justification of the survival analysis used in company submissions to the National Centre for Pharmacoeconomics (NCPE). A further aim was to develop NCPE Guidance for the future handling of survival analysis. **METHODS:** Relevant submissions to the NCPE (economic evaluations which had dealt with advanced and/or metastatic cancer) were reviewed to determine the methods/justification of the survival analysis used. **RESULTS:** Twelve submissions were evaluated. Appropriately, the mean overall survival (OS) had been estimated and used in eight cases (67%). Median OS estimates had been estimated/used in three (25%). It was unclear which measure had been used in the remaining submission. The submissions which had used mean OS estimates were further investigated. Parametric model-based extrapolation techniques had been used to calculate the mean estimates in all eight. The most popular parametric models were the Weibull (n=3) and the loglogistic (n=3). The methods used to fit the parametric models varied. Most commonly the model was fitted using individual patient-level data. Some justification for the choice of extrapolation technique was offered in five submissions; AIC +/or BIC were estimated in three and visual inspection was reported in two. **CONCLUSIONS:** Survival analysis has not been conducted appropriately in all HTAs. Justification of the choice of model is not always offered. Moving forward, NCPE Guidance is required to ensure that survival analysis using patient-level data is conducted appropriately. These will be presented.

CANCER – Cost Studies

PCN38
BUDGET IMPACT OF METASTATIC CASTRATE-RESISTANT PROSTATE CANCER (CRPC) TO GERMAN PAYERS
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OBJECTIVES: The 2010 Urological Association Guidelines for Management of Castrate-Resistant Prostate Cancer (CRPC) recommend docetaxel plus prednisone for first-line chemotherapy for symptomatic metastatic CRPC patients who have progressed from hormone therapy. Since 2010, several CRPC agents with better tolerability and longer survival have launched. These improved therapies are causing a shift in practice. The aim of our analysis was to 1) quantify the 3-year mCRPC budget impact for the German health system based on the practice shift, and 2) estimate the cost per additional month of progression-free survival (PFS). **METHODS:** A conceptual decision analytic model was developed for the German health system to estimate the impact on direct medical costs of a therapy shift in CRPC over three years. Guideline recommended regimens were represented in model with three lines of therapies: palliative, abiraterone, enzalutamide, docetaxel and cabazitaxel. Progression in therapy was measured as the duration of PFS. A targeted literature search identified US per-patient-per-month costs of docetaxel treated patients (hospitalization=€954, ambulatory=€765, ER=€32, MD=€318) and were adapted to the German health system by applying a published purchase price parity factor. Drug costs were based on Ex-factory pricing. Adverse event rates were used as a proxy to derive relative resource utilization of other treatments. Utilization of CRPC regimens was informed by interviews with EU opinion leaders. **RESULTS:** The shift in practice pattern is expected to increase the German health system's 3-year budget by €23 million. The additional cost/month of PFS is estimated to decrease by €99/month from €4,659 for current treatment mix to €4,560 for future treatment mix by year 3. **CONCLUSIONS:** From the German health system's perspective, a change in practice pattern will result in an increase in total budget of €23 million. The reduction in cost/month of PFS of €99/month indicates the shift in practice will use more efficient therapies.

PCN39
ECONOMIC IMPACT OF DENOSUMAB FOR SKELETAL RELATED EVENT PREVENTION IN PATIENTS WITH PROSTATE CANCER AND BONE METASTASIS FROM A UNITED STATE MANAGED CARE ORGANIZATION PERSPECTIVE
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OBJECTIVES: To evaluate clinical and economic impact of increasing denosumab use compared to zoledronic acid (ZA) in PrCa patients with BM to a MCO. **METHODS:** An economic model was developed to estimate clinical and economic impact to a 1-million-member US MCO of introducing denosumab as bone targeting agent (BTA) for prevention of SREs in PrCa patients with BM. Total number of patients receiving BTA was estimated based on disease prevalence and treatment eligibility in this population. The real-world SRE rates in ZA-treated patients were derived from a large commercial database and used together with the trial-

based treatment effect for denosumab versus ZA to estimate the denosumab SRE rate. Total number of SREs, total SRE management medical cost, BTA drug cost, and total cost were calculated. The impact of denosumab per-member-per-month (PMPM) at increasing utilization rates was assessed by comparing to a scenario without denosumab, i.e., all patients received ZA and reported. Additionally, impact of annual increase in denosumab use was conducted. **RESULTS:** A total of 63 PrCa patients with BM received BTA. In the scenario where all eligible patients receiving ZA, an annual total number of SREs was 120. An annual denosumab use of 20%, 35% or 45% resulted in 4.2%, 7.4%, and 9.5% reduction in total SREs and 5.3%, 9.3%, and 11.9% reduction in medical costs of managing SREs, compared to all patients receiving ZA. The drug cost was partially offset by the reductions in the medical cost and the increase in total cost was minimal (1.2%-2.7%). The PMPM ranged $0.002-$0.005. Consecutive-year analysis showed $0.001 increase in PMPM with 10% denosumab utilization increase. **CONCLUSIONS:** Due to superior efficacy of denosumab versus ZA in SRE prevention in PrCa patients with BM, increased denosumab use results in medical cost reduction in a US MCO. Overall, denosumab provides additional clinical value with limited budget impact.

PCN40

BUDGET IMPACT ANALYSIS OF IPILIMUMAB FOR THE TREATMENT OF ADVANCED MELANOMA IN THE VENETO REGION, ITALY

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OBJECTIVES: Ipilimumab is the first drug to be licensed in Italy for the treatment of advanced melanoma in adults who have received prior therapy. This study aims to estimate the budget impact of ipilimumab in patients who live in the Veneto Region. **METHODS:** Our analysis was performed from the perspective of the Italian health care system. Two scenarios were analyzed: one with the optimization of vials and the other without. Only drug acquisition costs (measured in euro) were considered into the analysis. All costs were referred to year 2013. **RESULTS:** Based on the incidence and mortality rates of the last three years, a total of 80 adult patients were assumed to be elegible for the treatment in the Veneto Region. The cost per mg of ipilimumab was €53,70: one 10 ml vial contains 50 mg of ipilimumab and one 40 ml vial contains 200 mg of ipilimumab. The recommended induction regimen is 3 mg/kg administered intravenously every 3 weeks for a total of 4 doses. The costs per patient of one year's therapy with ipilimumab ranged from €45.108 with vial optimization (considering 4-5 patients infused at the same time - average weight 70 kg) to €53.700 without. The Veneto Region identified a single center for the preparation/administration of treatment to minimize drug waste and to reduce the yearly treatment cost per patient, with a saving of €8.592 per patient/year. Applied to whole elegible patients (average weight 70-75 kg), it allows to obtain savings up to €430.000-690.000 per year. **CONCLUSIONS:** High prices for new cancer drugs are a growing concern to payers, given the large number of cancer drugs in development and the limited health care resources. Vial optimization may be an useful strategy to decrease waste, maximizing the use of health care resources and ensuring that eligible patients are treated.

PCN41

ECONOMIC EVALUATION OF EPOETIN ALFA HEXAL (BINOCRIT) COMPARED TO DARBEPOETIN ALFA (ARANESP) IN THE TREATMENT OF CHEMOTHERAPY INDUCED ANEMIA (CIA) IN GERMANY

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OBJECTIVES: To compare the budget requirements of utilizing epoetin alfa Hexal vs. darbepoetin alfa in the German health care system **METHODS:** Anemia is a common side effect observed in patients receiving myelosuppressive chemotherapy. The purpose of this pharmacoeconomic analysis was to evaluate the cost-effectiveness of the short-acting biosimilar ESAs epoetin-alfa Hexal (EA) 30,000 or 40,000 IU weekly (QW) versus long-acting erythropoiesis-stimulating agent (ESA) darbepoetin alfa (DA) 150 mcg weekly (QW) and 500 mcg once every 3 weeks (Q3W) for the treatment of CIA. A budget impact model was constructed employing a payer perspective, per patient plus 5 year time horizon. The treatment period considered was based on 12 weeks and was aligned with routine chemotherapy regimen administration. Model inputs included: medical treatment, outcomes, and health care service utilization from published clinical studies and summary of product characteristics recommendation. Effectiveness of therapeutic alternatives was determined by comparing hemoglobin maintenance rates. Initial treatment with biosimilar epoetin α 30,000 IU or 40,000 IU per week has been shown to produce a similar Hb response. Costs included only drug acquisition costs and reflect 2013 data. The analysis was performed from the perspective of the German health care system. **RESULTS:** The average expected pharmaceutical costs per patient were €4,843 for DA Q3W, €4,383 for DA QW and €2,944 for EA 30,000IU QW, €3,946 for EA 40,000IU QW. Cost-savings associated utilizing with utilizing Epoetin Alfa Hexal 30-40,000 are 11-49% to DA QW and were 23-64% relative to DA 3QW. **CONCLUSIONS:** In the treatment of CIA among cancer patients in Germany, epoetin alfa Hexal is projected to provide more efficient use of health care resources compared to alternative treatment strategies with darbepoetin alfa.

PCN42

A BUDGETARY IMPACT ANALYSIS MODEL FOR EVEROLIMUS IN THE TREATMENT OF ER+ HER2- METASTATIC BREAST CANCER IN ENGLAND AND WALES

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OBJECTIVES: Whilst the cost-effectiveness of everolimus + exemestane (EVE+EXE) versus placebo + exemestane (PBO+EXE) in patients with ER+ HER2- metastatic breast cancer has been demonstrated elsewhere, this is the first analysis to assess the implications for health spending at a population level. **METHODS:** The model uses a cumulative cohort approach, allowing incident patients to enter the model each year over a five-year period. The incident population was based on several factors: (i) the female population aged >15 years; (ii) the proportion of those women with advanced invasive breast cancer; (iii) the proportion who are post-menopausal; (iv) the proportion who are hormone receptor positive; (v) the proportion who are HER2-; (vi) the proportion with asymptomatic visceral disease, and (vii) the proportion for whom hormonal therapy is appropriate. Finally, the cohort was filtered to show those who had previously relapsed or progressed on NSAI. 'Per patient' treatment and adverse event costs were generated based on treatment-specific progression-free survival curves, and multiplied by the number of patients expected to receive each treatment according to market share data and likely uptake rates. An incremental analysis was performed, where two scenarios were compared: (i) a world without EVE+EXE, and (ii) a world with EVE+EXE. **RESULTS:** It is expected that a total of 1,052 patients will be eligible to receive EVE+EXE over a five-year period. In a 'world without EVE+EXE', the total five year cost was estimated as £1,652,904. Assuming an annual uptake rate of 10%, in a 'world with EVE+EXE' the total cost over the same period was expected to be £2,271,606. Therefore, the incremental cost associated with the introduction of EVE+EXE in England and Wales is £618,702 over five years. **CONCLUSIONS:** EVE+EXE was associated with modest increased health care costs but has, separately, been demonstrated to lead to incremental health benefits compared with other treatments.

PCN43

INCORPORATING STAKEHOLDER INPUT INTO BUDGET IMPACT MODELS TO COMPARE STEM CELL MOBILIZATION STRATEGIES

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OBJECTIVES: There is a dearth of published health economic evidence on stem cell (SC) mobilization that can be leveraged effectively for transplant center decision making. Our objective was to develop representative budget impact models (BIM) for key decision makers to estimate the total financial impact of adopting plerixafor for SC mobilization patients undergoing autologous peripheral stem cell transplantation (ASCT) for multiple myeloma and lymphoma. The BIMs were developed for EU5 (France, Germany, Italy, Spain, UK) and United States (US). **METHODS:** Prior to BIM development, in-depth interviews were conducted in EU5 (n=33) and US (n=20), to determine the most influential decison maker(s) for choosing a mobilization regimen. The choice of inputs and outputs that are critical for the adoption of plerixafor at the hospital level, were determined. Additionally, the BIM was developed using inputs from published literature and market research. **RESULTS:** Primary research revealed that the center director and treating physician are the most influential decision makers, while hospital administrators, transplant coordinators, pharmacy directors, and apheresis directors have a more limited role. There was consensus on inputs critical for assessment: clinical (drug/regimen utilization, apheresis days, and success/failure rates) and economic (mobilization costs; drug costs; apheresis cost and hospitalization costs). Model outputs include: first mobilization success and total mobilization budget impact. Interviews with clinical experts, and primary literature review determined that the relevant mobilization regimen comparators for the models are Granulocyte-Colony Stimulating Factor (G-CSF) alone, G-CSF and plerixafor, G-CSF and chemotherapy mobilization with cyclophosphamide and the triple regimen G-CSF, chemotherapy mobilization and plerixafor. **CONCLUSIONS:** Conducting primary interviews with key stakeholders and using the latest clinical practice information for critical inputs/outputs is essential for developing a representative model that is applicable to decison makers.

PCN44

BREAST CANCER SCREENING PROGRAM IN THE BASQUE COUNTRY: COSTS AND HEALTH BENEFITS ASSESSMENT THROUGH DISCRETE EVENT SIMULATION

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OBJECTIVES: In the Basque Country (Spain), mammographies have been done in biennial basis to women in their fifties and sixties since 1996. The main objective of this project was the evaluation of the impact of the Screening program in terms of costs and health in the Basque women population since 1996. **METHODS:** A discrete event simulation model was built to represent the natural history of breast cancer in women invited to the breast cancer screening program in the Basque Country. The disease progress was described in three main states (healthy, preclinical and clinical) in the model. We assumed all women would be diagnosed at the beginning of the clinical stage unless it had been diagnosed previously through the screening program. The data collected among the 15 years when the screening program was held allowed model's validation. In order to compare the economic impact of these scenarios mammography and treatment costs – depending on the diseasestage at diagnosis – were included. The health impact assessment was based on quality adjusted life expectancy of cancer patients. **RESULTS:** Since the screening program started working, 8,925 cancers were detected among 313,475 women who attended the screening which represents the 76% of the invited ones. 60% of the diagnosed cancers were detected through the screening program. All the mammographies carried out during the evaluated years costed 46 million Euros. Each cancer detected in the screened scenario costs 29,581.06€, in the

background scenario the cost was 29,639.22€. In terms of total costs the background scenario had a lower cost on average until the year 2009. **CONCLUSIONS:** Early detection of breast cancer improves survival prognosis and decreases treatment costs for each detected cancer. In the future, the costs of the early detection program will be balanced by the savings in treatment costs.

PCN45

ESTIMATING THE BUDGET IMPLICATIONS OF RADIUM RA 223 DICHLORIDE IN CASTRATION-RESISTANT PROSTATE CANCER PATIENTS WITH NON-VISCERAL BONE METASTASES TREATED IN INFUSION CENTERS IN THE UNITED STATES

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OBJECTIVES: Metastatic prostate cancer (MPC) results from the spread of cancer to distant parts of the body and is associated with markedly decreased survival. First line therapy for prostate cancer involves androgen deprivation, however most MPC patients progress in spite of castration levels of testosterone. A recently approved infusion product, Radium Ra 223 dichloride (Radium-223), has been introduced in the U.S. market adding to concerns about the costs for end-stage treatments. We sought to estimate the budget impact of Radium-223 on infusion center expenses in the U.S. **METHODS:** We developed a financial model to estimate budget impact from a hospital-based infusion center perspective. Using data from the U.S. Census, SEER, and the Premier Perspective Database, we estimated the eligible population using a theoretical hospital's catchment area. We modeled use, treatment costs and reimbursement for three radiopharmaceuticals (Radium-223, Samarium-153, and Strontium-89) and two common chemotherapies (docetaxel and cabazitazel) in terms of drug cost, infusions, and laboratory monitoring. Reimbursement for these treatments was estimated at both commercial and Medicare rates using the Average Sale Price and relevant Common Procedural Technology codes. We calculated total cost and reimbursement for one year with the current utilization from Premier and then estimated the incremental net budget impact associated with adoption of Radium-223 at 1, 3, and 5% of patients. **RESULTS:** In a catchment area of 1 million lives, an estimated 45 MPC patients with non-visceral bone metastases would be treated with current agents and incur approximately $500,000 in treatment costs for radiopharmaceuticals and chemotherapy. Adding Radium-223 to the treatment mix and assuming adoption rates of 1% to 5%, the annual net impact on the infusion center budget would range from $600 to $3,000. **CONCLUSIONS:** Radium-223 presents a new treatment option for MPC patients with non-visceral bone metastases and a positive net impact for infusion centers.

PCN46

ESTIMATING THE BUDGET IMPACT OF ADDING AVASTIN (BEVACIZUMAB) TO FRONT LINE TREATMENT FOR ADVANCED OVARIAN CANCER IN BRAZILIAN SUPPLEMENTARY HEALTH CARE SYSTEM

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OBJECTIVES: Ovarian cancer (OC) is one of the most lethal gynecologic cancers worldwide. According to Brazilian Institute of Cancer (INCA), 6,190 new OC cases were estimated in 2012. During the last 15 years, carboplatin plus paclitaxel (CP) has been established as front-line (FL) standard of care therapy for advanced ovarian cancer, with no significant advances in treatment ever since. Bevacizumab (Bev) in combination with CP was approved in Brazil for FL treatment of advanced epithelial OC on May/2013. Therefore, this study aimed to estimate the economic impact of bevacizumab reimbursement for advanced OC in Brazilian Supplementary Healthcare System. **METHODS:** The potential number of eligible patients for CP + Bev in FL therapy for advanced OC was estimated following an epidemiologic approach. It was assumed that Supplementary Healthcare System attendance accounts for 40% of all patients. Additional drug costs and infusion fees were evaluated. The ex-factory price (VAT 18%) and labeled dose were considered. Average therapy duration of CP + bevacizumab was 15 months based on GOG-0218 trial. Costs were reported in Brazilian Reais (BRL1.00≈USD0.44; Jun/2013). A total health assistance budget of BRL 88.1 billion was forecasted for 2013, based on the last updated data from Brazilian National Regulatory Agency for Private Health Insurance and Plans (ANS). **RESULTS:** A total of 1,287 eligible cases in CP + Bev FL therapy for advanced OC are expected in 2013 in the private setting. Adding bevacizumab to the treatment of all these potential patients would yield an increase of BRL 267 million, corresponding only to an increment around 0.30% on health assistance expenses. **CONCLUSIONS:** Treating all eligible FL advanced OC patients with CP + Bev will potentially result in a low impact in Supplementary Healthcare System budget, associated to unprecedented clinical benefits for this population with a high medical unmet need.

PCN47

THE FRENCH PUBLIC HEALTH CARE SYSTEM: AN ORIGINAL WAY FOR COST SAVING

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OBJECTIVES: The patent expiries of leading biologic products and development of biosimilars create opportunities for cost saving. The french public health policies has established a complementary means encouraging heathcare facilities (HF) to save money : the "écart médicament indemnisable" (EMI). We explored the evaluation of EMI on the erythropoietic factors class. **METHODS:** We've carried out a comparative study in french HF, representing about 65% of national hospital beds, on the price of erythropoietic factors. The data have been collected on procurement procedures operative as at January 1, 2012. **RESULTS:** A total of 25 care facilities or group of care facilities agreed to participate in the study. The overall sales turnover reached 15 millions euros (M€). All HF granted a discount from 5% to 69% on the prices fixed by negociation between the Comité Economique des Produits de Santé and the manufacturers. The average discount ranges from 11% to 73%. The average EMI varies between 1.42 and 2.69 € excluding value added tax (EVAT) per 1000 international units and between 0.09 and 0.22 € EVAT per microgram according to the medicinal product. The average amount refunded to HF can be estimated at january 1, 2012 at 3.37 M€, or 22.6% of the total budget. We assessed annual prices trends based on starting dates of contract, and we could figure out EMI trends. According to the product, the EMI quickly decline, remain broadly stable or increase. **CONCLUSIONS:** Many of top-selling biologics are due to lose patent protection over the next years. The emergence of competition in pharmaceutical market contributes to better control expenditure in our health system. The great potential for cost savings concerning erythropoietic factors in our study could be investigated in other class of medicinal products.

PCN48

BUDGET IMPACT ANALYSIS OF FENTANYL BUCCAL TABLET FOR THE TREATMENT OF CANCER BREAKTROUGH PAIN

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OBJECTIVES: To assess the economic impact of Fentanyl Buccal Tablet for the management of breakthrough cancer pain (BTcP) in Spain **METHODS:** A 4-year budget impact model was developed for the period 2012-2015 for patients with BTcP from the perspective of the Spanish National Health System. BTcP products included in this model were rapid onset opioids containing fentanyl products (buccal, sublingual, or nasal transmucosal). Prevalence data on cancer, BTcP, opioid use and number of BTcP episodes were obtained from literature. Input data on direct medical resources associated with opioid use and opioide-induced side effects (OISEs) were obtained by consulting experts in oncology from different Spanish hospitals. Resource utilisation included drugs, medical and emergency visits, other non-pharmacological treatments and the treatment of OISEs. Unit costs were obtained from literature and a 3% discount rate was applied to costs. Based on the unit costs for drugs and medical resources the annual BTcP treatment costs per patient associated with each product were determined, to estimate the overall budget impact based on the total treatment population and the percentage of drug utilisation associated with each product **RESULTS:** Patients treated with oral opioids for BTcP was estimated at 23,291 in 2012 with an increase up to 23,413 in 2015. The average annual budget savings with an increase of Fentanyl Buccal Tablet, Fentanyl Sublingual Tablet and Intranasal Fentanyl Spray and a decrease of Oral Transmucosal Fentanyl Citrate, was estimated at €2.6 million over the next four years **CONCLUSIONS:** The increase in the use of Fentanyl Buccal Tablet leads to overall savings in the budget impact for the Spanish NHS. Although the economic impact of BTcP treatment showed to increase over the next four years due to population growth the average annual cost per patient reduced with €29 by the increase in the use of Fentanyl Buccal Tablet.

PCN49

ECONOMIC IMPACT OF DENOSUMAB FOR SKELETAL RELATED EVENT PREVENTION IN PATIENTS WITH BREAST CANCER AND BONE METASTASIS FROM A UNITED STATE MANAGED CARE ORGANIZATION PERSPECTIVE

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OBJECTIVES: To evaluate clinical and economic impact of increasing denosumab use compared to zoledronic acid (ZA) in BrCa patients with BM to a MCO. **METHODS:** An economic model was developed to estimate clinical and economic impact to a 1-million-member US MCO of introducing denosumab as bone-targeting agent (BTA) for prevention of SREs in BrCa patients with BM. Total number of patients receiving BTA was estimated based on disease prevalence and treatment eligibility in this population. The real-world SRE rates in ZA-treated patients were derived from a large commercial database and used together with the trial-based treatment effect for denosumab versus ZA to estimate the denosumab SRE rate. Total number of SREs, total SRE management medical cost, BTA drug cost, and total cost were calculated. The impact of denosumab per-member-per-month (PMPM) at increasing utilization rates was assessed by comparing to a scenario without denosumab, i.e., all patients received ZA. Additionally, impact of annual increase in denosumab use was conducted. **RESULTS:** A total of 122 BrCa patients with BM received BTA. In the scenario where all eligible patients receiving ZA, an annual total number of SREs was 155. An annual denosumab use of 20%, 35% or 45% resulted in 4.5%, 7.9%, and 10.2% reduction in total SREs and 5.7%, 10.1%, and 12.9% reduction in medical costs of managing SREs, compared to all patients receiving ZA. The drug cost was partially offset by the reductions in the medical cost and the increase in total cost was minimal (2.4%-5.5%). The PMPM ranged $0.008-$0.017. Consecutive-year analysis showed $0.004 increase in PMPM with 10% denosumab utilization increase. **CONCLUSIONS:** Due to superior efficacy of denosumab versus ZA in SRE prevention in BrCa patients with BM, increased denosumab use results in medical cost reduction in a US MCO. Overall, denosumab provides additional clinical value with limited budget impact.

PCN50

POTENTIAL LONG-TERM COST SAVINGS DUE TO SIGNIFICANT CLINICAL BENEFIT OF OBINUTUZUMAB (GA101) IN COMBINATION WITH CHLORAMBUCIL IN PREVIOUSLY UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA

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OBJECTIVES: Obinutuzumab is the first, glycoengineered type II antibody demonstrating increased Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) and

direct cell death compared with rituximab (Rtx) and is pending regulatory approval (in combination with chlorambucil (Clb)) for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL). Obinutuzumab+Clb has shown >85% reduction in the risk of progression, relapse or death in comparison to treatment with Clb alone (HR 0.14), a broadly accepted treatment option for many patients with co-existing medical conditions. In a majority of markets the health economic consequences will be assessed in terms of affordability. **METHODS:** A health economic model was developed analyzing the cost impact of obinutuzumab on further lines of treatment due to the number of reduced refractory patients compared to Clb and Rtx. Market share information for obinutuzumab, ofatumumab, Rtx, Clb and Bendamustine and the different relevant combinations were entered for Germany and Canada (Ontario province only). **RESULTS:** Based on a 39% reduction in numbers of refractory patients treated with obinutuzumab+Clb compared to Rtx+Clb cost savings per year per patient (PYPP) for further line treatments in Canada (Ontario) range between Ca$950 and Ca$3,091, which leads to maximum cost savings for the whole eligible population (401 patients) up to $Ca1,239,491. In Germany the cost savings range PYPP between €2,556 and €8,318, which leads to maximum cost savings for the whole eligible population (1,302 patients) up to €10,830,036. The big difference in the cost savings PYPP between the two countries is mainly due to the different market share assumptions for ofatumumab. Key cost drivers were treatment duration and price/cost of further line treatments. Scenario analyses on cost, efficacy and market share data confirmed these findings. **CONCLUSIONS:** Obinutuzumab+Clb shows significant patient-relevant clinical benefits and potential cost savings in further line treatments in patients with previously untreated CLL.

PCN51

PHARMACOECONOMIC ASPECTS OF CHRONIC PAIN MANAGEMENT IN RUSSIAN CANCER PATIENTS

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OBJECTIVES: To assess the cost-effectiveness of the new transdermal therapeutic system (TTS) of fentanyl and subcutaneous injections (SIs) of morphine hydrochloride in the treatment of chronic pain and predict potential budget impact of the implementation of fentanyl TTS in routine clinical practice. **METHODS:** The pharmacoeconomic model was developed based on the results of Russian observational study, included 45 patients with terminal cancer: 25 patients received fentanyl TTS and 20 – SIs of morphine. At the first stage, the cost-effectiveness ratios (CERs) of therapies during the first month was measured as total costs of medicines and expenses for ambulance services for acute pain relief per one patient without side-effects. At the second stage, the CERs of therapies during subsequent three months was measured as costs of medicines per one unit of pain intensity (PI) reduction (visual pain scale). **RESULTS:** During the first month of therapy the frequency of ambulance use was significantly lower in patients received fentanyl TTS (0.32 vs 1.05 per one patient per week in the morphine group), this was reflected in lower total costs (12 611, 42 RUB and 23,037.54 RUB per one patient, respectively). Patients in the fentanyl TTS group were less likely to have side effects. The estimated CERs for fentanyl TTS and SIs of morphine were 13,001.46 RUB and 27,756.07 RUB per one patient without vomiting and 23,354.47 RUB and 82,276.93 RUB per one patient without constipation, respectively. Long-term treatment with fentanyl TTS was resulted in decreased PI as compared to SIs of morphine. The three-month CERs were 4,897.05 RUB and 7,869.30 RUB per one unit of PI reduction, respectively. **CONCLUSIONS:** The present study has demonstrated that administration of new transdermal therapeutic system of fentanyl has the better cost-effectiveness profile in the treatment of Russian cancer patients.

PCN52

BUDGET IMPACT OF LIPEGFILGRASTIM FOR THE MANAGEMENT OF CHEMOTHERAPY-INDUCED NEUTROPENIA

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OBJECTIVES: Chemotherapy-induced neutropenia (CIN), a commonly-occurring adverse event in cancer patients undergoing chemotherapy, and particularly febrile neutropenia (FN), have potentially life-threatening and costly consequences. The standard of care for patients at risk of FN comprises prophylactic administration of recombinant granulocyte colony-stimulating factor (G-CSF) with pegfilgrastim, a long-acting formulation of G-CSF, and the most widely used in Europe. Lipegfilgrastim is a novel, pegylated and glycosylated long-acting G-CSF designed for use in the same patient population as pegfilgrastim. We developed a model to estimate the economic impact over five years of managing G-CSF-eligible chemotherapy patients at risk of FN with lipegfilgrastim rather than pegfilgrastim in Scotland. **METHODS:** The eligible patient population was estimated based on cancer incidence in Scotland and current uptake of G-CSF by patients initiating chemotherapy to prevent neutropenia. Drug, monitoring and event costs were taken from the British National Formulary, Unit Costs of Health and Social Care and Scottish National Tariff. As lipegfilgrastim was shown to be non-inferior to pegfilgrastim (in a phase III study in breast cancer patients), the efficacy and safety of pegfilgrastim and lipegfilgrastim were assumed to be identical. Non-statistically significant trends towards fewer neutropenic events and dose modifications with lipegfilgrastim were explored in scenario analyses. **RESULTS:** The model estimated that 315 patients currently receive pegfilgrastim annually. A progressive increase in lipegfilgrastim uptake was associated with cost savings ranging from £2,814 in year 1 to £16,883 in year 5, totalling £61,904 over five years. Savings were attributable to the low drug acquisition cost of lipegfilgrastim. Using event rates from the pivotal phase III breast cancer study, scenario analyses suggested that using lipegfilgrastim instead of pegfilgrastim generated savings of £145,312, avoided 81 neutropenic events (including 11 occurrences of FN) and 50 dose modifications, and caused 34 additional treatment-emergent adverse events. **CONCLUSIONS:** Lipegfilgrastim was cost-saving compared with pegfilgrastim.

PCN54

SAFETY PROFILE AND COSTS OF RELATED ADVERSE EVENTS OF TRASTUZUMAB EMTANSINE COMPARED TO OTHER REGIMENS IN THE CANADIAN HEALTH CARE SYSTEM

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OBJECTIVES: Trastuzumab emtansine (T-DM1) is an antibody–drug conjugate comprised of the microtubule inhibitory cytotoxic agent DM1 and trastuzumab which, in addition to its antitumor properties, targets T-DM1 to HER2–overexpressing cells. The overall safety profile of T-DM1 was investigated in the phase III EMILIA trial (comparing T-DM1 [n=496] to capecitabine plus lapatinib [CAP+LAP, n=495]) in patients with HER2-positive locally advanced or metastatic breast cancer (MBC) previously treated with trastuzumab and a taxane, and the phase II TDM4450g trial (comparing T-DM1 [n=67] to trastuzumab plus docetaxel [TRAZ+DOCE, n=70]) in patients with previously untreated MBC. Both trials demonstrated clinically meaningful differences between T-DM1 and its comparators. The objectives were to estimate and compare the Canadian costs of managing the treatment-related adverse events (AEs) of T-DM1 as reported in the two trials, from the perspective of Canadian public payers. **METHODS:** An Excel based spreadsheet model was utilized for the analysis. Costing information was obtained from the literature, clinical experts, and Canadian standard costing sources. Costs were reported as 2012 CAD. The AEs that were considered were all treatment-related grade ≥3 AEs as well as grade 2 AEs that occurred in ≥5% of patients in both arms of either study. **RESULTS:** The management of treatment-related AEs as reported in the EMILIA trial resulted in higher per patient costs ranging from $3,060 - $10,499 for CAP+LAP versus $1,376 - $2,463 for T-DM1, yielding savings of $1,684-$8,036. In the TDM4450g trial, the management of treatment-related AEs resulted in higher per patient costs ranging from $5,124 - $27,617 for TRAZ+DOCE versus $798 - $2,215 for T-DM1, yielding savings of $4,326-$25,402. **CONCLUSIONS:** This analysis demonstrated that utilizing T-DM1 for the management of HER2-positive metastatic breast cancer results in significant cost savings of related AEs management due to the improved safety profile compared to CAP+LAP and TRAZ+DOCE.

PCN55

A COST-ANALYSIS OF STEREOTACTIC RADIOTHERAPY IN LUNG CANCER

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OBJECTIVES: Stereotactic radiation therapy is an innovative technique with high therapeutic potential due to excellent local control and increased survival rate. A cost analysis investigating stereotactic radiation therapy modalities either with linear accelerator (Cone Beam Computed Tomography (CBCT), Exac-trac) or Cyberknife was conducted. **METHODS:** The cost-analysis was performed prospectively based on a multicenter study. Patients included were treated for lung carcinoma (T1-T2, N0, M0). Cost calculations were strictly based on a micro costing approach according to the hospitals' point of view. Only direct costs were taken into account. Productivity losses of personnel involved in the process, costs of administrative personnel, costs of logistics and general management were not taken into account. Time horizon included radiation therapy (preparation for radiation therapy and the fraction itself). All costs were given in 2011 euros. Uncertainty was captured by one-way and probabilistic sensitivity analyses using a non-parametric bootstrap method. **RESULTS:** 113 patients were enrolled in 11 French centers from April 2009 to December 2011. 98 economic questionnaires were exploitable. The costs of preparation for stereotactic radiation therapy were 430€ (SD: 101€) with Cyberknife and 433€ (SD: 199€) with linear accelerator. When required, costs of implementation of fiducial markers with one/two days of inpatient care were 1,619€. The costs of stereotactic radiation therapy (all fractions included) were 1,811€ (SD: 760€) with Cyberknife and 817€ (SD:403€) with linear accelerator. Costs per fraction were 550€ (SD: 224€) with Cyberknife and 201€ (SD: 97€) with linear accelerator. Depreciation periods of the accelerator played a major role in costs. **CONCLUSIONS:** This is to our knowledge the first study highlighting costs incurred by different stereotactic radiation therapy modalities in lung cancers. Cost-effectiveness studies have to be conducted in order to shed further light on which modality to focus on.

PCN56

COST OF ADVERSE EVENTS DURING TREATMENT WITH EVEROLIMUS PLUS EXEMESTANE OR SINGLE-AGENT CHEMOTHERAPY IN PATIENTS WITH ADVANCED BREAST CANCER

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OBJECTIVES: Everolimus plus exemestane (EVE+EXE) recently received approval for the treatment of patients with HR+/HER2- advanced breast cancer that recurs or progresses during/after non-steroidal aromatase inhibitors. This study was designed to evaluate the expected costs of managing adverse events during EVE+EXE therapy and single-agent chemotherapy in the western European region. **METHODS:** An economic model was developed to estimate per-patient cost of managing adverse events for patients receiving EVE+EXE or chemotherapies. Adverse event rates for EVE+EXE were collected from the phase III BOLERO-2 trial. Adverse event rates for capecitabine, docetaxel, and doxorubicin chemotherapies were collected from published clinical trial data. Grade 3/4 adverse events with at least 2% prevalence during any of these treatments were included in the study. The adverse event rate

estimates do not count multiple episodes of the same event. Costs of managing each adverse event were obtained from the literature and averaged across western European countries (UK, Germany, France, Italy, Belgium, Spain, Sweden, and Switzerland), where available. The costs were inflated to 2012 Euros (€). **RESULTS:** Expected per-patient costs of managing adverse events within the first year of treatment among patients with advanced breast cancer receiving EVE+EXE were €730. Among patients receiving capecitabine, docetaxel, or doxorubicin as single-agent chemotherapy, expected per-patient costs were €1721, €2390, and €1230, respectively. The most costly adverse event for patients treated with EVE+EXE was anemia (€152 per patient). The most costly adverse event for patients treated with capecitabine, docetaxel, or doxorubicin was lymphocytopenia (€861 per patient), neutropenia (€821 per patient), and leukopenia (€382 per patient), respectively. **CONCLUSIONS:** Expected costs of managing adverse events in patients with HR+/HER2- advanced breast cancer receiving EVE+EXE are about one-half to one-third of the costs for those receiving chemotherapies. This economic consideration can have important implications for health care spending in the advanced breast cancer setting.

PCN57

ECONOMIC IMPACT MODEL OF LIPEGFILGASTRIM TO PREVENT NEUTROPENIA IN CANCER PATIENTS IN SPAIN

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OBJECTIVES: To estimate the economic impact of managing chemotherapy patients at risk of neutropenia and eligible to receive Granulocyte-Colony Stimulating Factor (G-CSF) with lipegfilgatrim (LONQUEX, a new long-acting G-CSF) rather than pegfilgastrim in Spain. **METHODS:** Both the BIA and CMA were conducted from the Spanish-payer's perspective: they included direct drug cost, administration, neutropenic events and adverse event costs, but did not consider indirect costs. The drug acquisition cost of lipegfilgatrim used in the model was based on the anticipated price of lipegfilgatrim at the time of launch in Spain. All costs were expressed in EUROS-2013. A range of sensitivity, scenario and threshold analyses were performed. An additional analysis was performed within the BIA to explore the trend towards fewer dose modifications in the lipegfilgatrim arm of the XM22-03 trial. **RESULTS:** The CMA shows that treating a patient with lipegfilgatrim instead of pegfilgrastim resulted in a cost saving of 650,06€. At the population level, the BIA predicts that cost savings could range from 113.166€ in year 1 to 678.995€ in year 5, totaling to 2.489.648€ over five years. Furthermore, the BIA shows a potential to avoid 50 dose modifications with the use of lipegfilgatrim instead of pegfilgrastim. The model is most sensitive to the cost of pegfilgrastim and lipegfilgatrim, but results are robust, with the model estimating cost savings over a wide range of inputs. When the trend towards decreased NE and increased AE with lipegfilgatrim vs pegfilgrastim reported in the XM22-03 trial is explored, cost savings was about 30% compared to the default scenario, reaching 3.208.619 €., mainly due to decreased NE costs **CONCLUSIONS:** Lipegfilgatrim is cost-saving compared with pegfilgrastim. These savings are confirmed across a wide range of input values.

PCN58

THE RELATIVE ECONOMIC VALUE OF IPILUMUMAB IN COLOMBIA

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OBJECTIVES: There are relatively few treatment options for pre-treated metastatic melanoma (MM) patients. Clinicians have recently been provided access to a new option, ipilumumab that has demonstrated long-term survival benefits, in a subset of patients. Karweit J and colleagues (2012) present data to support the use of mean OS for agents with a right-skewed survival curve, where a subset of patients respond to treatment with long term survival -as is the case for ipilimumab. The research presents data for several oncology agents: ipilimumab for MM, bevacizumab for non-small cell lung cancer, sorafenib for hepatocellular carcinoma, lenalidomide for multiple myeloma, trastuzumab for metastatic breast cancer and vemurafenib for MM. The data reveals a greater mean OS improvement than median OS improvement, since mean OS accurately captures the complete survival benefits. In this analysis we select agents from the Krweit J et al study and who have received regulatory authorization in Colombia, to compare their relative economic value. **METHODS:** The economic value of each asset is presented in terms of cost per month of mean OS within the Colombian health care payer perspective. The analysis uses the cost to treat to mean progression of each asset divided by the months of mean overall survival improvement using current list prices of assets. **RESULTS:** Ipilimumab in comparison to bevacizumab, sorafenib, trastuzumab, sutinib, lenalidomide, and vemurafenib demonstrates a clinical and economic relative value. The cost per mean overall survival month gained for ipilumumab ($39,344,362 COP) is below the average of the comparator assets (range from $60,226,690 to $20,166,226). **CONCLUSIONS:** The relative clinical and economic value of ipilumumab in the context of a variety of oncologic assets is clearly documented. This data provides health care decision makers critical data when determining coverage of oncologic treatments.

PCN59

EXAMINING THE BURDEN OF ILLNESS OF VETERAN PATIENTS WITH PROSTATE CANCER IN THE UNITED STATES

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OBJECTIVES: To examine the economic burden and health care utilizations of prostate cancer patients in the U.S. veteran population. **METHODS:** Patients diagnosed with prostate cancer (ICD-9: 185.xx) were identified from the U.S. Veterans Health Administration (VHA) Medical SAS dataset from October 1, 2009 through September 30, 2011. The first diagnosis date was defined as the index date. A comparator group was created by identifying patients without prostate cancer but with the same age, region, gender, index year, and matched baseline Charlson Comorbidity Index. The index date for the comparator group was randomly chosen to reduce selection bias. A 1-year continuous health plan enrollment was required before and after the index date for both groups. Study outcomes, including health care costs and utilizations, were compared between the disease and comparator groups using 1:1 propensity score matching (PSM). **RESULTS:** Eligible patients (N=384,596) were identified for the prostate cancer and comparison cohorts and after applying PSM, a total of 112,693 patients were matched from each group and the baseline characteristics were well-balanced. Patients diagnosed with prostate cancer were more likely to be hospitalized (75.41% vs. 2.46%, p<0.01), and report more emergency room (9.30% vs. 5.45%, p<0.01), outpatient (99.77% vs. 61.15%, p<0.01) and pharmacy visits (85.65% vs. 63.77%, p<0.01). Patients diagnosed with prostate cancer also incurred higher costs for inpatient ($2,216 vs. $695, p<0.01), emergency room ($92 vs. $51, p<0.01), outpatient ($3,364 vs. $1,462, p<0.01), pharmacy ($582 vs. $413, p<0.01) and total costs (6,162 vs. $2,571, p<0.01) compared to the comparator group. **CONCLUSIONS:** Patients diagnosed with prostate cancer were associated with a higher burden of illness compared to their matched controls during a period of 12 months.

PCN60

COST OF CARE WITH EVEROLIMUS VERSUS AXITINIB FOR SECOND-LINE METASTATIC RENAL CELL CARCINOMA PATIENTS IN CANADA

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OBJECTIVES: Everolimus and axitinib are approved to treat patients with metastatic renal cell carcinoma (mRCC) following failure on various first-line therapies. This analysis assessed the cost of care with everolimus versus axitinib for second-line mRCC patients from a Canadian payer perspective. **METHODS:** Costs considered in this analysis included those related to drug acquisition and adverse events (AEs). Drug acquisition costs were based on the Ontario wholesaler price. Adverse event costs were based on the Ontario Case Costing Initiative and literature. Drug costs, adjusted for dose intensity, and AE costs, based on daily incidence rates, accrued for the duration of treatment in each arm; the sums of these costs were compared across treatments. The mean dose intensities, treatment durations and rates of AEs in the treatment arms were the calculated from trial data. Scenario analyses are presented to estimate the range of costs within the treatment arms. Costs are presented in 2011 Canadian dollars. **RESULTS:** In the base case analysis, the total cost of treatment with everolimus was estimated to be $24,931 while the total cost of treatment with axitinib was $39,010. The primary driver of the cost discrepancy was axitinib's high dose intensity, resulting in high drug acquisition costs. Despite analysis limitations, the trend of the results remained consistent across scenario analyses. When treatment duration was estimated from median progression-free survival estimates in each study's post-sunitinib populations, the total cost of treatment with everolimus was $8,339 less than with axitinib. Sensitivity analyses that assumed equivalent treatment durations between each arm also demonstrated lower overall treatment costs for everolimus patients. **CONCLUSIONS:** The analysis demonstrates that everolimus provides a less costly treatment option than axitinib for patients requiring second-line therapy. Significant uncertainty remains regarding axitinib's treatment duration and dosing, which could result in higher costs to the health care system compared to everolimus.

PCN61

RELATIVE CLINICAL AND ECONOMIC VALUE OF IPILIMUMAB IN MEXICO

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OBJECTIVES: Ipilumumab is a clinically proven treatment option for pre-treated metastatic melanoma (MM). Ipilumumab has clearly demonstrated survival benefit, that is prolonged in a proportion of the responding patients. Karweit J and colleagues (2012) demonstrated that mean overall survival (OS) can be particularly useful for agents with a right-skewed survival curve where a subset of patients respond to treatment with long term survival. The research has demonstrated that several agents, including ipilimumab for MM, bevacizumab for non-small cell lung cancer, sorafenib for hepatocellular carcinoma, lenalidomide for multiple myeloma and trastuzumab for metastatic breast cancer (among others) have shown greater mean OS improvement than median OS improvement, reflecting the long term survival benefit for some patients. In this analysis we select oncologic agents that have demonstrated mean OS benefit in the above mentioned study and have received license in Mexico. We compare the relative economic value delivered by each asset, which broadly represent the therapeutic oncologic class. **METHODS:** The economic value of the analogues is estimated for the Mexican private perspective in terms of cost per month of mean OS versus comparators. The analysis relies on the cost to treat to mean progression by the months of mean OS improvement. **RESULTS:** Cost per month of OS for ipilimumab ($15,993 USD) when compared to bevacizumab, sorafenib, trastuzumab, sunitinib, lenalidomide and vemurafenib is below the average relative cost of the assets (range from $35,871 to $9,845 USD). **CONCLUSIONS:** This study demonstrates that ipilimumab is a competitive asset in terms of value for money. The analysis allows to evaluate within a clear and robust analytical framework, the reimbursement decisions across the oncologic therapeutic class in Mexico.

PCN62

COSTS OF PILOT PROGRAMS EMPLOYING ALLIED HEALTH PROFESSIONALS WITHIN THE CENTERS FOR POPULATION HEALTH AND HEALTH DISPARITIES

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OBJECTIVES: To measure the costs of two pilot interventions within the National Institutes of Health-funded Centers for Population Health and Health Disparities (CPHHD) designed to improve health outcomes in medically underserved commu-

nities through the utilization of allied health professionals. **METHODS:** Two local CPHHD programs with prospective randomized controlled trial designs (a virtual team care intervention aimed at reducing depressive symptoms in older adults with depression and cardio-metabolic syndrome, and a patient navigator program to increase mammography screening for breast cancer) provided the underlying data for this analysis. The programs collected detailed resource use data along with several clinical measures. Costs were measured from a payer perspective. The navigator program involved in-person or remote navigator consultations, and costs were based on a wage rate of $15 per hour. The depression program involved multiple services and all costs reflected institution-specific billing data. **RESULTS:** There were 949 patients in the patient navigator intervention. On average, these patients received 8.28 minutes of navigator services per patient over the phone and 1.23 minutes via in-person visits, translating to a per-patient cost of $2.38. For the six patients enrolled in the team care intervention for depression, resources used included social worker case management and individual psychotherapy, translating to program costs of $145 per patient over 12 months. Spillover health care service costs were similar between the intervention and control groups (intervention = $55 per patient, control = $64 per patient). **CONCLUSIONS:** Costs are an important consideration for evaluating pilot, team-care based interventions to improve patient health. The two programs evaluated here offer insight into the potential impact of interventions that employ allied health professionals and demonstrate a relatively low cost per patient. Future work will examine these costs in comparison with measured effects of the program.

PCN63

ASSESSING THE BURDEN OF CAREGIVING FOR PATIENTS WITH LUNG CANCER IN EUROPE

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OBJECTIVES: To investigate the self-reported burden imposed by care of lung cancer (LC) patients in the European Union (EU). **METHODS:** The study included respondents to the 2010 and 2011 EU National Health and Wellness Survey from France, Germany, Italy, Spain, and the UK who reported being caregivers for a relative with LC versus respondents who did not report being caregivers for a relative with any condition (control). Outcome measures included Short Form (SF)-6D health state utilities and mental and physical health status (all derived from the SF-12v2), stress-related comorbidities, health care resource use during the past 6 months, and work/activity impairment during the past week using the Work Productivity and Activity Impairment (WPAI) questionnaire. Productivity losses were converted into costs using the human capital method by applying median hourly wages per country (from Eurostat 2006 personal income inflated to 2010) to the total number of hours lost using results from WPAI. Multivariable analyses were used to test the potential impact of LC patient caregiving on health care resource use and work/activity impairment, as well as costs specifically associated with work impairment. **RESULTS:** A total of 107 caregivers for patients with LC and 103,868 non-caregivers were identified. Compared with non-caregivers and adjusting for covariates, caregivers had higher mean levels of impaired presenteeism (27.1% vs. 14.8%), overall work impairment (32.4% vs. 18.0%), and activity impairment (32.8% vs. 21.8%; all $p<0.005$); higher odds of impact across all measures of the WPAI including absenteeism (all $p<0.01$); and higher annual costs associated with impaired presenteeism (€5,672 vs. €3,429) and overall work impairment (€6,905 vs. €4,147; both $p<0.05$). Health care resource utilization and mean level of absenteeism did not differ significantly. **CONCLUSIONS:** LC patient caregiving in the EU is associated with significantly higher work/activity impairment and related costs relative to non-caregivers. Costs associated with LC caregiver burden deserve further attention.

PCN64

DIRECT MEDICAL COSTS (DMC) OF TREATING CHRONIC LYMPHOID LEUKEMIA (CLL) PATIENTS IN THE PUBLIC HEALTH CARE SYSTEM IN BRAZIL: RESULTS FROM A RETROSPECTIVE ANALYSIS OF AN ADMINISTRATIVE DATABASE

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OBJECTIVES: To determine direct medical costs of treating patients with Chronic Lymphoid Leukemia (CLL) from the Brazilian Public Healthcare System perspective. **METHODS:** A retrospective longitudinal analysis of the Government administrative claims database (Datasus) was performed. Eligibility criteria were patients starting CLL (ICD-10 code C911) chemotherapy from Jan/2008 to Dec/2011, with complete information and no inconsistency in date of birth, gender. Outpatient and inpatient databases were combined through deterministic linkage. Outcome was direct medical costs (DMC), calculated as the sum of the medical claims for each patient included in the analysis, for a maximum period of 5 years or death or loss of follow-up, whichever comes first. DMC was categorized in chemotherapy, hospitalizations, and other outpatient costs. **RESULTS:** From 5100 patients with CLL identified in the database, 613 met eligibility criteria. Median follow-up time was 25 months. This population cohort had 54% males with average age at start of treatment of 66.4 ± 11.7 years. Patients received an average of 12.0 ± 9.4 months of chemotherapy treatment, with 71% of them treated by one type of chemotherapy regimen. Total DMC in this population was R$ 7,021,631.48 (average cost of R$ 6,404.52 ± 6,133.37 per patient-year), from which R$ 5,384,552.12 (77%) are related to chemotherapy, R$ 1,062,978.98 (15%) to hospitalizations and R$ 574,100.38 (8%) to other outpatient costs. Outpatient laboratory exams accounted for 6% (R$ 397,050.07) of total DMC. 30 (5%) patients underwent radiotherapy treatment, with total costs of R$ 53,944.96 (<1% of DMC). A total of 862 hospitalizations were identified in 287 (46.8%) patients, with an average cost of R$ 1,233.15 ± 3,879.86 per hospitalization. **CONCLUSIONS:** Patients with CLL represent a significant economic burden to the public health system. Chemotherapy and hospitalization costs accounts for more than 90% of the total costs.

PCN65

REAL WORLD MANAGEMENT AND COSTS IN UNRESECTABLE METASTATIC MELANOMA (MM) PATIENTS: UPDATE OF A PILOT STUDY BASED ON AN INSTITUTIONAL PATIENT REGISTRY

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OBJECTIVES: To assess the management and associated lifetime costs in MM patients as from the diagnosis of unresectable metastatic disease until death. **METHODS:** A retrospective patient chart review was performed at the Antwerp University Hospital to obtain data on medical consumption related to the management of unresectable MM (uMM). A complete registry of all melanoma patients who visited the hospital between 2007 and May 2013 was compiled. Eligible for this retrospective chart review were patients with uMM with sufficient data available and who deceased before May 2013. Data on demographics, disease characteristics and management of uMM were collected. Direct costs were calculated by multiplying each item of resource use with its unit cost (2013, €) using the Belgian public health care payer's perspective (PHCP) and patient's perspective. Average (bootstrap 95%CI) overall costs per patient were calculated. **RESULTS:** Out of 338 registered melanoma patients, 35 were eligible and included in this chart review. The median overall survival time (OS) in all patients was 6.2 months. 88.6% (n=31) of patients were treated by systemic treatment(s) of which 17% (n=6) received up to 4 different treatment lines. Ten patients received "new drugs": ipilimumab (1 to 4 cycles): 10; vemurafenib: 2. Fifty-six (41%) of the 137 hospitalizations were for treatment administration. The mean overall cost per patient was €43,429 (bootstrap 95% CI: 33,372 - 54,351), of which € 42,367 (95%CI: 32,481 - 52,976) was reimbursed. The PHCP cost was driven by systemic treatments costs (46% of cost). Mean PHCP cost was € 87,468 (95 % CI: 77,372-97,307) for patients treated with "new drugs" versus € 24,327 (95 % CI: 18,617 - 30,634) for patients not treated with "new drugs". Median OS was 9 and 4.9 months, respectively. **CONCLUSIONS:** Management of uMM results in considerable costs for the PHCP, mainly driven by systemic treatment costs.

PCN66

MANAGEMENT COSTS OF THE FIRST FIVE YEARS AFTER DIAGNOSIS IN BREAST CANCER BY STAGE IN FRANCE

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OBJECTIVES: Few recent data are available on breast cancer treatment costs, especially by stage of the disease at diagnosis. This study was designed to estimate the management costs in breast cancer for the first 5-year period following diagnosis. Costs have been distinguished by stage of severity. **METHODS:** A patient-level analysis was performed from a French physician survey database, collecting data on patient demographics, cancer history from diagnosis and treatment patterns. Data were extracted for all breast cancer cases with at least 1 year of follow-up after diagnosis using data collected from 2011 to 2012. Cost analyses were conducted from a health care payers' perspective adjusting for stage (stages I-IV) at diagnosis and year from diagnosis. **RESULTS:** A total of 1,157 patients were included in the analysis. The stages at diagnosis distribution was respectively from stage I to IV 29.7%, 39.2%, 15.0% and 16.1%. The mean (SD) age at inclusion was 62.5 (12.4) and the mean (SD) time from diagnosis was 5.0 years (5.1). The mean annual cost (SD) over the 5-year period after diagnosis was ranging from 4,293€ (9,526€) for stage I to 12,111€ (19,070€) for stage IV. The mean (SD) annual costs for the 1st year after diagnosis were estimated at 11,647€ (9,883€), 13,226€ (11,575€), 17,254€ (14,535€) and 24,003€ (24,888€), respectively for stage I to IV at diagnosis. The main cost contributors in early stages were radiotherapy and surgery while cytotoxic treatments, hormonotherapy and supportive care droved it for the late stage. The mean annual costs for the following years after diagnosis (2nd to 5thyear) decreased, ranging from 1,827€ (8,964€) for Stage I to 5,370€ (10,662€) for stage IV. **CONCLUSIONS:** : The mean annual cost was strongly related to the clinical stage at diagnosis and the year from diagnosis. These estimates could be useful to populate models that explore impact of treating and preventing breast cancer.

PCN67

THE HUMANISTIC AND ECONOMIC BURDEN OF VENOUS THROMBOEMBOLISM IN CANCER PATIENTS: A SYSTEMATIC REVIEW

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OBJECTIVES: To systematically review the humanistic and economic burden of cancer-related venous thromboembolism (VTE). **METHODS:** A literature search was carried out on Pubmed, Cochrane Central Register of Controlled Trials, Econlit, Science Direct, JSTOR, Oxford Journals and Cambridge Journals. The search was limited to humanistic studies published from January 2000 to December 2012. Additional studies were also identified by searching reference lists of relevant published reviews and included studies. The identified studies were independently reviewed by two reviewers against pre-determined inclusion and exclusion criteria. A quality assessment of the selected studies was also conducted by using standard methods . The data of selected studies were extracted onto a data extraction form and consequently synthesized. **RESULTS:** Fifty five studies were included in our review. It was found that cancer patients experience between 2-fold and 20-fold higher risk of developing VTE in comparison to non-cancer patients. Cancer patients are more likely to experience a VTE event in the first 3 or 6 months after cancer diagnosis and the onset of chemotherapy. Additionally, an increased risk of VTE in patients with distant metastases and certain types of cancer (i.e. pancreatic or lung) was identified. VTE strongly affects the prognosis of cancer patients as it has been found that it is a leading cause of death in this group of patients. The annual average total cost for cancer patients with VTE was found to be almost 50% higher compared to that of cancer patients without VTE

in the USA in 2002. Inpatient care costs accounted for more than 60% of total cost. **CONCLUSIONS:** Although the economic impact of the VTE in cancer patients as well as the impact of VTE on patients' quality of life is not well studied, the present review demonstrate that there is a substantial humanistic and economic burden associated with VTE in cancer patients.

PCN68

A MICRO-COSTING OF THE INPATIENT MANAGEMENT OF FEBRILE NEUTROPENIA IN THE IRISH HEALTH CARE SETTING

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OBJECTIVES: Febrile neutropenia (FN) is a potentially life-threatening complication of chemotherapy which generally prompts immediate hospitalisation. The study objective was to evaluate the resource use and cost of hospitalisation for FN within the Irish Health care setting. Micro-costing techniques were used. The health payer perspective was adopted. **METHODS:** This was a single centre study. Adult cancer patients undergoing chemotherapy, who were subsequently admitted for FN, were identified prospectively. Patient medical records were reviewed retrospectively. **RESULTS:** Patient demographics and resource utilisation data (pertaining to the management of FN) were obtained from a cohort of 32 patients (69% female, mean age = 58.8 years). Twenty-five percent of patients had more than one FN episode. In total, 42 FN episodes were captured; 60% of episodes had occurred within the first two cycles of chemotherapy. The bootstrap estimation was used to determine mean hospital length of stay (LOS) with standard deviation (± SD) and mean costs (± SD). The mean LOS was 7.3 (± 0.5) days. The mean cost per FN episode was €8,915 (± 718). The major cost driver was hospital bed-stay (mean cost of €6,851 (± 549)). Other cost drivers included antibacterial treatment at €760 (± 156), laboratory investigations at €538 (± 47) and the requirement for blood bank products at €525 (± 189). **CONCLUSIONS:** To our knowledge, this is the first investigation of the cost of chemotherapy induced FN within the context of the Irish Health care setting. Our results will be used in cost-effectiveness analyses of novel chemotherapeutic agents and interventions which prevent or treat FN.

PCN69

THE COST OF NSCLC IN FRANCE

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Though lung cancer, and the most common subtype, non-small cell lung cancer (NSCLC), occur frequently, there are limited data quantifying the economic burden of these cancers in Europe.**OBJECTIVES:** To describe the burden of NSCLC in three European countries using patient-level data from commercially available health care data. **METHODS:** Patient-level data were obtained for France from the PMSI (French National discharge database; containing data from publicly-funded hospitals) from 2008 to 2011 while excluding patients with a prior-hospitalization for lung cancer in the preceding 24-month period (2006-2007). As NSCLC does not have a separate ICD-10 code, expert opinion was used to eliminate patients diagnosed with non-NSCLC, based on particular procedures and tests. Hospital resource use was valued using French DRG tariffs. Chemotherapy regimens were valued using official rates. **RESULTS:** A total of 61,144 patients were identified with lung cancer in 2008. 19,099 were excluded because of prior lung cancer diagnoses. Of this cohort of 42,043 patients, 25,054 were exclusively treated in the public setting; 15,061 were identified as NSCLC and were considered in this analysis. Hospital-related costs cumulated over the follow-up period were estimated at €337,382m, with chemotherapy costs representing 9%. Mean cumulated hospital-related cost per-patient were estimated at €22,401 over the follow-up period. Terminal care represented a mean per-patient cost of €10,440. Adverse events triggering hospital-expenses represented a mean per-patient cost of €5,694. Patients ≤ 55 years incurred higher costs per-person over the follow-up period than patients >55 years; €25,386 vs. €21,368. These extra costs were mostly driven by chemotherapy costs(€13,287 vs. €10,561). Patient with metastases incurred higher costs over the follow-up period than patients without these, €23,118 vs. €21,934. **CONCLUSIONS:** This is one of the first analyses quantifying the economic burden of NSCLC. The burden for France is substantial. Subsequent analyses will allow for comparisons of this burden across other countries.

PCN70

CHEMOTHERAPY TREATMENT PATTERNS, HEALTH CARE COSTS, AND MORTALITY OF LUNG CANCER PATIENTS IN TAIWAN – A LONGITUDINAL STUDY BETWEEN 2000 AND 2008

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OBJECTIVES: To examine chemotherapy treatment patterns, health care costs, and mortality of lung cancer patients in Taiwan. **METHODS:** This study analyzed medical and pharmacy claims from a random sample of one million taken from all beneficiaries covered under Taiwan's national health insurance in 2000. Newly diagnosed lung cancer patients between 2000 and 2008 (first observed diagnosis as the index date) were identified based on medical claims with associated diagnoses. Patients were followed until death or the end of 2008. Per patient per month [PPPM] total health care costs (in USD) and median survival were reported. Chemotherapy treatment patterns during the follow-up were examined. **RESULTS:** This study included 3,343 lung cancer patients (mean age: 67.1 years; 34.5% female; 35.4% secondary lung cancer). Median survival was 8.1 months. PPPM costs were $2,322 USD (interquartile range $450-$2,902). Lifetime costs from diagnosis among those who died during the study period were $12,788 USD (interquartile range $2,674-$17,546). Of the 1,633 patients who received chemotherapy during the follow-up, 375 received only one chemotherapy agent (gemcitabine 35.7%, vinorelbine 20.5%, platinum-based agents 20.3%, UFUR 8.3%, taxanes 7.7%, etoposide 7.5%). Close to three quarters (74.8%) of treated patients received combination therapy with platinum-based agents. Of 1,221 patients treated with platinum-based combination therapy, the therapy most commonly used includes gemcitabine (37.5%), taxanes (21.5%), and vinorelbine (18.2%), while 21.4% of patients received two or more other agents. We observed longer median survival in patients with a higher number of chemotherapy agents received. **CONCLUSIONS:** Lung cancer patients in Taiwan incurred considerable health care costs after diagnosis. More than half of patients were treated with chemotherapy, in particular with multiple chemotherapy agents. Future research comparing cost-effectiveness among different treatment options is warranted.

PCN71

AUSTRALIAN STANDARD COSTS AND CONSEQUENCES OF FOUR CHEMOTHERAPY ADVERSE EVENTS

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OBJECTIVES: This work aimed to develop rigorous models of the Australian costs of four common chemotherapy adverse event (diarrhoea, vomiting, anaemia and neutropenia), which provide standard cost estimates and can be used in future models of chemotherapy cost effectiveness. **METHODS:** Decision analytic modelling was used to identify the costs and consequences of AEs. These are not only stand alone models, but also form decision tree sections to be incorporated into larger models of chemotherapy cost effectiveness. Model structures are based on best-practice clinical pathways, and incorporate efficacy of side effect treatment, quality of life and chemotherapy dose. Literature reviews identified clinical inputs. Costs of treatment were obtained from standard Australian sources such as the Pharmaceutical Benefits Schedule. The perspective was the Australian health care system. One-way sensitivity analyses explored uncertainty in the models. **RESULTS:** The base case average cost per patient of diarrhoea ranged from $19 (mild AE) to $4,821 (severe AE); those for anaemia ranged from $51 (mild AE) to $17,100 (moderate AE) depending on the type of chemotherapy and anaemia treatment. Vomiting prevention base case costs ranged from $0.84 (low risk chemotherapy) to $157.55 (high risk chemotherapy requiring breakthrough and refractory management). Neutropenia base case costs ranged from $2,235 (outpatient management) to $12,054 (intensive care required). Where possible, the impact on quality of life and chemotherapy total dose was also modelled. Estimates of AE costs vary widely in the literature, however our estimates appear consistent with studies of similar methodology. **CONCLUSIONS:** The four models presented represent best-practice modelling techniques for chemotherapy AEs. Each has been designed to enable either the results or the model structure to be incorporated into larger models of chemotherapy cost effectiveness. This allows model builders to incorporate rigorous, Australian-specific estimates of the costs and consequences of chemotherapy AEs into models of chemotherapy cost effectiveness.

PCN72

HORMONAL RECEPTOR POSITIVE, HER2 NEGATIVE METASTATIC BREAST CANCER (MBC HR+HER2-): PRE AND POST-PROGRESSION COSTS UNDER THE PUBLIC HEALTH CARE SYSTEM (SUS) AND SOCIETAL PERSPECTIVES IN BRAZIL

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OBJECTIVES: To estimate direct medical costs and productivity costs of hormonal receptor positive, HER2 negative metastatic breast cancer (MBC HR+ HER2-) under the public health care system (SUS) and societal perspectives in Brazil, being MBC cost data very scarce in Brazil so far. **METHODS:** A systematic literature review was performed in the following databases: Cochrane, MEDLINE via Pubmed, LILACS, EMBASE and CRD until FEB 2013. Gray literature was also included. National guidelines search and expert validation was carried out specifically for the direct medical cost estimations. Direct medical costs were stratified as pre and post-progression costs and terminal costs. Pre and post-progression costs considered outpatient, inpatient and monitoring costs. For post-progression, metastasis treatment costs were also estimated, including bone, lung, liver and brain metastasis. For the productivity costs, the Human Capital method was chosen. Days of absenteeism were obtained from the literature and a Markov model was used to estimate the loss of productivity in 1 year (as the mean age of MBC in Brazil is 59 and official retirement at 60 years of age). Unit costs were obtained from Brazilian official lists and IBGE (income). All costs are expressed in 2012 Brazilian Real (BRL). **RESULTS:** Pre, post-progression and terminal costs of MBC HR+HER2-were estimated in BRL308, BRL731 and BRL4.164 respectively, under SUS perspective. Post-progression metastasis treatment costs presented an average of BRL12.047 under SUS perspective. The productivity costs were estimated in BRL26.056 under the societal perspective considering the available treatments at SUS for MBC HR+HER2- patients. **CONCLUSIONS:** MBC HR+HER2- post-progression costs impose a significant economic burden under SUS perspective as well as productivity losses to the society. Novel therapies that postpone progression in those patients may reduce costs associated.

PCN73

ESTIMATING THE COST OF HPV-RELATED DISEASES IN TURKEY: A DELPHI APPROACH

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OBJECTIVES: Very limited data is available on the cost and burden of HPV-related diseases in Turkey. The aim of our analysis is to evaluate the corresponding cost through understanding the current clinical practices, use of resources and treat-

ment algorithms based on expert opinion. **METHODS:** This study uses the Delphi method to reach experts' consensus on the clinical practices currently being used in Turkey. Delphi method has been widely used in medical areas where empirical data is scarce. The survey developed for this study includes questions to understand the clinical resource use in order to calculate the associated costs. Although the panelists' answers are unlikely to change after the second iteration according to the literature, a three-iteration panel was needed to reach a consensus in practice. The consensus is then used to calculate the cost of an episode of care for genital warts (GW), CIN 1, CIN 2/3, different cervical cancer stages from the payer's perspective. **RESULTS:** TDP-HPV included a total of 10 experts, including gyneco-oncologists, dermatologists and a medical oncologist. The cost of a GW episode of care is approximately USD 263.58 to the government. CIN 1 cases are only treated if the disease persists for 2 years, which happens in about 5% of cases. The cost of a CIN 1, CIN 2/3 episode of care is calculated as USD 127, USD 262 to the government, respectively. The cervical cancer (CC) stages are divided into local CC, regional CC, and distant CC. The costs associated with these states are USD 1,340, USD 4,345, and USD 8,150. **CONCLUSIONS:** Early diagnosis and treatment is crucial from the cost perspective too as a more severe disease costs more. GWs are sometimes left out when HPV-related diseases are considered. However, this study mentions that GW presents a serious burden to the society.

PCN74

COSTS OF HER 2 NEGATIVE, HORMONAL RECEPTOR POSITIVE, METASTATIC BREAST CANCER (MBC-HR+) TREATED WITH EVEROLIMUS (EVE) + EXEMESTANE (EXE) IN THE BRAZILIAN PRIVATE SYSTEM (BPS): A REAL WORLD (RW) AND PUBLISHED LITERATURE ANALYSIS

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OBJECTIVES: EVE in association with aromatase inhibitor was recently approved by ANVISA (Brazilian Regulatory Agency) for MBC-HR+ patients. EVE redefines the role of endocrine therapy in MBC-HR+ reversing endocrine resistance. The aim of this study is to determine the costs associated to the introduction of EVE + EXE for the Brazilian private system population. **METHODS:** A previous study from real-world (RW) data between 2011-12 (large private database of medical claims for chemotherapy (CT), Evidencias Database) and published data identified MBC-HR+ patients and evaluated costs of treatments and adverse events (AEs), by a micro-costing approach. Patients were divided into three groups, according to metastasis: bone exclusive (B), Visceral exclusive (V) and Bone plus Visceral (BV). For this study the financial impact of the adoption of EVE+EXE was calculated in this population, based on the previous findings. Direct medical costs of EVE, hormones, CT, hospitalization, supportive care, radiation, monitoring and AEs were considered. A cohort of 100 patients with MBC-HR+ was simulated in a decision tree to obtain the costs for each group and the mean cost/ patient. Costs were estimated in 2013 Brazilian Real (R$). **RESULTS:** RW data showed the following distribution of patients: B 38%, V 42% BV 20%. Lengths of treatment (months) were B 25.1-30, V 16.1; BV 14-19.6. Mean costs/patient/group, before EVE+EXE adoptions, were B R$135.744 (US$67,872), V R$129.079 (US$64,539) and BV R$117.172 (US$58,568). If EVE+EXE substituted 80% or 50% of the current treatments, the incremental percentage of costs would be B (5%; - 9%), V (5,7%; -16%) and BV (22%; 14%). Costs with AEs were at least 50% lower with the use of EVE+EXE. **CONCLUSIONS:** EVE adoption in association with EXE may be cost saving for some groups of MBC-HR+ patients. For other groups, the incremental cost is not superior to 22%.

PCN75

ESTIMATED COSTS OF HER2-POSITIVE METASTATIC BREAST CANCER FOR PATIENTS INITIATING AN ORAL ANTICANCER TREATMENT: RESULTS FROM A FRENCH PROSPECTIVE OBSERVATIONAL STUDY

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OBJECTIVES: To assess the cost of HER2-positive (HER2+) metastatic breast cancer (mBC) for patients initiating an oral anticancer treatment (OAT) from the perspective of the French National Health Insurance (NHI). **METHODS:** A prospective observational multicenter study was conducted among 284 HER2+ mBC patients treated by 68 oncologists initiating a treatment containing an OAT between March 2011 and February 2012. Costs data were available for 199 patients. Clinical characteristics, treatment patterns, quality-of-life, adherence and health care resources data were collected. Health care resource use data on hospitalization, medical consultation, drug and radiation-therapy were reported by oncologists at treatment initiation and after each 3-month period during a 9 months maximum period. Cost estimations were based on unit costs from national databases (French Diagnosis Related Group cost database and NHI database for drug unit cost). **RESULTS:** A total of 109 patients (55%) received an OAT only and 90 (45%) received oral and intravenous (IV) drugs. Thirty patients (15%) were treated with radiation therapy and 43 patients (22%) with hormonal-therapy in addition to chemotherapy. The overall average cost of management per patient was 28,482€ ± 14,914 for all patients, 19,412€ ± 9,462 for patients with an OAT only and 39,467€ ± 12,770 for patients with oral and IV drugs. Drug costs were 27,669 € ± 14,976 and they represented 97% of the total hospital cost of management (hospitalizations, consultations and drugs). **CONCLUSIONS:** This prospective observational study conducted among HER2+ mBC patients shows that the route of drug administration has an impact on treatment costs. Nevertheless, the study design does not allow concluding that OAT were associated with lower costs and cost savings. These finding however warrants further exploration within the context of micro-costing studies from the hospital and community perspective in order to better understand the health care resources used that are required to manage patients treated with OAT.

PCN77

INPATIENT HOSPITAL COSTS OF FEBRILE NEUTROPENIA (FN) AS A CONSEQUENCE OF CHEMOTHERAPY (CHT) FOR BREAST CANCER (BC) AND NON-HODGKIN LYMPHOMA (NHL) IN SWITZERLAND

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OBJECTIVES: FN can be a serious complication of CHT, increasing mortality risk and health care costs. Incidence and inpatient hospital costs of FN in Switzerland are currently not reported; therefore this study aimed to: 1. Estimate the number of FN-related hospitalizations. 2. Assess inpatient hospital costs per FN event in Switzerland. **METHODS:** The main data source was MedStat, a comprehensive database of all Swiss hospitalizations from 1997-2010. BC and NHL cases were identified from ICD-10-GM codes. Hospitalizations for FN were identified by a simultaneous code of BC or NHL and neutropenia. Incident cases of cancer were identified as patients treated in 2010 for the first time since 2002. Results were compared to data from the Foundation National Institute for Cancer Epidemiology and Registration (NICER). Cost data stems from the cantonal hospital of Winterthur. **RESULTS:** Using MedStat data, 645 male and 557 female NHL patients and 6'391 female BC patients were hospitalized in 2010 for the first time. Corresponding annual incidence data from NICER were 780 male and 688 female NHL patients and 5'388 female BC patients. The proportion of hospitalizations due to FN was 8.2% (190/2'311) among male and 6.0% (123/2'063) among female NHL patients, and was 2.6% (255/9'650) among female BC patients. In-hospital mortality of FN cases was 9.5% for men and 5.7% for women with NHL, and 4.3% for BC. Median inpatient treatment costs for an FN event were CHF 8'399 (mean: CHF 14'006) in NHL and CHF 4'208 (mean: CHF 10'020) in BC. Nursing time was the most important cost component and length of stay was the most important driver of total inpatient cost. **CONCLUSIONS:** 3% to 8% of all hospitalizations in NHL and BC patients were due to FN. Our results suggest that FN leads to considerable risk of death and incurs high in-hospital care cost in Switzerland.

PCN78

COST ASSESSMENT OF METASTATIC AND NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENT-MANAGEMENT IN SPAIN

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OBJECTIVES: To compare annual management costs of castration-resistant prostate cancer (CRPC) patients at high risk of developing bone metastases (BM) versus those that already had BM in Spain. **METHODS:** An expert panel of 5 urologists and 3 oncologists from Spanish health centres was asked to estimate the mean annual resource use in the management of non-metastatic CRPC patients and in the first, second and subsequent years after developing BM. Hospital resources were stratified into four major categories: 1) general resources [medical visits, diagnostic and monitoring procedures, hospital admission and surgeries], 2) hormone therapy, 3) chemotherapy and 4) analgesic treatments. The last three categories included: drug costs, adverse event (AE) management-costs and pre-medication costs. Skeletal-related events (pathological fracture, radiation or surgery to bone and spinal cord compression) often suffered by BM patients were excluded from the analysis as Spanish cost-related data had recently been published. Unit costs (€, 2013) for each identified resource were obtained from a national cost-database. **RESULTS:** Total management-related annual costs for non-metastatic CRPC patients were €2,691.57; €978.51 were hormone therapy drug costs, €11.10 analgesics costs and €243.55 AE management costs. No chemotherapy was administered in these patients. Annual management cost for BM patients was €6,000.37 the first year, €14,468.35 the second year and €14,313.87 in subsequent years. Hormone therapy drug costs accounted for €946.67, €948.13 and €948.13 in the first, second and subsequent years, while chemotherapy costs accounted for €1,892.21 (32.2%); 9,485.41 (66.2%) and €9,143.92 (64.4%), respectively. Analgesic costs increased from €597.29 (first year) to €915.16 and €1,031.20 (second and subsequent years) and AE management costs increased from €595.63 (first year) to €758.58 (second year) and €732.14 (subsequent years). **CONCLUSIONS:** CRPC patients with BM had higher management costs than non-metastatic patients especially after the first year of treatment, which was mainly due to chemotherapy drug costs.

PCN79

ECONOMIC BURDEN OF TOXICITIES ASSOCIATED WITH ADVANCED MELANOMA TREATMENTS IN FRANCE, ITALY, THE NETHERLANDS, AND SPAIN

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OBJECTIVES: Little is known about costs of managing adverse events (AEs) associated with currently-available therapies in advanced melanoma. This study identifies and estimates the costs of these AEs in France (FR), Italy (IT), The Netherlands (NL), and Spain (ES). **METHODS:** A comprehensive literature search was conducted to identify common grade 3/4 AEs from product labels and published phase II/III advanced melanoma studies in PubMed, conference abstracts, and European treatment guidelines. Resource utilizations for the management of each type of AE in typical inpatient/outpatient treatment setting were determined via in-depth interviews with 5 melanoma clinicians in each country. Outpatient and inpatient 2012 costs were then estimated for each type of AE by applying country-specific tariffs, except in Spain where costs were obtained from government database or best published sources. **RESULTS:** Most frequent grade 3/4 AEs associated with chemotherapies included neutropenia, vomiting, and anemia. Vemurafenib was commonly associated with cutaneous squamous cell carcinoma (CSCC)/keratoacanthoma, rash, and

elevated liver enzymes, while dabrafenib was most often associated with CSCC and pyrexia. The most common AEs associated with trametinib were hypertension and rash. Common ipilimumab AEs were immune-related diarrhea/colitis, dyspnea, anemia, vomiting, and less frequently, hypophysitis. In the outpatient setting, the most costly AEs per incident included anemia (€1,431, €1,309, €1,276; ES, IT, FR) and CSCC (€1,058; NL). Other costly outpatient treatments include those for hypophysitis (€463, €449, €321; NL, ES, IT), febrile neutropenia (€593, €430; IT, ES), and CSCC (€483, €292; ES, IT). In the inpatient setting, the most costly AEs per hospitalization per country were hypophysitis (€10,189; ES), elevated liver enzymes (€6,868; FR), anemia (€2,826, €2,628; NL, IT). Additional inpatient treatments with high costs were diarrhea (€4,083; ES), neutropenia (€2,322; IT) and vomiting (€2,036; NL). **CONCLUSIONS:** Costs of managing AEs can be substantial, and effective new treatments with reduced AE profiles would be valuable.

PCN80

THE COST OF TREATING SQUAMOUS CELL CARCINOMA OF THE ANUS (SCCA) IN ENGLAND: RESULTS FROM AN EMPIRICALLY CALIBRATED MODEL

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OBJECTIVES: Squamous cell carcinoma of the anus (SCCA) generally requires a number of complex interventions as part of a multidisciplinary approach to treatment. This research aimed to combine available data on disease progression and treatment in order to estimate the average cost of treating a case of SCCA in England. **METHODS:** Data on primary treatment, disease progression and follow-up were obtained from the Association of Coloproctology of Great Britain and Ireland's anal cancer position statement, supplemented by expert opinion where necessary. First, decision trees were constructed to estimate the costs of diagnosis, staging and primary treatment. A Markov model was then developed to simulate disease progression and follow-up based on the mode of primary treatment (combined modality therapy versus radiotherapy alone). Values for unknown parameters were jointly selected from within plausible ranges and model outputs for each simulation were then compared to empirical data on overall mortality and locoregional relapse. Goodness of fit was estimated using ordinary least squares. All costs applied to treatments and interventions were taken from the 2010/11 National Tariff, with the 2010/11 Reference Costs used for off tariff payments. A one-way sensitivity analysis was also performed. **RESULTS:** The cost of treating a case of SCCA was estimated to be in the range of £16,448-£16,630 when future inflation was taken into account, and £16,278-£16,455 when it was not. In the one-way sensitivity analysis, the adjusted value ranged between £14,309-£23,264 (unadjusted £14,139-£23,077), with the results most sensitive to changes in the mode of admission for primary treatment and the costs of staging/diagnosis. **CONCLUSIONS:** Despite limitations in the approach resulting from a lack of available data, these results indicate that the cost of treating SCCA is significant. Further observational work is required in order to verify these findings.

PCN81

ECONOMIC BURDEN OF TOXICITIES ASSOCIATED WITH ADVANCED MELANOMA TREATMENTS IN THE UNITED STATES

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OBJECTIVES: Information on the costs of managing adverse events (AEs) associated with currently-available treatment regimens in advanced melanoma is limited. This study identifies treatment-related AEs associated with commonly-used regimens recommended in US guidelines, and estimates the costs of treating these AEs in the US. **METHODS:** Grade 3 and 4 AEs were identified by a comprehensive literature search of product labels and published English-language phase II/III advanced melanoma studies in PubMed, conference abstracts, and NCCN guidelines. In-depth interviews with 5 US melanoma clinicians were performed to obtain resource utilization and treatment setting information for managing each type of AE. Costs (2012$) were then estimated for each type of AE in outpatient and inpatient settings, using Medicare reimbursement rates for the outpatient setting, and Healthcare Utilization Project estimates for the inpatient setting. **RESULTS:** The most common grade 3 and 4 AEs associated with chemotherapy regimens included neutropenia, vomiting, and anemia. Cutaneous squamous cell carcinoma (CSCC)/keratoacanthoma, rash, and elevated liver enzymes were most common AEs associated with vemurafenib, while CSCC and pyrexia were most often associated with dabrafenib. The most common AEs associated with trametinib were hypertension and rash. Common ipilimumab AEs included immune-related diarrhea/colitis, dyspnea, anemia, and vomiting, and less frequent hypophysitis. The highest cost per incident in the outpatient setting among these AEs was neutropenia ($2,039), followed by CSCC ($369), vomiting ($342), and dyspnea ($222). The highest costs per hospitalization were for CSCC ($18,906), followed by hypophysitis ($15,721) and febrile/afebrile neutropenia ($11,125). Other costly AEs in the inpatient setting include hypertension ($8,113), diarrhea ($6,881), dyspnea ($6,826), vomiting ($6,046), anemia ($6,014), and elevated liver enzymes ($5,942). All hospitalizations due to AEs were more than $4,000 per incident. **CONCLUSIONS:** The costs of managing treatment-related AEs in advanced melanoma are considerable, and there is need for effective treatments with improved toxicity profiles.

PCN82

HEALTH ECONOMIC EVALUATION OF A COMPLEMENTARY BIOMARKER FOR HYPOTHETICAL PROSTATE CANCER SCREENING IN GERMANY

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OBJECTIVES: Prostate cancer (PCA) is the most common cancer in men worldwide. However, there is disagreement about the benefits of existing screening programs. This is mainly due to low specificity of currently utilized biomarkers. This can lead to both inappropriate medical treatment and increasing costs of care. For the future, many biotechnological developments are promising, but not all will be affordable for routine screening. The question is how much a complementary biomarker to prostate-specific antigen (PSA)-test may cost which would be applied to avoid false-positive results. **METHODS:** Conduct of a hybrid discrete-event and system-dynamics simulation by applying AnyLogic. Based on clinical guidelines and expert knowledge, a hypothetical PCA screening workflow was developed and supplemented by a proposed innovative biomarker. Demographic and patient behavior information, disease related data on incidence as well as sensitivity and specificity of PSA, digital-rectal examination and prostate biopsy were further implemented in the model. Economic consequences were calculated by considering costs for examinations, biopsy diagnosis and complications. **RESULTS:** In Germany, annual screening would be recommended for 18.8 million men aged ≥45 years. Assuming a biomarker specificity of 80%, approximately 70% of prostate biopsies could be avoided. This could lead to a reduction of biopsy caused complications. Regarding the latter, mean costs of 204.17€ were calculated. Due to prevented check-ups and biopsy-complications, cost neutrality for the supposed biomarker will be reached when applying a price of 48.50€. **CONCLUSIONS:** A complementary biomarker could lead to more precise diagnosis and additional value for patients and health insurance funds. Although the price may not be high, an implementation may nevertheless be feasible for companies due to the high number of examinations. Funded by the German Federal Ministry of Education and Research (BMBF) as part of the National Cluster of Excellence Medical Technology - Medical Valley EMN (Project grant No. 01EX1013B).

PCN83

RESOURCE USE AND COST OF DIAGNOSIS AND MANAGEMENT OF BREAST CANCER BY STAGE IN AN IRISH TEACHING HOSPITAL

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OBJECTIVES: To estimate the cost of diagnostic investigation and treatment for breast cancer in an Irish teaching hospital from a health payer perspective. **METHODS:** Retrospective population based resource utilisation data for n=611 patients treated for primary breast cancer in a university teaching hospital in Ireland were available for the period 2009-2011. Health care resource use included diagnostic investigations and all treatments. Unit costs for diagnosis & surgical procedures, laboratory tests, and radiotherapy were derived from DRG costs, hospital finance departments, clinical opinion and literature review. Chemotherapy costs were estimated from local hospital protocols, pharmacy departments and clinical opinion. Associated pharmaceutical cost, including oral hormonal therapy, were estimated from the HSE Primary Care Reimbursement Services claims database. Overall and mean costs by stage of breast cancer are presented with bootstrap 95% confidence intervals (CIs). **RESULTS:** Total cost of diagnosis, treatment and follow-up was estimated at €15.2 million over the 3 year period, with an average cost of €24,863 per patient (95% CI; €22,628, €27,197). Chemotherapy and other pharmaceuticals accounted for 47%, radiotherapy 19%, surgery 19%, diagnostics 5%, radiology 2% and follow-up 8% of total expenditure. The biological agent trastuzumab accounted for 43% of total pharmaceutical expenditure. Costs varied by stage at diagnosis. The average cost per patient by stage at diagnosis was estimated as follows; Stage 1 (n = 186) €23,821 (95% CI; €20,113, €27,846); Stage 2 (n=248) €24,919 (95% CI; €21,358, €28,626); Stage 3 (n=121) €30,172 (95% CI; €25,434, €35,366); Stage 4 (n=56) €16,570 (95% CI; €7,964, €25,836). **CONCLUSIONS:** This study demonstrates the value of using existing data from national and local databases in estimating the cost of diagnosis and management of breast cancer from a health payer perspective and highlights the impact of trastuzumab on overall costs.

PCN84

ANALYSIS OF PUBLIC AND PRIVATE HOSPITAL DATABASES (PMSI) 2010 / 2011 TO ESTIMATE THE FREQUENCY AND ASSOCIATED COSTS FOR FEBRILE NEUTROPENIA IN FRANCE

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OBJECTIVES: To estimate the frequency and costs of hospital stays for cancer patients receiving cytotoxic chemotherapies inducing febrile neutropenia (FN), in public and private hospitals in France. **METHODS:** The French Hospital National Database (PMSI) is a comprehensive claims database which includes information on diagnoses an procedures and allows record linkage. Hospital stays for patients admitted with hematologic or solid tumors in 2010/2011 were extracted and an *ad hoc*algorithm selected those for which the primary admission reason was FN, as well as those due to an infectious syndrome resulting from FN. Economic valuations were based on 2010 public national tariffs and National Scale Costs (ENCC). **RESULTS:** A total of 14,685 hospital stays were analyzed (3,776 stays for the treatment of hematologic tumors and 10,909 for solid tumors) corresponding to 10,721 patients treated for FN (2,386 patients first treated for hematologic tumor and 8,343 first treated for solid tumor). The proportions of patients hospitalized for FN were 12.2% for hematologic tumors and 7.0% for solid tumors. The average length of stay was 7 days for patients with hematologic tumors and 6.5 days for patients with solid tumors. In the sub analysis, non-Hodgkin's lymphoma (11.7%) and lung cancer (11.8%) were, respectively, the most common hematologic and solid tumor types in patients hospitalized for FN. The mean costs of treatments associated with FN per patient were 7,820.67€ for hematologic tumors, 4,907.83€ for solid tumors and, in the sub-analysis, 6,816€ for non-Hodgkin's lymphoma and 4,907€ for lung cancer. **CONCLUSIONS:** The PMSI is a useful source to estimate the treatment costs associated with FN in France. In 2010/2011, febrile neutropenia induced a total of 14,685 stays and a total cost of 59.6 million euros for the Statutory Health Insurance.

PCN85

THE ANALYSIS OF COSTS AND REIMBURSEMENTS FOR LUNG CANCER TREATMENT IN THE CZECH REPUBLIC

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OBJECTIVES: Lung cancer is the most frequently diagnosed oncologic disease worldwide, annually diagnosed in nearly 1.4 million patients. In 2010, the incidence in men was 89.7 per hundred thousand people (in 1996, it was 102.3), while in women 35.2 (against 22.9 in 1996). The severity of the disease is also reflected by the high mortality rate, which was 74.8 per hundred thousand people in men and 27.4 in women in 2010. **METHODS:** Identifying the costs spent by a clinic/hospital is difficult in the Czech Republic, as the majority of hospitals work with cost related data in the "confidential" mode. The costs were estimated and verified based on expert opinions of pulmonologists, oncologists, head physicians and staff members of technical and economic departments of five pneumo-oncologic centres and university hospitals in this study. **RESULTS:** Totally 32 procedures (process maps) were identified in lung cancer treatment (10 in diagnostic, 22 in therapeutic processes). Each procedure consists of diagnostics, therapy and subsequent monitoring of patients. Costs for respective steps were assessed, and total costs for each therapeutic scheme were calculated. **CONCLUSIONS:** The calculations imply that treatment costs significantly differ depending on the selected diagnostic/ therapeutic procedure. The setting of the reimbursement system generates different stimuli for providers who may reach both positive and negative balances. This fact may have an effect on economic results leading, in its consequence, to the preference of alternatives more suitable in terms of reimbursement regardless of the optimum procedures for a specific patient.

PCN86

TREATMENT PATTERNS AND COSTS ASSOCIATED WITH CHRONIC LYMPHOCYTIC LEUKEMIA CHEMOTHERAPY UNDER THE BRAZILIAN PRIVATE HEALTH CARE PERSPECTIVE: A RETROSPECTIVE ANALYSIS OF THE ORIZON DATABASE

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OBJECTIVES: To identify the chemotherapeutic treatment patterns and associated costs in patients with chronic lymphocytic leukemia (CLL) in the Private Healthcare System. **METHODS:** A retrospective analysis of the Orizon database, containing inpatient and outpatient claims data of a pool of 102 HMOs (34% of the total Private Health System), from January 2009 to December 2012 was conducted. Eligibility criteria were patients starting CLL (ICD-10 code C911) chemotherapy treatment from April 2009 to December 2012. This cohort of patients was followed until December 2012, death or loss of follow-up. Chemotherapy regimens were identified based on the agents reported in the claims. Line of treatment was defined based on meaningful interruption (>6 months) and/or change in the chemotherapy regimen. Descriptive statistics (average, standard deviation and percentage) of treatment regimens, duration of treatment and costs were performed. **RESULTS:** A total of 163 patients representing 859 cycles of chemotherapy met eligibility criteria; 43.6% of the patients underwent more than one line of treatment, with total chemotherapy costs of R$84,979.63 per patient. The three most widely used chemotherapy regimen were: fludarabine, cyclofosfamide and rituximab (FCR), used in 81 (54.9%) patients with average treatment duration of 3.54 cycles and total costs of R$69,241.91 per patient; rituximab monotherapy, used in 44 (27.0%) patients, with average treatment duration of 4.05 cycles and total costs of R$59,543.12 per patient; and fludarabine and cyclofosfamide (FC), used in 19 (11.7%) patients, with average duration of 2.22 cycles and total costs of R$7,075.95 per patient. Chemotherapy drugs accounted for 72.8% of the total costs, followed by other medicines (11%), disposable devices (5.5%) and hospital facility fees (5.0%). **CONCLUSIONS:** FCR is the standard of care in CLL patients treated in the Brazilian Private Health System, and almost half of the patients undergo more than one treatment line, creating a significant financial burden to private payers.

PCN87

COST OF CANCER IN THE AUSTRIAN HOSPITAL SETTING

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OBJECTIVES: In Austria, 38,000 people are yearly diagnosed with cancer, which is the world's leading cause of death (Austria: 19,547), followed by heart disease and stroke. Advances in early detection, prevention and treatment have led to decreasing cancer death and more favorable outcomes. Moreover, significant increases in the cost of cancer care have come in parallel with these advances. The cost factor related to modern cancer treatment is increasingly a matter of debate. Hence, the aim of the analysis was to evaluate the cost of cancer expressed as reimbursed lump-sums of the DRG system, number of inpatients stays and Length-of-Stay (LOS) in the inpatient setting to bring more transparency in the discussion and bridge the information-gap. **METHODS:** We performed a retrospective claim-based analysis with Austrian DRG-System (LKF Leistungsorientierte Krankenanstaltenfinanzierung) data. The DRG-System is based on ICD-10 codes. Payment consists of one or several case-based lump-sums. Our analysis included all cancer hospital admissions. The cost-evaluation is based on the refunded lump-sums of the DRG-System for the year 2011. **RESULTS:** In 2011, 353,883 inpatient stays with a diagnosis of cancer were monitored. Hospital stays due to cancer accounts for 14% of the entire inpatient stays in Austria. The average LOS in cancer patients was 4.35 days and was associated with average costs per stay of 3,730 Euros. Compared with the total number of admissions these numbers are below average (LOS: 5.43; costs per stay: 3,949 Euros). Furthermore, cancer patients received medical services to the value of 927 million Euro or 14.2% of total reimbursed lump-sums (6.53 billion Euros) in Austria. 224 million Euros fall upon medical tumour therapy. With regard to monoclonal antibody therapies, 56 million Euros was refunded. **CONCLUSIONS:** The current development in modern cancer therapies leads to efficient treatment pathways expressed in higher survival rates, reduced hospital days and an improved quality-of-life.

PCN88

COST-ANALYSIS IN THE TREATMENT OF PATIENTS AFFECTED BY MALIGNANT ASCITES IN ITALY

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OBJECTIVES: The objective of this project was to identify the treatment cost of malignant ascites from the Italian NHS perspective through a cost-analysis. Three reference centers in Italy contributed to this study during year 2012. **METHODS:** Three centers (Scientific Institute of Romagna for Cancer Studies and Treatment-I.R.S.T; Medical Oncology Unit of San Gerardo Hospital; Department of Gynecology of University Hospital Agostino Gemelli) were chosen due to the fact that they treat a representative sample of patients with malignant ascites in Italy. Each center was asked to complete three case report forms: the first identifying the costs for the pre-procedure diagnostic tests, the second identifying the specific procedure costs (paracentesis) and the third identifying the specific costs due to treatment of complications. All these reports had to be completed for the last 5 patients diagnosed with malignant ascites in order to prevent selection bias. A total cost for each patient was calculated by DRG analysis (standard cost – tariff). The DRG analysis assessed: day hospital, admission number, hospitalization, number of hospitalization days, principal diagnosis, main procedure/intervention, number of paracentesis procedures performed on the same patient with the same diagnosis, DRG type, DRG code, refund value for day hospital/ refund value for ordinary hospitalization. **RESULTS:** The analysis shows an average cost of € 1,464.42 per patient with malignant ascites using the DRG reimbursement rate (minimum value: €1,405.63; maximum value: €1,525.37). Analysis using DRG with complications resulted in a mean value of €1,524.84 (minimum value: €1,429.69; maximum value: €1,625.55). The key cost driver of malignant ascites treatment was the paracentesis procedure. **CONCLUSIONS:** The economic impact of paracenteses is high, especially when procedures must be repeated. The reduction in the number of paracenteses could reduce the costs while improving the QoL of the patients.

PCN89

ECONOMIC EVALUATION OF AN ELECTRICAL IMPEDANCE SPECTROSCOPY (EIS) DEVICE USED AS AN ADJUNCT TO COLPOSCOPY

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OBJECTIVES: Colposcopy is an essential part of the screening process for the prevention of cervical cancer by diagnosing and treating precancerous lesions known as cervical intra-epithelial neoplasia (CIN). The objective of this study was to assess the cost and health impact of using an electrical impedance spectroscopy (EIS) device to aid in the diagnosis of precancerous lesions compared to standard colposcopy. A threshold for the EIS device that resulted in a similar sensitivity and higher specificity than standard colposcopy was used. **METHODS:** Two models to assess the cost and health impacts were developed; a short term model representing the initial colposcopy treatment pathway and a longer term Markov model that included colposcopy follow-up. Sensitivity and specificity of colposcopy were derived from the EpiCIN trial of the EIS device. Two referral thresholds were defined in the analysis, the threshold for 'See and Treat' on colposcopic impression alone (CI) and a lower threshold for referral for biopsy to determine disease presence (DP) prior to treatment. Costs of colposcopy were estimated using data from Sheffield Teaching Hospitals. Different colposcopy clinic scenarios were modelled to represent the different ways colposcopy clinics manage patients. Health related quality of life (HRQoL) decrements were applied for colposcopy, biopsy and treatment. One-way sensitivity analyses were also conducted. **RESULTS:** The analysis suggests that the use of the EIS device can result in fewer biopsies being taken, a reduction in overtreatment with an associated small improvement in HRQoL, and a lower colposcopy cost per woman with CIN2+ treated for some colposcopy clinic scenarios. The results are sensitive to changes in colposcopy costs. **CONCLUSIONS:** The use of the EIS device with a higher specificity and similar sensitivity to standard colposcopy has the potential to lead to a reduction in the colposcopy cost per woman with CIN2+ treated for some clinic scenarios.

PCN90

ESTIMATION OF THE EPIDEMIOLOGICAL AND ECONOMIC IMPACT OF THE QUADRIVALENT HPV VACCINATION IN GIRLS AND BOYS IN SPAIN

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OBJECTIVES: To estimate the epidemiological and economic benefits of a quadrivalent HPV vaccination in girls and boys compared with vaccination only in girls in Spain. **METHODS:** A population-based compartmental dynamic transmission model of HPV developed in the US was partially adapted to the Spanish setting updating epidemiological data of HPV related diseases, the vaccination coverage and direct costs of the diseases. The analysis was performed from the National Health System (NHS) perspective. The strategy of cervix cancer screening (CCS) and vaccination of only girls from 11 to 26 years (S1) was compared to CCS and vaccination of girls and boys from 11 to 26 years (S2) with the quadrivalent vaccine. Assuming the duration of protection against vaccine HPV types is lifetime, the results over a 100-year time horizon, were estimated applying a discount of 3% on costs. In order

to assess the uncertainty on the parameters, univariate sensitivity analyses were performed. **RESULTS:** At 100 years, compared to only screening for cervix cancer, S2 scenario reduced 73% of the genital warts cases, 92% of the cancer cases in women and 87% of the cancer cases in men; while S1 strategy only reduced 56%, 87% and 63% the cases of the different diseases, respectively. S2 strategy was less costly compared with S1: during the first 10 years reduced more than €25 million for the NHS and more than €282 million over 100 years. The savings over 100 years varied between €141 million and €1,268 million when considering a 5% or 0% discount, respectively. **CONCLUSIONS:** Vaccinating boys and girls between 11 and 26 years would significantly reduce the epidemiological and economic burden of HPV related diseases in Spain.

PCN91

COMPARATIVE COST-CONSEQUENCE ANALYSIS OF THE BIVALENT AND QUADRIVALENT VACCINES AGAINST HPV IN SPAIN

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OBJECTIVES: To compare the impact of the quadrivalent (QV) (HPV 6/11/16/18) and bivalent (BV) (HPV 16/18) vaccines against HPV in Spain. **METHODS:** A population-based compartmental dynamic transmission model of HPV developed in the US was partially adapted to Spain updating epidemiological data of HPV related diseases, the vaccination coverage and direct costs of the diseases. The reduction of the number of cases related to HPV and savings associated with the following strategies were compared: A) cervix cancer screening (CCS) of women between 25-65 years, every 3-5 years and a vaccination program of girls between 11-26 years with the QV vaccine; B) CCS+BV vaccine. The analysis was performed from the National Health System (NHS) perspective, costs were discounted by 3% and the time horizon was 100 years. Univariate sensitivity analyses were performed to assess the uncertainty on the parameters. **RESULTS:** At 100 years, considering the current indications of the vaccines, lifetime protection against HPV vaccine types and 20 years of cross-protection, both strategies reduced 208 cases of vulvar and vaginal cancers and 22,796 cases of CIN2+. The strategy CCS+QV vaccine reduced 18,689 additional cases of genital warts due to the protection against 6/11 HPV types, but 4 less cases of cervix cancer and 359 less cases of CIN2+ due to better cross-protection of the BV vaccine. Nevertheless, savings accumulated during 100 years due to the reduction of genital warts cases (€215.7 million) compensated the cost associated to cervix cancers and CIN2+ that the BV vaccine additionally reduced (€3 and €27.1 million, respectively). Therefore, during 100 years the QV vaccine saves €185.4 million more than the BV vaccine. The sensitivity analyses confirmed the stability of the results. **CONCLUSIONS:** The QV vaccine provides higher cost savings to the NHS compared to the BV vaccine due to the additional efficacy against HPV 6/11 types.

PCN92

ONE LINE DOES NOT MAKE A PICTURE: REAL-WORLD COST-EFFECTIVENESS OF MULTIPLE MYELOMA TREATMENTS USING A FULL DISEASE MODEL

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OBJECTIVES: As with many types of cancer, treatment of multiple myeloma (MM) is characterised by sequential treatment lines consisting of innovative expensive drugs such as thalidomide, bortezomib and lenalidomide. While cost-effectiveness of single treatments has been studied, a full disease model evaluating treatments sequentially is currently lacking, consequently, high uncertainty exists on incremental cost-effectiveness ratios. Therefore, we aimed to take a look at the big picture and calculate real-world costs and effects for commonly used treatment pathways for MM. **METHODS:** We developed a patient-level simulation (PLS) for elderly (>65) MM patients diagnosed since 2004. Real-world data (N=621) including patient and disease characteristics, treatment information as well as resource use was collected from hospital registrations and medical files. Five treatment categories per line were observed resulting in 19 commonly used treatment pathways. Parametric survival models including patient characteristics such as age, performance status, comorbidities and laboratory values were used to predict time to an event, i.e. the start of a new treatment or death. Logistic regression determined which of the two competing events occurred. The sensitivity of parameters was explored through sensitivity analyses. **RESULTS:** In total, the costs and effects of 19 treatment pathways were calculated. Depending on the treatment sequencing, total costs ranged from €40,810 (Melphalan/Prednison-Thalidomide-Other) to €132,613 (Bortezomib-Lenalidomde-Other) while overall survival ranged from 28 to 50 months for Bortezomib-Lenalidomide-Thalidomide and Lenalidomide-Bortezomib-Other, respectively. Costs per quality-adjusted-life-year (QALY) were between €21,881 (Melphalan/Prednison-Thalidomide-Other) and €57,743 (Bortezomib-Lenalidomide-Other). Compared to real-world prescription, QALYs could be increased at a cost of €33,785 per QALY (Lenalidomide-Thalidomide-Other). **CONCLUSIONS:** The cost-effectiveness of 19 treatment pathways for MM patients was calculated and revealed that real-world treatment could be improved at a cost of €33,785 per QALY. Our PLS model proved to be a reliable and robust approach to study entire treatment pathways for MM.

PCN93

COMPARATIVE EFFECTIVENESS OF CONSERVATIVE THERAPY VERSUS CYSTECTOMY FOR NON-MUSCLE INVASIVE BLADDER CANCER PATIENTS

Dinh T

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OBJECTIVES: Non-muscle invasive bladder cancer (NMIBC) is a complex disease with wide variation in risks of recurrence and progression, treatment efficacy and complications, and patient co-morbidities. To assist in medical decision making from clinical and cost perspectives, we have developed a simulation model that synthesizes the evidence on NMIBC using the Archimedes Model platform. **METHODS:** The NMIBC model consists of a patient generation component in which virtual patients are constructed from SEER case listings; a natural history component that captures recurrence, progression, and bladder cancer mortality; a health care component that captures the effects of treatments, tests, and surveillance; and a cost component that tracks the costs relevant to bladder cancer care. Using this model, we performed a 5-year virtual clinical trial of 350 NMIBC patients with demonstrated Bacillus Calmette-Guerin failure, randomized to either immediate cystectomy or conservative treatment with Mitomycin C (MMC) intravesical therapy. The model is integrated within the Archimedes Model platform, which captures the effects of both NMIBC and patient co-morbidities. This model, validated against 5 published studies, gives recurrence and progression rates within ±20% of published results. **RESULTS:** The virtual clinical trial shows a 5-yr cystectomy rate of 51% in the MMC arm, with an average delay to cystectomy of 0.84 yr (median 0.44 yr). The immediate cystectomy arm saves 0.26 life years (LY) and $5598 in total bladder cancer cost per patient compared to the MMC arm. **CONCLUSIONS:** We have constructed a dynamic, quantitative model of NMIBC that can predict clinical and economic outcomes and help optimize treatment and surveillance guidelines. The virtual clinical trial quantifies LY and cost outcomes for immediate cystectomy versus conservative therapy, and provides a valuable tool for trial design and health economic analyses.

PCN94

THE COST-EFFECTIVENESS OF BENDAMUSTINE-RITUXIMAB VERSUS FLUDARABINE-RITUXIMAB FOR PATIENTS WITH INDOLENT NON-HODGKIN'S LYMPHOMA (INHL) WHO HAVE PROGRESSED FOLLOWING TREATMENT WITH RITUXIMAB OR A RITUXIMAB-CONTAINING REGIMEN IN COLOMBIA

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OBJECTIVES: To determine the cost-effectiveness of bendamustine-rituximab (Ben-R) versus fludarabine-rituximab (Fdb-R) in patients with iNHL who have progressed following treatment with rituximab or a rituximab-containing regimen in Colombia. **METHODS:** An economic model was constructed from the Colombian health system perspective, with a 35-year (lifetime) horizon and a discount rate of 3%. The model included three health states, progression-free (PF), progressive disease (PD), and death, which were associated with utility weights of 0.81, 0.62 and 0, respectively. Clinical inputs (response rates, Kaplan-Meier curves, hazard ratios (HRs) and adverse event rates) were from the Stil NHL 2-2003 study. Resource use data were from interviews with three Colombian hematologists treating iNHL patients. Unit costs were from ISS and SISPRO report and were expressed as 2013 Colombian Pesos. Univariate and probabilistic sensitivity analyses were conducted to determine the key drivers of cost-effectiveness, and uncertainty around the results, respectively. **RESULTS:** Total lifetime cost of Ben-R was $291,192,912 and total cost of Fdb-R was $260,463,392. Ben-R patients accrued more LYs (6.47 vs. 5.15), QALYs (4.66 vs. 3.56), and PFLYs (3.57 vs. 2.05) compared to Fdb-R patients. The ICERs were $23,286,360 (cost per LY), $27,956,124 (cost per QALY) and $20,259,063 (cost per PF LY). Univariate sensitivity analysis revealed that the ICER per LY was most sensitive to the PFS and OS HRs for Ben-R vs Fdb-R, the number of treatment cycles, and the cost of bendamustine. Probabilistic sensitivity analysis with 1,000 iterations estimated that Ben-R had a 52% chance of being cost-effective, compared to Fdb-R, at a willingness to pay (WTP) of $59M per LY, rising to a plateau of about 93% at a WTP of $175M and above. **CONCLUSIONS:** At a willingness-to-pay of $59M (three times the GDP per capita of Colombia) Ben-R is a cost-effective alternative to Fdb-R.

PCN95

COST-EFFECTIVENESS OF THE OPTICAL IMAGING AGENT HEXAMINOLEVULINATE FOR PATIENTS WITH NON-MUSCLE INVASIVE BLADDER CANCER

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OBJECTIVES: Hexaminolevulinate (HAL) is an optical imaging agent used as an adjunct to white light cystoscopy (WLC) in the diagnosis and management of non-muscle invasive bladder cancer (NMIBC). The objective of this study was to model the cost-effectiveness of HAL-assisted blue light cystoscopy (HAL-BLC) compared to WLC alone when used at initial transurethral resection of bladder tumours (TURB) from the perspective of the National Health Service (NHS) in England and Wales using available clinical data. **METHODS:** A two-part model was developed to estimate the incremental cost-effectiveness of HAL-BLC at initial TURB for patients positively diagnosed in the outpatient setting with NMIBC over a lifetime horizon. This consisted of a short-term decision tree, which estimated the outcome of the outpatient diagnostic procedure and inpatient TURB, and a Markov cohort model, used to extrapolate long term outcomes. Clinical effectiveness evidence on recurrence was taken from a recent meta-analysis of NMIBC with HAL-BLC, costs were derived from NHS reference costs, and utilities and disease evolution were from the literature. **RESULTS:** Despite additional treatment and equipment costs, base case results suggest that HAL-BLC is a dominant strategy as an adjunct to WLC compared to WLC only, when used at initial TURB for patients diagnosed with NMIBC. HAL-BLC is expected to be associated with 0.060 incremental QALYs and cost-savings of £391 per patient resulting from fewer recurrences and fewer associated surgical procedures (33 avoided TURBs/149 positively-diagnosed patients), in turn due to improved completeness of lesion resection and better tumour staging. Probabilistic sensitivity analyses indicated that HAL-BLC was dominant in 91.9% of iterations. **CONCLUSIONS:** HAL-BLC as an adjunct to WLC was shown to be a domi-

nant strategy over WLC alone when used at initial TURB for patients diagnosed with NMIBC in England and Wales, with improved patient outcomes and cost-savings expected to offset investment in HAL.

PCN96

UNCERTAINTY AND COST-EFFECTIVENESS ANALYSIS OF THE SEQUENTIAL APPLICATION OF TYROSINE KINASE INHIBITORS FOR THE TREATMENT OF CHRONIC MYELOID LEUKEMIA

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OBJECTIVES: Currently, there are several tyrosine kinase inhibitors (TKI) approved for the treatment of chronic myeloid leukemia (CML). The aim of our study was to evaluate the long-term cost-effectiveness of different therapy regimens for CML focusing on the evaluation of the uncertainty using probabilistic sensitivity analysis (PSA). **METHODS:** We performed a cost-effectiveness analysis using a state-transition Markov model. The model evaluates seven treatment strategies including different combinations of TKIs as well as chemotherapy or stem cell transplantation. For model parameters, we used published trial data, and Austrian clinical, epidemiological, and economic data from the Austrian CML registry, statistical and economic databases. We performed a cohort simulation over a lifelong time horizon, adopted a societal perspective with an annual 3% discount rate. We conducted extensive uncertainty analyses and contrasted different methodological approaches to define parameter uncertainty distributions from our source data. We compared the base-line derived from the mean parameter values with the mean outcomes of all PSA scenarios. **RESULTS:** In the base-case efficiency frontier, nilotinib without second-line TKI resulted in an ICUR (1) of 118,600 €/QALY compared to the baseline strategy imatinib without second-line TKI. Imatinib followed by nilotinib after failure yielded an ICUR (2) of 123,900 €/QALY compared to nilotinib without second-line TKI. Nilotinib followed by dasatinib after failure resulted in an ICUR (3) of 149,400 €/QALY compared to imatinib followed by nilotinib after failure. The remaining strategies were excluded due to absolute or extended dominance. The PSA resulted in ICURs of (1) 116,200 €/QALY (2) 130,300 €/QALY and (3) 130,300 €/QALY. **CONCLUSIONS:** Based on our analysis, we recommend imatinib followed by nilotinib as the most cost-effective treatment strategy including a second-line TKI. Mean results from PSA show only small deviation from the base-case analysis. When new path to cure data are available, results will need to be updated.

PCN97

A SYSTEMATIC REVIEW AND CRITICAL APPRAISAL OF ECONOMIC EVALUATIONS OF RADIOTHERAPY FOR CANCER

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OBJECTIVES: To review published cost-effectiveness studies which evaluate radiotherapy in individuals with breast, cervical, colorectal, head and neck, or prostate cancer. To compare the economic methods used with the guidelines used in the appraisal programme for the National Institute of Health and Care Excellence (NICE) in the UK. **METHODS:** Systematic searches of seven databases (Medline, EMBASE, CDSR, NHSEED, HTA, DARE and EconLit) were conducted in July 2012. In addition, research registers, the NICE website and conference proceedings were searched. Studies that reported results of economic evaluations of radiotherapy interventions in terms of incremental quality adjusted life-years or life-years for individuals diagnosed with cancers were included. The quality of these studies was assessed in terms of meeting, essential, preferred and UK NICE-specific requirements for economic evaluations. **RESULTS:** Twenty-nine studies satisfied the inclusion criteria (breast=14, colorectal=2, prostate=10, cervical=0, head and neck=3). The majority (13) of the studies were set in the US with just 2 conducted in the UK. Considering essential methodological criteria, only 3 (10%) studies used estimates for clinical effectiveness which were identified by systematic literature review. Just a quarter (8/29) used health related quality of life data from patients with the particular cancers. While the majority of studies used one-way sensitivity analyses, only a third (10/29) reported the results of a full probabilistic sensitivity analysis. Additional essential criteria such as the use of an appropriate horizon, a clear description of both the comparators and the patient group indication were generally satisfied. However, as only 2 of the studies were conducted in the UK, the majority of the UK NICE specific requirements were not met. **CONCLUSIONS:** This review indicates there is little robust evidence of the cost-effectiveness of radiotherapy interventions in these cancers and very little evidence which could be used to support decision making in the UK.

PCN98

SELECTIVE INTERNAL RADIOTHERAPY (SIRT) USING RESIN YTTRIUM-90 MICROSPHERES FOR CHEMOTHERAPY-REFRACTORY METASTATIC COLORECTAL CANCER: AN ITALIAN COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: SIRT using resin microspheres of yttrium-90 can be used to treat liver metastases resulting from colorectal cancer (CRC). A retrospective cohort study found a survival advantage from SIRT compared to standard care in chemotherapy-refractory patients. This study was used in combination with other sources to model the cost-effectiveness of SIRT vs best supportive care (BSC) in this indication. **METHODS:** A state-transition model was developed, with three health states, based on survival outcomes from a retrospective cohort study in chemotherapy-refractory mCRC comparing yttrium-90 resin microspheres (SIR-Spheres; Sirtex, Sydney, Australia) *vs.* BSC. The model was developed from the perspective of the National Health Service in Italy. The model included costs for treatment acquisition, pre-treatment work-up and delivery of microspheres, and chemotherapy received in addition to, instead of, or after, SIRT. In addition costs of managing AEs and a cost of death were included. Costs were obtained from the University Hospital in Bologna, Agenzia Italiana del Farmaco, and the literature. Utility data was not available from the study, so was taken from a recent NICE economic evaluation in the same indication. **RESULTS:** SIRT increased survival resulting in a life-year gain of 1.35 (2.12 vs 0.98) life years and a quality-adjusted life year (QALY) gain of 0.83 (1.52 vs 0.70). The costs of SIRT, monitoring and further treatment were greater in the SIRT arm with partial cost-offset through a reduction in adverse events. Overall, SIRT lead to an increase in costs of €24,626 (€39,973 vs €15,347), resulting in a cost/QALY of €29,850. Probabilistic sensitivity analysis showed a 97% chance of SIRT being cost-effective at a threshold of €50,000/QALY. **CONCLUSIONS:** The analysis demonstrates that SIRT using resin yttrium-90 microspheres has the potential of being a cost-effective option in the treatment of patients with chemotherapy-refractory liver metastases resulting from colorectal cancer.

PCN99

THE COST-EFFECTIVENESS OF BENDAMUSTINE VERSUS FLUDARABINE FOR THE FIRST-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) IN MEXICO

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OBJECTIVES: To determine the cost-effectiveness of bendamustine versus fludarabine for the first line treatment of CLL in Mexico. **METHODS:** An economic model was constructed from the Mexican public payer perspective, with a 25-year (lifetime) horizon and a discount rate of 5%. The model included three health states, progression-free (PF), progressive disease (PD), and death. Clinical inputs (Kaplan-Meier curves, response rates, hazard ratios (HRs) and adverse event (AE) rates were from a phase 3 trial comparing bendamustine and chlorambucil, and from a network meta-analysis. Resource use data were from interviews with Mexican hematologists treating CLL. Resource use for PF patients was weighted based on treatment response. Unit costs were obtained from Mexican Social Security Institute (IMSS) and were expressed in 2013 Mexican Pesos. Univariate and probabilistic sensitivity analyses were conducted to determine the key drivers of cost-effectiveness, and the uncertainty around the results, respectively. **RESULTS:** Total lifetime costs for bendamustine and fludarabine were $660,796 and $536,068, respectively. Bendamustine patients accrued more LYs (6.83 vs. 5.98), QALYs (5.13 vs. 4.25), and PF LYs (2.97 vs. 1.13) compared to fludarabine patients. The ICERs were $146,848 (cost per LY), $142,853 (cost per QALY) and $67,647 (cost per PF LY). Univariate sensitivity analysis revealed the cost per LY ICER was most sensitive to number of bendamustine cycles, the PFS for bendamustine vs. chlorambucil and the cost of bendamustine. Probabilistic sensitivity analysis with 1,000 iterations predicted bendamustine had a 48% chance of being cost-effective, compared to fludarabine, at a willingness to pay (WTP) of $125,000. **CONCLUSIONS:** At a WTP of $125,000 (GDP per capita of Mexico) bendamustine is cost effective versus fludarabine.

PCN100

COST-EFFECTIVENESS OF INDUCTION TREATMENT WITH BORTEZOMIB ADDED TO THALIDOMIDE AND DEXAMETHASONE IN NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS ELIGIBLE FOR AUTOLOGOUS STEM CELL TRANSPLANTATION IN GERMANY

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OBJECTIVES: To estimate the cost-effectiveness of bortezomib, thalidomide, and dexamethasone (VTD) induction therapy, versus TD alone in newly diagnosed multiple myeloma (ndMM) patients eligible for autologous stem cell transplantation (ASCT) in Germany. **METHODS:** A life-time Markov model with monthly cycles is used to model disease progression and generate cost per quality-adjusted life years (QALY). It includes five health states; four of which are related to the lines of treatment, and death. Patients enter the first line state at randomisation and receive induction usually followed by ASCT. Patients can move to the next line upon progression or die within a line, until they enter the final (4+) line where they remain until death. Transition probabilities are derived from multi-state survival analysis of patient level data from the PETHEMA-trial for first line, the APEX-trial for second and third line, and an observational data set (eVOBS) for further lines. The model uses ASCT and time dependent utilities from the literature and trial estimated grade ≥3 adverse events (AEs) associated disutilities to calculate the QALYs. Cost estimates related to treatments, transplant and AEs are based on German specific sources. A payer's perspective is chosen. Discount rates of 3% for both cost and utilities are applied. **RESULTS:** Total life years of 6.38 VTD and 5.06 for TD with first line duration of 50.47 versus 32.85 months respectively. Incremental costs of VTD versus TD are 22,179€ [95%CI:6,950€;33,528€] and incremental QALYs are 0.72 [95%CI:0.33;1.20], resulting in an ICER of €30,655 per QALY gained. The univariate analyses show that the model is most sensitive

to induction cost and percentage transplants. At a willingness-to-pay threshold of 35,000€ per QALY gained, VTD has a 57.1% probability to be cost-effective in this setting. **CONCLUSIONS:** VTD induction is a cost-effective strategy for ndMM patients eligible for ASCT in Germany compared to TD.

PCN101

A COST-EFFECTIVENESS ANALYSIS OF CISPLATIN PLUS PEMETREXED DOUBLET INDUCTION TREATMENT FOLLOWED BY PEMETREXED MAINTENANCE COMPARED WITH BEVACIZUMAB PLUS CISPLATIN PLUS GEMCITABINE TRIPLET INDUCTION TREATMENT FOLLOWED BY BEVACIZUMAB MAINTENANCE FOR NON-SQUAMOUS NSCLC IN SWEDEN

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OBJECTIVES: This analysis compares the cost effectiveness (CE) of an induction and maintenance sequence of a cisplatin plus pemetrexed (cis+pem) doublet followed by pemetrexed, with that of a bevacizumab (7.5mg or 15mg) plus cisplatin plus gemcitabine (bev+cis+gem) triplet followed by bevacizumab (7.5mg or 15mg) for the treatment of non-squamous non-small cell lung cancer (NSCLC) in Sweden. **METHODS:** As no head-to-head trial data are available comparing these relevant regimens in the first-line induction and maintenance treatment settings, decision modelling and evidence synthesis were used to estimate CE. A series of network meta-analyses were performed to obtain hazard ratios for overall survival (OS) and progression-free survival (PFS) for each induction and maintenance comparator, and odds ratios for response for induction comparators. Bevacizumab doses were pooled in the meta-analyses. The CE model was structured using an area-under-the-curve approach. Costs and benefits were discounted at 3% per annum, consistent with Swedish practice. **RESULTS:** Cis+pem induction followed by pemetrexed maintenance was associated with a higher median PFS, OS, total life-years gained and quality-adjusted life-years (QALYs) than the bevacizumab triplets. Total costs were 416,478Kr for the bev(7.5mg)+cis+gem induction triplet plus bevacizumab 7.5mg maintenance sequence, 478,862Kr for the cis+pem doublet followed by pemetrexed maintenance sequence, and 541,677Kr for the bev(15mg)+cis+gem induction triplet followed by bevacizumab 15mg maintenance sequence. Total QALYs were 0.73 and 0.97 for the bevacizumab triplets and pemetrexed induction and maintenance sequence. The incremental cost-effectiveness ratio (ICER) of cis+pem followed by pemetrexed compared with bev(7.5mg)+cis+gem followed by bevacizumab 7.5mg was 260,831Kr (30,477Euro). The higher bevacizumab dose of 15mg was dominated by the cis+pem followed by pemetrexed sequence. The results of the probabilistic analysis support these results. **CONCLUSIONS:** The results of the CE analysis suggest that cis+pem doublet induction followed by pemetrexed maintenance is a cost-effective treatment sequence compared with the bevacizumab options for NSCLC in Sweden.

PCN102

A COST-EFFECTIVENESS ANALYSIS OF AXITINIB AND SORAFENIB FOR 2ND LINE TREATMENT OF ADVANCED RENAL CELL CARCINOMA AFTER FAILURE OF CYTOKINES IN THE UNITED STATES

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OBJECTIVES: To assess the cost-effectiveness of axitinib compared to sorafenib from the perspective of a US third-party payer for second-line treatment of patients with advanced RCC who failed cytokines. **METHODS:** Phase III AXIS trial reported that axitinib increased median progression free survival (PFS) compared to sorafenib (12.0 vs. 6.6 months, p<0.0001), while overall survival (OS) showed no difference (29.4 vs. 27.8 months, p=0.144) in patients failing treatment with cytokines. A cohort partition model was constructed to estimate direct medical costs and health outcomes, discounted at 3.0% per annum. Patients were apportioned into 3 health states (progression-free, progressed and dead) based on OS and PFS Kaplan-Meier curves from the AXIS trial. Active treatment was applied until progression, followed by best supportive care (BSC) thereafter. The wholesale acquisition costs and adverse event (AE) costs were obtained from published sources. AE rates and utility values were informed by the AXIS trial. US administrative claims data (MarketScan®) was analyzed to estimate routine care costs. Probabilistic sensitivity analysis (PSA) was conducted. **RESULTS:** The total per-patient lifetime costs were estimated to be $242,750 for axitinib and $168,880 for sorafenib and 84% of the cost difference was due to the higher total medication cost of axitinib. The quality-adjusted life-years (QALY) gained on axitinib vs. sorafenib was 1.3 vs. 1.2 and the incremental cost-effectiveness ratio (ICER) was $683,209/QALY. 100% of the PSA iterations showed that axitinib was more expensive than sorafenib and the QALY difference between axitinib and sorafenib was no greater than 0.7. **CONCLUSIONS:** For post-cytokine subgroup, axitinib resulted in an ICER > $650,000/QALY versus sorafenib due to high drug costs and lack of OS benefit, indicating that axitinib may not present good value for money as 2nd line treatment of advanced RCC when compared to sorafenib in the US.

PCN103

COST-EFFECTIVENESS OF COBAS® EGFR MUTATION TEST VERSUS SANGER SEQUENCING IN THE TREATMENT OF LOCALLY ADVANCED OR METASTATIC NSCLC: A PAYER PERSPECTIVE IN THE UNITED KINGDOM

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OBJECTIVES: We explored the cost-effectiveness of using the CE-IVD marked cobas® EGFR Mutation Test versus Sanger sequencing for identifying EGFR mutations in locally advanced or metastatic NSCLC patients from a UK payer perspective. **METHODS:** A decision-tree model was developed to compare testing methodologies and resulting treatment pathways in a hypothetical NSCLC population in the UK with a baseline EGFR mutation prevalence of 16.6%. Model inputs included parameters describing mutation testing accuracy, treatment response (EGFR inhibitor, standard chemo therapy or best supportive care) and adverse events arising from treatment. Inputs were based on published literature and costs in the NHS in England and Wales. The model examined cost-effectiveness over the patients' lifetime. A one-way sensitivity analysis was conducted. **RESULTS:** Using £32,500/QALY as a threshold, the cobas EGFR Mutation Test was cost-effective at an incremental cost per QALY gained of £18,394 for the target population as a result of better test accuracy and lower detection limit relative to Sanger sequencing. The cobas EGFR Mutation test was able to correctly identify more patients with EGFR mutations (lower rate of false negatives) and more appropriately direct patient treatment than Sanger sequencing. **CONCLUSIONS:** The cobas EGFR Mutation Test, by correctly identifying more patients for proper treatment, can be considered a cost-effective strategy for identification of EGFR mutations in locally advanced or metastatic NSCLC patients from a UK payer perspective.

PCN104

A CRITICAL APPRAISAL OF COST-EFFECTIVENESS ANALYSES OF HUMAN PAPILLOMAVIRUS TESTING IN CERVICAL SCREENING: MAKING APPROPRIATE COMPARISONS AND USEFULLY INTERPRETING RESULTS

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OBJECTIVES: To critically appraise published cost-effectiveness analyses (CEAs) of human papillomavirus (HPV) testing in cervical screening regarding the appropriateness of comparisons between strategies and the usefulness of the interpretation of cost-effectiveness estimates. **METHODS:** The PubMed database was searched for relevant CEAs of cervical screening using HPV testing. The identified CEAs were carefully appraised for their quality of analyses, reporting and interpretation of results. Specific examples of modelling shortcomings were selected as illustrations of what to avoid when estimating the cost-effectiveness of HPV-based screening. **RESULTS:** The review identified 29 relevant CEAs. Regarding basic errors, 11 of the 29 calculated the incremental cost-effectiveness ratios (ICERs) either partly or completely incorrectly. Ten studies failed to fully report costs and effects; either simply reporting ICERs or depicting a cost-effectiveness plane. Regarding more fundamental errors, 23 failed to include sufficient screening interval comparators against which to meaningfully estimate ICERs; effectively leading to average cost-effectiveness ratios being mistakenly identified as ICERs, which biases cost-effectiveness ratio estimates downwards. Finally, none of the studies gave specific consideration to the magnitude of the change in costs and effects of adding HPV testing to a given strategy, either with a simple graphical interpretation or with a formal interpretation using the net benefit framework. **CONCLUSIONS:** Model specification is typically the most difficult part of a model-based CEA, whereas simulating relevant strategies is relatively straightforward once the model is built. Similarly, once results have been generated, their correct presentation and interpretation is relatively straightforward. However, this analysis shows that these relatively easy aspects of CEA are being performed poorly in the HPV screening literature. Consequently, a few simple improvements to basic aspects of CEAs of HPV-based screening could greatly enhance the usefulness of such analyses to decision makers.

PCN105

COST-EFFECTIVENESS OF EML4-ALK FUSION TESTING AND FIRST-LINE CRIZOTINIB TREATMENT FOR PATIENTS WITH ADVANCED ALK POSITIVE NON-SMALL CELL LUNG CANCER IN A PUBLICLY FUNDED SYSTEM (ONTARIO, CANADA)

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OBJECTIVES: ALK-targeted therapy with crizotinib offers significant improvement in clinical outcomes for the treatment of EML4–ALK fusion positive NSCLC. We estimated the cost-effectiveness of EML4-ALK testing in combination with first-line crizotinib for ALK positive NSCLC in Ontario. **METHODS:** A cost-effectiveness analysis was conducted, using a Markov model from the Canadian public health (Ontario) perspective and a lifetime horizon in Stage IV NSCLC patients with non-squamous histology. Transition probabilities and mortality rates were calculated from the Ontario Cancer Registry and Cancer Care Ontario New Drug Funding Program (CCO NDFP). Costs were obtained from the Ontario Case Costing Initiative, CCO NDFP, University Health Network and the literature. Population-based ALK testing included initial IHC testing followed by FISH confirmation for positive cases. **RESULTS:** The strategy of genomic testing linked to targeted crizotinib treatment gained 0.11 QALYs compared to no testing or crizotinib treatment in the advanced non-squamous NSCLC population. The incremental cost was CAD $4,179 per patient compared to the previous standard of care without ALK testing; the incremental cost-effectiveness ratio for the base case was $392,538 per QALY. The incremental cost and ICER for crizotinib therapy in known ALK positive advanced NSCLC patients was $96,554 and $254,617/QALY. The cost of testing was less relevant to the ICER at a biomarker frequency of 7% and higher. The major drivers of cost-effectiveness are drug cost and low biomarker frequency in the population. **CONCLUSIONS:** EML4–ALK genomic testing in combination with crizotinib treatment for all Stage IV non-squamous NSCLC patients is not cost-effective in the setting of high drug costs and a low biomarker frequency in the general population. Modifying these key drivers will be important in improving the cost-effectiveness and accessibility to novel therapies with major clinical benefit in advanced NSCLC.

PCN106

OVERVIEW ON COST-EFFECTIVENESS RESULTS OF DECISION-ANALYTIC STUDIES FOR THE TREATMENT OF MULTIPLE MYELOMA

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OBJECTIVES: To provide an overview on published decision-analytic models evaluating treatment strategies for multiple myeloma (MM) focusing on the cost-effectiveness results. **METHODS:** A systematic literature search was performed in the electronic databases Pubmed, NHS EED and the Tufts CEA Registry to identify studies evaluating MM treatment strategies using mathematical decision-analytic models. To meet the inclusion criteria, models were required to compare different treatment strategies, to be published as full text articles in English, and comprise relevant clinical health outcomes over a defined time horizon and population. We used evidence tables to summarize methodological characteristics and economic results. For comparability, all economic results were transferred into 2012 US Dollar. We used Purchasing Power Parity to convert the currency into US Dollar of the same year. For converting US Dollar from step one into US Dollars 2012, we used Consumer Price Index rates for the relevant year. **RESULTS:** We found eleven decision-analytic modeling studies. Economic evaluations were included in all studies. Eight studies reported cost-utility results. The modeling approaches applied included a decision tree model, Markov cohort model, discrete event simulations, partitioned survival analyses and area under the curve models. Time horizons ranged from seven years to lifetime. Half of the models chose the perspective of the health care system, while other perspectives were societal, third party payer and government payer. Among others, two studies reported cost-effectiveness of autologous transplantation vs. standard-dose melphalan with an ICER of $31,263 /life-year gained (LYG) and $36,778/LYG. One study reported that bortezomib vs. lenalidomide plus dexamethasone is cost saving, while another comparable study reported an ICUR for lenalidomide plus dexamethasone vs. bortezomib of $22,301/QALY. **CONCLUSIONS:** We identified several well-designed cost-effectiveness/cost-utility models using a broad variety of different modeling approaches. Results of most of the studies were not comparable due to different treatment strategies, target population and settings.

PCN107

ECONOMIC EVIDENCE OF SURGICAL PROCEDURES IN CANCER: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: To examine the empirical and methodological cost-effectiveness evidence of surgical interventions for breast, colorectal, and prostate cancer. **METHODS:** Systematic searches of seven databases including MEDLINE, EMBASE, CDSR,HTA, DARE, EconLit and NHSEED, research registers, the National Institute of Health and Care Excellence (NICE) website and conference proceedings was conducted in April 2012. Studies were included if they evaluated the cost-effectiveness of a surgical procedure in either breast, colorectal or prostate cancer and reported cost per quality adjusted life-year or cost per life-year results. The quality of the studies included was assessed in terms of meeting essential, preferred, and UK specific requirements for economic evaluations. **RESULTS:** The 17 (breast=3,colorectal=7,prostate=7) studies which satisfied the inclusion criteria covered a broad range of settings with 9 set in European and 8 in non-European locations. Just a third (11/17) was published within the last 10 years. In terms of the essential quality criteria; the populations, interventions and comparators were generally well defined. However, very few studies were informed by the results of literature reviews or synthesised clinical evidence. Although the interventions had potential differential effects on recurrence and mortality rates, some studies used relatively short time horizons. Although univariate sensitivity analyses were reported in all studies, less than a third characterised all uncertainty with a probabilistic sensitivity analysis. While a third of studies incorporated patients' health-related quality of life data, only 4 of the 17 studies used social tariff values. **CONCLUSIONS:** There is very little recent robust evidence describing the cost-effectiveness of surgical interventions in these indications. Many of the more recent publications did not satisfy the essential methods requirements, such as using synthesising clinical evidence informed by a systematic literature review. Given the ratio of potential benefit and harm associated with surgery in cancer, there is an urgent need to conduct additional robust economic evaluations in this area.

PCN108

ABIRATERONE ACETATE VERSUS ENZALUTAMIDE FOR METASTATIC CASTRATION-RESISTANT PROSTATE CANCER POST CHEMOTHERAPY: COST EFFECTIVENESS ANALYSIS

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OBJECTIVES: With approvals of abiraterone acetate (AA) and enzalutamide (ENZA) in the past 2 years, the treatment landscape has shifted dramatically for metastatic castration-resistant prostate cancer (mCRPC) patients who failed docetaxel-based chemotherapy. There is increasing interest in the relative cost-effectiveness of these therapies. The objective of this study was to assess the cost-effectiveness of AA versus ENZA among individuals with mCRPC post chemotherapy from a payer perspective. **METHODS:** A survival-based Markov cohort model consisting of 3 health states, progression-free, progressed, and dead, was developed to project over 10 year period. Progression between states was determined by overall survival (OS) and radiographic progression free survival (rPFS). An indirect treatment comparison was conducted to determine the relative efficacy of AA and ENZA (data reported separately). Utilities were mapped from FACT-P to EQ-5D based on a review of the literature. Drug acquisition costs in the US were used since ENZA was approved only in the US at the time of analysis. Costs of scheduled and unscheduled follow-up visits were obtained from the Centers for Medicare Services Drug Payment Table and Physician Fee Schedule and represented in 2013 US dollars. Average wholesale prices for a 30-day supply of AA and ENZA were $7,674 and $8,940, respectively. One-way sensitivity analyses were performed against all probability, utility, and cost values incorporated into this cost-effectiveness model. **RESULTS:** In this analysis, AA provides substantial saving with $13,322 per patient versus ENZA. The main drivers of the model are drug costs, health utility values, and efficacy (OS and rPFS). The robustness of the results was supported by sensitivity analyses. **CONCLUSIONS:** Given similar OS benefits, AA is cost saving compared with ENZA for the treatment of patients with mCPRC post-docetaxel based on US data.

PCN109

COMPARATIVE STUDY OF THE COST-EFFECTIVENESS OF TRASTUZUMAB IN THE TREATMENT OF BREAST CANCER IN DIFFERENT COUNTRIES

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OBJECTIVES: Pharmacoeconomic evaluations are more critical in developing countries in which economic effects of new and expensive therapies have significant impact on patients, insurance companies and the health systems. Since cost-effectiveness studies are too costly and time consuming, in these countries new medications are often being used in daily practice before being well documented as cost-effective interventions. This would force health organizations to perform comparative studies as alternatives to cost-effectiveness analysis. Trastuzumab, an anti-cancer monoclonal antibody which was approved by FDA in 1998, is an expensive medicine introduced to the Iranian pharmaceutical market since 2003, with an annual usage cost of 308,352,730,640 Rials ($ US 25,000,000) in 2010. **METHODS:** A systematic review on electronic medical databases including the Cochrane, CRD, EMBASE, HEED, MEDLINE, and PubMed, covering the years 2000 to 2009, was performed using relevant key words to extract publications investigating cost-effectiveness and efficacy of trastuzumab in breast cancer treatment. The Incremental Cost-Effectiveness Ratios (ICERs) were compared with a criterion introduced by WHO. **RESULTS:** The reported ICERs were between $90,118/QALY to $217,264/QALY and $13,361/QALY to $65,250/QALY in metastatic and adjuvant breast cancer therapy, respectively. The metastatic ICERs were 8 to 20 folds of the GDP per Capita in Iran whereas the adjuvant phase ICERs were 1.2 to 6 folds of it. Sensitivity analysis showed the results are more sensitive to discount rate, drug regimen cost, duration of survival benefits, as well as the risk of relapse and metastasis. **CONCLUSIONS:** Trastuzumab therapy in metastatic breast cancer cannot be cost effective in Iran, however as adjuvant therapy it is still a challenging issue. Unlimited access to this medicine would not be rational and recommendations with an approach to optimize its usage, e.g. administration in younger patients with poor prognosis and higher risk of relapse or using clean rooms to reduce drug wasting, are strongly advised.

PCN110

THE COST-EFFECTIVENESS OF BENDAMUSTINE-RITUXIMAB VERSUS FLUDARABINE-RITUXIMAB FOR PATIENTS WITH INDOLENT NON-HODGKIN'S LYMPHOMA (INHL) WHO HAVE PROGRESSED FOLLOWING TREATMENT WITH RITUXIMAB OR A RITUXIMAB-CONTAINING REGIMEN IN MEXICO

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OBJECTIVES: To determine the cost-effectiveness of bendamustine-rituximab (Ben-R) versus fludarabine-rituximab (Fdb-R) in patients with iNHL who have progressed following treatment with rituximab or a rituximab-containing regimen in Mexico. **METHODS:** An economic model was constructed from the Mexican public payer perspective, with a 35-year (lifetime) horizon and a discount rate of 5%. The model included three health states, progression-free (PF), progressive disease (PD), and death, which were associated with utility weights of 0.81, 0.62 and 0, respectively. Clinical inputs (response rates, Kaplan-Meier curves, hazard ratios (HRs) and adverse event rates) were from the Stil NHL 2-2003 study. Resource use data were from interviews with Mexican hematologists treating iNHL patients. Unit costs were obtained from Mexican Social Security Institute (IMSS) and were expressed as 2013 Mexican Pesos. Univariate and probabilistic sensitivity analyses were conducted to determine the key drivers of cost-effectiveness, and uncertainty around the results, respectively. **RESULTS:** Total cost of Ben-R was $1,726,828 and total cost of Fdb-R was $1,640,024. Ben-R patients accrued more LYs (5.82 vs. 4.73), QALYs (4.22 vs. 3.29), and PF LYs (3.37 vs. 1.96) compared to Fdb-R patients. The ICERs were $79,890 (cost per LY), $92,788 (cost per QALY) and $61,486 (cost per PF LY). Univariate sensitivity analysis revealed that the ICER per LY was most sensitive to the PF survival (PFS) and overall survival (OS) HRs for Ben-R vs Fdb-R and the use of bone marrow transplants in the PD state. Probabilistic sensitivity analysis with 1,000 iterations estimated that Ben-R will be cost effective over 90% of the time at a willingness-to-pay threshold of $125,085. **CONCLUSIONS:** At a willingness-to-pay of $125,085 (GDP per capita of Mexico) Ben-R is cost effective versus Fdb-R.

PCN111

A COST-EFFECTIVENESS ANALYSES OF USING SUNITINIB (SU) IN FIRST LINE OF METASTATIC RENAL CANCER IN ROMANIAN JURISDICTION

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OBJECTIVES: In Romania the estimated incidence of metastatic renal cancer (mRCC) is about 1500 cases; less than 400 patients receive full reimbursement for

their therapy. Our objective was to assess the cost-effectiveness of Sunitinib (SU) in the first-line treatment of mRCC patients in comparison with Bevacizumab (BEV) + IFN- and Sorafenib (SO) -at the level of 2011 year- based on the latest clinical evidence. **METHODS:** A Markov model (comprised of four states: 1st line treatment, 2nd line, Best Supportive Care and Death) was validated in several countries and was adapted for the Romanian jurisdiction. The model was set to 6 weekly cycles for a period of 10 years, which corresponds with a lifetime length scenario. Costs for medication and application were derived from hospital databases, expert panels and structured interviews. Experts that managed more than 60% of all local mRCC were consulted. These experts identified several scenarios related to outpatient and inpatient treatment decisions predominantly based on social reasons; all these scenarios have been tested. A WHO methodology was used to set a threshold of price per QALY (3 x local GDP) **RESULTS:** Cost per cycle in 1st line was lower than both 2nd line and BSC – consistent with other international findings. Neutropenia, proteinuria and heart failure have been identified as the most costly adverse events. The QALYs for SU was 1.86 compared to BEV 1.7 and SO 1.69. Incremental cost per QALY SU versus SO was 14.000 EURO and, respectively, -141.000 EURO versus BEV. **CONCLUSIONS:** Sutent is cost effective versus SO and dominant to BEV in the treatment of mRCC in the study settings. The model was very sensible to price of medication and cost of BSC.

PCN112

THE POTENTIAL COST-EFFECTIVENESS OF OBINUTUZUMAB (GA101) IN COMBINATION WITH CHLORAMBUCIL IN CHRONIC LYMPHOCYTIC LEUKEMIA

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OBJECTIVES: Obinutuzumab is the first, glycoengineered type II antibody demonstrating increased Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) and direct cell death compared with rituximab, and is pending regulatory approval (in combination with chlorambucil (Clb)) for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL). Obinutuzumab+Clb has shown a > 85% reduction in the risk of progression, relapse or death in comparison to treatment with Clb alone (HR 0.14, 95% CI 0.09-0.21, p <.0001), a broadly accepted treatment option for many patients with co-existing medical conditions. The cost-effectiveness of this innovative therapy will need to be assessed in countries using incremental cost-effectiveness thresholds to make reimbursement decisions. **METHODS:** A four-state Markov lifetime model from the UK NHS perspective was developed for patients with existing medical conditions utilizing the patient-level information from the underlying clinical trial comparing obinutuzumab+Clb versus rituximab+Clb and versus Clb alone (CLL11 trial). Transition probabilities from PFS to progression were derived from this study's data. Post-progression survival was estimated using published data and was part of the sensitivity analyses. Cost data (e.g. administration and adverse events), utilities and the prices for rituximab and Clb were retrieved for the UK. As obinutuzumab is not yet approved a range of price assumptions of similar innovative oncology therapies has been applied. **RESULTS:** Based on this early evaluation, obinutuzumab+Clb showed a cost per QALY in the base case analysis of £18,000 to £19,000 when compared to Clb and £29,000 to £32,000 when compared to rituximab+Clb. Probabilistic and deterministic sensitivity analyses confirmed these findings. **CONCLUSIONS:** Obinutuzumab+Clb showed significant patient-relevant clinical benefits and might be a potential cost-effective therapy in comparison to the current standard of care and could hence support access for a maximum number of patients with previously untreated CLL.

PCN113

COST-EFFECTIVENESS OF BREAST CANCER SURVEILLANCE BY LIFETIME RISK IN WOMEN AGED LESS THAN 50 YEARS

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OBJECTIVES: National programmes of breast cancer screening are common for women over the age of 50 at average risk. For women aged less than 50, surveillance may be offered to those at elevated risk either due to family history or because of identified genetic risk factors, such as a BRCA1 mutation. The lifetime risk for these women is not known with certainty. The purpose of this study was to examine the cost-effectiveness of different screening strategies as a function of lifetime risk. **METHODS:** A Markov model was developed to evaluate the cost-effectiveness of different MRI- and digital mammography-based surveillance strategies between the ages of 30 and 49. Costs and benefits were calculated to life expectancy. The perspective was that of the publicly funded health care system in Ireland. Lifetime risk of developing breast cancer was varied between 4% and 94%. A cost-effectiveness threshold of €45,000/QALY was applied. **RESULTS:** The probability of cost-effectiveness increased with increasing lifetime risk. For women at moderate risk (i.e. lifetime risk of between 17% and 30%), cost-effectiveness was only achieved with annual surveillance from the age of 40 to 49 when lifetime risk reached 28% to 30%. For women with high familial risk, cost-effectiveness was achieved for surveillance from the age of 40 to 49. For women with a BRCA1 mutation, surveillance from the age of 40 to 49 was cost-effective for all levels of lifetime risk, while MRI from age 30 was only cost-effective for a lifetime risk of over 65%. **CONCLUSIONS:** Risk levels for breast cancer encompass wide ranges of lifetime risk. The cost-effectiveness of different surveillance strategies is sensitive to lifetime risk and suggests the need for individualised surveillance programmes.

PCN114

COLLABORATIVE CARE FOR DEPRESSION MANAGEMENT IN CANCER: A COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: Collaborative care interventions for comorbid depression have demonstrated their beneficial impact on health outcomes. Depression in cancer patients is associated with decreased quality of life, and poorer health outcomes. Therefore, there may be considerable gains in the adequate treatment of depression in oncology patients. We explored the cost-effectiveness of a collaborative care intervention specifically developed for the treatment of depression in cancer patients compared to usual practice. **METHODS:** A cost-effectiveness analysis comparing a collaborative care intervention for depression management, Depression Care for People with Cancer (DCPC), in addition to usual care with usual care alone, based on data from the second Symptom Management Research Trials in Oncology (SMaRT-2). SMaRT-2 was a large (n=500), multicentre study, in depressed patients with a relatively good cancer prognosis, in a secondary care setting. Outcomes included costs expressed as UK sterling in 2010-11 prices and health outcomes in quality-adjusted life-years (QALYs), estimated from a National Health Service and Personal Social Services perspective. Scenario analyses were performed to determine the impact on cost-effectiveness of alternative costing assumptions, and uncertainty was characterised through cost-effectiveness acceptability curves and probabilities of cost-effectiveness at key cost-effectiveness thresholds. **RESULTS:** DCPC in addition to usual care was associated with greater costs, but also improved health outcomes. DCPC was found to be cost-effective at accepted cost-effectiveness thresholds. Results were robust across alternative scenarios, with probabilities of cost-effectiveness higher than 90% for cost-effectiveness thresholds ranging between £20,000-30,000 per QALY. **CONCLUSIONS:** Compared to usual care, DCPC in addition to usual care is likely to be cost-effective at current UK cost-effectiveness thresholds. This contributes to the growing evidence on the cost-effectiveness of collaborative care interventions for the treatment of comorbid depression. Future research will use a decision modelling approach to extrapolate trial-based results across a longer time horizon, and incorporate other relevant sources of evidence.

PCN115

PHARMACOECONOMIC EVALUATION OF ABIRATERONE ACETATE VERSUS CABAZITAXEL IN THE TREATMENT OF METASTATIC CASTRATION-RESISTANT PROSTATE CANCER IN KAZAKHSTAN

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OBJECTIVES: The purpose of this study was to explore the cost-effectiveness of abiraterone acetate (abiraterone) vs. cabazitaxel in metastatic castration-resistant prostate cancer (mCRPC) patients who progressed after docetaxel in Kazakhstan. **METHODS:** Since no head-to-head trial data were not available for Abiraterone against cabazitaxel, indirect profitability model was developed using clinical data (progression-free survival (PFS), overall survival (OS), adverse events (AEs)) from the pivotal Phase 3 clinical trials COU-AA-301 (Abiraterone) and TROPIC (cabazitaxel). The basic assumption in the model was that the two comparator arms in the trials were "palliative" and are therefore equivalent. Using the resources, in particular for controlling the adverse events was calculated based on data Kazakhstan. For validation purposes, a secondary analysis was conducted using international resources use data. The analysis used a local expenditures 2011-2012, undiscounted. Hospitalization, day hospital visits, medications, and laboratory tWe developed a Markov microsimulation model with a lifetime horizon and a direct health-care cost perspective. The patient history was recorded and was used in calculations of transition probabilities, utilities, and costs. ests were taken from the public officially published rates. The cost of purchasing drugs came from recent price lists . Calculations were based on the average duration of treatment for each agent. **RESULTS:** The total cost of treatment was lower for Abiraterone compared with cabazitaxel. Higher costs for the purchase of medicines for Abiraterone were offset by lower administrative expenses and lower AE management costs. Results were confirmed by secondary analysis. All sensitivity analyzes from the point of view of the model parameters and modeling assumptions are consistent with the expected findings, which confirmed both internal and external consistency of the model. **CONCLUSIONS:** Abiraterone is a potentially cost-effective option compared with cabazitaxel in the health care system in Kazakhstan.

PCN116

REDUCING THE LENGTH OF ANTIBIOTIC PROPHYLAXIS IN CLINICAL CONDITIONS

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OBJECTIVES: The aim of this study was to evaluate duration and cost of prophylactic use of antibiotics, as well as occurrence of postoperative infection in the patients (pts) with laryngeal and pharyngolaryngeal carcinoma during 2005 and 2010. **METHODS:** Histories from 87 pts (2005) and 92 pts (2010) who were treated during the year 2005 and 2010 from laryngeal and pharyngolaryngeal carcinoma at the ENT Clinic, Clinical Center of Vojvodina, Novi Sad, Serbia, have been used. All pts received triple drug therapy perioperatively. Since 2009, additional hygienic measures and education of staff (in terms of the proper use of antibiotics) have been taken to improve hospital treatment. From the patients' histories, we followed: average length of hospital stay,average length of administrating antibiotics, occurrence of infection or other postoperative complication (fistula) and the price of used antibiotics. **RESULTS:** During 2005, antibiotics were administrated as follows: aminoglycosides (amikacin) 2x500mg during 10 days, cephalosporin (cefazolin amp. 2x1g, cefrtriakson 2x1g) 10 days, metronidazole (solutio) 3x500mg 10 days.During 2010, same anibiotics were administerd for an average of 3 days. The average length of hospital stay was in 2005. was 13.5 days, x+/- SD=13.5+/-4.2, and in 2010 was 11.18 days, x+/- SD=11.18+/-5.9. The average length of administrating antibiotics was 9.4 days in 2005 (x+/- SD=9.4+/-1.1) and in 2010 was 3.4 days (x+/- SD=3.4+/-1.7). Occurrence of infection was in 4 pts (2005) and 6 pts (2010). The cost of used antibiotics in 2005.was 775748 dinars (9320 euros), and in 2010. was 366159 dinars (3698euro). **CONCLUSIONS:** With reducing the length of administrating same antibiotics, after additional hygienic and educative measures have been taken, it is possible to significantly reduce the length of hospital stay (while the number of postoperative infections is not significantly increased) and cost of used antibiotics, which altogether leads to reduction of overall cost of hospital treatment.

PCN117

SELECTIVE INTERNAL RADIOTHERAPY (SIRT) USING RESIN YTTRIUM-90 MICROSPHERES FOR CHEMOTHERAPY-REFRACTORY METASTATIC COLORECTAL CANCER: A UK COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: Treatment options for chemotherapy-refractory liver metastases resulting from colorectal cancer are limited. The safety and efficacy of SIRT using resin yttrium-90 microspheres was studied in this population. The objective of this analysis was to assess the cost-effectiveness of SIRT compared to best supportive care (BSC) from the perspective of the UK NHS. **METHODS:** A state-transition model was constructed, based on survival curves from a retrospective cohort study of yttrium-90 resin microspheres (SIR-Spheres; Sirtex, Sydney, Australia) *vs.* BSC in chemotherapy-refractory mCRC. The model included costs for treatment acquisition, pre-treatment work-up and delivery of microspheres, and chemotherapy received in addition to, instead of, or after, SIRT. In addition, costs of managing AEs and a cost of death were included. Costs were microcosted using NHS reference costs and the British National Formulary 64. Utility data were taken from a recent NICE economic evaluation in metastatic colorectal cancer. **RESULTS:** The results showed an increase in survival for patients receiving SIRT compared to BSC (2.09 *vs.* 0.97 years), with a corresponding increase in quality adjusted life years (1.50 vs 0.69). The associated costs were £35,487 *vs.*£12,730 for SIRT and BSC, respectively. The additional costs were due to the SIRT treatment and the cost associated with extension to life. The cost per QALY was £28,216 (cost per life year £20,323). The results were robust to alternative assumptions tested in scenario analyses; survival functions, utilities or the time spent pre- and post-progression. However, one-way sensitivity analysis showed results were most sensitive to the parameters for the survival functions. Data shown here were also consistent with published clinical studies. **CONCLUSIONS:** The analysis demonstrates that SIRT using resin yttrium-90 microspheres has the potential of being a cost-effective option in the treatment of patients with chemotherapy-refractory liver metastases resulting from colorectal cancer.

PCN118

PHARMACOECONOMIC ANALYSIS OF INTRAVENOUS TEMOZOLOMIDE FOR THE TREATMENT OF NEWLY DIAGNOSED GLIOBLASTOMA MULTIFORME IN RUSSIA

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OBJECTIVES: To perform comparative pharmacoeconomic analysis of concomitant, adjuvant and second-line intravenous temozolomide (ITMZ) for the treatment of newly diagnosed glioblastoma multiforme versus initial radiotherapy and second-line therapy with ITMZ. **METHODS:** Analysis of the published clinical trials was conducted to evaluate comparative efficacy and safety of the studied therapy options. Direct medical costs included drug therapy and hospital treatment. All prices were for Moscow region, year 2013. Expected difference in direct medical costs was calculated in Excel based model. For the cost-effectiveness analysis, survival was expressed as 2.5 years restricted mean estimates from EORTC-NCIC study. The incremental cost-effectiveness ratio (ICER) was estimated. One-way sensitivity analysis was made. **RESULTS:** According to published trials the treatment of newly diagnosed glioblastoma multiforme with ITMZ was associated with a significant improvement in overall survival. The difference in 2.5 years restricted mean survival between the treatment arms was 0.25 life-years and the ICER was 76,982.6 USD per life-year. The one-way sensitivity analysis showed that the results are more sensitive to the variations of key model parameter, such as price of ITMZ. **CONCLUSIONS:** The concomitant, adjuvant and second-line ITMZ was more effective and economically justified treatment option for patients with newly diagnosed glioblastoma multiforme.

PCN119

COST-EFFECTIVENESS OF BENDAMUSTINE VERSUS FLUDARABINE FOR FIRST-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) IN COLOMBIA

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OBJECTIVES: To determine the cost-effectiveness of bendamustine versus fludarabine for first line treatment of CLL in Colombia. **METHODS:** An economic model was constructed from the Colombian health system perspective, with a 25-year (lifetime) horizon and a discount rate of 3%. The model included three health states, progression-free (PF), progressive disease (PD), and death. Clinical inputs (Kaplan-Meier curves, response rates, hazard ratios (HRs) and adverse event (AE) rates) were from a phase 3 trial comparing bendamustine and chlorambucil, and from a network meta-analysis. Resource use data were from interviews with three Colombian hematologists treating CLL. Resource use for PF patients was weighted based on treatment response. Unit costs were from ISS and SISPRO report and were expressed in 2013 Colombian Pesos. Univariate and probabilistic sensitivity analyses were conducted to determine the key drivers of cost-effectiveness, and the uncertainty around the results, respectively. **RESULTS:** The total lifetime costs for bendamustine and fludarabine were $61,982,845 and $20,432,209, respectively. Bendamustine patients accrued more LYs (7.52 vs. 6.50), QALYs (5.61 vs. 4.60), and PF LYs (3.09 vs. 1.14) compared to fludarabine patients. The ICERs were $40,530,919 (cost per LY), $41,117,127 (cost per QALY) and $21,264,817 (cost per PF LY). Univariate sensitivity analysis revealed the cost per LY ICER was most sensitive to progression-free survival and overall survival HRs for bendamustine vs. fludarabine, the number of treatment cycles, and the cost of bendamustine. Probabilistic sensitivity analysis with 1,000 iterations predicted bendamustine had a 71% chance of being cost-effective, compared to fludarabine, at a willingness to pay (WTP) of $59M per LY, rising to a plateau of about 80% from a WTP of $80M and greater. **CONCLUSIONS:** At current WTP of $59M (three times Colombian GDP per capita) bendamustine is a cost effective alternative to fludarabine.

PCN120

COST-EFFECTIVENESS OF CABAZITAXEL IN MHRPC IN TURKEY

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OBJECTIVES: To determine the cost-effectiveness of cabazitaxel, based mainly on the TROPIC trial in 2nd line treatment of mHRPC relative to the standard of care at the time of launch of the drug. **METHODS:** A Markov model was developed to comprise set of different health states each associated with costs, effects and probabilities of moving to other state. In simulation, a cohort of defined patients are run through the model during the time period of choice, it's assumed that transitions between states only occurs at equidistant time-points and the interval is called a cycle. Because of the relatively short survival time of mHRPC patients, cycle length in the model was set at 3 weeks, corresponding to the length of one chemotherapy administration cycle. Transition rates between different states representing mHRPC disease progression were estimated based on progression of disease and survival rates from the TROPIC trial. **RESULTS:** According to the approved labeling in Turkey, a subgroup of patients with ECOG PS 0-1 and measurable disease at baseline was identified on TROPIC results with a secondary analysis. The result of this analysis shows a similar OS outcomes with decreased death rates. Cabazitaxel was cost-effective compared mitoxantrone with cost per LYG of TRY66,862 given the threshold of TRY68,409 per LYG for the subgroup of the patients at ECOG PS 0-1 and with measurable disease at baseline. Although there has been no formal threshold for the cost-effectiveness ratio in Turkey, a threshold of TRY68,409 per LY gained was assumed based on WHO-CHOICE criteria (3xGDP percapita). **CONCLUSIONS:** It is difficult for the results of the analysis to be interpreted because there is no official cost-effectiveness threshold in Turkey. However, from the WHO perspective; results showed that cabazitaxel is a cost-effective treatment with all ICER values compared to mitoxantrone, below TRY68,409.

PCN121

EVALUATING THE COST EFFECTIVENESS OF GENE EXPRESSION PROFILING AND IMMUNOHISTOCHEMISTRY TESTS

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OBJECTIVES: Gene expression profiling (GEP) and expanded immunohistochemistry (IHC) tests aim to improve decision-making relating to adjuvant chemotherapy for women with early breast cancer (EBC) at intermediate or high risk of recurrence following primary surgery. **METHODS:** A probabilistic model was developed to evaluate the cost effectiveness of treatment guided using the OncotypeDx and IHC4 tests compared with current clinical practice in England and Wales. Analysis was undertaken for women with oestrogen receptor positive (ER+), lymph node negative (LN–), and HER2– EBC from a NHS perspective. In the comparator arm, cancer registry data was used to inform the proportion of patients receiving chemotherapy under current practice. In the intervention arm (new test in addition to current practice) patients were classified into different risk categories based on the result of the new test. The likelihood of receiving chemotherapy was dependent on this classification. The natural history of breast cancer was then simulated using a state transition Markov model, taking into account the reduction in the risk of recurrence associated with chemotherapy. **RESULTS:** The economic analysis suggested that treatment guided using IHC4 has the most potential to be cost-effective at a threshold of £20,000 per QALY gained; however the evidence base to support IHC4 needs further research to confirm the analytical validity of the test and to clarifiy the cost of the test in clinical practice. OncotypeDX has a more robust evidence base, but further evidence on the impact on decision making in the UK and the predictive ability of the test in an ER+, LN-, HER- population receiving current treatment regimens is needed to confirm whether or not it constitutes a cost-effective option in the UK. **CONCLUSIONS:** GEP and IHC tests have the potential to constitute a cost effective option in the UK, but further research is needed to confirm this finding.

PCN122

PHARMACOECONOMIC ANALYSIS OF USING APREPITANT PLUS STANDARD ANTIEMETIC THERAPY FOR PREVENTION OF NAUSEA AND VOMITING ASSOCIATED WITH HIGHLY AND MODERATELY EMETOGENIC CANCER CHEMOTHERAPY IN RUSSIA

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OBJECTIVES: To perform comparative pharmacoeconomic analysis of aprepitant plus standard antiemetic therapy – 5-hydroxytriptamine-3 antagonist and corticosteroid - for prevention chemotherapy-induced nausea and vomiting (CINV) versus standard antiemetic therapy. **METHODS:** Analysis of the published clinical trials was conducted to evaluate comparative efficacy and safety of three-drug combination. Cost-effectiveness analyses was performed. Direct medical costs of treatment with studied drugs were considering for each option: cost for 1-cycle and 6-cycle cancer chemotherapy (CCT) with highly emetogenic drugs and for 1-cycle and 4-cycle CCT with moderately emetogenic drugs for 1 patient. The calculation of costs was based on drugs' prices from the List of Vital and Essential Drugs in Moscow region. The incremental cost-effectiveness ratio (ICER) was estimated. One-way sensitivity analysis was made. **RESULTS:** According to published trials the using aprepitant plus standard antiemetic therapy in patients receiving highly and moderately emetogenic chemotherapy was associated with a significant improvement in control of CINV. The ICER was 593.7 USD per 1-cycle and 2906.6 USD per 6-cycle CCT with highly emetogenic drugs for 1 patient. The ICER was 852.7 USD per 1-cycle and 4570.1 USD per 4-cycle CCT with moderately emetogenic therapy. The one-way sensitivity analysis showed that the results are more sensitive to the variations of

aprepitant price. **CONCLUSIONS:** The using aprepitant plus standard antiemetic therapy was more effective and economically justified treatment option for prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy.

PCN123

ECONOMIC EVALUATION OF FULVESTRANT 500 MG VERSUS GENERIC NON-STEROIDAL AROMATASE INHIBITORS IN PATIENTS WITH ADVANCED BREAST CANCER IN NORWAY

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OBJECTIVES: In Norway, breast cancer represented 23% of all new cancer cases between 2004 and 2008, and was a leading cause of mortality representing 13% of all cancer deaths. The objective of this study was to perform an economic evaluation of fulvestrant 500 mg compared with anastrozole and letrozole used as second line endocrine therapies in the treatment of advanced breast cancer in post-menopausal women in Norway. **METHODS:** The economic analysis was conducted by using a simulation model estimating progression-free survival, overall survival and associated costs and utility gains over the expected lifetime of the patients. As there are no head-to-head trials comparing fulvestrant 500 mg with aromatase inhibitors, the clinical evidence for the comparative effectiveness was obtained from a network meta-analysis. The economic evaluation was conducted from a health care perspective, with costs and resource use based on published sources and expert assessment. **RESULTS:** The cost-effectiveness ratio of fulvestrant 500 mg versus anastrozole 1 mg was 36,000 EUR per quality-adjusted life year (QALY), with incremental costs of 9,600 EUR and incremental QALYs of 0.27. The cost-effectiveness ratio of fulvestrant 500 mg versus letrozole 2.5 mg was 62,000 EUR per QALY, with incremental costs of 21,000 EUR and incremental QALYs of 0.34. In the sensitivity analysis the results were stable for variations of key parameters, such as the time horizon, the hazard ratios for overall survival, the choice of parametric distribution for progression-free survival and the discount rate. **CONCLUSIONS:** Given an informal cost-effectiveness threshold of around 70,000 EUR/QALY in Norway, the results of the economic evaluations suggest that fulvestrant 500 mg is a cost-effective treatment compared with alternative treatments such as anastrozole and letrozole. These findings indicate that fulvestrant 500 mg is a valuable treatment option for patients with advanced breast cancer in Norway.

PCN124

COST-EFFECTIVENESS OF THE SYSTEMATIC IDENTIFICATION AND TREATMENT OF COMORBID MAJOR DEPRESSION FOR PEOPLE WITH CHRONIC DISEASES: THE EXAMPLE OF CANCER

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OBJECTIVES: Comorbid major depression occurs in approximately ten percent of people suffering from a chronic medical condition such as cancer. A 'collaborative care' approach can be used to systematically identify and treat comorbid major depression. However, we lack information on cost-effectiveness of overall approach as economic evaluations published to date have focused solely on the treatment stage. We therefore aimed to use the best available evidence to estimate the cost-effectiveness of the whole approach (both systematic identification and systematic treatment) compared with usual practice, for patients attending specialist cancer clinics. **METHODS:** A cost-effectiveness analysis using a decision analytic model structured to reflect both the identification and treatment processes. Evidence was taken from reviews of relevant clinical trials and from observational studies, together with data from a large depression screening service. Sensitivity and scenario analyses were undertaken to determine the effects of variations in depression incidence rates, time horizons, patient characteristics and alternative estimates of treatment effect. Probabilistic sensitivity analysis was also undertaken. **RESULTS:** Systematic depression management generated more costs than usual practice, but also more quality adjusted life years (QALYs). The incremental cost-effectiveness ratio was £11,765 per QALY and the probabilities of systematic depression management being cost-effective at thresholds of £20,000 and £30,000 per QALY were 0.998 and 1 respectively. Findings were robust to tests of variation in key model parameters. **CONCLUSIONS:** A combined approach to the systematic identification and treatment of comorbid major depression in cancer patients is likely to be cost-effective at widely accepted threshold values. Systematic depression management may be a better way of generating QALYs for cancer patients than some existing medical and surgical treatments. It could potentially be applied to other chronic medical conditions.

PCN125

PET-BASED RADIOTHERAPY TREATMENT PLANNING IS HIGHLY COST-EFFECTIVE COMPARED TO CT-BASED PLANNING: A MODEL-BASED EVALUATION

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OBJECTIVES: PET-based radiotherapy planning for selective lymph node irradiation is an example of the current tendency to individualize treatment in cancer. We evaluated the cost-effectiveness of individualized radiotherapy planning, comparing PET-CT-based to CT-based radiotherapy treatment planning in non-small cell lung cancer. **METHODS:** Our analysis uses a previously developed decision model. The model was based on data for 200 NSCLC patients with inoperable stage I-IIIB, provided by the Maastro Clinic. Transition rates in the model were estimated by multi-state statistical modelling and include the impact of patient and tumour features on disease progression. Resource use estimates, costs and utilities were obtained from the database of the Maastro Clinic, the literature and Dutch guidelines. Primary outcomes were the difference in life years (LY), quality adjusted life years (QALY), costs and the incremental cost-effectiveness and cost-utility ratio (ICER and ICUR) of PET-CT versus CT based radiotherapy planning. Model outcomes were obtained from averaging the outcome for 50 000 simulated patients. To present uncertainty, a probabilistic sensitivity analysis was done. In scenario analyses, we explored the effect of varying the input parameters for costs and QALYs and the effect of changing the assumptions regarding the multi-state model. **RESULTS:** The incremental costs of PET-CT based planning were € 534 (95% CI: €-4670 – €6080) for 0,43 incremental LYs (95% CI: 0,31 – 0,52) and 0,33 QALYs gained (95% CI: 0,26 – 0,45). The base-case scenario resulted in an ICER of € 1242 per LY gained and an ICUR of € 1618 per QALY gained. The probabilistic sensitivity analysis gave a 41% probability that PET-CT based planning improves health outcomes at reduced costs and a 59% probability that PET-CT based planning is more effective at slightly higher costs. **CONCLUSIONS:** PET-based radiotherapy planning for non-small cell lung cancer is highly cost-effective compared to CT-based planning.

PCN126

COST-EFFECTIVENESS OF SYSTEMATIC TESTING FOR LYNCH SYNDROME IN PATIENTS NEWLY DIAGNOSED WITH COLORECTAL CANCER IN THE UNITED KINGDOM

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OBJECTIVES: The cost-effectiveness of genetic testing for Lynch Syndrome for patients newly diagnosed with colorectal cancer in the UK has not previously been estimated. Therefore, the cost-effectiveness of nine testing strategies were simultaneously compared using a detailed and rigorous mathematical model. **METHODS:** In the base case analysis, probands were tested only if aged 50 or below. Testing strategies included use of family history, tumour-based tests and genetic testing. The clinical pathways of thousands of individual patients diagnosed with colorectal cancer (CRC) and their relatives were simulated. For each person, the total costs and quality-adjusted life years (QALYs) were calculated using methodology recommended by the National Institute of Health and Care Excellence (NICE). Simulated clinical events included incidence of CRC and endometrial cancer (EC); surgery for CRC and EC, colonoscopies (including bleeding and perforation), mortality from CRC, EC, colonoscopy and background causes. A proportion of people diagnosed with Lynch Syndrome were assumed to receive prophylactic hysterectomy and to undergo biennial colonoscopies (assumed to reduce the incidence and stage of colorectal cancer). The costs of treating patients with CRC with surgery, chemotherapy, radiotherapy, stoma care and palliative care were captured. Similarly, the costs of treating patients with EC with chemotherapy and radiotherapy were included. **RESULTS:** The life expectancies of probands and relatives with Lynch Syndrome are estimated to increase by up to 1.6 years, depending on the strategy for genetic testing. All testing strategies are predicted to offer good value for money versus no testing, with all incremental cost-effectiveness ratios below the UK basic cost-effectiveness threshold of £20,000 per QALY. Universal genetic testing is predicted to offer poor value for money versus targeted genetic testing. **CONCLUSIONS:** Results suggest that targeted genetic testing for Lynch Syndrome for patients with newly diagnosed CRC in the UK is a good use of limited financial resources.

PCN127

COST-EFFECTIVENESS ANALYSIS OF CAPSULE ENDOSCOPY IN SCREENING FOR COLORECTAL CANCER IN JAPAN

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OBJECTIVES: The PillCam COLON2 is a colon capsule endoscopy (CCE) that makes a minimally-invasive colonoscopy possible and is expected to improve detailed examination rate which have been identified as a problem concerning a population-based colorectal cancer (CRC) screening system in Japan. The objective of this analysis was to evaluate the cost-effectiveness of CCE if newly introduced into the current population-based CRC screening system in Japan. **METHODS:** The subject of this analysis was a sequential screening system for which CCE has been incorporated (immunochemical fecal occult blood test (IFOBT) → detailed examination by CCE → detailed examination by colonoscopy) and the comparator was the conventional sequential screening system (IFOBT → detailed examination by colonoscopy). The target population includes asymptomatic adults aged 40 years old and a lifelong simulation was conducted using a Markov model which consists of 8 states, no polyp, adenomatous polyp (≤ 5mm, 6-9mm and ≥ 10mm), localized CRC, regional CRC, distant CRC and death. The efficacy measures were life year and quality-adjusted life year (QALY). The analysis was conducted from the perspective of the payer and only direct medical costs were considered. **RESULTS:** The incremental cost effectiveness ratio (ICER) observed when incorporating CCE into the conventional screening system was €59,911 per QALY, €25,060 per QALY and €14,905 per QALY when assuming a 10%, a 20% and a 30% improvements in detailed examination rates (1 Euro=128 JPY). Therefore, the introduction of CCE was determined to be cost-effective if the detailed examination rate increased by 20% or more relative to current rate with CCE introduction. **CONCLUSIONS:** Based on this analysis, the introduction of CCE into the conventional population-based screening system in Japan is shown to be cost-effective. The cost-effectiveness of CCE is primarily dependent on the degree of improvement in the current detailed examination rate.

PCN128

COST-EFFECTIVENESS OF FIRST-LINE TREATMENT OF ADVANCED METASTATIC NON SMALL CELL LUNG CANCER- A SYSTEMATIC REVIEW OF ECONOMIC MODELS

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OBJECTIVES: To summarize the modeling methods used in published cost-effectiveness evaluations of first-line treatment for advanced NSCLC patients. **METHODS:** To identify relevant studies, a systematic literature search was performed in Medline®, EMBASE®, Medline-In-Process and the CRD database from 2000 to 2013. In addition, Technology Appraisals (TA) were identified by searching the NICE, SMC and pCODR websites. Studies were included for review based on the following pre-defined criteria; 1) description of cost-effectiveness or cost-utility analysis; 2) inclusion of a comparison of drug interventions in first-line treatment of advanced NSCLC patients; and 3) results were expressed as cost per LY or QALY gained. **RESULTS:** Out of 1009 unique citations, 21 publications and 18 TA met the inclusion criteria. The identified cost-utility and cost-effectiveness analyses were all performed from a payer perspective for a variety of countries in Europe, Asia and North America. The economic value of targeted therapies for first-line and maintenance treatment for advanced NSCLC patients were evaluated for different subpopulations according to histology type (non-squamous, squamous). The most commonly used modeling approach was the state-transition model with health states reflecting stable disease, progression, and death. Transitions between these health states were based on either fixed or time varying transition probabilities. Cost-effectiveness analyses that were based on a synthesis of clinical efficacy evidence primarily relied on the constant hazard ratio assumption. The impact of structural modeling assumptions on cost-effectiveness findings was frequently not reported. **CONCLUSIONS:** Based on a review of published cost-effectiveness evaluations, it was concluded that the rational for certain modeling choices are frequently not provided. In particular, choices pertaining to methods for clinical evidence synthesis and the impact on cost-effectiveness findings need to be justified in a more structured way.

PCN129

COST-MINIMIZATION ANALYSIS (CMA) OF DIFFERENT STRATEGIES TO TREAT NEWLY DIAGNOSED LOCALLY CONFINED LOW-RISK PROSTATE CANCER (LCLRPC) IN GERMANY: RESULTS OF THE HAROW STUDY

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OBJECTIVES: The optimal treatment choice for the about 64,000 men diagnosed with prostate cancer each year in Germany still remains unclear. The objectives therefore were to estimate and compare costs under day-to-day conditions of caring for men in Germany with newly diagnosed LCLRPC using hormonal therapy (HT), active surveillance (AS), radiotherapy (RT), operation (OP), or watchful waiting (WW) – HAROW. **METHODS:** The long-term observational multi-centre HAROW study combined data collection from urologists (clinical data; utilized outpatient medical services, OMS) and from patients (employment status, QoL by EQ-5D, numerous health resource use items). Resource use was valued by year 2010 official prices in €. Direct costs (DC) were given by hospital treatment, OMS and drugs, inpatient rehabilitation, patients' co-payments. Indirect costs (IC: sick leave, premature retirement, premature mortality) were estimated by 2010 gross domestic product/capita/day. Costs and quality-adjusted life-years (QALYs) were discounted by 3% per annum. Strategies without significant differences in QALYs/patient-year (PY) were compared by cost-minimization analysis (CMA) using mean costs/PY, remaining strategies by cost-utility analysis. **RESULTS:** From 07/2008 to 03/2013, 3063 LCLRPC patients (T1a–T2c, N0, M0; 67.3±7.5 years) were included from 257 urologists: AS n=452, RT n=378, HT n=210, HT+RT n=80, combination therapy (CT) n=137, OP n=1647, other therapy (OT) n=18, WW n=141. Observation period: average 1.9 years, maximum 4.6 years. From the societal perspective (DC+IC), HT+RT had the lowest cost/PY (€1033), followed by AS (€1265), RT (€1313), WW (€1316), HT (€1522), CT (€3209), OT (€5705), and OP had highest cost/PY (€6656). From the perspective of DC, WW showed he lowest cost/PY (€894), followed by RT (€905), HT+RT (€987), AS (€1014), HT (€1169), OT (€2176), CT (€2204), and OP had highest cost/PY (€5374). **CONCLUSIONS:** The HAROW study provides meaningful results on costs of different LCLRPC treatment strategies under day-to-day conditions of care in Germany to support decision making.

PCN130

HEALTH TECHNOLOGY ASSESSMENT OF CONTRAST-ENHANCED ULTRASOUND (CEUS) TECHNIQUES

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The second generation of contrast-enhanced ultrasound (CEUS) techniques combines the advantages of ultrasound techniques and the additional information provided by the contrast agent. **OBJECTIVES:** To prove that sulphur hexafluoride microbubbles contrast agent used for CEUS is as effective in detecting and analyzing abnormal-looking areas in the liver as currently used imaging techniques (contrast-enhanced CT and MRI: CECT and CEMRI), however the costs of CEUS are considerably lower. **METHODS:** Cost-minimization analysis was based on literature review (last 5 years MEDLINE research, evidence level 1++) and on Hungarian financing data. National medical protocols were also considered. **RESULTS:** Average cost per patient of CEUS was 64,5 EUR, while costs of currently used techniques were 129 EUR. According to the literature 70% of currently used CT and MRI techniques could be replaced by CEUS. Results made it evident that the equally effective contrast-enhanced ultrasound technique is more cost-effective than the currently used contrast-enhanced CT and MRI techniques. Health technology assessment suggested that the change for the new technology would save 64 509 million EUR for the National Health Insurance Fund at the end of the third year of application, counting with 5000 cases. **CONCLUSIONS:** The widespread use of cost-effective CEUS technology is highly recommended as it is an evidently cost-saving technique from the insurer's point of view. Further assessment is recommended to measure clinical parameters, burden of radiology and other quality of life parameters of patients, possibly by using a control group if this is ethically viable.

PCN131

COST-EFFECTIVENESS OF BENDAMUSTINE-RITUXIMAB IN FIRST-LINE INDOLENT NHL: A PATIENT-LEVEL SIMULATION

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OBJECTIVES: To evaluate the cost-effectiveness of bendamustine-rituximab (B-R) compared with standard of care as first-line treatment for patients with advanced indolent non-Hodgkin's lymphoma (NHL) in England and Wales. **METHODS:** A patient-level simulation was adapted from the model used by the University of Sheffield School of Health and Related Research (ScHARR) in a health technology appraisal of rituximab for first-line treatment of follicular lymphoma (the most common type of indolent NHL). This approach allowed modelling of the complex treatment pathways in indolent NHL; specifically, first-line maintenance and second-line treatment choice could be modelled as a function of patient age, and prior treatment choice and outcome. Data from a Phase 3 randomised, open-label trial by the Study group indolent Lymphomas (StiL) in Germany were used to compare B-R with CHOP-R (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab). The relative efficacy of CHOP-R and CVP-R (cyclophosphamide, vincristine, prednisone, rituximab) was estimated as per the original ScHARR approach. The analysis was conducted from the perspective of the National Health Service, using a lifetime time horizon. One-way sensitivity and scenario analyses were conducted, including one using recently published randomised trial data comparing CVP-R with CHOP-R. **RESULTS:** The base-case deterministic incremental cost-effectiveness ratio (ICER) was £5,249 per quality adjusted life year (QALY) for B-R *vs.* CHOP-R, and £8,092 per QALY for B-R *vs.* CVP-R. The alternative scenario using direct data comparing CVP-R with CHOP-R more than halved the ICER for B-R *vs.* CVP-R to £3,468. Owing to its better toxicity profile, B-R reduced the cost of treating adverse events by over £1,000 per patient *vs.* CHOP-R. None of the one-way sensitivity or scenario analyses increased the ICER above £20,000. **CONCLUSIONS:** The ICERs for B-R *vs.* CHOP-R and CVP-R were below the thresholds normally regarded as cost-effective in England and Wales (£20,000 – 30,000 per QALY).

PCN132

COST-UTILITY OF GRANULOCYTE-COLONY STIMULATING FACTORS (G-CSFS) FOR PRIMARY PROPHYLAXIS (PP) OF CHEMOTHERAPY INDUCED FEBRILE NEUTROPENIA (FN) IN BREAST CANCER PATIENTS IN THE NETHERLANDS

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OBJECTIVES: To assess number needed to treat to avoid an episode of FN (NNT) and cost-utility in The Netherlands of PP with once-per-cycle pegfilgrastim vs. no prophylaxis and vs. PP with daily G-CSF filgrastim (11-days as per label or 6-days suboptimal use) for reducing FN incidence in women with primary breast cancer receiving high risk chemotherapy for FN (e.g. TAC, a frequently used reference regimen in The Netherlands). **METHODS:** A decision-analytic model was constructed from health care-payer perspective. Costs were from official list prices (April 2013) or literature and included drugs, drug administration and FN-related medical costs and hospitalisations. Effectiveness inputs in terms of relative risk reduction (RRR) for FN were based on a recent meta-analysis. Survival and utility inputs were modeled from available data for breast cancer patients in the US and the UK. Outcomes included NNT and incremental cost effectiveness ratio (ICER) as cost per quality-adjusted life-year gained (QALY). Univariate sensitivity analyses evaluated the robustness of the model. **RESULTS:** NNT with pegfilgrastim PP was lowest at 4.4, with filgrastim 11-days at 5.6 and filgrastim 6-days at 13.4. In terms of cost-utility, pegfilgrastim PP was dominant vs. 11-days filgrastim PP and was considered cost-effective vs. no prophylaxis (€29,896/QALY) and vs. PP with 6-days filgrastim (€7,615/QALY). In a scenario analysis reducing the prices of daily G-CSFs by 40%, pegfilgrastim PP remained cost-effective. The sensitivity analyses revealed that most sensitive variables were FN effectiveness (relative risk reductions), incremental survival assumptions and cost of G-CSFs, and overall the model was robust to sensitivity analyses. **CONCLUSIONS:** In a Dutch setting, pegfilgrastim PP offers a cost-effective approach to PP of FN. In the cost-utility analysis pegfilgrastim PP was dominant vs. 11-days filgrastim PP and cost-effective vs. no prophylaxis and 6-days filgrastim PP.

PCN133

COST-EFFECTIVENESS ANALYSIS OF ABIRATERONE ACETATE AS SECOND LINE TREATMENT FOR METASTATIC CASTRATION-RESISTANT PROSTATE CANCER AFTER DOCETAXEL TREATMENT IN JAPAN

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OBJECTIVES: Abiraterone acetate improves overall survival of patients with metastatic castration-resistant prostate cancer (CRCP). The NICE in the UK has recommended abiraterone as a second line treatment for CRCP after docetaxel. Ministry of Health, Labour and Welfare (MHLW) has begun to discuss whether or how to use cost-effectiveness data for reimbursement or pricing. The purpose of this study is to evaluate cost-effectiveness of abiraterone plus prednisolone compared to prednisolone alone in Japan. **METHODS:** Cost-effectiveness analysis was performed using a Markov model (TreeAge Pro 2013) based on data from the randomized control trial (COU-AA-301 study) and literature review conducted from the public health care payer's perspective. The (1) abiraterone (1,000 mg once daily and orally) plus prednisolone (5 mg twice daily and orally) was compared with (2) prednisolone alone. The base case was assumed to be a 69 year-old man with metastatic CRPC. The model used a time horizon of 10 years. Outcomes were measured in quality-adjusted life years (QALYs), and incremental cost-effectiveness ratio (ICER) was calculated. MHLW has yet to approve abiraterone due to the delay in development, and drug cost was estimated based on prices in the UK and the US. Both cost and outcomes were discounted at a 2% annual rate based on Japanese guidelines for eco-

nomic evaluation. Sensitivity analyses were conducted to explore the uncertainties surrounding the assumptions. **RESULTS:** Abiraterone plus prednisolone indicated higher QALYs than prednisolone alone, though it was more expensive. In the base-case analysis, ICER for abiraterone plus prednisolone exceeded JPY 10 million (EUR 80,000) per QALY gained. The one-way sensitivity analysis for discount rate (0 to 4%) showed no affects on the results. **CONCLUSIONS:** The present study concludes that the ICER may be more than JPY 10 million. Further deliberate discussion on cost-effectiveness of abiraterone in Japan is needed to consider the Japanese price and clinical outcomes.

PCN134

ECONOMIC EVALUATION OF HPV VACCINATION PROGRAM IN SOUTH KOREA

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OBJECTIVES: To assess the cost-effectiveness of a national HPV vaccination program that vaccinates 12 year-old girls with cervical cancer screening and the only current cervical cancer screening. **METHODS:** We analyzed the effect of HPV infection reduction by HPV vaccination on reduction of CIN and cervical cancer and finally conducted cost-utility analysis applying QALYs to which takes into account life span expansion and the quality of life. With the societal perspective, patient time costs, caregiver costs, and transportation costs were all considered as well as medical costs. Markov model was used with one year cycle and life time analysis period. Markov states in this model were classified well, HPV infection, CIN 1, CIN 2/3, cervical cancer (initial cancer), follow-up cervical cancer, recurrent/persistent cancer, follow-up recurrent/persistent cancer and death. The HPV infection was limited to infections caused by HPV specific types 16 and 18. **RESULTS:** When HPV vaccination program is introduced to 12-year old cohort, it was indicated that cervical cancer patients with HPV vaccination program would be 2,042 patients and cervical cancer patients with present screening program 3,709. It results that cervical cancer patients would be decreased to 1,667 by HPV vaccination. From this, it was estimated that all the cohorts would get an additional life expectancy of 1,648 LYG and quality adjusted life years of 1,849 QALYs. According to cost-utility analysis result, additional 1849 QALYs cost KRW 59.8 billion when HPV vaccination program implement, and the incremental cost-utility ratio was estimated to be KRW 32 million per a QALY. Considering the threshold of Korean cost-effectiveness, the vaccination program is decided not to be cost-effective. **CONCLUSIONS:** Though the HPV vaccination program for 12-year old girls was not cost-effective at the current condition of Korea, it is advisable to consider that cost-effectiveness varies sensitively.

PCN135

COST UTILITY ANALYSIS OF EVEROLIMUS IN THE TREATMENT OF METASTATIC RENAL CELL CANCER IN THE NETHERLANDS

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OBJECTIVES: Metastatic renal cell cancer (mRCC) is becoming an important part of Dutch health care expenditure due to expensive pharmaceutical options for disease control and lack of adequate prevention methods. New targeted therapeutics, such as sunitinib, sorafenib and everolimus, have recently emerged with relevant benefits on progression-free survival (PFS) for mRCC patients. This study aims to assess the cost-effectiveness of the most recent of these introductions, i.e. everolimus, in comparison to best supportive care in second line treatment of mRCC patients in The Netherlands. **METHODS:** A Markov model was designed in line with Dutch treatment protocols. Transitions between health states were modeled by time-dependent probabilities extracted from published Kaplan-Meier curves for PFS and overall survival (OS). The cohorts were followed over 18 cycles, each cycle lasting 8 weeks. Annual discount rates of 1.5% for health and 4% for costs were applied and a health-care perspective was taken. One-way and probabilistic sensitivity analyses (PSA) were performed to test the robustness and uncertainty around the base-case estimate. **RESULTS:** The incremental cost-effectiveness ratio (ICER) for everolimus was esimated at €92,258/QALY. Sensitivity analysis identified the hazard multiplier, an estimate of OS gain, as the main driver of everolimus' cost-effectiveness. Through PSA a wide 95% confidence interval around the base-case ICER estimate was revealed (€49,677 - €453,941/QALY). Additionally, at the threshold of three times GDP per capita (€95,700 in The Netherlands) everolimus had a 54% probability of being cost-effective. **CONCLUSIONS:** The base-case ICER was just below the upper cost-effectiveness limit recommended by WHO, indicating that everolimus might be a cost-effective option in the Dutch setting. However, reasonable uncertainty of the main finding resulted from everolimus' unpredictable gain in OS. Efforts should be undertaken to perform an integral assessment of the economic attractiveness of all current and new therapeutics in mRCC.

PCN136

COST-UTILITY ANALYSIS (CUA) OF DIFFERENT STRATEGIES TO TREAT NEWLY DIAGNOSED LOCALLY CONFINED LOW-RISK PROSTATE CANCER (LCLRPC) IN GERMANY: RESULTS OF THE HAROW STUDY

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OBJECTIVES: The optimal treatment choice for preserving quality of life (QoL) of the about 64,000 men diagnosed with prostate cancer each year in Germany still remains unclear. The objectives therefore were to estimate cost utility under day-to-day conditions of caring for men in Germany with newly diagnosed LCLRPC using hormonal therapy (HT), active surveillance (AS), radiotherapy (RT), operation (OP), or watchful waiting (WW) – HAROW. **METHODS:** The long-term observational multi-centre HAROW study combined data collection from urologists (clinical data; utilized outpatient medical services, OMS) and from patients (employment status, QoL by EQ-5D, numerous health resource use items). Resource use was valued by year 2010 official prices in €. Direct costs (DC) were given by hospital treatment, OMS and drugs, inpatient rehabilitation, patients' co-payments. Indirect costs (IC: sick leave, premature retirement, premature mortality) were estimated by 2010 gross domestic product/capita/day. Costs and quality-adjusted life-years (QALYs) were discounted by 3% per annum. Strategies with significantly different QALYs/patient-year (PY) were compared by CUA, remaining strategies by cost-minimization analysis. **RESULTS:** From July 2008 to March 2013, 3063 LCLRPC patients (T1a–T2c, N0, M0; 67.3±7.5 years) were included from 257 urologists: AS n=452, RT n=378, HT n=210, HT+RT n=80, combination therapy (CT) n=137, OP n=1647, other therapy (OT) n=18, WW n=141. Observation period: average 1.9 years, maximum 4.6 years. From the societal perspective (DC+IC), AS and RT each dominated HT, i.e. there were savings/PY (€257 and €208) and QALYs gained/PY (0.0811 and 0.0587) with AS and RT, respectively, versus HT. When comparing OP to HT, there were additional cost (DC+IC) of €5134/PY and 0.0784 QALYs gained/PY for OP versus HT leading to €65,525 per QALY gained. **CONCLUSIONS:** The HAROW study provides meaningful results on cost utility of AS, OP, RT, and HT as LCLRPC treatment strategies under day-to-day conditions of care in Germany to support decision making.

PCN137

A COST-UTILITY ANALYSIS OF EVEROLIMUS PLUS EXEMESTANE FOR THE TREATMENT OF ER+ HER2- METASTATIC BREAST CANCER IN THE UNITED KINGDOM

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OBJECTIVES: This study evaluated the cost-effectiveness of everolimus + exemestane (EVE+EXE) versus placebo + exemestane (PBO+EXE) in patients with ER+ HER2- metastatic breast cancer in the UK. Whilst the effectiveness of treatment has been demonstrated previously, this is the first analysis to assess the cost of the intervention alongside those benefits. **METHODS:** A Markov model was developed to compare treatment with EVE+EXE versus PBO+EXE in patients with ER+ HER2- metastatic breast cancer over a lifetime time horizon (UK health care perspective). Follow-up data on progression-free survival and overall survival were taken from the BOLERO II trial. Weibull functions were used to extrapolate trial data beyond the follow-up period. Utilities from published sources were combined with trial data to calculate quality-adjusted life years (QALYs) associated with each treatment. Drug costs (list prices) and background health state costs (i.e. non-intervention costs) were applied to calculate incremental costs offset. **RESULTS:** Over a ten year time horizon, EVE+EXE led to a life expectancy of 3.27 years, compared to 2.41 for PBO+EXE. EVE+EXE resulted in 1.91 QALYs, compared to 1.31 for PBO+EXE. Therefore, the incremental gains in life years and QALYs were 0.85 and 0.60 respectively. Drug costs were £22,074 and £628 for the two arms respectively, whilst non-drug costs were £22,332 and £21,108 respectively. Therefore, the EVE+EXE arm had an incremental cost of £22,670. The incremental cost per QALY was, therefore, £37,719 over a ten-year time horizon. Probabilistic sensitivity analysis demonstrated that, at a threshold of £30,000 per QALY gained, EVE+EXE had a 27.3% likelihood of being cost-effective. At a threshold of £55,000 per QALY gained, the likelihood of cost-effectiveness was 77.4%. **CONCLUSIONS:** EVE+EXE was associated with increased health care costs, but was also estimated to lead to health gains in terms of both LYs and QALYs.

PCN138

COST-EFFECTIVENESS OF GEMCITABINE PLUS CISPLATIN VERSUS GEMCITABINE ALONE FOR TREATMENT OF ADVANCED BILIARY TRACT CANCER IN JAPAN

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OBJECTIVES: Gemcitabine plus cisplatin is a common use for chemotherapy patients with advanced biliary tract cancer in Japan. This study aims to assess the cost-effectiveness of this combination therapy compared to monotherapy for biliary tract cancer in Japan. **METHODS:** A Markov model of three states and monthly transmissions was constructed based on a phase II trial. Transition probabilities between states were derived from the trial conducted by Valle, J. et al (2010). and converted to appropriate parameters for input into the model. The associated cost components, obtained from literature published in Japan, were inpatient, outpatient, and medication for biliary tract cancer as well as those for palliative care. We estimated cost-effectiveness per quality-adjusted life year (QALY) at a time horizon of thirty two months. An annual discount for cost and outcome was not considered. **RESULTS:** The model demonstrate no statistical significance in the hazard ratio of 0.625, as compared to an actual ratio of 0.63 (95% confidence interval: 0.51–0.77) retrieved from the clinical trial. The base case outcomes indicated that combination therapy would be more cost-effective than monotherapy when the incremental cost-effectiveness ratio (ICER) was approximately 720,000 YEN per QALY gained, retrospectively. A tornado diagram depicting the deterministic sensitivity analysis of the ICER revealed that the death rate resulting from the combination therapy influenced the base case, but robustness of the base case was identified. A probabilistic analysis resulting from 5,000 Monte Carlo simulations demonstrated efficacy at willingness to pay (WTP) thresholds of 5,000,000 YEN per QALY gained in approximately 95% of the population. **CONCLUSIONS:** In Japan, combination therapy is a cost-effective treatment option for advanced biliary tract cancer.

PCN139

HEAD TO HEAD ECONOMIC EVALUATION OF TWO GENOMIC PROFILES OF RECURRENCE RISK FOR BREAST CANCER, MAMMAPRINT VERSUS ONCOTYPE DX, IN SPAIN

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OBJECTIVES: Cost effectiveness analysis of MammaPrint in the diagnosis of early breast cancer from the Spanish NHS perspective. **METHODS:** Markov model

assuming a 60-year-old women cohort with negative-lymph node, positive estrogen receptors and negative HER2 breast cancer. Costs and effects of the treatment by identifying recurrence risk using A!O, MammaPrint or OncotypeDX were compared at 5 years, 10 years and lifetime horizons. Probability of low or high risk of recurrence by A!O was fixed 50/50 (ratios between 40/60 and 60/40 for sensitivity analysis). Risks predicted by OncotypeDX and MammaPrint were assumed to be the same. Cost of chemotherapy (2.825€), recurrence (6,357€) and other direct health care costs were derived from local data. Three health states (free of recurrence, recurrence, death) were defined in a given period of time. **RESULTS:** A total of 31% patients required adjuvant chemotherapy with MammaPrint classification (36.6% with OncotypeDX, 56.3% with A!O). MammaPrint showed a life expectancy of 23.55 years at lifetime Differences in chemotherapy costs, worse prognosis rates and a higher cost of the genomic profile (3,200€ vs. 2,675€) explained higher cumulative costs for OncotypeDX over both alternatives at any time. MammaPrint instead of OncotypeDX showed savings of at least 1,273€ after 5 years. MammaPrint resulted dominant (less costly and more effective) against OncotypeDx at any time horizon and would be cost-effective from the 6th year versus A!O (43,912€, 6,169€ and 287€ per QALY gained at 5, 10 years and lifetime; 30,000€/QALY gained threshold assumed). Sensitivity analysis confirmed base case results with MammaPrint remaining cost-effective until a willingness-to-pay threshold below 275€/QALY gained. Utility of recurrence, age at baseline and probability of A!O low risk were the key drivers at 10 years. **CONCLUSIONS:** MammaPrint in predicting risk of recurrence in these patients and avoiding chemotherapy overtreatment is a dominant strategy over OncotypeDX and it is highly cost-effective against A!O.

PCN140

EARLY-STAGE ECONOMIC EVALUATION OF STRATIFIED MEDICINE IN MULTIPLE MYELOMA

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OBJECTIVES: The clinical utility of biomarkers is often uncertain and difficult to demonstrate in an experimental setting. Modeling techniques can be used at the preclinical phase to evaluate their potential therapeutic and economic value. In multiple myeloma (MM), subgroup analyses of pivotal trials show that only patients presenting with adverse prognostic biomarkers demonstrate significantly improved survival with bortezomib-based versus some alternative therapies. A cost-utility analysis was conducted to evaluate the potential value of a risk-stratified treatment (RST) approach versus uniform treatment (UT) in Dutch daily practice MM. **METHODS:** A Markov-type decision analytic model compared total health benefits and costs for two strategies: 1) UT where all patients received the standard of care consisting of bortezomib induction/maintenance and 2) RST where treatment was stratified according to clinical and tumor biomarkers only, molecular biomarkers only, or any biomarker. In RST, high-risk patients received bortezomib while other patients received chemotherapy and thalidomide. Input data originated from clinical trials, literature reviews, observational studies and national tariffs. Various sensitivity and scenario analyses were performed. **RESULTS:** RST dominated UT, with average health gains of 0.007-0.059 LYs (0.009-0.040 QALYs) and cost-savings of €1,842-€4,924 depending on detection method. A scenario analysis for RST where all high-risk patients received an experimental treatment increased health by 0.40 LYs (0.30 QALYs) and costs by €2,567 compared to UT. Influential parameters included the price of bortezomib and survival and quality-of-life-related parameters. **CONCLUSIONS:** An economic evaluation of biomarkers in the preclinical development phase provided evidence that RST in MM may improve health outcomes and lower costs. Modeling techniques made it feasible to assess the circumstances under which RST would be promising and hence guide the prioritization of designing experimental studies to evaluate clinical utility. These findings should encourage payers and users to support the clinical development and adoption of RST approaches in MM.

PCN141

COST-UTILITY OF ACTIVE SURVEILLANCE FOR THE TREATMENT OF LOCALIZED PROSTATE CANCER IN THE CONTEXT OF THE GERMAN HEALTH CARE SYSTEM

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OBJECTIVES: There is an on-going debate about whether to perform surgery on early, localized prostate cancer and put up with common long term side effects of prostatectomy like incontinence and erectile dysfunction. Alternatively such patients could be closely monitored and counselled (active surveillance). This study investigates the cost-utility of active surveillance compared to radical prostatectomy. **METHODS:** A Markov model comparing prostatectomy and active surveillance over a lifetime horizon was programmed in TreeAge. Comparative disease specific mortality was based on the Scandinavian Prostate Cancer Group trial and a review and meta-analysis of comparative effectiveness studies. Resource use was identified via national treatment guidelines and expert interviews covering in-patient, out-patient, medication, aids & remedies as well as out of pocket payments. Utility values were literature-based and used as factor weights to age specific German HRQoL values. Uncertainty is assessed deterministically and probabilistically. **RESULTS:** Our results suggest that active surveillance is a cost saving treatment strategy generating more QALYs at reduced overall costs. The probability of developing metastases under AS and the probability of recurrence as well as utility weights of patients under AS and after prostatectomy were major drivers of cost-effectiveness. Monte Carlo simulation suggests that PE is likely to become at willingness to pay thresholds > €400,000. **CONCLUSIONS:** Active surveillance is likely to be a cost effective treatment option from the perspective of the German Statuary Health Insurance. An improved way of identifying cancers with a high probability of progression could favour active surveillance more clearly. It is not clear yet how the use of individual utilities for side effects would alter the results.

PCN142

AN OVERVIEW OF DOMESTIC CANCER DRUGS IN TURKEY: 2008-2012

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OBJECTIVES: Cancer is among the most common causes of death in Turkey. Cancer diagnosis and treatment management were substantially improved by the Ministry of Health. Generic market and price movements of different kinds of drug groups show different characteristics. In this study we aimed to demonstrate the impact of domestic manufacture of cancer drugs on import cancer drug sales in Turkey in terms of both boxes and cost sale trend analysis between 2008 and 2012. **METHODS:** This study was designed as an observational, retrospective study. Domestic oncology drugs were chosen from the base oncology drug groups. The sales data of the domestic oncology drugs and both original and generic import drugs which have the same active ingredient with the domestic drugs was obtained from the Information Medical Statistics (IMS) database from September 2007 to July 2012. Sales data is evaluated with segmented regression analysis for interrupted time series. **RESULTS:** Oncology drug sales report showed that the market share of domestic products increased approximately 38% at 2012 from 0,5% at 2008. Before the cut point, there was a statistically significant increase in the sales level of import oncology drugs, but after the cut point sales trend showed a statistically significant decrease. Import oncology drugs' unit price per box decreased from 196.5TL between September 2007 and October 2008 to 172.6TL between November 2008 and July 2012. But domestic oncology drugs' unit price per box was 91.8TL between November 2008 and July 2012. **CONCLUSIONS:** In conclusion, domestic drug manufacturing has important contributions to a country's economy including low drug prices, supplying for the domestic consumption, creation of employment opportunities and also as export potentials. Price cut in 2009 and 2011 in Turkey and "Reference Pricing System" should be taken into consideration for this price change evaluation in the case of domestic product manufacturing.

PCN143

SHORT-TERM DISABILITY (STD) ASSOCIATED WITH SKELETAL RELATED EVENTS (SRES) IN COMMERCIALLY INSURED PATIENTS WITH BONE METASTASES (BM) SECONDARY TO SOLID TUMORS

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OBJECTIVES: Patients with BM frequently experience SREs including pathological fracture, surgery or radiation to bone, or spinal cord compression .The study objective was to estimate STD (work hour loss) and associated costs in patients with SREs in a population with BM secondary to solid tumors. **METHODS:** Patients with diagnosis of solid tumors and BM were extracted from MarketScan® Health Productivity and Management Database and Commercial Database in 2002-2010. Eligible patients were 18-64 year-old full-time employees, had STD benefit eligibility, and had ≥6 months continuous pre-index enrollment (pre-period) and ≥1 month follow-up. For SRE patients, index date was the first SRE claim. For patients without SREs, index date was assigned per the distribution of index dates from SRE patients. Monthly STD hours and costs associated with STD were estimated during the first (up to) 6 months and the first (up to) 12 months. Generalized linear models estimated the marginal impact of having SRE on STD hours and associated costs, controlling for baseline STD hours and patients' characteristics. **RESULTS:** A total of 854 patients with SREs and 701 patients without SREs were included, with a mean age of 52.1 and 51.6 years, respectively. 52.2% of SRE patients reported STD during the 6-month follow-up, compared with 19.1% of patients without SREs. For SRE patients, the mean STD hours were 21.2 per month in pre-period and 61.3 during follow-up. The hours for patients without SREs were 8.6 and 14.4, respectively. Multivariate analysis indicated that SREs were associated with significantly increased STD hours (39.4 per month) and associated costs ($613 per month) during the 6-month follow-up period. Results from the 12-month follow-up period were similar. **CONCLUSIONS:** SREs were associated with significantly increased STD hours and associated costs. Therapies that prevent or delay the development of SREs may reduce work loss and costs associated with it.

PCN144

ECONOMIC ACTIVITY OF CANCER SURVIVORS IN POLAND

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OBJECTIVES: Although cancer is one of the leading causes of mortality worldwide, the number of cancer survivors is constantly growing due to improved treatment. Growing number of cancer survivors goes in line with trends to increase retirement age and this together leads to increase number of cancer survivors at economically active age. The aim of this study was to analyze economic activity of cancer survivors in Poland. **METHODS:** Data on disability (the number of medical certificates awarded because of incapacity for work) due to cancer and other diseases were retrieved from the Social Insurance Institution annual report for the year 2009. Data included the number of medical certificates issued for the first time and the number of certificates reissued, their periods of validity, age of population and disability severity (complete or partial inability to work, inability of independent existence). **RESULTS:** Cancer was the second (after cardiovascular diseases) cause of medical certificates issued for the first time because of incapacity to work and account for 22% of all certificates awarded for the first time. However, the number of certificates reissued was significantly lower – cancer accounted for 7% of all certificates reissued (cardiovascular diseases still accounted for the largest number of certificates reissued – 25%). The mean age of population with cancer was above the mean age of overall population with medical certificates awarded because of incapacity to work, however lower than those for cardiovascular or pulmonary diseases. Significant differences in disability severity structure exist. Significant higher percentage of cancer patients were judged as either incapable of independent existence (19.9%-24.9% compare to 4.4%-6.5% in overall population) or complete incapable to work (45.9%-71.1% compare to 23.4%-32.9% in overall popula-

tion). **CONCLUSIONS:** Disability in cancer survivors is very common and is more severe than in other diseases.

PCN145
IMPACT OF NURSING AND PHARMACY CARE BETWEEN CAPECITABINE AND 5-FLUORURACIL REGIMENS IN THE MANAGEMENT OF ADVANCED ESOPHAGO-GASTRIC CANCER IN HONG KONG
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OBJECTIVES: To compare the possible time savings from reduction of nursing and pharmacy time to manage advanced esophago-gastric cancer (AEGC) patients using capecitabine-based regimens versus traditional 5-FU based intravenous (IV) chemotherapy in the Hong Kong public hospital setting. **METHODS:** This was a time-and-motion study conducted in 2 public hospitals of Hong Kong based on the simulation of previously data on both capecitabine-based regimen (XELOX and XP) and IV 5-FU-based regimen (FOLFOX and FP). The preparation, dispensing and administration time for XELOX, XP, FOLFOX and FP were compared. The capital item utilization including hospital bed, infusion pump etc and length of patient attendance were recorded. Each subject was based on 24-week cycle in the analysis. The projected cost saving in nursing and pharmacy time was estimated if all AEGC in Hong Kong were prescribed capecitabine-based regimen. **RESULTS:** The average nursing time for FOLFOX and FP was 83.7 and 83.4 minutes versus XELOX and XP was 33.7 and 39.8 minutes respectively. The average pharmacy dispensing time for FOLFOX and FP was 25.3 and 71.4 minutes versus XELOX and XP was 18.7 and 19.9 minutes respectively. The total time saved for each patient for a 24-week cycle in FOLFOX versus XELOX was 734.8 minutes in nursing and 154.0 minutes in pharmacy as well as in FP versus XP was 182 minutes in nursing and 269.2 minutes in pharmacy. Nursing and pharmacy could potentially spare 3.3 full time equivalent (FTE) and 1.5 FTE if all AEGC patients were converted to capecitabine-based chemotherapy. **CONCLUSIONS:** Capecitabine-based chemotherapy regimens saved in both nursing and pharmacy time as compared to traditional 5-FU based IV chemotherapy in the Hong Kong public hospital setting.

PCN146
WORKFORCE PARTICIPATION AND PRODUCTIVITY LOSSES AFTER HEAD AND NECK CANCER
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OBJECTIVES: There has been no estimate of the productivity losses associated with head and neck cancer (HNC) conducted using bottom-up data, or beyond premature mortality. The aim of this work is to investigate workforce participation, and estimate the productivity losses associated with temporary and permanent work absence, reduced work hours, and premature mortality in individuals with HNC in Ireland. **METHODS:** Survey data were collected from a cancer registry identified cohort of individuals in Ireland diagnosed with head and neck cancer between January 1994 and December 2011. Data collected included employment status at time of diagnosis and workforce participation patterns following diagnosis. These data were combined with population-level survival estimates and national wage data to estimate the value of temporary and permanent work absence, reduced work hours and premature mortality using a Human Capital Approach. **RESULTS:** Of the survey respondents, 276 were in paid work at the time of diagnosis. 88% had time off following diagnosis, with 63% of these returning to work. The mean (median) time off work was 9 months (6 months), range of 0 to 65 months. Seventy percent of individuals returning to work reported reducing the hours they worked, by an average of 20 hours per week. Preliminary results show the average productivity losses per person associated with temporary and permanent work absence and reduced work hours are €222,000. Productivity losses associated with premature mortality and the results of sensitivity analyses to test discount and wage growth rates will also be presented. **CONCLUSIONS:** Head and neck cancer and its treatment can have a profound impact on workforce participation. This affects not only the individuals' and their families, but also society in terms of productivity costs. These costs should be considered in economic evaluations of cancer treatments and health service delivery in this population.

PCN147
HOSPITAL RESOURCES CONSUMPTION ASSOCIATED WITH TRASTUZUMAB TREATMENT IN BREAST CANCER IN PORTUGAL
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OBJECTIVES: Determine the costs associated with the preparation and administration, considering the material resources (MR) consumption and time spent by the health care professionals (HP), of Her2 positive breast cancer treatment with trastuzumab intravenous (iv) and to estimate the difference compared with a subcutaneous (sc) formulation. **METHODS:** Data were collected in face to face interviews with the pharmacist and nurse responsible for the preparation and administration of trastuzumab in each hospital. The cost of the HP time was calculated by multiplying the value of each HP hour by the average time of each procedure; MR costs were determined based on the values presented in official sources or in price table provided by the manufacturer. **RESULTS:** Five public and two private Hospitals from mainland Portugal, with an average of 12 patients with HER2 + breast cancer treated with trastuzumab iv, per week, participated in the study. The average time spent by the HP in trastuzumab preparation and administration was 79 minutes for iv and 18 minutes for sc. Per treatment cycle, the estimated average overall cost of each treatment was €43.22 (HP - €26.01; MR - €17.21) for iv, and €3.18 (HP - €3.13; MR - €0.05) for sc. Considering the total course of treatment (18 cycles), the treatment with trastuzumab iv is estimated at €777.96 versus €57.19 on sc treatment. **CONCLUSIONS:** Trastuzumab sc formulation would potentially allow savings of approximately €720 per patient, and provide an important benefit to the patients. Trastuzumab sc would also contribute to maximize the efficiency and effectiveness of health resources. This study presents a limitation regarding the subjectivity inherent to costs determination based on answers given by the HP. Moreover values may be underestimated due to lack of information regarding fixed costs.

PCN148
RESOURCE USE OF NON-SMALL CELL LUNG CANCER IN SLOVAKIA
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OBJECTIVES: Data on economic burden of advanced or metastatic non-small cell lung cancer (NSCLC) are lacking in Slovakia. Therefore, the objective of this cost of illness study was to measure the resource utilisation and the costs associated with treating advanced or metastatic NSCLC in Slovakia and provide a basis for cost-effectiveness evaluations. **METHODS:** The project was run in two phases: in the first phase an Expert panel took part in the survey and developed the diagnostic and treatment algorithms to reflect the local medical practice and quantify the use of resources associated with anticancer drug treatment, management of adverse events and best supportive care. Then, in the second step, 2012 management costs were applied to the resources. All types of health care used in the NSCLC management were evaluated (outpatient and inpatient visits, diagnostics, prescription drugs and examinations). The analysis was performed from the Slovakian health insurance perspective reflecting direct medical costs only. The structure of cost data follows the requirements of pharmaco-economic modelling in NSCLC. **RESULTS:** Monthly costs of advanced or metastatic NSCLC management during the active treatment (before progression) count for €1055.67, during the disease progression €1101.21 and on the best supporting care €1561.22. The most frequent regimens were cisplatin+gemcitabine (20.6%) and cisplatine+pemetrexed (19.1%) in the first line, erlotinib (49.1%) in the second line and gemcitabine (29.6%) in the third line. The most costly side effects were renal toxicity (€1060.85), febrile neutropenia (€902.92), hemoptysis (€717.08), anaemia (€668.84), pain (€631.34), leukopenia/neutropenia (€629.58), dyspnoe (€628.35), thrombocytopenia (€578.60), nausea/vomiting (€562.72) and fatigue (€523.19). **CONCLUSIONS:** Cost-effectiveness must be demonstrated in order to get reimbursement in Slovakia and local resource use data are key drivers for health economic modelling and can guide resource allocation decisions in NSCLC. This study provides important information to support these decisions.

CANCER – Patient-Reported Outcomes & Patient Preference Studies

PCN149
ADHERENCE RATES FOR INTRAVENOUS CHEMOTHERAPY REGIMENS TO TREAT COLON CANCER
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OBJECTIVES: It is widely thought that adherence rates to intravenous (IV) chemotherapy regimens for colon cancer are high. However, there are no known formal assessments of this issue. **METHODS:** A retrospective analysis was performed using the Optuminsight Oncology claims database. Patients aged 18 years and older, diagnosed with CRC between July 1, 2004 and December 31, 2010, who were insured by a commercial health plan were included in the study. Adherence to the following IV chemotherapy regimens was assessed using the National Comprehensive Cancer Network (NCCN) guidelines as the standard for expected cycle/regimen duration: FOLFOX, FOLFOX+bevacizumab, FOLFIRI, and FOLFIRI+bevacizumab. Adherence was assessed using the medication possession ratio (MPR), calculated as the number of days a patient was covered by their chemotherapy regimen, according to NCCN guidelines, divided by the number of days elapsed from the first to the last infusion of that regimen. **RESULTS:** A total of 46,941 chemotherapy cycles in 6,880 patients were analyzed. Overall, adherence rates to IV chemotherapy was fairly high, with mean MPR ranging between 0.84 and 0.88 for these regimens. However, a substantial proportion of patients for each regimen experienced low adherence. Twenty five percent of patients receiving FOLFOX, FOLFOX+bevacizumab, and FOLFIRI+bevacizumab regimens experienced MPR<0.8. Additionally, approximately 35% of patients receiving FOLFIRI experienced an MPR<0.8. At least 10% of patients receiving FOLFOX regimens had an MPR less than 0.7; while at least 10% of patients receiving FOLFIRI regimens had an MPR of less than 0.6. **CONCLUSIONS:** Although overall rates of adherence were fairly high, a substantial subpopulation experienced low adherence to each of these IV regimens per NCCN guideline recommendations. The reasons for the low adherence rates need to be explored as this could have an impact on efficacy. These results also highlight the drawback of relying solely on summary statistics at the population level.

PCN150
PERSISTENCE IN PATIENTS WITH BREAST CANCER TREATED WITH TAMOXIFEN OR AROMATASE INHIBITORS- ANALYSIS BASED ON ONCOLOGY ANALYZER DATABASE
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OBJECTIVES: Lack of non-compliance is often underestimated in breast cancer treatment. The aim of our study was to analyze the persistence with tamoxifen (TAM) and aromatase inhibitors (AI) in women with breast cancer (BC) and to identify reasons of treatment discontinuation and determinants of non-persistency. **METHODS:** We used data of the Oncology Analyzer database, which includes individual information on patient history related to the treatment of patients across all cancer types. This enables a complete overview of cancer patient care from diagnosis onward, facilitating research in areas such as treatment changesn, dosing and regimen compliance, market sizing and off-label use. We identified 7063 breast cancer patients with a start of TAM or AI therapy from 1990 until 2011 and with a treatment duration of at least 365 days. **RESULTS:** After

one year of follow up, 11.2% of TAM, and 18.4% of AI treated patients discontinued their treatment. In these patients with , the reasons for stopping were: progressive disease including local and distant progression (68.1%), side effects (15.5%), patient's choice (8.6%) and other reasons (7.8%). The multivariate hazard ratios of the cox regression models showed that patients younger than 50 were most likely to discontinue initial therapy when compared with the reference group of women over 70 years of age (HR: 2.30, p=0.01). In contrast, patients treated in gynaecologist or oncologist practice had significantly longer persistence than patients who obtained their prescriptions in general hospital or academic cancer facility (HR: 0.47, p=0.02). Additionally, patients with therapy initiation in gynecological practices had significantly longer persistence than in oncological practice (HR: 0.68, p=0.04). Additionally, metastases were associated with strongly increased risk of treatment discontinuation (HR: 3.81, p<0.01). **CONCLUSIONS:** The proportion of breast cancer patients with therapy discontinuation within first year after therapy start is high and needs to be significantly increased to improved outcome in clinical practice.

PCN151

HEALTH STATE UTILITY VALUES IN ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS

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OBJECTIVES: Lung cancer has an important impact on Health related Quality of Life (HRQoL). LUCEOR2 is a multi-country prospective study which aimed to measure HRQoL and EQ-5D utility values in Non Small Cell Lung Cancer patients (NSCLC). Previous results presented utility values calculated on the whole LUCEOR2 population and on the French subgroup using the UK tariff for the EQ-5D. Our aim was to calculate utility values with the French tariff for the application in French cost-effectiveness studies. **METHODS:** Data from the LUCEOR2 study that included all patients from participating countries which provided a meaningful sample size for data analysis. Patients were stratified in 7 health states defined by the response of treatment (progressive or stable) and the line of treatment (1st, 2nd, 3rd/4thand BSC). EQ-5D health states were valued using the French tariff. **RESULTS:** A total of 319 patients were recruited in LUCEOR2, HRQoL were available for 258 of them (73 in France). Mean utilities for progression-free patients on 1st, 2nd and 3rd/4th lines were 0.690 (n=116; standard deviation [sd]: 0.258), 0.697(n=46; sd: 0.221) and 0.609(n=25; sd: 0.324) respectively. For patients with progressive disease, values were 0.608(n=26; sd: 0.237), 0.550(n=17; sd: 0.353) and 0.418(n=21; sd: 0.399). Overall, patients with progressive disease had lower mean utility than patients with stable disease (0.530 vs. 0.682 ; p=0.001). Utilities calculated using the French EQ-5D tariff are lower than the utilities calculated using the UK tariff. **CONCLUSIONS:** This study presents the French utility values for patients with NSCLC. It demonstrates the impact of the disease on the HRQol. Further investigations will be made on the potential differences in scores between countries.

PCN152

ESTIMATING HEALTH STATE UTILITIES FOR PATIENTS WITH RELAPSED/ REFRACTORY (R/R) HODGKIN LYMPHOMA (HL) AND SYSTEMIC ANAPLASTIC LARGE-CELL LYMPHOMA (SALCL) IN MEXICO AND BRAZIL

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OBJECTIVES: Benefits of treatment can be measured by utility values. Health utilities typically range between 0 (dead) and 1 (full health) and reflect health-related quality of life (HRQL) in a given health state. Societal values for health states can be captured using the time trade-off (TTO) methodology. Currently, no values exist for health states depicting stages of R/R HL and sALCL for Latin American countries. The aim of this study was to collect utility values from members of the public in Mexico and Brazil for R/R HL and sALCL health states. **METHODS:** Health states were developed using recognized methods, including a literature review, patient and clinician interviews, and cognitive debriefing. States included stages of R/R HL and sALCL (complete response [CR], partial response [PR], stable disease, and progressive disease), and adverse events (AEs) including B-symptoms, acute/chronic graft-versus-host disease (GVHD), and grade I/II or grade III peripheral sensory neuropathy (PSN). Members of the public in Mexico (n=100) and Brazil (n=101) valued each health state using the TTO methodology. **RESULTS:** Participants showed a clear preference for the treatment response states; CR was valued as the state least likely to affect HRQL, with utility gains of 0.13–0.14 over stable disease. The experience of any AE was associated with a large decline in quality of life. The most burdensome AEs were acute GVHD and grade III PSN. Experiencing acute GVHD gave a disutility from stable disease of 0.190 (for Brazil) and 0.125 (for Mexico). Only minor discrepancies existed between the mean utilities for the two countries, the largest being for PR (Mexico, 0.633; Brazil, 0.717). **CONCLUSIONS:** Societal valuation of health states for R/R HL and sALCL revealed the notable perceived benefit of a treatment response and the significant disutility associated with AE experience. Utility values for Mexico and Brazil were broadly consistent.

PCN153

UTILITY VALUES FOR PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMORS (GIST) TREATED WITH REGORAFENIB VERSUS PLACEBO IN THE PHASE III GRID TRIAL

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OBJECTIVES: To estimate utility values by health states for regorafenib and placebo-treated subjects from the phase-3 *GIST – Regorafenib In Progressive Disease* (GRID) trial, and test the assumption that utility values remained constant over successive cycles of treatment in the same health state. **METHODS:** The GRID study included a double-blinded phase, plus an open-label regorafenib phase for those whose disease progressed. The EQ-5D index was evaluated using paired-samples comparison as the primary analysis, and repeated measures as a sensitivity analyses. **RESULTS:** A total of 185 subjects were included; 63% males, with an overall average age of 58 years; 55% received study treatment as 3rd-line, the rest as 4th-line or later. 67% were randomized to receive regorafenib as initial double-blind therapy. Average utility at baseline was 0.767 units. There were no differences in baseline characteristics or EQ-5D for either treatment arm, or those whose disease progressed. The paired-samples analysis compared progression-free EQ-5D index versus any first, post-progression assessment. Of those with available data (N=77) there was a difference of -0.120 units (p=0.001). In the repeated analysis, the Δ-EQ-5D between progression-free disease and disease progression (in double-blind phase) was -0.041 units (p=0.051). The mean EQ-5D index following discontinuation of open-label treatment due to secondary progression was much lower, with a difference of -0.231 units (p<0.001). Whilst adjusting for disease status and treatment, the cycle number did not significantly influence the EQ-5D index (p=0.341). **CONCLUSIONS:** Heath-related utility remained stable over successive treatment cycles after controlling for disease status and treatment type, suggesting that for subjects treated with regorafenib who remained progression-free, that active treatment did not lead to deterioration in utility. Due to the cross-over design, the repeated measures analysis did not contain a homogenous, group of people whose disease had progressed. Thus, the paired-sample analysis provides a better estimate of utility.

PCN154

ASSOCIATIONS BETWEEN OVERALL CARE EXPERIENCE RATINGS AND UTILITY AND PSYCHOLOGICAL WELL-BEING IN MEN RECENTLY DIAGNOSED WITH PROSTATE CANCER: FINDINGS FROM A POPULATION-BASED STUDY

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OBJECTIVES: Patient experience is increasingly recognised as an important measure of quality of care. A few studies have suggested that patients who report higher levels of satisfaction with care also have higher quality-of-life and higher psychological wellbeing, and are more likely to cooperate with treatment. In Ireland, this area is under-researched. The PiCTure 2 study aimed to assess the care experiences of men recently diagnosed with prostate cancer – the most common cancer among men in Ireland - and investigate associations between experiences and health-related quality-of-life (utility) and psychological wellbeing (depression, anxiety and distress). **METHODS:** Men diagnosed with invasive prostate cancer (ICD10 C61) 5-20 months prior to study commencement were identified through the National Cancer Registry. The patient experience questionnaire was based on the Prostate Care Questionnaire (Baker et al. 2007), modified for Ireland. Utility and psychological wellbeing were assessed using the EQ5D-5L and Depression Anxiety and Stress Scale (DASS-21). The questionnaire was administered by post to 2,180 men during January-April 2013. EQ5D-5L responses were converted to EQ5D-3L health states and valued with UK valuations. **RESULTS:** A total of 1499 valid questionnaires were received (response rate=70%). Men rated their overall care very highly; however, there were variations with those (i) further from diagnosis, (ii) in poorer health, (iii) younger, (iv) with third level education and (v) with private health insurance significantly more likely to report poorer care experiences. Almost half of men reported maximum utility scores; one-fifth had depression, one-fifth anxiety and one-eighth stress. Lower global experience scores were significantly associated with lower utility values and poorer psychological well-being (p<0.001). **CONCLUSIONS:** While men recently diagnosed with prostate cancer report quite high overall care experience ratings, variations were reported and associations with lower utility and psychological well-being were observed. These results provide further rationale for initiatives to improve quality of care.

PCN155

UTILITY MAPPING OF THE EORTC QLQ-C30 ONTO EQ-5D IN PATIENTS WITH SOFT TISSUE SARCOMA

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OBJECTIVES: The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) is one of the most commonly used quality of life instruments in clinical trials of anti-cancer agents. Here we present an algorithm for mapping between the QLQ-C30 and EQ-5D preferences in an adult population with advanced soft tissue sarcoma (aSTS) who participated in the PALETTE trail, building upon mapping work performed in other tumours. **METHODS:** Data from the PALETTE trial assessing pazopanib versus placebo for the treatment of aSTS (n=369) was used, where EQ-5D was assessed at baseline and week 4, and the QLQ-C30 at baseline plus weeks 4, 8 and 12. Ordinary least squares (OLS) and generalised linear model regression using a generalised estimating equations (GLM/GEE) approach was employed with the EQ-5D disutility value as the dependent value. A variety of model forms were tested with different link functions and error term distributions, as well as using two stage models and including factors other than QLC-C30 terms (i.e., age, sex, ECOG status). **RESULTS:** There was relatively little variability in the root mean square error (RMSE) and R-squared across 28 different models tested, with the RMSE ranging from 0.16 to 0.18 and the R-squared ranging from 0.54 to 0.63. Using GLM/GEE vs. OLS, adding non QLQ-C30 terms, two-stage models, and squared terms for QLQ-C30 scores all improved R^2, albeit slightly. All the models overestimated the disutility for assessments with zero disutility and underestimated the disutility for assessments with large disutilities, as has commonly been reported for such algorithms. **CONCLUSIONS:** The mapping algorithms tested had reasonable predictive validity. These algorithms were used in cost-effectiveness evaluations of pazopanib in aSTS patients and may be useful for future cost-effectiveness evaluations of other therapies for this indication.

PCN156

COMPARATIVE RESPONSIVENESS OF DIRECT AND MAPPED SF-6D PREFERENCE-BASED MEASURES IN COLORECTAL CANCER

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OBJECTIVES: This study examined the responsiveness of preference-based measures based on the anchor of self-reported change in general health condition of patients with colorectal cancer (CRC). **METHODS:** A baseline sample of 333 patients was recruited at the specialist outpatient clinic of academic teaching hospital in Hong Kong between September 2009 and July 2010, and was surveyed prospectively at 6-month follow-up. SF-6D preference-based indices were derived from the generic SF-6D measure ($SF\text{-}6D_{Direct}$), from the Short Form-12 Health Survey ($SF\text{-}6D_{SF\text{-}12}$) and also mapped from the condition-specific Functional Assessment of Cancer Therapy-Colorectal ($SF\text{-}6D_{FACT\text{-}C}$). The responsiveness of three measures was assessed using the internal responsiveness and external responsiveness. The 95% bias-corrected and accelerated bootstrapping confidence intervals were performed to compare the internal responsiveness statistics measured by standardized effect size, standardized response mean, and responsiveness statistic. External responsiveness was evaluated by receiver operating characteristic (ROC) curve analysis that examined the ability to detect score changes with global health condition changes or discriminate between the worsened and unchanged/improved groups. **RESULTS:** Over half of patients reported no change in global health condition based on the self-reported anchor, whilst 15.1% and 32.9% of patients rated better and worse in current health condition compared to baseline respectively. In worsened group, internal responsiveness was satisfactory for the $SF\text{-}6D_{Direct}$ and $SF\text{-}6D_{FACT\text{-}C}$ preference-based indices. The $SF\text{-}6D_{SF\text{-}12}$ and $SF\text{-}6D_{FACT\text{-}C}$ indices were significantly more responsive to detect positive changes than the $SF\text{-}6D_{Direct}$ index in improved group. The $SF\text{-}6D_{Direct}$ and $SF\text{-}6D_{FACT\text{-}C}$ indices were more externally responsive based on ROC curve. The $SF\text{-}6D_{FACT\text{-}C}$ index was generally more responsive to changes in health status compared with other indices. **CONCLUSIONS:** Direct SF-6D measure was more responsive than mapped preference-based measures in improved group but the direction was reversed in worsened group. Use of a preference-based index mapped from a condition-specific measure captures both negative and positive important changes in HRQOL score among CRC.

PCN157

QUALITY OF LIFE IN PATIENTS WITH METASTATIC COLORECTAL CANCER (MCRC): A UTILITIES STUDY IN THE UNITED KINGDOM AND THE NETHERLANDS

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OBJECTIVES: To elicit utility values from EQ-5D for patients with various stages of mCRC. **METHODS:** An observational cross-sectional study consisting of one-time EQ-5D completion at enrollment was conducted in five hospitals in The Netherlands and the United Kingdom (UK). Patients were categorized into stable or progressed cohorts based on investigator assessment. Patients with mCRC were eligible if on second or subsequent lines of treatment or best supportive care [BSC], received prior oxaliplatin, no prior irinotecan, and had Eastern Cooperative Oncology Group (ECOG) performance status scores of 0-2 at second line initiation similar to the VELOUR trial. Chart data on patient demographics, clinical history, prior/current treatments, serious adverse events (SAEs) were collected. Average utilities were estimated; uni- and multivariate analyses were conducted. **RESULTS:** A total of 75 patients were enrolled, 42 patients stable on second line or third line following an AE on second line and 33 progressed patients. Mean age was 63 (standard deviation [SD]=10); 52% male. Most patients in the stable (98%) and progressed (88%) cohorts had ECOG scores of 0-1 at enrollment. 7% and 15% of patients in stable and progressed cohorts respectively had ongoing SAEs at enrollment. Mean utility scores were 0.741 (SD=0.230) and 0.731 (SD=0.292) for stable and progressed patients respectively. Higher proportions of patients reported increased anxiety/depression (36% vs. 12%) and fewer problems with daily activities post-progression (64% vs. 38%). 83% and 42% of patients in stable and progressed cohorts respectively, were on treatment at enrollment. **CONCLUSIONS:** While the majority of the stable cohort had good performance status and few SAEs ongoing at enrollment, utility values were not much higher compared to the progressed cohort. Higher values in the progressed cohort may be attributed to exclusion of patients in palliative care centers, radiological versus symptomatic disease progression and patients remaining on treatment, having few SAEs and good performance status at enrollment.

PCN158

UTILITY VALUES USED IN NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE) TECHNOLOGY APPRAISALS OF MEDICINES FOR 4 METASTATIC CANCERS

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OBJECTIVES: National Institute for Health and Care Excellence (NICE) considers the quality-adjusted life year (QALY) to be the most appropriate generic measure of health benefit that reflects both mortality and health-related quality of life effects. The QALY is the sum of a person's length of life in each health state multiplied by a quality-adjustment weight (that is, utility value) associated with that health state. Cost-effectiveness results are often sensitive to the choice of utility value, but relevant and comparable utility values are not always available leading to debate about the most appropriate utility values to include. The objective of the research was to review the health-related utility values used in economic models across NICE technology appraisal guidance for 4 metastatic cancers. **METHODS:** A cross-sectional review of manufacturer submissions and reports produced by independent academic groups was carried out to identify the health-related utility values used. Information relating to the methods used to elicit utility values that were selected for use in cost-effectiveness analyses were compared with methods specified by NICE as the reference case in its 2004 and 2008 Methods Guides. The review focused on guidance published before June 2013 for medicines treating metastatic breast cancer, metastatic colorectal cancer, metastatic hormone-refractory prostate cancer and metastatic non-small-cell lung cancer. Nineteen technology appraisals published between March 2002 and August 2012 met the inclusion criteria. **RESULTS:** Common themes or variations that exist between utility values selected by manufacturers and independent academic groups for each metastatic cancer and between the 4 metastatic cancers were analysed. The research also explored the methodological issues that were considered by the Appraisal Committee relating to the selection of utility values. **CONCLUSIONS:** Therefore, this research provides insight to the methodological considerations regarding incorporation of utility values that have informed health technology assessment decision-making in England for 4 metastatic cancers.

PCN159

PATIENTS' AND CAREGIVERS' PREFERENCES FOR BONE METASTASES (BM) TREATMENTS IN THE UNITED STATES

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OBJECTIVES: Patients with BM from solid tumors often experience skeletal-related events [SREs]; commonly defined as pathologic fracture, radiation or surgery to bone, and spinal cord compression. Several bone-targeted agents are approved for the prevention of SREs. This study evaluated US patients' and caregivers' preferences in relation to available treatment options in the US. **METHODS:** Adults with or adult caregivers of patients with a self-reported physician diagnosis of BM from a solid tumor completed a web-enabled discrete-choice experiment survey comprising a series of 10 choices between pairs of hypothetical medication profiles. Each profile included 6 medication attributes within a pre-defined range (primarily based on prescribing information and real-world practice): months until first SRE (10, 18 and 28 months); months until worsening of pain (3, 6, 10 months); annual risk of osteonecrosis of the jaw (ONJ; 0%, 1%, 5%); annual risk of renal impairment (0%, 4%, 10%); mode of administration (subcutaneous injection, 15-minute infusion, 120-minute infusion); and monthly out-of-pocket cost to patients ($25, $75, $150, $330). Choice questions were based on an experimental design with known statistical properties. The survey was pretested with 15 patients and 11 caregivers using open-ended interviews. A separate main-effects random parameters logit model was estimated. **RESULTS:** In total, 187 patients and 197 caregivers completed the survey. Among the attribute levels included, out-of-pocket cost to patients, risk of renal impairment, and months until first SRE were most important to both patients and caregivers. For those attributes, better outcomes were preferred to worse outcomes ($p<0.05$) except that risk of renal impairment between 4% and 10% was not significant for patients; costs between $25 and $75 were not significant for either group. **CONCLUSIONS:** When considering treatment choices for preventing skeletal complications associated with BM, patients and caregivers focused mainly on out-of-pocket cost to patients, avoiding renal impairment, and delaying SREs.

PCN160

CLINICAL OUTCOME ASSESSMENTS IN FDA ONCOLOGY LABELS SINCE 2010

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OBJECTIVES: In 2009, the FDA released Final Guidance on Patient-Reported Outcomes (PROs) and has stated that standards for PROs apply equally to Clinician and Observer Reported Outcomes (ClinROs, ObsROs; collectively, clinical outcome assessments - COAs). The objective was to survey labels for oncologic drugs approved in the three years since the "PRO Guidance" was finalized and to characterize any COAs in these labels. **METHODS:** CenterWatch maintains a list of FDA approved drugs following definitions established by the Tufts Center for the Study of Drug Development, including only drugs or NMEs newly approved by the FDA Center for Drug Evaluation and Research. From 2010 to the time of this review in 2013, 45 oncologic drugs were approved by the FDA. The FDA approved product labels of each of these drugs was reviewed and each was tabulated according to its inclusion of COAs. **RESULTS:** Few of the approved product labels reviewed included any reference to, much less data collected using PROs, ClinROs, or ObsROs. Several (e.g., carfilzomib) had clear statements to indicate that approval for the product was based on a predefined response rate rather than any "improvement in survival or symptoms." The notable exceptions are fentanyl sublingual tablets and spray and abiraterone, with PRO data on pain. **CONCLUSIONS:** There are several explanations for the low rate of COAs in oncology labels, especially that oncology trials tend to be unblinded. The FDA has stated that open label designs cannot support PRO claims. Yet there is still a heavy reliance on outcomes such as progression free and overall survival. Three labels were identified with PRO data on pain, two of which were specifically indicated for pain rather than tumor control. This review suggests there are opportunities for sponsors and the FDA to increase the degree to which the patient's voice is heard during the regulatory decision making process.

PCN161

SYSTEMATIC REVIEW OF PATIENT REPORTED OUTCOMES IN CHRONIC MYELOID LEUKEMIA

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OBJECTIVES: Patient reported outcomes (PRO) are becoming useful tools for collecting and generating evidence for new medical products to show improvements in health-related quality of life (HRQoL). Chronic myeloid leukemia (CML) is now a chronic disease in which HRQoL is becoming important. The objective of this study was to review, analyze, and understand trends in the PRO instruments used in patients with CML. **METHODS:** A systematic literature search for CML randomized controlled trials (RCTs) with PROs endpoints was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interven-

tions, year, PRO instrument, and results for PROs. Analysis was conducted to identify trends in commonly used PRO instruments and results were categorized as positive, neutral, or negative. **RESULTS:** Eight RCTs with a total of 3,342 patients were identified. In these studies, there were eight different PROs instruments identified: FACT-Leu, SF-36, FSI, PSQI, MSAS-SF, FACT-BRM, EQ-5D, and MDASI-CML. The most commonly used instruments were FACT-Leu (used in 1,336 patients) and FACT-BRM (used in 1,199 patients). Five studies reported positive results with improvement in quality of life (QoL) symptoms versus comparator treatments. Two studies reported results highlighting significant deterioration in QoL versus patients with no cancer. One study reported QoL in various types of CML and showed significant deterioration in patients with chronic phase CML versus those with acute and blast phase CML. Studies also identified two QoL domains, depression and fatigue, which matter most for patients with CML. **CONCLUSIONS:** Patients with CML have significant deterioration in their QoL. PRO instruments such as FACT-Leu and FACT-BRM can aid in generating evidence to show which therapies improve patient QoL.

PCN162

PATIENT REPORTED OUTCOMES IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

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OBJECTIVES: Patient reported outcomes (PRO) are becoming useful tools for collecting and generating evidence for new medical products to show improvements in health-related quality of life (HRQoL). Castration-Resistant Prostate Cancer (CRPC) is a chronic disease with high importance for patient HRQoL. The objective of this study was to review, analyze, and understand trends in the PRO instruments used in patients with CRPC. **METHODS:** A systematic literature search for CRPC randomized controlled trials (RCTs) with PROs endpoints was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interventions, year, PRO instrument, and results for PROs. Analysis was conducted to identify trends in commonly used PRO instruments and categorize results as positive, neutral or negative. **RESULTS:** Ten RCTs with a total of 5,797 patients were identified. In these studies there were thirteen different PROs instruments were identified that were FACT-P, FACT-G, BPI-SF, EQC30, EQPR25, FLIC, SDS, SUF, PDA, IPDA, PROSQOLI, SF-36, and QOLM-P14. The most commonly used instrument were FACT-P (used in 4,297 patients) and EQC-30 (used in 1,091 patients). Six studies reported positive results with improvement in quality of life symptoms (QoL) versus comparator treatments. Fours studies reported results with deterioration in (QOL). Three studies reported improvement in pain scores. **CONCLUSIONS:** Patients with CRPC have relatively longer survival and hence QoL is an important consideration for these patients. PRO instruments such as FACT-P and EQC-30 have been commonly used to generate evidence to show which therapies improve patient QoL.

PCN163

ARE "DIZZY" AND "LIGHTHEADED" THE SAME CONCEPT OR SEPARATE CONCEPTS? CHALLENGES IN CONCEPTUAL EQUIVALENCE OF THESE TERMS IN 20 LANGUAGES

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OBJECTIVES: Feeling "dizzy" or "lightheaded" are common concepts in patient-reported outcome (PRO) instruments in a number of conditions. The Functional Assessment of Cancer Therapy – Anemia (FACT-An) subscale contains an item assessing "feeling dizzy (lightheaded)" as one concept while other instruments propose to assess the symptoms as two separate concepts or items. The purpose of this study was to translate and assess conceptual equivalence of this concept across 20 languages (21 countries). **METHODS:** The FACT-An was translated following the FACIT Translation methodology which is consistent with ISPOR guidelines for translation and cultural adaptation of PRO measures (Wild et al., 2005). The translation process for each language consisted of: 2 forward translations by native translators, reconciliation of the forward translations, 1 back-translation by an English-speaker fluent in the target language, 3 reviews by native translators or clinicians, final reconciliation by a native speaking linguist, and harmonization. Interviews were conducted among 456 native-speaking patients in 21 countries. Data were analyzed to assess linguistic and cultural validity of the FACT-An in each language and confirm conceptual equivalence. **RESULTS:** Mean age of the sample (N=456) was 55 years, (range 19-88) and 58% were male. During the translation phase, 12 of the 20 languages translated the concept of dizzy (lightheaded) using only one term, and the remaining 8 languages provided two terms. The rationale was that one word was used to describe this set of symptoms and it would be a complicated explanation to address the second term. The translations were well understood and considered relevant. **CONCLUSIONS:** The majority of languages in this study provided only one term for the concept of dizzy (lightheaded) indicating that it may be problematic to assess the concept as two separate symptoms in future questionnaires in other languages where this concept is not separated as it is in English.

PCN164

PRO CLAIMS IN JAPANESE ONCOLOGY PRODUCT LABELING

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OBJECTIVES: There is a growing use of patient-reported outcomes (PRO) in the US and Europe but little is known about Asia. Oncology in particular is an area of growing interest. This study sought to review PRO labeling within oncology products over the last five years in Japan. **METHODS:** Oncology labels were identified by reviewing the Pharmaceutical and Medical Devices Agency (PMDA) postings of label changes for the past 5 years (2007-2012). For identified products with label changes, labels and Interview Forms (IF) were acquired and reviewed. The IF is used as a supplement to the label in Japan to provide additional data that will not fit within the package insert. Only PROs used for potential promotion were evaluated. Symptoms such as pain listed in the adverse events or safety sections were not included in this review. **RESULTS:** A total of 84 active ingredients had new indications or label changes. After removal of 25 duplicate ingredients (or updated again during this timeframe), 59 labels and IFs were identified and reviewed. No product labels contained PRO information. However, in contrast 20 (34%) IFs contained PRO information. 10 of these IFs only stated that "QOL" or "PRO" was assessed without details on the questionnaires or results. The EORTC (European Organisation for Research and Treatment of Cancer) and FACT (Functional Assessment of Cancer Therapy) were explicitly stated as measures in four and three IFs, respectively. There were also three pain assessments; two Visual Analog Scale assessments and one utilizing the Brief Pain Inventory – Short Form (BPI-SF). **CONCLUSIONS:** Although no oncology labels contained PRO information, the IFs contained PRO information. 1/3 of product information contained a mention of PROs which can be used in discussions with clinicians.

PCN165

CHANGES IN PATIENT-REPORTED OUTCOMES AMONG PEDIATRIC LEUKEMIA AND LYMPHOMA PATIENTS DURING THE FIRST 2-YEARS POST ALLOGENEIC STEM CELL TRANSPLANTATION (ALLOSCT)

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OBJECTIVES: To explore changes in child-reported quality of life (QOL) of pediatric leukemia/lymphoma patients receiving alloSCT. **METHODS:** Hierarchical linear modeling was used to explore trends in select PedsQL 4.0 sub-scales and individual items of 43 children ≥5 years of age. QOL was assessed once pre-alloSCT and on days 100, 180, 365, and 730, post-alloSCT. **RESULTS:** Median age: 13.54 years, Range: 4.66-23.12 years; leukemia: 76.7%; lymphoma: 23.3%; reduced-toxicity conditioning (RTC)/myeloablative conditioning (MAC): 44%/56%; chronic graft-versus-host disease (cGVHD): 27.9%. Emotional and social functioning was stable pre-to-post-alloSCT and comparable to a normative pediatric sample ($p>.05$), whereas physical functioning was 19 points lower pre-alloSCT ($M=67.42$; $p<.01$; $ES=1.26$SD) with improved scores approaching norms by Day +730. 51-65% of children at baseline reported difficulties with sports/exercise, strength, pain, and fatigue. Significant improvements from baseline ($M=51.41$) were observed in sports/exercise at a rate of 1.06 points-per-month (ppm)/12.90 points-per-year (ppy) ($t=2.57$; $p=.01$) and strength ($M=47.47$; $t=2.05$; $p=.04$) at a rate of 0.84 ppm (10.21ppy). Recipients of RTC significantly improved at a rate of 14.04ppy (slope=1.16; $t=2.41$; $p=.02$) compared to children who received MAC (-4.01ppy; slope=-0.33). Similarly gains in strength were significantly better for the RTC group (12.94ppy; slope=1.06; $t=2.25$; $p=.02$) than the MAC group (-10.62ppy; slope=-0.83). Levels of pain ($M=64.82$; slope= 0.05ppm; $t=0.15$; $p=.88$) and fatigue ($M=58.01$; slope=0.39ppm; $t=1.14$; $p=.26$) remained unchanged irrespective of conditioning regimen. Emotional functioning of children ages 8-12 significantly improved from baseline ($M=70.18$; slope=1.78ppm; $t=2.89$; $p=.01$), whereas children ≥13 significantly declined post-alloSCT ($M=72.61$; slope=-1.34ppm; $t=-2.64$; $p=.01$). Presence of cGVHD did not significantly affect outcomes scores. **CONCLUSIONS:** Improvements in exercise and strength were seen with RTC regimens whereas pain and fatigue remained unchanged independent of conditioning regimen. Older children may have more emotional difficulties post-alloSCT. These results highlight the importance of including QOL to monitor patients and further define outcomes for this population.

PCN166

QUALITY OF LIFE IN PATIENTS WITH OSTOMY IN POLAND: MULTICENTRE CROSS-SECTIONAL STUDY USING WHOQOL-BREF QUESTIONNAIRE

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OBJECTIVES: To assess quality of life of Polish patients with a stoma using validated generic questionnaire. **METHODS:** Adult patients with colostomy, ileostomy or urostomy performed in Poland between July 2009 and December 2010 were included. Patients completed satisfaction survey at the discharge from the hospital, and The World Health Organization Quality of Life-BREF (WHOQOL-BREF) generic questionnaire at 3 months after surgery. **RESULTS:** The study involved 1519 patients (71.5%, 16.8%, 11.7% with colostomy, ileostomy and urostomy, respectively). The studied population was highly diversified in terms of: pain and discomfort, dependence on medical treatment and acceptance of physical appearance. 57% of patients with a stoma defined their quality of life as good or very good (mean 3.54 points; range: 1 to 5; SD 0.73). The subjects were characterized by low quality of life assessment in the physical health and psychological domains (53.5 and 60.0 pts.) and by high evaluation in the environment and social relationships domains (69.6 and 70.2 pts.). Respondents highly assessed: the level of social support, home environment, physical environment, personal relationships. Low assessment was related to: sexual activity, ability to work, dependence on medical treatment, financial resources, satisfaction with health. **CONCLUSIONS:** This is the first Polish study on the quality of life of patients with a stoma, based on validated generic questionnaire. The results should help improve standards of care for patients with a stoma.

PCN167

INFLUENCE OF ANXIETY AND DEPRESSION ON 1-YEAR HEALTH RELATED QUALITY OF LIFE IN COLORECTAL CANCER PATIENTS

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OBJECTIVES: To assess the impact of anxiety and depression measured by Hospital Anxiety and Depression Scale (HADS) on 1-year HRQoL measured by EuroQol-3L (EQ-5D) and EORTC-QLQ-C30 on patients with colorectal cancer. This aspect of continuity

of care could be nowadays a major issue **METHODS:** This prospective study carried out in 12 Hospitals. At baseline patients fulfilled EQ-5D questionnaire (utility and VAS scale), EORTC-QLQ-C30 (physical, role, emotional, cognitive and social functioning, and global health) and HADS. One year post-surgical management they completed the EQ-5D and EORTC-QLQ-C30. We used general linear models to establish the influence of baseline anxiety (HADS-A) and depression (HADS-D) on changes in HRQoL, adjusted by baseline score and gender. We have used the recommended cut-off points of HADS ≤7 (normal); 8-10 (uncertain) and ≥11 (problem). **RESULTS:** There were 778 patients. The mean age (SD) was 67.4 (10.4). Males represented the 62.7%. At baseline, in the HADS-A there were 282 (36.4%) of patients scoring higher than 7 points (17.6% higher than 10 points). In the HADS-D 137 (17.6%) scored higher than 7 and 9.3% were higher than 10 points. Both anxiety and depression at baseline influence the changes in EQ-5D, with less gains in patients with more level of anxiety or depression ($p<0.0001$). Regarding the EORTC-QLQ-C30 domains, baseline anxiety level impacts significantly in all domains, except in physical functioning, with gains around 5 to 11 points lower in patients with anxiety problems comparing with those classified as normal (all $p<0.05$). Baseline depression level impacts significantly on changes in role and social functioning, and global health, with gains around 10 to 13 points lower in patients with depression problems (all $p<0.01$). **CONCLUSIONS:** This study supports the importance of providing psychological interventions for cancer patients before surgical management.

PCN168

A PROPOSED 6-ITEM REDUCTION FOR THE EUROPEAN ORGANIZATION FOR THE RESEARCH AND TREATMENT OF CANCER-QUALITY OF CORE QUESTIONNAIRE (EORTC QLQ-C30) - CUBAN GROUP OF TRIALISTS ON EPIDERMAL GROWTH FACTOR (CGT-EGF)

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OBJECTIVES: To develop an unidimensional and short version of the QLQ-C30 to be used as a patient-perceived quality of life in cancer trials. **METHODS:** We analysed data of 873 patients diagnosed with non-small-cell lung cancer who participated in 4 Cuban multicenter trials of immunotherapy against the epidermal growth factor. The analysis followed a 4-step approach. First, we conducted a Mokken nonparametric item response analysis to ascertain the QLQ-C30 dimensionality and separate several scales if appropriate. Second, we conducted a parametric Samejima's graded response model (GRM) to assess the item characteristics and information. Third, we did a confirmatory factor analysis (CFA) to test the scales unidimensionality and to obtain standardised factor loadings to suggest a reduced version of the QLQ. Finally, we assessed the discriminative validity of the reduced version by using receiver-operator curve (ROC) analysis. **RESULTS:** Mokken analysis of the QLQ-C30 resulted in a unidimensional scale, with an overall scalability of 0.43 that defined a medium scale. The unconstrained GRM showed that most items presented appropriate difficulty and discrimination parameters. The CFA supported an underlying unidimensional latent structure for the whole QLQ-C30 (CFI = 0.98; RMSEA = 0.05) with modification indexes pointing to important redundancy of information. The selection of items with standardized factor loadings > 0.70 lead to a 6-item QLQ that showed good discriminative validity against independent criteria of quality of life (ROC area = 0.76; 95% CI = 0.72 to 0.80) as compared with the values for the whole scale (ROC area = 0.70; 95% CI = 0.66 to 0.74). **CONCLUSIONS:** The EORTC QLQ-C6 suggested in this study presents good psychometric properties and includes an unidimensional structure of patient-perceived quality of life.

PCN169

EVALUATING THE BURDEN OF BONE METASTASES (BM) ON PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER (CRPC) AND THEIR TREATING PHYSICIANS: FINDINGS FROM A ROUTINE PRACTICE STUDY IN 13 MEDIUM-SIZED EUROPEAN COUNTRIES

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OBJECTIVES: To evaluate the burden of BM on patients with CRPC and their treating physicians. **METHODS:** A total of 167 physicians (100 oncologists and 67 urologists) completed a prospective 5-day workload form, interview and average of 8 patient record forms (PRFs, October 2012–March 2013) for non-metastatic and metastatic CRPC patients. Data from 142 workload forms, 167 interviews and 1,274 PRFs (including 475 CRPC patients at 'high risk' of BM, 505 CRPC patients with BM only, 102 CRPC patients with BM and VM and 192 CRPC patients with VM only) were included in these analyses. **RESULTS:** Physician interviews showed 92%, 63% and 60% of the physicians believed the greatest patient burden of BM was back pain, reduced ability to perform daily activities and fractures, respectively (from a predetermined list where 'other' was specified). PRF data confirmed that Eastern Cooperative Oncology Group (ECOG) performance status was significantly worse in patients with BM (with/without VM) when compared with patients at high-risk of developing BM ($p<0.0001$). 92% of the patients at 'high-risk' (defined by treating physician) of developing BM (n= 475) had a PSA doubling time (PSADT) ≤6 months. The biggest burden of BM on treating physicians was seeing patient deterioration (70% [n=117]; 67% of oncologists; 75% of urologists), inability to propose effective treatment (57% [n=95]; 60% of oncologists; 52% of urologists), managing complex regimens (29% [n=49]; 27% of oncologists; 33% of urologists) and transferring patients for respite/hospice care (23% [n=38]; 26% of oncologists; 18% of urologists). **CONCLUSIONS:** These data highlight the burden of BM on patients with CRPC and the perceived burden on physicians treating this population. BM are associated with a significant reduction in patients' performance status and an increased burden on the patient. There is a need for treatments to prevent or delay the onset of BM and their associated burden.

PCN170

AN EXPLORATORY ANALYSIS OF THE ASSOCIATION BETWEEN EORTC-QLQ C30 DOMAINS AND PROGRESSION FREE/OVERALL SURVIVAL IN ADVANCED MELANOMA AFTER 12 WEEKS OF TREATMENT ON IPILIMUMAB COMPARED TO GP100 IN A PHASE III CLINICAL TRIAL

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OBJECTIVES: This study analyses the association between health-related quality of life (HRQL) domains and progression free (PFS) and overall survival (OS) for ipilimumab, ipilimumab + gp100, and gp100 alone during the 12 week treatment induction period compared to baseline. The aim of this study was to assess whether outcomes reported in the EORTC-QLQ-C30 summary domains impact the hazard of progressing and/or dying after 12 weeks of treatment. **METHODS:** Data from the MDX010-20 trial, including 676 previously treated patients with unresectable stage III or IV melanoma, was analysed. A domain correlation plot (excluding Global domain) was constructed to determine whether the EORTC-QLQ-C30 domains showed a high level of correlation for baseline scores. It was then used to derive two components summarising fourteen domain scores, Principal Components 1, containing 10 domain scores (Pain, Appetite Loss, Nausea, Finance, Dyspnoea, Constipation, Diarrhoea, Role, Social and Physical) and 2 containing 4 domains scores (Fatigue, Sleep Disturbance, Emotional and Cognitive), based on the correlation level between domains. These two Principal Components were entered as additional covariates in the Cox model for PFS/OS and hazard ratios were determined. **RESULTS:** In the Cox regression model, Principal Component 1 showed a 30% increase in hazard of progression when comparing the upper to the lower quartile of the Principal Component score , while a lower Principal Component 1 score indicated a better HRQL at baseline. It was also showed a rate of death twice as high in the upper quartile than the lower quartile. Principal Component 2 neither affected significantly PFS nor OS. **CONCLUSIONS:** In advanced melanoma treated by ipilimumab compared to gp100, PFS and OS were associated with most of the HRQL domain scores. These findings suggest that poor baseline HRQL could be predictive of poor PFS/OS, while higher baseline HRQL could predict a better outcome.

PCN171

QUALITY OF LIFE (QOL) DURING TREATMENT OF NEWLY DIAGNOSED LOCALLY CONFINED LOW-RISK PROSTATE CANCER (LCLRPC) IN GERMANY: RESULTS OF THE HAROW STUDY

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OBJECTIVES: The optimal treatment choice for preserving QoL of the about 64,000 men diagnosed with prostate cancer each year in Germany still remains unclear. The objectives therefore were to generate long-term information under day-to-day conditions on QoL of men in Germany cared for newly diagnosed LCLRPC using hormonal therapy (HT), active surveillance (AS), radiotherapy (RT), operation (OP), or watchful waiting (WW) – HAROW. **METHODS:** The long-term observational multi-centre HAROW study was undertaken. The urologist provided all relevant clinical data of the patient. The patient provided inter alia data on QoL using the EQ-5D. Utilities derived from the EQ-5D based on the German value set were used to construct quality-adjusted life-years (QALYs). QALYs were discounted by 3% annually and standardised to mean QALYs per patient-year (PY) for each initial treatment strategy. Differences between strategies were tested using the Kruskal-Wallis test (Bonferroni-corrected $p=0.0018$ due to 28 tests). **RESULTS:** Between July 2008 and March 2013, 3063 patients (mean age 67.3 ± 7.5 years) with LCLRPC (T1a–T2c, N0, M0) were included from 257 urologists. Data on QoL were documented by patients as follows (% of patients/strategy): AS n=353 (78%), RT n=291 (77%), HT n=149 (71%), HT+RT n=68 (85%), combination therapy (CT) n=109 (80%), OP n=1167 (71%), other therapy (OT) n=9 (50%), WW n=93 (66%), over a mean time of between 1.6 (OT) and 2.5 years (CT). AS showed the highest undiscounted/discounted QALYs/PY (0.9297/0.9103) followed by OP (0.9289/0.9075), RT (0.9075/0.8878), CT (0.9071/0.8820), OT (0.8954/0.8818), HT+RT (0.8875/0.8699), WW (0.8646/0.8465), and HT (0.8485/0.8292). Compared to HT, QALYs/PY were significantly higher with AS ($p<0.0001$), with OP ($p<0.0001$), and with RT ($p=0.0002$). Tests with undiscounted/discounted QALYs/PY adjusted for age, tumor stage and comorbidity showed no different results. **CONCLUSIONS:** According to the HAROW study, active surveillance yielded the highest QALYs of the different LCLRPC treatment strategies in Germany evaluated.

PCN172

HR-QOL DATA IN THE AMNOG EARLY BENEFIT ASSESSMENT: INDUSTRY AND IQWIG/GBA PERSPECTIVE

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OBJECTIVES: To explore how often and which types of quality of life (QOL) data are included in the dossiers submitted for the AMNOG early benefit assessment and analyze how a drug's effect in QOL is interpreted by the industry and the evaluating committee. **METHODS:** The published value dossiers up to June 15, 2013 and the corresponding benefit assessments were reviewed. Types of QOL data and the statements concerning QOL in the value dossier and the benefit assessments were collected and summarized. **RESULTS:** A total of 46 cases were analyzed. In 6 cases no dossier was submitted. Of the rest, 13 dossiers (32.5%) did not include any QOL data, 13 (32.5%) included disease-specific QOL data only, 5 (12.5%) included generic QOL data only, and 9 (22.5%) both types. The QOL instruments used were considered as valid by the assessors. However, outcomes such as pain severity, fatigue, work productivity, and health care resource use were not regarded as QOL measures. Of 27 dossiers that have included QOL data companies have claimed an added benefit in QOL, either for the whole population or a specific subgroup, in 15 (56%) cases. However, the assessors rec-

ognized the added benefit claim in 2 cases only. In an additional 2 cases no clear scoring was provided for the QOL outcome and in the remaining 11 cases no additional benefit was acknowledged. The main reasons were missing statistical significance of results or the submitted QOL data were regarded as not usable. **CONCLUSIONS:** In a majority of value dossiers companies included QOL data and also most often claimed an added benefit in QOL. However, the assessors have accepted this added value in exceptional cases only. In order to get an added value recognized showing both statistical and clinical significance of results is required.

PCN173

FEASIBILITY OF A SURVEY ON THE WILLINGNESS-TO-PAY FOR COLORECTAL CANCER SCREENING USING SOCIAL NETWORKS

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OBJECTIVES: To investigate the feasibility of a online survey using social media (facebook) to estimate the willingness to pay (WTP) for a new diagnostic blood test to determine the risk of colorectal cancer. According to the approval documents of the manufacturer the new biomarker test shows a better performance, better handling and improved compliance of patients and physicians compared to standard fecal occult blood tests (FOBT). **METHODS:** A standardized questionnaire was accompanied by background information on colorectal cancer and alternative screening approaches. WTP was asked for in categories (e.g. <100 or >100 EUR) and maximum values. Other parameters such as age, sex, insurance status, income, family history of cancer and risk factors were determined in categories. The survey ran for 14 days in November 2012 and was started via 6 facebook accounts with the possibility of further distribution. **RESULTS:** Overall 123 completed questionnaires were submitted anonymously. The average age was 24,2 years and in 94% the monthly income was below 1500 EUR due to their student status. 68% of the participants had cases of cancer in the family and 36% knew about the colorectal cancer. The most important quality aspects of screening tests for were accuracy (69%), handling (14%), price (11%) and the time to result (6%). 24% stated that their WTP is lower than 100EUR and the mean WTP for S9 was 271EUR. Higher income, family history of colorectal cancer and private insurance status were positively correlated with a higher WTP. **CONCLUSIONS:** WTP and patient preference studies via social networks such as facebook are feasible, easy to perform and reveal plausible results. Advantages of online surveys in social networks are that the results are gained voluntarily and anonymously avoiding interviewer bias. Disadvantages obviously lie in a selection of young and healthy populations.

CANCER – Health Care Use & Policy Studies

PCN174

CANCER PATIENTS MAY HAVE A DIFFERENT POINT OF VIEW ON ONCOLOGY DRUG COVERAGE DECISIONS THAN NON-PATIENTS

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OBJECTIVES: Recently a major cancer center in the United States decided not to offer treatment using a newly launched oncology drug citing comparative effectiveness and cost as reasons. This study looked at health care consumer opinions about the decision to restrict treatment options based on outcomes and price. **METHODS:** The nationally representative Truven Health PULSE Healthcare Survey gathered responses from 2,615 US households via landline telephone, cell phone or Internet. Respondents were asked their opinion regarding a decision by providers not to offer a new cancer treatment because it demonstrated the same benefit as an existing drug with the same side effects, but its cost was higher. Demographic data were gathered and respondents were asked if they are being/have been treated for cancer, and if a friend, family member or loved one is being/has been treated for cancer. **RESULTS:** Overall, 40.5% of respondents agreed with the decision; 37.5% disagreed. Agreement with the decision varied with the respondents' exposure to cancer. Those who had a family member, friend or loved one with cancer were least likely to agree (36%), while those who not only had a family member, friend or loved one with cancer, but also had cancer themselves were the most likely to agree (50.8%). Respondents who had cancer themselves with no family member, friend or loved one with cancer or had no experience with cancer were equally likely to agree with the decision (44%) (P<0.0001). **CONCLUSIONS:** Findings suggest that fear and experience may play roles in consumers' opinions regarding restrictions on cancer medications. Individuals who have experienced cancer may place more value on outcomes, side effects, and/or out-of-pocket costs than those with no personal experience or may have more realistic expectations for treatment. Additional research is warranted to better understand the drivers of consumer opinion regarding cancer treatment coverage decisions.

PCN175

ADDITIONAL INVESTMENTS, ADDED VALUE, REAL WORLD EVIDENCE AND ADDITIONAL CLINICAL BENEFIT IN THE CONTEXT OF SUBGROUPS OF SPECIAL INTEREST

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OBJECTIVES: Definition of target profiles for new compounds and lifecycle planning lead to clinical studies in the context of a clinical trial program. Currently subgroups of special interest such as elderly, pediatrics or females/males are normally not separately included in these research programmes, most of the time not even stratified for. The objective of this research is to analyze the inclusion of patient-relevant endpoints in special patient subgroups during the clinical trial programme which would thereafter increase the pricing opportunity of this new compound in the German market. **METHODS:** New oncology therapies which were authorized by the European Medicine Agency (EMA) after January 1, 2011 were included and assessed with respect to their evidence for special subgroups. Regulatory guidelines were compared against the IQWIG evaluation methods with respect to the handling of subgroups and its impact on the clinical benefit assessment. Furthermore GBA decisions and potential price impact with the GKV-Spitzenverband are taken into account for the pricing impact of new evidence with special subgroups based on target profiles developed. **RESULTS:** Overall, ten new compounds were approved by the EMA in the last 2.5 years for which no subgroup trials were presented. Regulatory guidelines and IQWIG methods differ significantly with respect to subgroup handling from a statistical and health policy perspective. Most important clinical trials with a special focus on subgroups of interest could even have a negative outcome on the market access of such a compound with respect to subgroup-only reimbursement (in case of positive subgroup results) or exclusion of subgroups (in case of negative results) based on target profiles included in the analyses. **CONCLUSIONS:** Incentives from a health policy and investment decision perspective are low for the pharmaceutical industry in terms of research focus towards subgroups of special interest. Further research with respect to incentives is needed.

PCN176

DOES PERSONALISED HEALTH CARE (PHC) IN ONCOLOGY REQUIRE NEW APPROACHES TO CLINICAL DEVELOPMENT, REGULATORY ASSESSMENT, AND ECONOMIC EVALUATION?

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OBJECTIVES: To identify the extent to which current approaches to clinical development, regulatory assessment, and economic evaluation of personalised health care drugs in oncology are aligned with real world clinical practice at product launch. To identify and critically evaluate alternative approaches that should be factored into future clinical development and health technology assessment (HTA) planning. **METHODS:** Structured interviews were undertaken with physicians and payers (n=50) to identify the key issues surrounding the phased development and early use of personalised health care drugs in oncology. Analogue analyses were undertaken, based on "treatment tracking", to develop a comparison between theoretical RCT (randomised control trial) evidence based, licensure aligned, utilisation and that observed in real world clinical practice Gap Analyses identified drivers of differences. The utility and limitations of retrospective and prospective observational registries in addressing these were explored. **RESULTS:** Early results indicate that the level of unmet need, the magnitude of incremental clinical benefit, the timing of biomarker testing in the treatment algorithm and, increasingly, the number and prioritisation of diagnostic tests for an increasing number of different biomarkers are drivers of real world utilisation. Differences exist between countries. The greatest differences between theoretical and real world utilisation are in markets where decisions are driven by considerations of relative clinical effectiveness rather than cost effectiveness. Comparative SWOT analyses were developed of current and alternative clinical development, regulatory and health technology assessment systems. These highlight areas where improvements in approach would be beneficial. **CONCLUSIONS:** Additional evidence sources should be used to reinforce the regulatory and health technology assessment of PHC products in oncology with the aim of bringing closer alignment between the RCT approach to drug development and assessment – and the utilisation and outcomes (economic, clinical, and humanistic) seen in real-world clinical practice.

PCN177

THE UNITED STATES PHYSICAN SURVEY TO POPULATE A DECISION-ANALYTIC MODEL FOR THE TREATMENT OF CHRONIC MYELOID LEUKEMIA

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OBJECTIVES: The overall goal of our project is to adapt an Austrian decision-analytic model for the treatment of chronic myeloid leukemia (CML) to the U.S. context. We conducted an electronic survey to gain expert knowledge about the state-of-the-art in CML treatment. **METHODS:** The expert survey was constructed as an online questionnaire and contained 14 questions. The questionnaire was developed in collaboration with ONCOTYROL project partners and distributed to CML experts at the Huntsman Cancer Institute in Utah. Data were generated using Qualtrics and discussed with experts in order to incorporate the findings into the model. **RESULTS:** Four out of six experts (67%) stated that effectiveness of second-line TKI depends on the response to first-line TKI therapy. NCCN and ELN guidelines are the most frequently used guidelines when treating CML patients. Furthermore, expert opinion, literature and personal characteristics influence decision making. Patients younger than 50, or between 50 and 54 years, most frequently receive stem cell transplantation after TKI failure. The recently approved TKIs bosutinib and ponatinib are used by 17% and 100% respectively. Experts stated that quality of life (QoL) on dasatinib is better (17%)/ about the same (50%)/ worse (33%) compared to imatinib. QoL on nilotinib is better (17%)/ about the same (83%) in comparison to imatinib. QoL on ponatinib is better (17%)/ about the same (67%)/ worse (17%) compared to imatinib. Although bosutinib is rarely (67%) used, experts answered that is better (17%) or about the same (17%) compared to imatinib. **CONCLUSIONS:** The results provide valuable insights into the state-of-the-art of CML treatment in the U.S. context. Due to the small sample size and the limitation to the region of Utah, results should be interpreted carefully. However, the responses for ponatinib and bosutinib are particularly valuable for the model due to lack of QoL and long-term data.

PCN178
BURDEN OF HOSPITALIZATION IN PATIENTS WITH ADVANCED LUNG CANCER IN THE UNITED STATES
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OBJECTIVES: To assess the burden of hospitalization in advanced lung cancer patients in the United States. **METHODS:** Oncologists (N=101) actively involved in management of advanced lung cancer in United States were invited to participate in a lung cancer disease specific program. Each consenting physician was asked to complete patient record forms for 12 advanced (stage IIIB/IV) lung cancer patients seen in their practice and receiving 1st, 2nd or 3rd line of therapy for advanced lung cancer. The study period extended from Oct- Dec 2011. Data on hospitalization that included reasons of hospitalization and the length of stay (LOS) over the past year was provided by physicians from patient records. **RESULTS:** Majority of the patients (N=1200) were male (56%), Caucasian (71%) and Stage IV (78%), with an average age of 65 years. Hospitalization records were obtained for 93% (n=1110) of the patients among which 22% (n=248) of the patients ≥1 hospitalization events in the previous year with an average (SD) LOS of 4 (2.4) days and a median LOS of 3 days. The reasons reported for the 293 hospitalization events were disease symptoms (61%), surgery (19%) and therapy side effects (43%). The LOS for surgery related hospitalization (n=57) ranged from 1-12 days (mean (SD): 6 (2.9) days; median: 5 days). Among disease symptoms reported as reasons for hospitalization, the most frequent were pain (51%), dyspnea (47%) and cough (47%) respectively. Among side effects reported as reasons for hospitalization anemia (25%), febrile neutropenia (21%) and fatigue (20%) were most frequently reported. **CONCLUSIONS:** Burden of hospitalization in advanced lung cancer patients is significant in the United States. Innovative therapies with favorable side effect profile that also alleviate need for surgery and are effective in improving lung cancer symptoms could help significantly in decreasing hospitalization burden in advanced lung cancer patients.

PCN179
PERCEPTION OF COUNTRY-SPECIFIC HEALTH CARE REFORM AND CONSIDERATION OF REAL WORLD EVIDENCE IN ROUTINE PRACTICE: SURVEY OF ONCOLOGISTS IN EUROPEAN UNION, UNITED STATES, CHINA AND BRAZIL
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OBJECTIVES: To assess oncologist perception of their country-specific health care reforms and the consideration of 'Real World Evidence' (RWE) when prescribing medications in the EU, US, China and Brazil. **METHODS:** A multi-country cross-sectional survey was conducted in top-5 EU countries (UK, Germany, Spain, France, Italy), US, Brazil and China in February 2013 using an online physician panel in the respective geographies; oncologists were randomly selected for survey participation to be geographically representative in each country. Surveys assessed the oncologist perceptions of health care reforms in their respective countries, and their consideration of the following, when prescribing oncology medications: RWE on product effectiveness/safety, patient quality-of-life (QoL) and product cost/patient affordability. Descriptive statistics are reported. **RESULTS:** A total of 257 oncologists participated in the survey. Specialties included: medical oncology-69%, haemato-oncology-11%, radiation-oncology-9%, surgical-oncology-5%, gynecologic-oncology-3%, pediatric-oncology-2%, other-2%. Geographic distribution of oncologists was: 5EU-36%, US-33%, China-17% and Brazil-14%. Overall, 40% of oncologists indicated that they were 'not sure whether their country's health care reform is heading in the right direction' (5EU:39%, US:40%, China:44%, Brazil:36%); 38% indicated that they were 'concerned of country's health care reform's implications for them and their practice' (5EU:30%, US:50%, China:44%, Brazil:19%); 23% indicated that the health care reform 'did not have enough focus on RWE needs and cost-effectiveness of medications' ((5EU:16%, US:24%, China:37%, Brazil:19%). When prescribing oncology medications, consideration of following attributes 'all the time' differed across the countries (Overall/5EU/US/China/Brazil): RWE on product effectiveness and safety (37%/29%/38%/47%/42%), patient QoL (54%/48%/59%/42%/69%), product cost/patient affordability (23%/15%/20%/42%/28%). **CONCLUSIONS:** Across markets, a significant proportion of oncologists raised concerns regarding their country-specific health care-reforms, and between one-third and half of the oncologists reported considering RWE data while prescribing medicines. As the health care reforms evolve in the studied countries, its actual implications warrant closer scrutiny to alleviate physician concerns and improve care delivery and outcomes.

PCN180
THE EXPECTED HEALTH ECONOMIC VALUE OF USING CIRCULATING TUMOR CELLS TO PERSONALIZE CANCER TREATMENT
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OBJECTIVES: Research has shown that circulating tumor cells (CTCs) in the blood can give valuable information about the prognosis and treatment options in oncology. A new approach, CTC therapeutic apheresis (CTCtrap) is being developed for use in breast and prostate cancer. At the moment it is not clear where in the diagnostic track CTCtrap could be of most value. The goal of this study is to estimate the health impact of using CTCtrap in 1) screening for breast cancer; 2) early staging of tumors; and 3) therapy response monitoring. **METHODS:** A systematic literature study and experts' interviews were used to document the diagnostic track in breast cancer. Headroom analysis and early health economic modelling was used to estimate the health impact of implementing CTCtrap at the three different purposes. **RESULTS:** Dependent on the assumption of sensitivity, the CTCtrap could decrease the total screening costs. Yet, it is expected that this application only has limited clinical utility. In the early staging, the CTC trap can replace the currently used FDG-PET-CT. The CTCtrap could provide additional staging information and therapy can be selected more specifically, eliminating unnecessary costs. Finally, CTCtrap as a monitoring tool enables personalising therapy by analysing discordance in hormone receptor (HR) and Human Epidermal Growth Factor Receptor 2 (HER2) expression in CTCs compared to solid tumors in metastatic breast cancer patients. It is estimated that in total 4,41% of metastatic breast cancer patients could be treated in a more efficient way, leading to increase in progression free survival of 5,59 months. Increase in clinical utility is expected to be the most important consequence of this implementation option. **CONCLUSIONS:** CTCtrap as a monitoring tool is expected to be of most value. In this stage, a more appropropiate prescription of expensive therapies can be administered to patients who are sensitive for these therapies.

PCN181
THE IMPACT OF AMNOG ON ONCOLOGY DRUGS
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OBJECTIVES: The implementation of the 2011 German health care reform (AMNOG) introduced pricing mechanisms which oblige newly launched patented drugs to undergo an early evaluation of their additional benefit by IQWiG, with a final resolution given by the G-BA. Medicines which demonstrate an incremental therapeutic benefit versus an appropriate therapeutic comparator – with an innovation score ranging from 1 to 4 – enter the preferable pricing negotiation system; those failing to prove benefit – a score of 5 or 6 – are relegated to the reference pricing system. The study aims to discern how oncology drugs, which began the process of benefit assessment during 2012, fared under the new system, and whether survival data influenced the decisions. **METHODS:** We reviewed both IQWiG and G-BA documents relating to eight cancer drugs assessed during 2012 to determine whether each drug received a positive or negative early benefit assessment. Reasons for each specific decision were then investigated. **RESULTS:** Of the five drugs qualifying for pricing negotiations, vemurafenib (Roche, Switzerland) was the only drug to demonstrate a statistically significant improvement in overall survival (OS) at the time of assessment. It received the highest innovation score of the five qualifying drugs. For the three drugs not qualifying for pricing negotiations, the G-BA cited an incomplete dossier or issues with comparators as the reason for rejection. **CONCLUSIONS:** Although OS is considered the favoured clinical endpoint, the study results show that this endpoint is not always necessary to enter pricing negotiations. However, when OS is not proven, the G-BA often gave a positive assessment to only a small portion of eligible patients. Additionally, two of the qualifying drugs were orphan drugs, which entails exemption from the need to prove an additional benefit if annual sales are below EUR50 million.

PCN182
DEVELOPING PERSONALIZED MEDICINE DRUGS - INCENTIVES FOR PHARMACEUTICAL COMPANIES
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OBJECTIVES: Stratification of oncology drug therapy by genetic marker diagnostics can reveal additional patient benefit but also might influence the development process of drug manufacturers. The objective of this study is to identify and describe the most important incentives for pharmaceutical companies to develop personalized medicine drugs. **METHODS:** To describe the main factors influencing the decision-making process in the development of personalized medicine drugs. The main factors influencing the process and their priority ranking were determined by structured expert interviews with pharmaceutical companies, test manufacturers and other key stakeholders such as regulatory bodies, reimbursement decision makers and payers. **RESULTS:** In contrast to small companies big international companies constantly look for suitable companion diagnostic tests to select subgroups of high responder. The most important key factor for market success is the extent of clinical efficacy in comparison with competitors respectively the current treatment standard. Stratification of patient populations according to treatment response or frequency of adverse events using biomarker is regarded to increase clinical efficacy of the target indication. The test performance is important due to unsolved safety issues although not regarded as crucial for the success of the drug. In contrast to other stakeholders pharmaceutical companies did not consider personalized medicine to relevantly decrease development costs or marketing efforts respectively to increase the price potential for new drugs. A low prevalence of the remaining patient population after testing is not seen as a factor which might lead to a stop of the development of a new drug by pharmaceutical companies. **CONCLUSIONS:** Genetic stratification is seen as a breakthrough in cancer therapy by pharmaceutical companies and physicians. Due to the current need for improvement of approval and reimbursement processes for personalized medicine approaches in oncology especially in Europe future sales are more difficult to predict.

PCN183
ARE ICER THRESHOLD VALUES MALLEABLE? THE CASE OF LIFE-EXTENDING CANCER TREATMENTS AT THE END OF LIFE
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OBJECTIVES: HTA bodies treat end of life (EOL) conditions differently than other conditions? And if so does this depend on whether they have a specific policy for EOL? **METHODS:** NICE's website was searched for single technology appraisals of cancer drugs evaluated between January 2009 to May 2013 for which NICE's supplementary advice for EOL treatments was accepted. The websites of other agencies – SMC (Scotland), TLV (Sweden), PBAC (Australia), pCODR (Canada, except Quebec) and INESSS (Quebec) – were searched for HTAs of the drugs deemed to have met NICE's EOL criteria. A literature search was performed to identify estimated willingness-to-pay ICER threshold values (WTP-ICER) for each agency and to determine if the agency has a specific EOL policy. These were compared against the final ICERs of the retained HTAs. **RESULTS:** Seventeen drugs were identified for which NICE's EOL supplementary advice was accepted. Several of these were also evaluated by other agencies, but only those with final ICERs below the WTP-ICER were retained:

11 SMC; 9 PBAC; 3 TLV; 4 pCODR; 3 INESS. The literature search revealed the following WTP-ICERs: NICE (20,000 - 30,000 GBP); SMC (30,000 GBP); PBAC (45,000 – 75,000 AUD); TLV (777,000 SEK); pCODR and INESS (50,000 – 70,000 CAD). Of the agencies with specific EOL policies, the number of drugs recommended as cost-effective despite final ICERs greater than the respective WTP-ICERs were 11 (65%) NICE; 5 (45%) SMC; 0 PBAC and 1 (33%) INESSS. The corresponding figures for the agencies with no specific EOL policy were 0 TLV and 4 (100%) pCODR. **CONCLUSIONS:** The evidence suggests some HTA bodies treat EOL conditions differently, however the example of pCODR suggests this need not depend on having a specific EOL policy. In fact, the results for PBAC and INESSS show that having a specific EOL policy is no guarantee EOL conditions are treated differently.

PCN184

TREATMENT PATTERNS OF CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS UNDER THE BRAZILIAN PUBLIC HEALTH CARE PERSPECTIVE

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OBJECTIVES: To identify the chemotherapeutic treatment patterns in patients with chronic lymphocytic leukemia (CLL) treated in the Brazilian Public Healthcare System. **METHODS:** A retrospective longitudinal analysis based on Government administrative claims database (Datasus) was performed from January 2008 to December 2012. Eligibility criteria were patients with CLL (ICD code C911) diagnosed until January 2012 and starting their first chemotherapy regimen from January 2008 to January 2012. This cohort of patients was followed until December 2012, death or loss of follow-up. Patients without interruption during treatment and without change in medication were considered in the same chemotherapy regimen. Descriptive statistics (average, standard deviation and percentage) of treatment regimens, treatment free interval (TFI), age at treatment start, gender and length of treatment were performed. **RESULTS:** A total of 1,538 patients with CLL representing 15,371 APACs (Authorization for High Complexity Procedures) met eligibility criteria. The population cohort comprised 56.6% men with an average age of 67.4±12.1 years. 55.0% of the patients had only one chemotherapy regimen, whereas 44.9% had two and 19.4% had three or more chemotherapy regimens. Time between diagnosis and beginning of treatment was 4.3±7.6 months. The most widely used first chemotherapy regimen was chlorambucil (54.9%), followed by cyclophosphamide, vincristine and prednisolone (CVP) (9.1%), fludarabine and cyclophosfamide (FC) (8.1%) and chlorambucil and prednisone (7.0%). Average length of treatment was 6.3±5.7 months. For second chemotherapy scheme, the most widely used regimen was chlorambucil (45.3%), followed by FC (11.0%), CVP (7.8%), chlorambucil and prednisone (6.2%) and CHOP (3.5%). The average length of treatment was 4.9±3.6 months, with an average TFI of 3.5±5.0 months. **CONCLUSIONS:** Chlorambucil was the most used therapy as both first and second chemotherapy regimen. There was a decreasing of Chlorambucil and an increasing of FC in second scheme. The length of treatment was longer in first scheme.

PCN185

EVOLUTION OF ORAL ANTICANCER TREATMENTS USE IN FRANCE FROM 2004 – 2012: RE-ACTOR STUDY (RETROSPECTIVE ANALYSIS OF CANCER TREATMENTS GIVEN ORALLY)

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OBJECTIVES: Within the last decade market authorizations for oral anticancer treatments (OATs) have increased but no published data are available on their use over time. This analysis aimed at describing the evolution of OATs use in France. **METHODS:** A retrospective analysis was performed from Oncology Analyzer™ (IMS Health, France), a physician survey database covering more than 10,000 cancer patients per year treated in both public and private institutions from multiple French regions. The database includes patient demographics, diagnosis and treatment patterns. Data were extracted for all cancers patients treated by oral and intravenous (IV) anticancer drugs from October 2004 to September 2012. Analyses included active anticancer treatments (chemotherapy, targeted therapy, hormonal-therapy, immunotherapy) excluding supportive care agents. **RESULTS:** The proportion of cancer patients receiving OATs increased from 2,241/7,891 (28%) to 2,410/7,426 (32%). Data showed an increasing use of OATs over time especially among patients aged over 70 years (i.e. 40% in 2004 vs. 46% for patients in 2012). The proportion of OATs among all anticancer drugs (oral and IV) remains stable over time (45.1% in 2005 (41/91) vs. 45.4% in 2012 (54/119). The number of molecules available in oral form was stable except for targeted therapies (4 in 2004 vs. 15 in 2012). Data related to some molecules available in both forms (oral and IV) such as melphalan, fludarabine, topotecan, confirmed the preferential use for the oral route of administration over time. **CONCLUSIONS:** The Re-ACTOR study confirms the increasing uptake of OATs in oncology in France. The number of patients receiving OATs increases over time especially for targeted therapies. This trend draws the attention of the necessity to reinforce measures to accompany the development of OATs in terms of safety and health care delivery, especially for the elderly who require specific attention to provide them with patient support tools and programs.

PCN186

THREE YEARS OF THE GEFITINIB UK SINGLE PATIENT ACCESS (SPA) SCHEME: DURATION OF TREATMENT FOR PATIENTS WITH EGFR MUTATION POSITIVE NSCLC IN NHS CLINICAL PRACTICE

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OBJECTIVES: The UK National Institute for Health and Clinical Excellence (NICE) recommended gefitinib as cost-effective for use first line in locally advanced or metastatic, EGFR mutation positive NSCLC, when supplied via the SPA scheme, based on the mean duration of treatment observed in the IPASS study (8.8 months). The single fixed payment under the scheme is triggered at the order of the third 30-day pack and covers a patient for their total supply of gefitinib treatment. An initial analysis of the first 18 months of the SPA scheme indicated that the length of gefitinib therapy was at least that anticipated by NICE. This study aims to validate the length of therapy in a larger cohort with up to 3 years follow-up. **METHODS:** The SPA administrative database contained information on packs (30-days therapy/pack) dispensed to patients from September 2009 to December 2012. This retrospective study included patients registered on the database prior to the end of 2012, fulfilling NICE eligibility criteria and receiving at least 3 packs for which the NHS was invoiced. Patients were considered censored if they had ≥1 pack recorded in the last 3 months of the database. Median time to treatment cessation was estimated from a Kaplan-Meier curve of packs supplied to patients and the mean number of packs dispensed per patients from a parametric failure time model. **RESULTS:** 883/1160 registered patients met the study eligibility criteria (460/883 censored). These 883 patients, for whom the NHS was invoiced the single fixed payment, received a median of 13 packs 95%CI[12,14], equivalent to 12.8 months to treatment cessation. A mean of 19.4 95%CI[18.0, 21.0] packs were dispensed per patient. **CONCLUSIONS:** The results of this observational study confirm the average length of gefitinib therapy and mean number of packs dispensed in the SPA scheme exceed that assumed by NICE.

PCN187

TREATMENT PATTERNS OF INDOLENT NON-HODGKIN LYMPHOMA PATIENTS UNDER THE BRAZILIAN PUBLIC HEALTH CARE PERSPECTIVE

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OBJECTIVES: To identify the chemotherapeutic treatment patterns in patients with indolent non-hodgkin lymphoma (NHL) treated in the Brazilian Public Healthcare System. **METHODS:** A retrospective longitudinal analysis based on the Government administrative claims database (Datasus) was performed from January 2008 to December 2012. Eligibility criteria were patients with indolent NHL diagnosed until January 2012 and starting their first chemotherapy regimen from January 2008 to January 2012. This cohort of patients was followed until December 2012, death or loss of follow-up. Patients without interruption during treatment and without change in medication were considered in the same chemotherapy regimen. Descriptive statistics (average, standard deviation and percentage) of treatment regimens, treatment free interval (TFI), age at the beginning of treatment, gender and length of treatment were performed. **RESULTS:** A total of 817 patients with indolent NHL representing 5,449 APACs (Authorization for High Complexity Procedures) met eligibility criteria. The population cohort comprised 50.7% men with an average age of 61.3±14.5years. 72.2% of the patients had only one chemotherapy regimen, whereas 18.2% had two and 9.1% had three or more chemotherapy regimens. Time between diagnose and the beginning of treatment was 3.6±6.2 months. The most widely used first chemotherapy regimen was cyclophosphamide, vincristine and prednisolone (CVP)(22.2%) followed by cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) and rituximab(15.7%), cyclophosphamide, vincristine and prednisolone (COP) and rituximab(5.6%), chlorambucil and prednisone(4.8%). Average length of treatment was 5.0±3.7months. For second chemotherapy scheme, the most widely used regimen was CHOP and rituximab(14.1%), CVP(7.5%), interferon(9.3%), chlorambucil and prednisone(6.2%). The average length of treatment was 4.0±4.1months, with an average TFI of 3.3±4.2months. **CONCLUSIONS:** The most used chemotherapy in first regimen was CVP. Rituximab in combinations was present in most patients in the first scheme. Rituximab in second scheme in combination with CHOP was the most used therapy. The length of treatment was longer in first scheme.

PCN188

CURRENT SITUATION OF ORAL ANTICANCER TREATMENTS USE IN FRANCE: THE ACTOR STUDY (ANALYSIS OF CANCER TREATMENTS GIVEN ORALLY)

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OBJECTIVES: Within the last decade market authorizations for oral anticancer treatments (OATs) have increased. This analysis aimed at describing the current situation of OATs and their modalities of use. **METHODS:** An analysis was performed from Oncology Analyzer™ (IMS Health, France), a physician survey database covering more than 10,000 cancer patients per year treated in both public and private institutions from multiple French regions. The database includes patient demographics, diagnosis and treatment patterns. Data was extracted for all types of cancers and described as number of patients treated by oral and intravenous (IV) anticancer drugs. Data was collected from October 2011 to September 2012. Analyses were split into different active anticancer treatment categories and excluded supportive care agents. **RESULTS:** A total of 7426 patients treated with oral and IV anticancer treatments in France were included in the analysis. The male/female ratio was 47%/53% and 58% of patients were aged over 60 years old. Patients receiving OATs were mainly diagnosed with a solid tumor (74%) such as breast cancer (34%), non-small cell lung cancer (8%) and colorectal cancer (7%). OATs represented 45% (54/119) of all molecules available (oral and IV) of which 44% (24/54) were cytotoxic chemotherapies, 28% (15/54) were targeted therapies, 22% (12/54) were hormonal-therapies and 6% (3/54) were immunotherapies. 32% of patients (2,410/7,426) received a regimen containing at least one OATs among them 78% received OATs only versus 18% received a combination of oral and IV drug. Sixty-one percent of patients aged over 80 years received OAT's, as compared to 26% of patients aged less than 60 years. **CONCLUSIONS:** The ACTOR study is the first analysis focused on the understanding of the pattern of use of OATs. One third of cancer patients in France are treated with OATs especially among the elderly. Further research is needed to understand the OATs uptake.

PCN189

A DISEASE MODEL OF METASTATIC COLORECTAL CANCER INCLUDING MULTIPLE TREATMENT LINES

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OBJECTIVES: To develop a decision-analytic model describing the current course of disease, including the available treatments, in metastatic colorectal cancer to serve as a baseline for the analyses of new developments. **METHODS:** A disease model was constructed containing six disease states, namely 'first-line treatment', 'progression of disease after first-line',' second-line treatment', 'progression of disease after second-line', 'third-line treatment' and 'death'. Time spent in each state was predicted using log-logistic, log-normal or Weibull survival models, utilizing simulated characteristics. All survival models and simulated characteristics were based on patient-level data, provided by the CAIRO trial (n=820). The model was validated by comparing various outcome parameters with the original data. **RESULTS:** The overall survival of the simulated cohort resulted in a median survival of 498 days. The original patient level data had a median OS of 508 days (95% CI: 463- 545). For the subgroups age and treatment line data continued to match consistently with patient-level data. Patients treated with sequential therapy in the RCT had an OS of 492 days (95% CI 416-557), the model predicted an OS of 489 days. Patients in the RCT with combination therapy had an OS of 525 days (95%CI 442-591days), the model predicted 509 days OS. Similar results were achieved in other subgroups and for various other outcome measures. **CONCLUSIONS:** The model constructed during this study is a good basis on which to model the effectiveness and cost-effectiveness of numerous new treatment options, including expensive drugs. It will also allow - in future - for the evaluation of these treatment options while accounting for the heterogeneous nature of colorectal cancer As such this model offers a method to aid in determining the optimal sequence of treatments for patients with metastatic colorectal cancer, both in terms of costs and effects.

PCN190

STAGE-BASED UTILIZATION OF CHEMOTHERAPY AGENTS IN A CANADIAN BREAST CANCER POPULATION

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OBJECTIVES: To describe the utilization of chemotherapy agents administered to women with a diagnosis of breast cancer, by stage of disease. **METHODS:** Chemotherapy utilization was extracted from two databases with population-level coverage [New Drug Funding Program (NDFP) and Activity Level Reporting (ALR) data] for women diagnosed with breast cancer between January 1, 2005 and December 31, 2009 and resident in Ontario, Canada. NDFP included expensive antineoplastics. ALR included only intravenous antineoplastics for agents administered at cancer centres. Each entry in the database represented one exposure to an antineoplastic medication administered and funded by the province. Hormonal therapies were not included in this analysis. All duplicate entries (same patient, same drug, same date of administration, same dose) were excluded. Overall utilization and utilization by stage of disease were determined. Chemotherapy regimen utilization was not analyzed, only individual drug use was. **RESULTS:** There were 39,656 breast cancer cases (34.4% Stage I; 31.8% Stage II; 12.0% Stage III; 3.9% Stage IV; 17.9% Unstaged) with a mean age of 61.6 ± 14.0 years. Among all cases (staged and unstaged), 17,383 (43.8%) received chemotherapy. The most common drugs administered across the entire cohort were cyclophosphamide (68.4%), docetaxel (52.8%), epirubicin (47.3%), fluorouracil (36.2%), doxorubicin (31.6%) and traztuzumab (24.3%). The drug utilization for Stage I/II was cyclophosphamide (72.9%), docetaxel (52.0%), epirubicin (49.6%), fluorouracil (37.9%), doxorubicin (31.2%), paclitaxel (23.0%) and traztuzumab (22.8%). For Stage III/IV utilization was as follows: cyclosphosphamide (68.3%), docetaxel (62.4%), epirubicin (45.6%), doxorubicin (36.1%), traztuzumab (27.8%) and paclitaxel (26.0%). **CONCLUSIONS:** This frequency distribution of chemotherapeutic agents provides population level data on the management of breast cancer, by stage. Future work will involve costing of these medications from a population perspective.

PCN191

RACIAL DISPARITY IN HEALTH CARE ACCESS AND OUTCOMES ASSOCIATED WITH PROSTATE CANCER IN THE UNITED STATES

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OBJECTIVES: Clinically significant prostate cancer is characterized by the growth of a tumor of more than 20 cc of cancerous cells within the prostate gland. Literature suggests significant disparities in prostate cancer prevalence and outcomes between Whites and African-Americans resulting in greater health services utilization. This study assessed the count of health care visits between White and African American prostate cancer patients. **METHODS:** This cross-sectional study used data from the 2010 Medical Expenditure Panel Survey. Negative binomial regression models were used to estimate the count of health services including emergency department visits, outpatient services and inpatient services associated with race in patients with prostate cancer while controlling for age and count of comorbidities. Patients who were not White or African-American were excluded due to the small numbers. **RESULTS:** The total sample consisted of 141 patients, of which 104 were White and 37 were African-Americans. Being White was associated with 43% less use of emergency services compared to being an African American while adjusting for age and comorbidities (IRR 0.57; 95% CI 0.33-0.97). Similarly, being White was associated with a 44% lower count of outpatient service use (IRR 0.56; 95% CI 0.32-0.99). No difference was found with inpatient services, most likely due to a low number of events. **CONCLUSIONS:** Being White was associated with less emergency and routine health care visits compared to being an African American, suggesting a disparity may exist among prostate cancer patients. More research should explore the sources of the disparity and whether this translates into other health care services like access to treatments.

PCN192

A FRAMEWORK FOR THE COST-EQUALITY ANALYSIS OF HEALTH CARE PROGRAMMES

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OBJECTIVES: To describe a methodological framework for the economic evaluation of health care programmes that addresses effects on unfair health inequality as well as overall health. The framework is designed to highlight the social value judgements required to define unfair health inequality and how these impact on the estimated level of inequality, and is distinct from equity weighting or multi-criteria decision analysis. Application of the framework comprises characterisation and quantification of the distribution of health, and this is illustrated using an existing decision model evaluating a bowel cancer screening programme. **METHODS:** The decision model of bowel cancer screening is restructured using additional information on the distributions of screening uptake, baseline health levels, quality-adjusted life expectancy and health opportunity costs in order to estimate the health distribution resulting from alternative bowel cancer screening policies. Standard screening is compared to two re-design policies wherein reminders are used to increase uptake. Different sets of social value judgements are applied to explore the robustness of the results, using different approaches to measuring inequality and to adjusting health distributions for fair sources of inequality. **RESULTS:** A universal reminder to participate in bowel cancer screening results in the greatest improvement in total population health, but increases inequality compared to no reminder or targeted reminders. Targeting reminders by deprivation and ethnicity reduces health inequality. The choice between screening policies depends on the type and level of inequality aversion and on the value judgements about which sources of health inequality are unfair. **CONCLUSIONS:** The framework imposes additional data requirements and requires that decision makers consider supplementary value judgements compared to standard cost-effectiveness analysis. Differential uptake of screening results in significant, potentially avoidable, health inequalities. This framework can provide decision makers with useful information to help address such inequalities while appropriately addressing any trade off with improving overall health.

PCN194

DECISION MAKING IN HIRA FOR 5 YEARS OF POSITIVE LIST SYSTEM

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OBJECTIVES: In Korea, the Positive List System was adopted in the end of 2006 and the cost-effectiveness had been important in decision making process for reimbursement. We tried to check the appraisal results. **METHODS:** Total of 5-years decision-making from 2007 to 2011 were reviewed and classified in several categories according to relative effectiveness and submission type of cost-effectiveness. **RESULTS:** Among 219 results which were made decision there were 149 recommendations(68%) for listing. Fifty submissions were cost-effectiveness(utility) analysis report but 26 submissions of those were improved relative effectiveness compared to the comparator. Twenty-four drugs were submitted CEA or CUA even though they didn't have evidence for improvement. If there was no evidence for the relative effectiveness or the new drug was inferior HIRA decided not to list. If new drug had evidence for non-inferiority it could be evaluated by cost-minimization analysis. Eleven drugs were decided to be listed among 12 submissions by CMA. There were 9 essential drugs to be appraised for 5 years. **CONCLUSIONS:** The most important factor in decision-making for reimbursement was relative effectiveness and the method of economic evaluation was determined by drug's relative effectiveness. In deciding acceptability in cost-effectiveness results the other factors are considered whether the drug used in severe disease or it was orphan drug, etc.

PCN195

HEALTH CARE RESOURCE UTILIZATION AND EXPENDITURES OF INCIDENT BREAST CANCER PATIENTS IN THE NETHERLANDS: RETROSPECTIVE ANALYSIS OF HEALTH INSURANCE DATA

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OBJECTIVES: Breast cancer generates a considerable economic burden. This study aims to quantify health care resource utilization and health care expenditures of breast cancer patients in The Netherlands. **METHODS:** A bottom-up cost-analysis was conducted using health insurance data retrieved from the AGIS Health Database in The Netherlands containing information on health care usage and –expenditures. Additionally, we estimated cost of in-hospital breast cancer medication in a top-down manner, based on Dutch National Breast Cancer treatment guidelines. Incident breast cancer cases (2008-2010) were included based on Diagnosis-Treatment-Combinations (DTC) codes containing the diagnosis of breast cancer. Health care resource utilization and expenditures were examined per phase of treatment (the year of diagnosis, second year, third year and last year of life). **RESULTS:** A total of 3494 newly diagnosed breast cancer patients were identified in the AGIS database, with an average age of 63 years at diagnosis. During the follow-up period, 220 patients died. Health care expenditures of Dutch breast cancer patients insured at AGIS were on average €17.120 per case in the year of diagnosis, €9.014 in the second year, €5.499 in the third year and €14.900 in the last year of life. The majority of the expenditures were related to health care utilized in the hospital setting. Additional costs of treatments with expensive drugs varied between €15.462 and €38.877, depending on the type of treatment. **CONCLUSIONS:** Health care usage and expenditures of Dutch breast cancer patients are substantial in the year of diagnosis, decrease in the second and third year after diagnosis, and then increase again in the last year of life. Treatment with expensive drugs adds a substantial cost burden.

PCN196
COST OF END OF LIFE PHARMACOTHERAPY IN CANCER PATIENTS: WHERE DOES THE BUDGET GO TO?
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OBJECTIVES: Costs of cancer treatment has received increased attention in the last decade mainly because of the very high expenses on new biological drugs. Total cancer treatment costs vary by tumor type and stage, with the highest costs usually incurring in the last year of life. In this study, we characterized the drugs that have the highest budget-impact in treating cancer patients in Israel, immediately before death. **METHODS:** Clalit Health Services (CHS), Israel's largest health-care organization with over 4 million members, serves 52% of the total population. Using CHS's comprehensive databases, we identified the three leading fatal cancers in 2012. We calculated CHS's acquisition costs for all pharmaceuticals provided to patients in their last three months of life, and extracted the top budget-consuming drugs used during this period. **RESULTS:** The leading fatal cancers in 2012 were colorectal (1551 deaths), breast (1273) and lung cancer (1174). The drugs with the highest budget-impact in colorectal cancer patients were (% of total drug-expenditure, # of patients treated (% of the total number of patients)): Cetuximab (20.2%, 38 patients (2.5%)), Bevacizumab (14.6%, 56 patients (3.6%)), Panitumumab (6.6%, 21 patients (1.4%), Fentanyl (6.5%, 278 patients (17.9%)), Irinotecan (4.0%, 77 patients (5.0%)). In breast cancer: Trastuzumab (12.0%, 23 patients (1.8%)), Fulverstant (6.4%, 42 patients (3.3%), Fentanyl (5.9%, 178 patients (14.0%)), Lapatinib (5.5%, 10 patients (0.8%)), Zoledronic acid (4.1%, 59 patients (4.6%)). In lung cancer: Erlotinib (21.4%, 77 patients (6.6%)), Gefitinib (12.8%, 42 patients (3.6%)), Pemetrexed (10.5%, 57 patients (4.9%)), Crizotinib (6.0%, 8 patients (0.7%)), Fentanyl (4.5%, 298 patients (25.4%)). **CONCLUSIONS:** A significant proportion of the pharmaceutical budget was spent on a relatively small portion of patients who received expensive novel targeted therapies during their last months of life although chances for success were minimal. A much higher portion of patients received palliative treatments for a substantially smaller proportion of the pharmaceutical expenditure.

PCN197
THE GERMAN QUOTA SYSTEM AS A MODEL FOR BIOSIMILAR COST SAVINGS IN EPOETIN TREATMENT
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OBJECTIVES: To demonstrate real-world benefits of biosimilar quota system used in Germany. **METHODS:** Long before recent economic challenges health care costs have represented a vast and unsustainable trajectory beyond western economies real GDP. Biologics have become a driver of payer expenditure with an 83% increase in global spend expected from 2010 to 2020. The introduction of biosimilars since 2006 represents an opportunity to reduce expenditure on biologics while maintaining the quality of patient care. Uptake of biosimilars and associated cost savings has been very different across markets. One mechanism, to encourage utilization of biosimilars, is to introduce quota style systems as in Germany. Using claims data from the KV regions to determine the use of biosimilar epoetin in relation to the quotas introduced by the 17 physician based regions in Germany, and the historic spend on epoetin treatment to calculate the budget expenditure reduction. **RESULTS:** Driven by the German quota system together with consultancy via KV- and SHI-pharmacists and physicians, biosimilar epoetins in Germany have obtained 57% of the German EPO market by Q3 2012. A reduction of 51% was experienced across historic public prices from January 2007 to August 2011. The increased penetration of biosimilar epoetin resulted in cumulative savings in Germany of €551 million. German real-world research demonstrated that biosimilar epoetin treatments did not experience any significant differences in efficacy and safety when compared with the originator. **CONCLUSIONS:** The quota system has become a significant driver of biosimilar epoetin uptake in Germany, which has resulted in substantial cumulative savings to the German health care system. Additionally this has allowed for extensive clinical experience with biosimilars which resulted in confirmation of the expected efficacy and safety outcomes. The biosimilar quota system provides markets with a mechanism to reduce biologic expenditure, increase patient access to biologic medicines and increase physician experience.

PCN198
A PROSPECTIVE TIME AND MOTION ANALYSIS COMPARING INTRAVENOUS (IV) VESUS SUBCUTANEOUS (SC) BORTEZOMIB IN PATIENTS WITH MULTIPLE MYELOMA (MM)
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OBJECTIVES: Bortezomib is an effective therapy for patients with MM. The recommended dosage is 1.3 mg/m^2 IV dosed on days 1, 4, 8 and 11 for eight, three week cycles. However, a recent randomized non inferiority trial demonstrated that the same dosage of bortezomib administered SC is equally effective, but with an improved safety profile. To measure the overall efficiency and cost savings of the SC route, a prospective time and motion study was undertaken in MM patients treated in a sample of U.S. community oncology clinics. **METHODS:** Time and motion and resource use data were collected from MM patients being treated with bortezomib IV (n=20) or SC (n=20) in seven U.S. community oncology clinics. Resource use and time impact on clinical staff were quantified using unit cost estimates. This included costs for drug preparation, wastage, administration, materials and supplies, premedication, patient chair time and all labor costs. **RESULTS:** The mean total time for IV and SC delivery (preparation, administration and total chair time) was 76.3 and 39.8 minutes ($p = 0.005$), with the associated (i.e. drug preparation and administration) cost being $U.S.189 and $U.S.90.84 respectively. With the inclusion of costs for drug wastage (i.e. mean of 1.2 mg for both IV and SC bortezomib, which is 34% of a 3.5 gram vial and costs approximately $U.S.500) and premedication, the cost for drug delivery was $U.S.808 (95%CI: $U.S.603 to $U.S.1011) and $U.S.596 (95%CI: $U.S.334 to $U.S.856) per dose of IV and SC bortezomib. Over a full cycle of therapy (i.e. 4 doses), the total cost for drug delivery including wastage and drug acquisition would be substantial at $U.S.7,113 and $U.S.6,327 for IV and SC bortezomib respectively. **CONCLUSIONS:** SC bortezomib resulted in a significant savings in drug delivery resources. However, drug wastage remained an important factor, regardless of the route of administration.

PCN199
RETROSPECTIVE ANALYSIS OF ONCOLOGY INDICATIONS UTILIZING DRUG EXPENDITURES FROM 2005 TO 2012 IN THE REPUBLIC OF SRPSKA
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OBJECTIVES: Analyses were conducted on Republic of Srpska (RS) Health Insurance Fund (HIF) national prescription database. Analyses explored health expenditure in pharmaceutical consumption of oncology medications for the fiscal year 2005 through 2012, in order to determine impact of introduction of public tenders in 2008. RS HIF provides coverage for a population of 1.2 million. **METHODS:** RS HIF national prescription database was explored. Key cost drivers and the differences were identified across all medications covered by the RS HIF. **RESULTS:** In 2005, total expenditure for all Oncology medication was €1.2 million. In 2012, total expenditure for all Oncology medications was €8 million. This increase of 681% is a result of two critical factors: 1) a national policy shift in 2004, of patient treatment switch from being treated abroad in Republic of Serbia to being locally treated; 2) exponential increase in Oncology indications incidence. In 2008 there was an introduction of public tenders that run every two calendar years, which allowed additional medications to be purchased by the RS HIF, as well at lower costs and hence it resulted in moderate decrease in expenditures, even though there was a steady increase in quantities purchased. This resulted in balanced and average expenditure from 2008 to 2012 of €9 million. Based on 2005 through 2012 consumption of Oncology medications, it is derived that over the years to date, top three Oncology indications are: a) Metastatic breast cancer, b) Metastatic colorectal cancer, c) Colorectal cancer Stage III. **CONCLUSIONS:** Results indicate that most of the patients treated abroad, transferred back to RS HIF for treatment by 2008. Top three Oncology indications show that there is a need for higher public awareness and patient education in RS related to them. This is in line with current RS public health care policies and strategies.

PCN200
MARKET ACCESS OF CANCER DRUGS IN EUROPEAN COUNTRIES: A MATTER OF SETTING PRIORITIES FOR RESOURCE ALLOCATION
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OBJECTIVES: Public health systems need to make well-founded choices in order to distribute their scarce resources in the most efficient way. Given the large number of cancer patients and their increasing life expectancy, public/private investments in oncology research, the growing launches of new anticancer agents and consequent high budget impact of cancer care, market access of cancer drugs has become delicate over the last decade. Furthermore, decision makers are challenged by ethical considerations and endeavor after fair and equal access to treatments for cancer patients. The aim of this study is to generate an overview of price setting and reimbursement procedures for cancer drugs in eight European countries. **METHODS:** Belgium, The Netherlands, France, Germany, Italy, Poland, UK and Sweden were selected as the countries of interest. Results were collected between January and March 2013 through a literature review and a qualitative questionnaire sent to authorities involved in price setting and reimbursement of drugs. The specific section of results for each country was validated by experts in the field. **RESULTS:** Diverse measures are introduced to optimize market access of cancer drugs such as adjusted cost-effectiveness thresholds and new market access agreements. Additionally, innovative cancer drugs are excluded from explicit cost control measures in some of the studied countries. Given the fact that each drug covered by the limited public health care budget might possibly exclude another one from reimbursement, results suggest preferential treatment of cancer drugs compared to drugs for other diseases. Besides societal preferences for treatments of severe diseases, there is no solid evidence that could justify prioritization of cancer. **CONCLUSIONS:** Price setting and reimbursement procedures seem to prioritize cancer above other disease areas. Further research needs to address the question if society attributes higher value to cancer drugs than to treatments for other diseases.

PCN201
A NOVEL ALGORITHM USING CLAIMS DATA TO IDENTIFY PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER (CRPC)
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OBJECTIVES: CRPC is an advanced form of prostate cancer with poor prognosis. The changing treatment landscape calls for use of real-world data to provide current information on disease epidemiology, treatment patterns, comparative effectiveness, and treatment cost. Administrative claims databases are a rich source of real-world data; however, they lack clinical values needed to identify CRPC patients. As currently there is no standard method to identify CRPC patients when clinical variables are unavailable, we developed and validated an algorithm using claims data to reliably identify CRPC patients. **METHODS:** Male patients with an ICD-9 code for PC between January 1, 2004 and November 30, 2012 were identified from IMS pharmacy and medical claims data. Metastatic PC was identified by additional tumors on or after the PC diagnosis. Surgical castration was determined using CPT and ICD-9 procedure codes for orchiectomy; medical castration was identified using codes for hormone therapies. The algorithm identified patients as having CRPC if they had any of the following: 1) switch in hormone therapy; 2) new metastases while on hormone therapy; 3) switch in treatment from any hormone therapy

to chemotherapy. The algorithm was validated against a PSA-based definition of CRPC (at least two PSA increases following castration or new metastases while on hormone therapy). **RESULTS:** A total of 269 patients met inclusion criteria and had 3 or more PSA measurements. The two methods agreed in 88% of patients; 220 (81.8%) were identified as CRPC by both methods and 17 (6.3%) were identified as not castration resistant by both methods. A statistical comparison of the two methods yielded a Cohen's kappa of 0.4491, indicating moderate agreement. **CONCLUSIONS:** The algorithm was concordant with a PSA-based definition of CRPC and serves as a new tool to identify CRPC patients using claims data. Future validation against a different data source is needed.

PCN202

INCREASED RISK OF CANCER INCIDENCE ASSOCIATED WITH REPEAT MEDICAL IMAGING: DESIGNING BETTER CLINICAL TRIAL PROTOCOLS

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OBJECTIVES: To assess the potential increase in lifetime attributable risk (LAR) of cancer incidence due to repeated exposure to medical imaging procedures for participants in clinical trials. **METHODS:** Medical imaging in clinical trials has grown exponentially in the last decade. We have developed an individual-based state-transition model to estimate the LAR of radiation-related cancer following a patient's exposure history, and site-specific dose according to age and gender. Monte Carlo simulations to vary effective doses, risk model coefficients, and the period for radiation-related cancer latency were performed. **RESULTS:** We examined two scenarios in a three year hypothetical clinical trial: minimal exposure describing a subject's radiation exposure as one abdominal CT scan per year; and frequent exposure consisting of five abdominal CT scans per year. For a 30 year old female the LAR of cancer incidence increased from 46 per 100,000 population in the minimal exposure scenario to 229 per 100,000 in the frequent exposure scenario. For a 30 year old male, the risk increased from 36 to 179 per 100,000. At age 30, females had a 30% higher risk than males, however, cancer incidence at ages 50, and 70 were similar for both sexes. At age 50 the LAR of cancer incidence increased from 31 to 151 per 100,000. At age 70 the risk increased from 15 to 71 per 100,000. The LAR of cancer incidence was one third lower in 70 year olds than in 30 year olds, and half the rate of 50 year olds. **CONCLUSIONS:** Although the LAR of cancer incidence of a single exposure seems to be relatively small, clinical trials that involve a comparatively large number of imaging procedures can lead to significantly higher risks. Examinations that deliver relatively high doses of radiation, such as CT, need to be clinically justified.

PCN203

TRENDS IN CHEMOTHERAPY SETTING AND COSTS FROM 2005 TO 2012: A CASE STUDY USING BEVACIZUMAB

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OBJECTIVES: The rising costs of cancer care are a major focus for clinicians, payers and patients. This analysis examines trends in bevacizumab chemotherapy administration and drug reimbursement. **METHODS:** Using the MarketScan© Research Databases, administrations of bevacizumab were identified from 1/1/2005 through 12/31/2012 for patients with commercial or employer-sponsored supplemental Medicare insurance. Bevacizumab claims were excluded if the claim had a diagnosis related to eye disease or the reimbursed amount was < $100. All claims were identified as occurring in an office-based setting (OBS), an outpatient hospital setting (OHS) or other setting. **RESULTS:** The percent of bevacizumab claims occurring in OHS increased from 6 to 34% among Medicare claims, and from 14 to 42% among commercial claims from 2005 to 2012. Medicare median drug reimbursement was $257 more for OHS than OBS in 2005, increasing to a difference of $3,022 in 2009 and declining to $1,722 in 2011 before narrowing to $165 in 2012. Medicare median reimbursements for chemotherapy administration in OHS were $408 more than OBS in 2005, dropping to a difference of $97 in 2008 and ending at $165 in 2012. Commercial differences in drug reimbursement for OHS and OBS settings continuously increased from $885 in 2005 to $3714 in 2011, declining slightly to $3676 in 2012. Differences in chemotherapy administration reimbursement were $176 more for OHS than OBS in 2005, the difference decreasing to $103 in 2007 and increasing to $236 in 2012. **CONCLUSIONS:** Although the difference in reimbursements to OHS and OBS has decreased over time for Medicare, the differences across settings for commercial insurance increased over time with a slight indication that cost increases are slowing. The higher reimbursements in OHS combined with the shift from OBS to OHS over the past 7 years has implications for the growth in cancer costs over the past decade.

PCN204

NOVEL MARKET ACCESS MODELS FOR CANCER DRUGS

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OBJECTIVES: Cancer drugs are the world's highest selling category of therapeutic products. Due to their premium price and budget impact, several new drug reimbursement models have been implemented worldwide by public and private payers. These models have potential implications for coverage and reimbursement of all branded products. This study reviewed recent cancer drug reimbursement models and developed lessons and implications for future products. **METHODS:** Reviewed cancer drug reimbursement schemes in developed and emerging markets. Interviewed payers and KOLs to develop lessons and implications for future products. **RESULTS:** Public and private payers worldwide have implemented several new models for cancer drug reimbursement to manage budgets and control costs. In the US, private payers are piloting single source compendia and third party protocols (eg. P4 Oncology) to limit off-label use of cancer drugs. In the UK, NICE has successfully negotiated lower price and discounts for first few cycles of therapy. In Italy, AIFA has implemented registry based patient access for cancer drugs. In India, several manufacturers have implemented novel pricing strategy for first few cycles of therapy. In Germany, IQWIG has proposed to use correlations between surrogate endpoints and patient relevant outcomes to determine value of cancer drugs. Due to increased cost pressure on payers, such models are likely to inspire novel reimbursement schemes for other branded products. **CONCLUSIONS:** Cancer drug reimbursement models are setting new benchmark for payers to manage access and control costs. These models have significant implications for other expensive branded products.

PCN205

THE RELATIONSHIP BETWEEN SUBMITTED LINE OF THERAPY AND REIMBURSEMENT DECISIONS IN SOLID STATE TUMOR CANCER DRUGS

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OBJECTIVES: To explore the relationship between lines of therapy and submission for reimbursement across disease conditions and types of therapy. **METHODS:** This study looked at 252 Health Technology Assessments from eight agencies: CADTH, CCO, HAS, HIS, NICE, PBAC, SMC, and pCODR. The data covered 41 drugs across seven solid-state tumor cancer conditions. **RESULTS:** Of the 41 drugs, 27% (11/41) were initially submitted for first-line therapy and 73% (8/11) were recommended for reimbursement. Similarly, 32% (13/41) were initially submitted for second-line therapy and 77% (10/13) were recommended for reimbursement. Cytotoxic drugs were most likely to be reviewed initially for first-line therapy at 35% (7/20) and second-line therapy at 25% (5/20); targeted therapies were most likely to be reviewed initially for second-line therapy at 38% (8/21) and adjuvant therapy at 24% (5/21). The percentage of drugs reviewed for two or more lines of therapy varied greatly across conditions. Colorectal Cancer, SCLC, and NSCLC had the greatest percentages of drugs reviewed for 2+ lines of therapy with 100% (4/4), 100% (1/1), and 83% (5/6), respectively. Melanoma, Prostate Cancer, and Ovarian had the lowest percentages with 0% (0/2), 14% (1/7), and 40% (2/5), respectively. Additionally, there was a positive correlation (r= 0.9) between the number of drugs reviewed and number of lines of therapy covered per disease condition. **CONCLUSIONS:** There was no discernable difference in the rate of reimbursement between drugs initially submitted for first-line therapy or second-line therapy. There were, however, differences in various trends across disease conditions and between types of therapy. Future research will focus on trends across agencies and will include a larger sample size covering more conditions as well as investigational case studies on frequently reviewed drugs.

PCN206

CLINICAL AND COST-EFFECTIVENESS OF NON-PEGYLATED LIPOSOMAL DOXORUBICIN FOR NON-HODGKIN LYMPHOMA: A SYSTEMATIC REVIEW

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OBJECTIVES: To systematically review the currently available clinical and cost-effectiveness evidence of non-pegylated liposomal doxorubicin (NPLD) for non-Hodgkin lymphoma (nHL). The hypothesis under verification was that the administration of NPLD lowers the cardiotoxicity typical for conventional anthracyclines while being able to sustain the clinical effect of treatment. **METHODS:** A systematic literature search was conducted for clinical and cost-effectiveness data for the nHL population treated with NPLD, using the main medical databases (PubMed, EMBASE, Cochrane Library). In addition, clinical trial registries were searched, reference lists of included studies and reviews were screened for missed studies. Searches took place in September 2012. **RESULTS:** The review generated 9 one-arm clinical trials and 1 retrospective study which met the inclusion criteria. One comparative parallel trial comparing R-CHOP with R-COMP in the DLBCL population is ongoing, with no results published. Generally, available evidence is poor – studies identified are characterized by many limitations, i.e.: small and heterogeneous study populations, relatively short observation period, not always specified inclusion and exclusion criteria, diversified treatment regimens (with R-CHOP dominating), shortened or/and presented selectively safety data. The majority of studies was performed in the DLBCL population. Cumulative interpretation of data was hindered due to essential differences in between trials. Lowering of LVEF was observed with a frequency of 0% to 31,7% of cases, while symptomatic lowering of LVEF with the development of chronic ischemic heart disease occurred with the frequency of 0 to 10%. The second most frequent cardiological event observed was arrhythmia. Clinical efficacy focused on surrogate endpoints (radiological responses), defined differently in between trials. No economic evaluations studies were found. **CONCLUSIONS:** There is limited evidence on the effectiveness and safety of NPLD in patients with nHL due to the lack of well-designed and well-reported comparative studies. Further research is needed to explore the hypothesis in question.

PCN207

IMPACT OF RECOMMENDED PHARMACEUTICALS ON CANCER MORTALITY: ANALYSIS OF REAL-LIFE DATA

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OBJECTIVES: To ascertain whether there were any trends in cancer mortality after hospital admittance and diagnosis that could be linked to recent approval of therapies by the National Institute for Health and Care Excellence (NICE). **METHODS:** Using information provided by Hospital Episode Statistics and the Office of National Statistics, yearly mortality data from both the inpatient and outpatient population between 2007 and 2010 were extracted. An analysis of 30-, 60-, and 90-day mortality following admittance to hospital was undertaken for malignancies which had seen therapies approved by NICE after 2006. **RESULTS:** Of the 37 cancer therapies assessed by NICE between 2006 and 2010 inclusive, 27 were recommended. Patients with lung cancer were found to experience one of the highest mortality rates overall. Interestingly, lung cancer also saw the largest number of therapies approved between 2006 and 2010 (7), along with a steady decline in the annual 90-day mortality over the three year period (29.6%, 28.4% and 27.1% in 2007-08, 2008-09 and 2009-

10, respectively). Similarly, patients admitted to hospital with oesophageal cancer experienced a high 90-day mortality rate, ranging from 22% to 21.9% in 2007-08 and 2009-10, respectively. However, between 2006 and 2010, no therapies were submitted for NICE appraisal for oesophageal cancer, suggesting that there may have been a lack of research interest and potentially explaining why there was no substantial decrease in mortality from 2007, as compared to indications where therapies had been approved, such as lung, colon and breast cancer. **CONCLUSIONS:** The recommendation of therapies and their uptake in the UK may at least partially explain the trends noted in this study, although other factors such as delay in therapy uptake and off-label use may also need to be taken into account.

PCN208

DO NICE EVIDENCE REVIEW GROUPS (ERG) FOCUS ON DIFFERENT ASPECTS OF MANUFACTURER SUBMISSIONS IN ONCOLOGY?

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OBJECTIVES: Evidence Review Groups (ERGs) provide a critical appraisal of the manufacturer submission in the NICE single technology appraisal (STA) process. As the academic centres may differ in experience and methodology, the objective of this study was to evaluate whether the focus areas and key criticisms differ between ERGs. **METHODS:** The NICE website was searched for all NICE oncology STAs, published between June 2010 and June 2013. The ERG reports were retrieved, and the main critiques were categorised for the five centres that performed the most evaluations. The focus areas of the ERGs were further studied. **RESULTS:** A total of 27 STAs were identified with evaluations performed by 9 different ERGs. The most evaluations were performed by Liverpool (9), followed by Sheffield (4), and PenTAG, West Midlands and York (3 evaluations each). All ERGs would report uncertainties related to the extrapolation and gain in overall survival (OS), maturity of data, trial comparator, and the quality of life (QoL) data. In addition all critiques covered submission quality and disease specific challenges, yet variation was found in focus area between ERGs. For example a specific focus area of Liverpool was the OS modelling method. Proposed changes to survival modelling included separating the survival curves for pre- and post-progression, and removing any survival advantage post-progression where this was considered inappropriate. Comments from other agencies on OS were mainly limited to the choice of parametric survival function. Other areas that differed between ERGs were the systematic review methods (more often reported by Sheffield) and comments on the QoL data (York). **CONCLUSIONS:** Although all ERGs focus on uncertainty around the evidence and quality of the manufacturer submissions, the focus areas differed between the groups. The key difference seems to relate to research focus of the academic centre.

PCN209

REVIEW OF NICE TECHNOLOGY APPRAISALS IN ONCOLOGY: HOW DOES CLINICAL EVIDENCE CHANGE OVER TIME?

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Drug licensing and reimbursement authorities worldwide are considering new ways to stimulate market access for innovative medicines such as accelerated approval and conditional coverage. Early release of pharmaceuticals calls for more responsive decision-making alongside continuous evidence generation throughout clinical development. We explore whether changing trends in clinical evidence considerations for health technology assessment (HTA) by the National Institute for Health and Care Excellence (NICE) may help inform future evidence requirements for rapid and early HTA. **OBJECTIVES:** We investigate how the submission and acceptability of clinical evidence for single, multiple and repeated assessments of cancer drugs by NICE have changed in the past decade. **METHODS:** We reviewed technology appraisals published online since February 2002 by NICE for pharmaceuticals in oncology. Information regarding the clinical evidence included and the methods used to analyse relative treatment effects across relevant comparators was extracted. Manufacturer submissions, assessment reports, and final appraisal determinations were considered for longitudinal comparison. **RESULTS:** Out of a total of 254 appraisals identified since 2002, 85 assessed cancer drugs and 76 of these were included for review based on available documentation. Only 11 products had been re-assessed to date with initial guidance superseded by a multiple technology appraisal or clinical guideline. We found a greater reliance on phase II and observational data in recent appraisals, particularly for novel therapies in areas of high unmet need. Limited data was also accompanied by an increase use of surrogate outcomes and extrapolation of observed short-term clinical benefits. Recent submissions were also marked by the uptake of network meta-analysis methodologies. **CONCLUSIONS:** NICE has previously recommended cancer drugs based on immature clinical data allowing for considerable uncertainty in 'real-world' effectiveness estimates. However, these examples remain the exception to the rule; moreover our review highlighted a need for methodological development to deal with early clinical evidence.

PCN210

G-BA ASSESSMENTS OF ONCOLOGY TRIALS: IS INCREASED OVERALL SURVIVAL A "MUST HAVE"?

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OBJECTIVES: Objective of this research was to provide an overview of Health Technology Assessments (HTAs) in oncology after introduction of AMNOG in Germany. **METHODS:** Quintiles' HTA database (HTA Watch) has been used to analyse HTAs in Germany. The timeframe chosen for analysis was 1st of January 2011 to 24th of June 2013. All reports have been analysed in detail to reveal key factors for success or failure, which are presented in the following. **RESULTS:** Since introduction of AMNOG in 2011, thirty percent (13 out of 43) of all completed assessments by the G-BA (Federal Joint Committee) evaluated cancer drugs. The products assessed were abiraterone acetate, axitinib, brentuximab vedotin, cabazitaxel, crizotinib, decitabine, eribulin, ipilimumab, pixantrone, ruxolitinib, vandetanib, vemurafenib and a combination of tegafur, gimeracil and oteracil. Across these oncology assessments a total of 19 patient subgroups have been evaluated. Eleven subgroups (58%) showed an additional benefit according to the G-BA. Eight subgroups (42%) received the rating "no additional benefit" or "less benefit than comparator". The comparators chosen by G-BA within subgroups vary widely depending on the indication. Key factors for the positive outcome of these assessments were increased overall survival, reduction of symptoms or improved quality of life. Main reasons for the G-BA to attest no additional benefit include inappropriate indirect comparison and lack of adequate patient subgroup analysis. **CONCLUSIONS:** Analysis of HTA reports in oncology shows that while overall survival is a strong end point, also increased quality of life and reduced side-effects can be sufficient to achieve a beneficial outcome (crizotinib: considerable benefit). Importantly, the provided data must be applicable to the German regulations under AMNOG, showing clinical evidence against the specified comparator. The amount of the additional benefit plays an important role in the reimbursement amount negotiations following the definition of the additional benefit by the G-BA.

PCN211

HEALTH TECHNOLOGY ASSESSMENT: IS IT THE RIGHT PIECE FOR THE JORDANIAN HEALTH CARE PUZZLE?

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OBJECTIVES: To study the pharmaceutical reimbursement/Coverage decision making processes in Jordan to highlight the importance of conducting formalized technology assessments **METHODS:** To review publically available data regarding the reimbursement/Coverage decision making processes in Jordan through searching related organization's websites and publically available regulations. **RESULTS:** Jordan is characterized with a fragmented health care system. Pharmaceutical registration and pricing are under the responsibility of the JFDA. Furthermore, it is responsible about medication selection for the Rational Drug List (the national formulary). The medication supply chain differs between the public and the private sectors in term of process and out puts. The medication selection process is not governed by criteria and not empowered by an independent review body to support decision making by the national appraisal committee (national P&T). The rational drug list is publically available but without details of the decision or the processes of decision making process. Listing of new medication is wide without indication specification or date of listing. The role of cost-effectiveness is limited and the tender prices are not linked to any type of cost effectiveness analysis **CONCLUSIONS:** The National Agenda, the National health Policy and the National Drug Policy tackled the high health expenditure in Jordan as an essential priority. This challenged is due to the characteristics of the Jordanian health care system that is fragmented with a divided funding system between public and private sectors. A more formalized medication selection processes empowered with drug information services that provide evidence based data and analysis in the form of technology assessment would play a role in decreasing health care expenditures. All of these recommendations should move parallel with improving the level of transparency and patient engagement.

PCN214

EPIDEMIOLOGY FOR ONCOLOGICAL DRUGS REGARDING THE BENEFIT DOSSIER PREPARATION IN GERMANY

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OBJECTIVES: An early benefit assessment of drugs after launch has been implemented since 2011 in Germany. The Institute for Quality and Efficiency in Health Care (IQWiG) assesses the benefit of the drug based on a dossier submitted by the pharmaceutical manufacturer. Based on this assessment and the statements by industry, scientific community and patient organizations the Federal Joint Committee (G-BA) reviews and decides on the extent of the additional benefit. The dossier needs also to contain information about the number of patients treated with the new drug. The objective is to investigate the sources considering the calculation of patient numbers for oncological drugs. **METHODS:** A review of oncological drugs which passed through the benefit assessment was conducted to evaluate which data sources and methods were used to calculate the potential patient number. The results were compared with IQWiG's assessment and the final decision by G-BA, to detect possible methodological difficulties. **RESULTS:** The data sources regarding German epidemiological data were mainly collected through publicly available sources such as national and local cancer registries. Difficulties occurred with small cancer entities or when specific data regarding patient subpopulations (e.g. through age, tumor stages, ECOG performance status or previous therapies) was needed. The pharmaceutical manufacturer's calculations were often challenged by IQWiG and G-BA without suggesting a precise alternative or more suited data source. **CONCLUSIONS:** The data collection and data availability within the benefit dossier process for oncological drugs is in most cases challenging and the efforts needed should not be underestimated. Authorities, industry and medical community should work on a common solution for a more valid and reliable calculation of the potential patient number in oncology.

PCN215

ECONOMICAL LOSSES DUE TO DISABLEMENTPARENTS CARRING FOR CHILDREN WITH ONCOHEMATOLOGICAL DISEASES

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OBJECTIVES: Socio-economic phenomena, caused by disease of children are reflected primarily in the formation of non-medical costs. Methodology for calculation of non-medical costs includes a number of parameters, including the cost of lost output by persons caring for children during the treatment period. **METHODS:** The study involved patients from Oncohematological Chelyabinsk Center for Children and Adolescents behalf of prof. V. Gerein been treated in the period from 2008 to 2013.

Patient selection was random. The basic condition for inclusion in the study was the availability of data necessary to meet the costs. The number of patients at this stage of the study was already 42 people. Age at diagnosis was 9 months to 12 years, the median age of the patients was 6,4 ± 5,6 years. All of the patients were in the hospital with their parents of working age. In the calculations have been included: - GRP Chelyabinsk region (Gross Regional Product-14 USD per day per capita) and GDP (Gross Domestic Product-44,4 USD per day per capita), which amounted on average in 2008-2012. The formula for the calculation of total costs:E $ = Nd x GRP / GDP (Nd-the number of days of disability) **RESULTS:** Comparing the various cost components of treatment revealed that the indirect costs are 66% of the total amount of all expenses for medical treatment. State losses caused by non-working period of hospitalized for care people and non-produced Gross Regional Product are 7758,5 ± 1076,1 USD per capita. Losses of GDP are 21449,6 ± 3748,8 USD per capita. **CONCLUSIONS:** The formation of regional budgets should be done with consideration of big loss connected with disability of people hospitalized for the care of the a sick child, adjusted for and with GRP/GDP taken into account of big potion non-medical costs.

PCN216

POPULATION BASED UTILIZATION OF RADIATION THERAPY BY A CANADIAN BREAST CANCER COHORT

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OBJECTIVES: To examine the trends in radiation therapy (RT) utilization by a population based breast cancer cohort in Ontario, Canada. **METHODS:** The provincial cancer registry maintains cancer specific databases and provided a breast cancer cohort based on diagnosis dates from April 1, 2005 to March 31, 2010. Staging information was also available. The cohort was then linked, by their encrypted health card number, to linkable administrative datasets that are maintained by the Institute for Clinical Evaluative Sciences (ICES) such as RT utilization. **RESULTS:** An all female breast cancer cohort (N=39,656) was identified over a five-year timeframe and the average age was 61.6 ± 14.0 years. Approximately, two thirds (N=25,225) of patients received RT and staging information was available for 22,988 patients (stage I = 9,541; stage II = 8,516; stage III = 4,050; and stage IV = 881). Patients had an average of 1.4 ± 0.7 (stage I) number of RT courses, 1.8 ± 1.1 (stage II), 2.5 ± 1.3 (stage III), and 2.8 ± 2.4 (stage IV). The percent ratio of conventional RT to intensity modulated RT (IMRT) was 70.9%:16.6% (stage I), 71.6%:11.3% (stage II), 74.6%:4.6% (stage III), and 72.7%:12.6% (stage IV). For the non-IMRT cohort with a primary cancer (N=30,887), the average number of fractions per course was 18.1 ± 9.2. **CONCLUSIONS:** From 2005 – 2010, almost two thirds of a Canadian female breast cancer cohort received RT and the average number of courses increased with stage. A similar trend was observed with the type of RT (coventional RT utilization increased with stage) but peaked at stage III and decreased at stage IV, likely due to palliation. The next step is to apply unit costs to the number of fractions per subgroup and to also obtain RT-planning and radiation therapist times.

PCN217

DEFINING ELIGIBLE PATIENT POPULATION IN SÃO PAULO STATE BASED ON CLEOPATRA TRIAL INCLUSION CRITERIA: A RETROSPECTIVE ANALYSIS OF FUNDAÇÃO ONCOCENTRO (FOSP) CANCER PATIENT REGISTRY (REGISTRO HOSPITALAR DO CÂNCER – RHC)

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OBJECTIVES: Breast cancer (BC) is the most common cancer affecting women and, despite advances in treatment, is still the leading cause of cancer death among women worldwide. Approximately 20%-25% of the women diagnosed with BC will have HER2-positive disease and those with metastatic disease (mBC) have a 5-year life expectancy of only 24%. Recently, pertuzumab (P) was approved as a new therapeutical option for first line HER2-positive mBC in Brazil. This study aims to define the proportion of BC patients that would be eligible for pertuzumab+trastuzumab+chemotherapy (P+T+C) combination therapy in São Paulo state by analyzing retrospectively (2000-March 2013) the Fundação Oncocentro (FOSP) cancer patient registry (Registro Hospitalar de Câncer – RHC). **METHODS:** Raw data of cancer cases reported from 2000-March 2013 was taken from the FOSP-RHC and mined according to the inclusion criteria of the CLEOPATRA trial. Only women with histologically/cytologically confirmed diagnosis of BC (ICD-50) and reported TNM classification at diagnosis were included in the analysis. P+T+C therapy eligible patients were those reported as stage IV at diagnosis (de novo mBC) or stages 0, I, II and III with evidence of progression at last tumour assessment (recurrent cases), excluding ones with evidence of central nervous system (CNS) metastasis. Was considered that all patients in the database would test for HER2 status and positivity rate was taken from literature (25%). **RESULTS:** During the analysis period 59,095 BC cases with TNM classification at diagnosis were reported. 4,660 cases were considered de novo mBC and 7,378 cases were considered as recurrent. According to the positivity rate 3,010 patients would be eligible for P+T therapy which accounts for approximately 5.1% of the overall cases of BC. **CONCLUSIONS:** First-line HER2-positive mBC is a targeted, clearly defined and limited patient population where pertuzumab based regimen provides significant and clinically meaningful benefits in overall survival and progression-free-survival.

PCN218

PHYSICIANS' PREFERENCES FOR BONE METASTASES TREATMENTS IN FRANCE, GERMANY AND THE UNITED KINGDOM

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OBJECTIVES: To evaluate European physicians' treatment preferences for preventing skeletal-related events (SREs) in patients with bone metastases from solid tumors. **METHODS:** Physicians completed an online discrete-choice experiment survey consisting of 10 choices between pairs of hypothetical medication profiles for a putative patient. Each profile included five attributes within a pre-defined range (based on prescribing information for the available bone-targeted agents [BTA]): months until first SRE (10, 18 and 28 months); months until worsening of pain (3, 6 and 10 months); annual risk of osteonecrosis of the jaw (ONJ; 0, 1 and 5%); annual risk of renal impairment (0, 4 and 10%); and mode of administration (oral tablet, subcutaneous injection, 15-minute infusion and 120-minute infusion). Choice questions were based on an experimental design with known statistical properties. The survey was pretested with 8 physicians using open-ended interviews. A separate main-effects random parameters logit model was estimated for each country. **RESULTS:** Physicians from France (n=191), Germany (n=192) and the UK (n=197) completed the survey. Among the attributes included in the survey, months until first SRE and the risk of renal impairement were the most important attributes in France and the UK, whereas in Germany months until first SRE and a delay in worsening of pain were the most important. For all these attributes, better levels were significantly preferred to worse levels ($p<0.05$). In all three countries, a 120-minute infusion every 4 weeks was the least preferred mode of administration ($p<0.05$). The annual risk of ONJ was judged by physicians to be the least important attribute in all three countries. **CONCLUSIONS:** Physicians generally make treatment decisions regarding choice of BTA for patients with bone metastases based on intent to delay the onset of SREs, managing risk of renal impairment and preventing the worsening of pain.

PCN219

NURSES' PREFERENCES FOR BONE METASTASES TREATMENTS IN THE UNITED STATES

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OBJECTIVES: Several bone-targeted agents (BTAs) are approved for the prevention of skeletal related events (SREs). Nurses work closely with physicans and patients in managing the disease. Whilst influencing treatment decisions, nurses preferences for alternative treatment options have not been assessed. This study evaluated US nurses' preferences for treatment attributes in preventing SREs among patients with bone metastases from solid tumors. **METHODS:** Nurses completed a web-enabled discrete-choice experiment survey consisting of 10 choices between pairs of hypothetical medication and patient profiles. Each profile included six medication attributes within a pre-defined range (primarily based on prescribing information and real-world practice): months until first SRE (10, 18 and 28 months); months until worsening of pain (3, 6 and 10 months); annual risk of osteonecrosis of the jaw (ONJ; 0, 1 and 5%); annual risk of renal impairment (0, 4 and 10%); mode of administration (subcutaneous injection, 15-minute infusion and 120-minute infusion); and out-of-pocket cost to patients ($25, $75, $150 and $330). Choice questions were based on an experimental design with known statistical properties. The survey was pretested with 6 nurses using open-ended interviews. A main-effects random parameters logit model was estimated. **RESULTS:** A total of 196 US nurses completed the survey. Among the attribute levels included in the survey, out-of-pocket costs to patients, risk of renal impairement, and months until first SRE were the most important attributes. For all attributes, better levels were significantly preferred to worse levels ($p<0.05$) except that no difference was observed between 0% and 1% ONJ attribute. Annual risk of ONJ was perceived by nurses to be the least important attribute. **CONCLUSIONS:** When working with physicians and patients on the choice of BTAs for patients with bone metastases, out-of-pocket costs to patients, managing the risk of renal impairment and delaying time to first SRE are the primary foci for nurses.

PCN220

PHYSICIANS' PREFERENCES FOR BONE METASTASES TREATMENTS IN THE UNITED STATES

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OBJECTIVES: Among the bone-targeted agents (BTAs) currently approved for the prevention of skeletal-related events (SREs), several characteristics may be considered by physicians when making treatment decisions. This study evaluated US physicians' treatment preferences for preventing SREs in patients with bone metastases from solid tumors. **METHODS:** Physicians treating patients with bone metastases completed a web-enabled discrete-choice experiment survey consisting of 10 choices between pairs of hypothetical medication and patient profiles. Each profile included six medication attributes within a pre-defined range (primarily based on prescribing information and real-world practice): months until first SRE (10, 18 and 28 months); months until worsening of pain (3, 6 and 10 months); annual risk of osteonecrosis of the jaw (ONJ; 0%, 1% and 5%); annual risk of renal impairment (0%, 4% and 10%); mode of administration (subcutaneous injection, 15-minute infusion and 120-minute infusion every 4 weeks); and out-of-pocket cost to patients ($25, $75, $150 and $330). Choice questions were based on an experimental design with known statistical properties. The survey was pretested with 8 physicians using open-ended interviews. A main-effects random parameters logit model was estimated. **RESULTS:** A total of 200 US physicians completed the survey. Among the attribute levels included, out-of-pocket cost to patients, months until first SRE and the risk of renal impairment were the most important attributes. For those attributes, better levels (outcomes) were significantly preferred to worse levels ($P < 0.05$). For mode of administration, subcutaneous injection was preferred over 15-minute infusion every 4 weeks ($P < 0.05$). **CONCLUSIONS:** When making treatment decisions regarding choice of BTA for patients with bone metastases, out-of-pocket cost to patients, delaying the onset of SREs and managing the risk of renal impairment are the primary foci for physicians.

PCN221

IDENTIFICATION OF THE TREATMENT PATHWAY OF METASTATIC CASTRATE-RESISTANT PROSTATE CANCER IN SCOTLAND: A CHART REVIEW

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OBJECTIVES: Chemotherapy with docetaxel was the first therapy approved for the treatment of metastatic Castrate-Resistant Prostate Cancer (mCRPC) while others came along rather recently. With all the treatment options available now, current treatment strategies to appropriately sequence these agents are not known. This study aims to describe mCRPC current treatment paradigms, with specific attention to docetaxel, in Scotland. **METHODS:** A retrospective chart review was conducted. A panel of Scottish physicians was contacted to identify patients diagnosed with mCRPC between 2008 and 2013. Collected data included demographics, disease history, sequencing of therapies (type, duration and time-to-event), reason for switch or discontinuation, drug-related serious adverse events and hospitalisations. Descriptive analyses were performed. Time-to-event was analysed using the Kaplan-Meier method. **RESULTS:** Twelve physicians in Scotland completed the survey and 34 patients were included in the analysis. Mean age at mCRPC diagnosis was 62 years (range 56-69 years). The mean duration between mCRPC diagnosis and the date of last contact was 1.20 years. Postcastration, most patients (19/34, 56%), received docetaxel as first-line. The second most frequent first-line was bicalutamide (14/34, 41%), alone (9/14, 64%) or in combination with LHRHa. Abiraterone was frequently prescribed as next (second or third) line of therapy after docetaxel (6/21, 29%). The median time to switch was 105 days (range 20-235 days) and did not differ between patients with docetaxel versus other as first-line ($p = 0.17$). Most patients switched after radiographic progression or PSA rise. Serious adverse events and hospitalisations were rarely reported. **CONCLUSIONS:** These findings provide insights into the treatment pathway of mCRPC patients in Scotland. Chemotherapy with docetaxel and hormonal agents appear to be the most utilised therapies. Switch from first-line treatment occurred in approximately 3.5 months and was facilitated by radiographic progression or PSA rise. A larger retrospective chart review is needed to confirm these results.

DIABETES/ENDOCRINE DISORDERS – Clinical Outcomes Studies

PDB1

EVALUATION OF ACUTE PANCREATITIS SIGNALS WITH INCRETIN ENHANCERS: REVISITING DISPROPORTIONALITY ANALYSIS OF THE ADVERSE EVENT REPORTING SYSTEM

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OBJECTIVES: There has been a rising concern about the association between incretin enhancers and acute pancreatitis (AP). Previous research showed conflicting findings, and this analysis of the FDA Adverse Event Reporting System (FAERS) aims at investigating signals of AP across pharmacological classes of anti-diabetes medications (ADM) and within incretin enhancers class. **METHODS:** Adverse event reports submitted to FAERS between 1997Q3-2012Q1 were analyzed. The outcome was defined by MedDRA Preferred Term (PT) "pancreatitis acute"; exposures were defined by generic names of ADM. Sensitivity analyses were conducted by creating a custom term (CT) for outcome: "autoimmune pancreatitis", "ischemic pancreatitis", "pancreatitis", "pancreatitis acute", "pancreatitis hemorrhagic", and "pancreatitis necrotizing". Reports of other pancreatic disorders were excluded. Disproportionality analysis by proportional reporting ratio (PRR) and 95% confidence interval (LL05-UL95) is applied to detect AP signals compared to all ADM. Associations with LL05≥2 are significant signals. **RESULTS:** A total of1183 AP PT and 4481 CT reports for ADM were identified (incretin enhancers, n=912 and n=3,704, respectively). Corresponding PRR and (LL05-UL95) were: metformin 0.98 (0.83-1.16) and 0.52 (0.47-0.59); sulfonylureas 0.53 (0.37-0.75) and 0.35 (0.28-0.43); thiazolidinediones 0.12 (0.09-0.16) and 0.12 (0.10-0.14); meglitinides 0.54 (0.31-0.93) and 0.39 (0.28-0.54); incretin enhancers 1.94 (1.87-2.00) and 2.09 (2.06-2.12); and combinations 0.65 (0.47-0.88) and 0.81 (0.70-0.93). Compared to all ADM, estimates for incretin enhancers were: exenatide 1.46 (1.37-1.55) and 1.54 (1.49-1.59); liraglutide 4.90 (4.37-5.48) and 4.00 (2.73-4.28); saxagliptin 4.47 (3.00-6.67) and 4.60 (3.73-5.67); and sitagliptin 2.33 (1.95-2.78) and 4.02 (3.75-4.31). There were no reports of AP PT for linagliptin, but 39 reports of CT with estimates of 6.41 (4.64-8.85) were identified. **CONCLUSIONS:** Compared to other ADM, incretin enhancers are associated with higher than expected reporting of AP. Prescribers should monitor patients with diabetes for signs and symptoms of pancreatitis while treated with incretin enhancers. Given limitations of spontaneous reporting systems, pharmacoepidemiological studies are required to test the generated hypothesis and to draw clinically rigorous conclusions.

PDB2

BAYESIAN NETWORK META-ANALYSIS TO ASSESS THE RELATIVE EFFICACY AND SAFETY OF CANAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) INADEQUATELY CONTROLLED ON METFORMIN AND SULPHONYLUREA (MET+SU)

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OBJECTIVES: To assess the relative efficacy and safety of canagliflozin (CANA), a sodium-glucose co-transporter inhibitor, as an add-on to MET+SU, versus DPP-4 inhibitors, GLP-1 agonists and insulin, using Bayesian network meta-analysis (NMA). **METHODS:** A systematic literature review was conducted according to NICE guidelines. Outcomes of interest included HbA1c, weight and hypoglycaemia. A Bayesian NMA using non-informative priors was conducted, based on linking trials with treatment and dose-specific common treatment arms. Assessment of model fit and selection of fixed versus random effects was based on the Deviance Information Criterion (DIC). Sensitivity analyses assessed the impact of individual trials and definition of priors. Consistency between direct and indirect evidence was assessed. **RESULTS:** Ten studies reporting results at 26 weeks +/- 4 weeks were identified. HbA1c-reduction (D) for CANA 100mg was comparable to DPP-4s (D between 0.05 and -0.14 versus sitagliptin and linagliptin respectively, with pairwise probabilities (P) of being more effective between 33-88%), and higher for CANA 300mg, which was comparable to GLP-1s (D=0.08;P=31% and 0.01;P=53%) versus liraglutide 1.8mg and exenatide 10µg respectively) and biphasic insulin (D=0.03;P=43%). CANA 300mg had the highest weight reduction with changes between 0.14kg;P=93% (vs. exenatide 10µg) and 5.13kg;P=100% (vs. biphasic insulin). The odds ratio for hypoglycaemia versus long-acting insulin were 0.31 and 0.39 for CANA 100mg and 300mg respectively, compared to 0.20-0.41 for other classes. **CONCLUSIONS:** NMA of add-on therapies to MET+SU suggests that glycaemic reductions for CANA at 26 weeks are at least as large for CANA 100 mg and greater for CANA 300 mg compared to DPP-4s. CANA 300mg was found to be comparable to liraglutide 1.8mg and biphasic insulin. Weight reduction was similar to GLP-1s and substantially higher compared to all other classes. All classes showed significantly lower hypoglycaemic event rates compared to insulin.

PDB3

COMPARATIVE EFFECTIVENESS OF LIRAGLUTIDE VERSUS SITAGLIPTIN IN TYPE 2 DIABETES IN THE UNITED KINGDOM: A RETROSPECTIVE STUDY IN PRIMARY CARE

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OBJECTIVES: Liraglutide is an incretin-based (GLP-1 analog) therapy indicated for the treatment of patients with type 2 diabetes (T2DM). This study aimed to assess whether phase 3 clinical trial data, showing significantly greater reductions in HbA1c and body weight vs. the DPP-IV inhibitor sitagliptin is translated into routine clinical practice. **METHODS:** This was a retrospective database analysis of the Clinical Practice Research Datalink (CPRD), a primary care database in the UK. Patients (≥18 years) diagnosed with T2DM and prescribed liraglutide or sitagliptin between July 2009 and July 2012, were included. Patients on insulin or fixed dose metformin combinations at therapy initiation were excluded. Outcomes included: % of patients achieving ≥1% HbA1c reduction; % of patients with HbA1c reduction ≥1% and weight reduction ≥3% (NICE criteria); % of patients achieving treatment target HbA1c <7%; absolute change in HbA1c, weight (BMI), systolic blood pressure and blood lipids. **RESULTS:** Baseline demographics: 294 liraglutide and 2790 sitagliptin patients with a mean age of 55.7 (SD 10.6) and 62 (SD 11.0) years and 36.4% and 40.5% female respectively. Patients had a baseline HbA1c of 8.9% (SD 1.9) and 8.6% (SD 1.5), a baseline BMI of 39.3 (SD 7.1) and 33.3 (SD 6.4) and had been diagnosed with diabetes 7.1 and 7.2 years prior to start of current treatment for liraglutide and sitagliptin respectively. Comparative effectiveness analysis demonstrated superior reductions for liraglutide vs. sitagliptin in HbA1c (%) (-0.89 vs. -0.57, p<.01), weight (Kg) (-3.78 vs. -1.12, p<.0001), BMI (-1.3 vs. -0.4, p<.0001) and systolic blood pressure (mmHg) (-4.1 vs. -0.37, p<.0005) after 6 months of therapy. No statistically significant differences were observed in total cholesterol and HDL reductions. **CONCLUSIONS:** The superior control and weight reduction of liraglutide vs. sitagliptin observed in clinical trials is reflected in routine primary care clinical practice.

PDB4

WEIGHT LOSS OF ≥3% IN TYPE II DIABETES PATIENTS IS ASSOCIATED WITH WEIGHT CHANGE PROPERTY OF NEWLY PRESCRIBED ANTI-DIABETIC MEDICINE IN ANTI-DEPRESSANT USERS OVER A 12-MONTH FOLLOW-UP PERIOD

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OBJECTIVES: Anti-depressant use could complicate the weight change effect of anti-diabetes (AD) medications. This study examined if different newly prescribed AD medications were associated with weight loss in a 12-months period in type II diabetes (T2D) patients who were on anti-depressants. **METHODS:** The study included patients who were on anti-depressants (selective serotonin reuptake inhibitors, SSRI, or tricyclic antidepressants,TCA) and prescribed a new AD during 1995-2011 from the UK Clinical Practice Research Datalink (CPRD.) Patients on more than one ADs are included if ADs are within same weight-change category, categorized as weight-gain agents (WG)(sulfonylureas (SU), thiazolidinediones (TZD)) and weight- neutral/ loss agents (WN/L)(metformin(MET), DPP-4 inhibitors (DPP-4), GLP-1 agonists (GLP-1). Descriptive analyses and multivariate regression examined the association between weight loss ≥3% and newly prescribed AD medications grouped by weight change category. **RESULTS:** This study included 3,445 T2D patients, of whom 2,041 were SSRI users and 1,404 were TCA users. Mean (sd) age was 60(±13.2) years for SSRI users and 64(±12.0) years for TCA users. Baseline mean (sd) weight was 92.86(±22.24) kg for SSRI users and 89.31(±19.86) kg for TCA users. At 12 months after initiation of AD therapy, with baseline age, weight, and other characteristics controlled, the likelihood of achieving weight loss of ≥3% was higher for those prescribed a WN/L agents versus those prescribed a WG agents regardless of the anti-depressant medicine currently used: For SSRI users OR= 2.84; 95% CI [1.89, 4.32]; for TCA users OR = 1.51; 95% CI [1.03, 2.23]. **CONCLUSIONS:** T2D anti-depressant users prescribed WN/L agents had higher odds of actual weight loss of ≥3%, compared to those prescribed WG agents. This association holds regardless of the anti-depressant medicine patients are currently taking. For T2D patients on anti-depressants, considering different weight change effects when initiating anti-diabetes therapy is needed.

PDB5

ECONOMIC IMPACT OF IMPROVING THE ACCURACY OF BLOOD GLUCOSE SELF-MONITORING ON THE SPANISH HEALTH SERVICE

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OBJECTIVES: The 15197:2003 ISO states that 95% of the glucose results shall fall within ±15 mg/dl of the concentrations ≤75 mg/dl and ±20% at those >75 mg/dl. The objective was to estimate the 1-year economic impact for the Spanish Health System of blood glucose self-monitoring by using glucose meters with different degrees of accuracy **METHODS:** A probabilistic model was designed to estimate the clinical and economic outcomes of a type 2 (T2D) or type 1 diabetes (T1D) cohort. A second-order Monte Carlo simulation was run, in order to estimate the frequency of non-detected hypoglycemia and hyperglycemia cases. The frequency of macro and microvascular events, associated with the non-detected readings, was calculated. Finally, the economic impact was assessed for better accuracy levels (±15; ±5%) **RESULTS:** We estimated a total prevalence of 96,169 type 1 and 3,115,866 type 2 treated diabetic patients in Spain. We included all the T1D patients and those insulin dependents T2D (23.4%). The average annual cost of associated events and those of monitoring blood glucose were estimated at 95,987,193 € for T2D and 11,501,292 € for T1D with a ±20% accuracy. When an accuracy of ±15% was analyzed, the annual costs for T2D were reduced to 88,349,485 € and to 9,180,317 € for T1D, showing a total saving of 9,958,682 € a year. If the accuracy rose up to ±5%, the results were 80,067,179 € in T2D and 6,084,776 € in T1D, for a total saving of 21,336.530 € a year. The total costs reduced by 9.3%, 15.4% and 19.9% with accuracy of ±15%, ±10% and ±5%, respectively, respect of the initial ±20% **CONCLUSIONS:** This study shows that if the accuracy of the glucose meters raises, several macrovascular and microvascular events and hypoglycemic episodes could be avoided. That can improve patients' quality of life and reduce significantly the associated costs

PDB6

BASELINE CHARACTERISTICS, WEIGHT AND GLYCAEMIC CHANGE AMONG PATIENTS IN THE UNITED KINGDOM WITH TYPE 2 DIABETES MELLITUS (T2DM) PRESCRIBED A NEW ANTIDIABETIC TREATMENT CLASS IN A REAL WORLD SETTING

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OBJECTIVES: Patients with T2DM have an increased risk of comorbidities associated with weight gain. Depending on patients' weight, treatment guidelines give preference to treatments that have favourable weight profiles, with weight gain being an important adverse event to avoid. This study aims to characterize baseline characteristics, weight and glycaemic change in patients prescribed new antidiabetic treatment. **METHODS:** Patients with T2DM diagnosis and receiving first new antidiabetic treatment class (index) between 01/01/05-01/01/12 were identified in UK CPRD primary care records. Index class could be first-line, switch or add-on. Demographics, baseline weight and glycosylated haemoglobin (HbA1c), and change at 6 months were described by index class. **RESULTS:** Of 23,987 included (of whom 133 were lost to follow-up) 64.7% initiated metformin (MET), 15.5% sulfonylureas (SU), (14.0%) thiazolidinediones (TZD), 2.1% dipeptidyl-peptidase-4-inhibitors (DPP4), 1.9% insulin, 0.7% glucagon-like-peptide-1-agonists (GLP-1), 0.6% 'other', 0.5% acarbose. About 57% were men; baseline mean age for different index classes ranged between 56.5 (insulin) and 63.1 years (acarbose). Mean baseline weight ranged between 88.0 (SU) and 112.4 kg (GLP-1) and mean baseline HbA1c between 72.6 mmol/mol (8.8%) (acarbose) and 84.7 mmol/mol (9.9%) (insulin). Among 14,438 patients with six-month follow-up data an increase in weight was found for subjects initiating SU (2.1%;95%CI: 1.9;2.4,n=2,223), TZD (1.9%;95%CI: 1.7;2.1,n=2,034) and insulin (1.8% ;95%CI: 1.0;2.6,n=285). A reduction in weight was observed for patients on GLP-1 (-3.4%;95%CI: -4.3;-2.5,n=119), DPP4 (-0.9%;95%CI: -1.4;-0.4,n=347) and MET (-0.8%;95%CI: -0.9;-0.7,n=9,278). A mean reduction in HbA1c over the six month period was seen for all antidiabetic classes but was not statistical significant for GLP-1 and 'other'. **CONCLUSIONS:** These results indicate that initiation of antidiabetic agents such as SU, TZD and insulin frequently are associated with weight gain. This underscores the need to choose agents with favourable weight profiles for overweight or obese patients, as recommended by UK T2DM treatment guidelines.

PDB7

GLYCEMIC, LIPID, AND BLOOD PRESSURE CONTROL AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN DUBAI

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OBJECTIVES: Inadequate glycemic, blood pressure (BP), and lipid control among type 2 diabetes mellitus (T2DM) patients is associated with increased risk of T2DM-related complications. Few data on these outcomes are available from the United Arab Emirates (UAE). The objective was to estimate the proportion of T2DM patients with glycemic, lipid, and BP control at a large centre in Dubai. **METHODS:** Charts from T2DM patients aged ≥18 years that visited the Dubai Hospital from October 2009 to March 2010 (enrolment period) were systematically sampled until the target (n=250) was reached. Results of haemoglobin A1c (HbA1c), low-density lipoprotein (LDL), and BP tests conducted from enrolment to September 2011 were abstracted from patient charts. The most recent test values were compared to guideline targets. The proportion of well-controlled (target met on all tests) and never-controlled patients (target not met on any test) over the study period was calculated. All analyses were stratified by T2DM duration. **RESULTS:** Thirty-three percent of the sample was male, and at enrolment, the mean (SD) age was 58 years (12), and T2DM duration, 14 years (8). At the most recent assessment, 58 patients (23%) had HbA1c <7%, 68 (27%) had HbA1c ≥9%, and 173 (71%) had LDL <100mg/dL. Although 74 patients (29%) met BP targets (<130/80mmHg), 50% had BP ≥140/90mmHg. HbA1c, LDL and BP were well-controlled in approximately 7.2%, 41.2%, and 8.6% of patients, respectively, while 59.2%, 7.8% and 21.3% of patients were never-controlled, respectively. The proportion of patients who were never-controlled for HbA1c increased with T2DM duration. **CONCLUSIONS:** Nearly 75% of patients met targets and over 40% were well-controlled for LDL; however, rates of control for HbA1c and BP were lower. Given the increased risk of complications associated with poor control, achieving higher rates of control could reduce the burden of T2DM in the UAE.

PDB8

A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF SECOND-LINE ANTI-DIABETES TREATMENTS FOR THOSE WITH TYPE 2 DIABETES MELLITUS INADEQUATELY CONTROLLED BY SULFONYLUREA MONOTHERAPY

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OBJECTIVES: To assess the efficacy and safety of EU-licensed anti-diabetes agents when added to sulfonylurea (SU). **METHODS:** A systematic review was conducted in MEDLINE, EMBASE and CENTRAL to identify randomised controlled trials in patients with type 2 diabetes mellitus inadequately controlled by a stable dose of SU monotherapy. Direct meta-analysis, Bucher indirect comparisons and Bayesian network meta-analysis (NMA) using WinBUGs were conducted. The effect of potentially confounding baseline factors was explored through covariate analyses. **RESULTS:** The search identified 2,976 articles of which 2,945 were excluded based on title/abstract. On reviewing remaining full-text articles, 5 studies were selected for analysis at 24 (+/- 6) weeks follow-up. All studies were comparable in terms of baseline characteristics, including: HbA1c, age and BMI. Three classes of agents had sufficient data for meta-analysis: DPP4 inhibitors ('DPP4s'), GLP1 analogues ('GLP1s') and SGLT2 inhibitors ('SGLT2s'; only dapagliflozin has an EU licence in this class). Based on the fixed-effect NMA, all three classes of treatment resulted in statistically significantly lower HbA1c at follow-up compared to placebo (based on the 95% credible interval [CrI]). SGLT2 treatment resulted in significantly lower weight at follow-up compared to placebo (–1.54 kg; 95% CrI –2.16, –0.92), which is in contrast to treatment with GLP1s (-0.65kg; 95% CrI -1.37, 0.07) and DPP4s (0.57 kg; 95% CrI 0.09, 1.06). The odds of hypoglycaemia for SGLT2 and DPP4 add-on treatment were similar to placebo, but significantly greater than placebo for GLP1 add-on treatment (10.89; 95% CrI 4.24, 38.28). Assessment of NMA model heterogeneity was hindered by the low number of studies within the network. **CONCLUSIONS:** All three classes of treatments used as add-on therapy to SU provided better short-term glycaemic control compared to SU monotherapy. However, DPP4s, GLP1s and SGLT2s may show variation in terms of impact on weight and incidence of hypoglycaemia.

PDB9

REAL LIFE EFFECTS OF LIRAGLUTIDE SUPPORTS THOSE SHOWN IN RCTS

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OBJECTIVES: In RCTs performed in patients with T2DM liraglutide reduced HbA1c by 1.0-1.5%-point and weight up to 3.7kg. Patients had disease duration of 7.7 years on average, baseline HbA1c of 8.4%. We assessed the effectiveness of liraglutide prescribed per guidelines in the analyzed cohort. **METHODS:** Patients from an Israeli HMO (Maccabi) treated with liraglutide ≥6 months during 2010-2012 were included. Prescription rules were BMI>30; HbA1c>8.0% after use of 2 oral hypoglycemic agents. Data was extracted from electronic records included in a registry of >90,000 diabetes patients. Assessments were performed within 180 days before the date of first prescription and at 6 months +/- 90 days. **RESULTS:** A total of 462 insulin naïve patients treated with liraglutide were identified. 52% males; age was 61.0 years (SD 8.67); diabetes duration was 10.5 years (SD 3.53). HbA1c decreased by 0.93%-points (SD 1.17) (p<0.0001 95% CI 0.82-1.03), down from 8.6% (SD 1.20). Mean time between HbA1c measurements was 222 days (SD 52.39). In 170 patients with available data, weight decreased by 2.5kg (SD 5.09) (p<0.0001 95% CI 1.71-3.2) from 99.9kg (18.17). Time between measurements of weight was 202 days (SD 63.2). Diabetes duration, HbA1c levels and change of the group with weight data were similar to the main cohort. 202 patients (43.7%) achieved ≥1%-point HbA1c reduction. In 31.2% (48 of 170), the reduction was without weight gain. 26 (16.9%) achieved the NICE criteria (decrease of HbA1c≥1% and weight≥3%). Baseline HbA1c and amount of liraglutide prescribed correlated with the degree of HbA1c reduction. **CONCLUSIONS:** Real life use of liraglutide significantly reduced HbA1c and weight, showing similar outcomes as those observed in RCTs. Compared to the RCTs patients in this cohort had more severe diabetes and were more obese, yet liraglutide retained its effects.

PDB10

A BAYESIAN MULTIPLE TREATMENT COMPARISON OF DULOXETINE, PREGABALIN, GABAPENTIN, AMITRIPTYLINE, AND THEIR COMBINATIONS FOR PAINFUL PERIPHERAL NEUROPATHY BASED ON PAIN REDUCTION REPORTED IN CLINICAL TRAILS

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OBJECTIVES: To compare the performance of treatment of painful diabetic peripheral neuropathy (PDPN) — duloxetine, pregabalin, gabapentin, amitriptyline, and their combinations based upon pain reduction reported in clinical trials, and inform a revised treatment algorithm. **METHODS:** Published studies of PDPN treatment through May 2012 were identified from MEDLINE(PubMed) database and extended manual search was conducted based on citations from identified studies. Inclusion criteria was restricted to randomized controlled trials lasting at least 5 weeks and at most 12 weeks and studies examining 30% pain reduction or equivalent. Direct and

indirect pairwise odds ratios (OR) were obtained. The study used Bayesian Analysis Using Gibbs Sampling in Windows (WinBUGS) version 1.4.3. and Monte Carlo Simulations to conduct a multiple treatment comparison. Results are reported in OR with 95% credible intervals (CI) and the median of ranking. **RESULTS:** There were a total of 10 studies with 23 treatment arms, representing 2,885 subjects enrolled, that were included in the analysis. The results from fix effects model indicated that duloxetine, pregabalin, gabapentin, and co-administration of duloxetine and gabapentin were significantly better than amitriptyline (OR= 3.22[95%CI, 1.54-7.17], OR = 2.53[95%CI, 1.11-5.94], OR = 4.00[95%CI, 1.33-11.69], OR = 2.86[95%CI, 1.09-7.48], respectively). The results from random effects model suggested that only duloxetine and pregabalin were significantly better than placebo (OR = 2.61[95%CI, 1.37-4.95] and OR = 1.97[95%CI, 1.01-3.62], respectively). There was no significant difference between amitriptyline and placebo in either fixed or random effects models. With regard to the median ranking, gabapentin was ranked first, followed by duloxetine, co-administration of duloxetine and gabapentin, pregabalin, placebo, and amitriptyline from the fix effects model. **CONCLUSIONS:** Treatment of PDPN with amitriptyline does not appear to be significantly different from placebo. Duloxetine and pregabalin appear to be better than both amitriptyline and placebo.

PDB11

RESULTS OF GALATA STUDY: GALVUS EFFICACY AND SAFETY ASSESSMENT IN TURKISH POPULATION

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OBJECTIVES: The GALATA study was the first observational study on DPP-4 inhibitors in Turkey and aimed to evaluate the efficacy, safety and tolerability of vildagliptin and metformin combination (VMc) in patients with type 2 diabetes mellitus (T2DM). **METHODS:** A total of 648 of the 682 screened T2DM outpatients (age >18 years) on VMc for at least 4 weeks prior to enrollment were included in this 24-week, multicenter, observational study. **RESULTS:** Of the 648 patients, 382 (59.0%) were female. The mean (standard deviation-SD-) age was 55.2 (10.2) years, the mean (SD) T2DM duration was 4.8 (5.2) years and 220 (34.0%) patients had T2DM for more than 5 years. Patients were followed for median (inter-quartile range-IQR-) 184.0 (74.0) days at median (IQR) 4.0 (2.0) visits. Median vildagliptin and metformin doses were 100.0 mg and 2000 mg, respectively. HbA1c decreased from 7.8% to 7.0% ($p<0.001$). A similar reduction in HbA1c from 7.6% to 7.1% was also seen in elderly patients (>65 years, 18.1% of patients) ($p<0.001$). The proportion of patients with HbA1c ≤6.5% increased from 13.3% to 42.7% ($p<0.001$) and those with HbA1c ≤7.0% increased from 26.6% to 65.3% ($p<0.001$). Mean fasting plasma glucose (FPG) decreased from 153.1 mg/dL to 136.5 mg/dL ($p<0.001$), whereas mean post-prandial plasma glucose (PPG) decreased from 217.6 mg/dL to 182.1 mg/dL ($p<0.001$). Eighty (12.3%) patients experienced 122 adverse events (AEs) including 3 serious AEs; 2 SAEs were not suspected to be related to VMc. AEs were mostly (94.3%) mild or moderate in severity and no action was taken for 44.3% of them; 76.2% of AEs resolved during follow-up. **CONCLUSIONS:** The results of the GALATA study suggested that VMc significantly decreased HbA1c, FPG and PPG, achieved glycemic control targets even in elderly patients and demonstrated good overall safety and tolerability in T2DM patients.

PDB12

EFFICACY AND SAFETY OF TREATMENTS OF TYPE 2 DIABETES MELLITUS (T2DM): A SYSTEMATIC REVIEW (SLR)

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OBJECTIVES: Collect randomized clinical evidence on the efficacy and safety of antidiabetic agents used in dual or triple therapy or add-on to insulin to provide a qualitative overview of the available evidence and undertake a meta-analysis. **METHODS:** A SLR was conducted in line with NICE guidelines to identify randomised controlled trials assessing agents received in combination with metformin (MET), a sulphonylurea (SU), MET+SU, MET+pioglitazone, or insulin. Interventions of interest included SGLT-2 inhibitors (canagliflozin and dapagliflozin), sulphonylureas, pioglitazone, DDP-4 inhibitors, GLP-1 analogues and insulin. Electronic searches were undertaken using Medline, Medline-in-process, Embase, and the Cochrane Library and supplemented with hand searches. An ad hoc search was conducted to identify the most recent data at 104 weeks. **RESULTS:** A total of 159 clinical trials met inclusion criteria. The frequency of studies by background therapy was as follows: MET (38%), mixed (trials containing treatment arms with different background therapies; 25%), insulin (21%), MET+SU (9%), and SU alone (8%). One study (assessing canagliflozin) featured a background of MET+pioglitazone. Studies varied in terms of treatment duration (12 to 104 weeks), presence and duration of run-in periods (57% studies with run-in, from 0.7 to 18 weeks), HbA1c eligibility criteria (minimum from 6% to 7%), body mass index (BMI; 37 studies focused on overweight and obese patients, two studies focused on obese patients) and age for inclusion (from ≥18 to ≤ 85 years). **CONCLUSIONS:** The outcome of this SLR will serve as input-data in a meta-analysis, to assess relative efficacy of T2DM treatments in different background therapy settings.

PDB13

RESULTS OF THE POST-MARKETING SURVEY OF VILDAGLIPTIN IN FRANCE

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OBJECTIVES: To assess the effectiveness, tolerability and maintenance of vildagliptin in type 2 diabetes (T2D) patients under real-life conditions in France, requested by the French Health Technology Agency. **METHODS:** A representative sample of T2D patients initiating a treatment with vildagliptin was enrolled in a 2 years follow-up observational cohort in 2010 by a national sample of endocrinologists and general practitioners. **RESULTS:** A total of 482 GPs and 84 endocrinologists included 1,700 patients. 60% were males, mean age=63 (±9) years, mean disease duration=7 (±6.5) years. Follow up visits were available for 96.3%, 90.7%, 86.5% and 81.8% of patients at respectively 6, 12 18 and 24 months. Mean HbA1c level decreased from 7.8% (sd=1.3) before vildagliptin prescription to 7.0% (sd=1.0) 0 to 6 months after vildagliptin initiation and remained stable thereafter: 7.0% (sd=1.0), 7.0% (sd=0.9) and 7.0% (sd=1.0) 6 to 12 months, 12 to 18 months and 18 to 24 months after vildagliptin initiation. The percentages of patients with alanine and/or aspartate aminotransferase above 120 UI were 0.5% before vildagliptin prescription and 0.3%, 0.5%, 0.1%, 0.0% at 0-6 months, 6-12 months, 12-18 months and 18-24 months after vildagliptin prescription. The mean glomerular filtration rate (MDRD formula) was 82.0 ml/minute before vildagliptin prescription and 82.4, 84.1, and 83.6 and 82.8, at 0-6 months, 6-12 months, 12-18 months and 18-24 months after vildagliptin prescription. The incidence of severe hypoglycemia (requiring third party assistance) has been estimated at 0.30/100 vildagliptin treated patients years (CI95%=[0.15,0.55]). All occurred in patients also treated with insulin and/or sulfamide The proportion of patients treated with vildagliptin remained high over the course of the study: 96.5% (CI95%[95.6,97.4]) after 6 months, 92.5% (CI95%=[91.2%,93.8%]) after one year and 88.8% (CI95%=[87.2%,90.4%]) after 2 years. **CONCLUSIONS:** Vildagliptin showed sustained effectiveness in terms of reduction in HbA1c over 24 months, with a low incidence of hypoglycemia.

PDB14

CLINICAL OUTCOMES AND HEALTH CARE COSTS EVALUATION OF SULFONAMIDES AND THIAZOLIDINEDIONES COMPARED WITH DIPEPTIDYL PEPTIDASE 4 INHIBITORS FOR THE TREATMENT OF UNCONTROLLED DIABETES

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OBJECTIVES: To compare clinical outcomes and the health care costs across two cohorts of uncontrolled diabetic patients who initiated treatment with Sulfonamides or Thiazolidinediones (SU/TZD) or Dipeptidyl Peptidase 4 (DPP-4) Inhibitors in a clinical practice setting. **METHODS:** A retrospective analysis using a large administrative database and a clinical registry containing laboratory results of three Italian Local Health Units was performed. The index-period ranged from July, 2008 and June, 2010. Patients were treatment naïve to SU/TZD or to DPP-4, but already treated with other oral antidiabetic agents. Demographics, concomitant therapies, Charlson comorbidity index, glycemic and lipid control level and previous hospitalizations were assessed at baseline. Adherence was measured by *Medication Possession Ratio* (MPR). We calculated unadjusted rates and used a Poisson regression model to estimate risk ratios for diabetes-related hospitalizations occurred during the 18-months follow-up period. Total annual costs included all the pharmacological treatments and the direct costs due to hospitalizations and outpatient services. **RESULTS:** We identified 1384 patients treated with SU/TZD and 199 treated with DPP-4. DPP-4 patients were significantly younger (mean age 59.2 years and 65.0 years; $p<0.001$) and with less previous hospital discharges for diabetes-related diseases. Baseline mean HbA1c was 8.1% for SU/TZD and 8.2% for DPP-4 patients. DPP-4 naïve resulted more adherent (MPR≥80%) than SU/TZD naïve (70.9% and 55.8%; $p<0.001$). The SU/TZD group showed a significant increased risk of diabetes-related hospitalizations (unadjusted rate was 9,17 vs 3,47 per 100 person-years, $p=0.002$; adjusted incidence rate ratio 1.83; $p=0.028$). The higher hospitalization rate resulted in higher total annual direct costs per patient (€2.719 vs €2.462 of those treated with DPP-4). **CONCLUSIONS:** Results indicate that uncontrolled diabetic patients who initiated treatment with DPP-4, compared with those initiating with SU/TZD, are associated with a reduced risk of diabetes-related hospitalizations and consequently with a lower overall total annual cost per patient.

PDB15

THE PRESENCE OF METABOLIC AND OTHER RISK FACTORS IN ADRENAL INSUFFICIENCY PATIENTS COMPARED TO AN UNMATCHED BACKGROUND POPULATION FROM THE SAME REGION IN THE UNITED KINGDOM

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OBJECTIVES: To describe epidemiological characteristics among adrenal insufficiency (AI) patients and describe the prevalence of risk factors in primary and secondary AI (PAI; SAI) and an unmatched, non-AI population. These analyses explore metabolic morbidity in AI, which literature suggests may be associated to a non-physiological cortisol profile. **METHODS:** Initial aggregated data from the FARSITE database were analysed. The prevalence of risk factors was evaluated, including hypertension, BMI, diabetes and depression, and compared across PAI, SAI and non-AI populations. Characteristics of non-AI patients were not matched with AI patients. **RESULTS:** A total of 261,638 patients were included; 62 PAI and 191 SAI. Prevalence of hypertension was 32% in PAI, 22% in SAI and 13% non-AI. 26% of hypertension in SAI was not on target according to QOF criteria (14% non-AI; 10% PAI). Hypercholesterolemia occurred in 13% of PAI and 6% of SAI patients (3% non-AI). Among SAI patients, 69% were overweight (BMI>25) or obese (BMI>30) (63% PAI; 39% non-AI). Diabetes (Type 1 and 2) was prevalent in 13% of PAI and 10% of SAI (5% non-AI), with HbA1c not controlled according to QOF criteria in 75% of PAI and 74% of SAI patients. Psychological risk factors were more prevalent among AI patients; 24% of PAI and 14% of SAI patients recently received anti-anxiety/depression treatment (6% non-AI). Hypnotics were recently prescribed to 6% of SAI patients (1% non-AI; PAI not reported). Bisphosphonates are used by 21% of PAI and 8% of SAI patients (2% non-AI). The hospital admission rate was 3% for SAI patients (1% non-AI; PAI not reported). **CONCLUSIONS:** The prevalence of metabolic and other risk factors is considerably higher among AI patients

than the non-AI population. Since the comparison was unmatched, results should be interpreted with caution. Ongoing analysis will include a detailed data assessment, with a stronger comparison against matched non-AI populations.

PDB16
REAL WORLD INCIDENCE OF TYPE 2 DIABETES (T2D) COMPLICATIONS LEADING TO HOSPITALIZATION IN FRANCE: THE RECODE STUDY
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OBJECTIVES: To estimate the cumulative incidence and cost of cardiovascular (CV) complications (stroke, acute coronary syndrome (ACS), acute heart failure (AHF) and peripheral vascular disease (PVD)) leading to hospitalization in T2D patients with a CV complication history in France. **METHODS:** We conducted an analysis of the Program for a Medicalized Information System (PMSI) databases which record all hospitalizations occurring in France including rehabilitation care. We identified all patients with a T2D diagnosis and hospitalized for any reason in 2006-2008 and selected patients with a documented CV complication history. We analyzed those patients as a retrospective cohort followed-up for 3 years from the index date (January 1st 2009) and calculated cumulative incidences of new CV complications. We considered death as a competing event. Mean hospital and rehabilitation costs were based on the National Scale of Costs. **RESULTS:** A total of 1,114,182 T2D patients were hospitalized in France in 2006-2008. Among them, 30.5% (n=339,328) had a CV complication history. Mean age was 70.6 (+/-11.1), and 61.9% were males. Hypertension, dyslipidemia, renal impairment and obesity were reported in 80.1%, 45.0%, 33.3% and 29.2% of the patients, respectively. The 3-year cumulative incidences for one or more new CV complication were: 3.6% [95%CI:3.5%;3.7%] for stroke, 5.6% [95%CI:5.5%;5.7%] for ACS, 6.8% [95%CI:6.7%;6.9%] for AHF and 15.0% [95%CI:14.9%;15.1%] for PVD with a mean cost per event of €5,724, €5 315, €4 726, €4 766, respectively. 21.8%, 10.5%, 11.4% and 9.5% of patients required rehabilitation care for stroke, ACS, AHF and PVD, at an additional mean cost of €12,000, €6 233, €6 987 and €9 219 per patient, respectively. **CONCLUSIONS:** CV complications represent an important burden for T2D patients and the health system in France. These results would be helpful for health technology assessment and for economic evaluation of upcoming interventions which reduce CV risk in T2D patients.

PDB17
STUDY AND EVALUATION OF MEDICATION ERRORS IN DIABETIC PATIENTS IN MEDICINE WARD OF A SECONDARY CARE COMMUNITY HOSPITAL AT MUMBAI, INDIA
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OBJECTIVES: While concerning to diabetic treatment, any suboptimum therapy may lead to medication error (ME). Objective of study was to report the causes, severity, increase in cost of therapy and outcomes of ME in patients undergone treatment for diabetes in medicine ward of a community hospital. **METHODS:** Prospective observational study (8 months). In-patients with type-II diabetes mellitus were chosen randomly and the details were followed till discharge. **RESULTS:** Incidences of 504 MEs were observed in 164 out of total patient pool of 230. The notable trends in MEs identified were- erroneous prescriptions 101(20.03%), inappropriate dosage-form 93(18.4%), incorrect-route 63 (12.5%), incident of drug interactions 129 on 55 patients (10.09%), failure to monitor lab levels 27(5.30%), failure to adjust doses according to lab levels 37(7.14%) and 21(4.16%) cases of incorrect-indications. On severity scale, MEs were classified as 143(28.37%) severe, 256(50.79%) moderate and 105(20.8%) mild. Predicted error outcome of 164 incidences which were reaches to patient classified as- no serious 85(51.8%), moderately serious 61(37.19%), 9(5.3%) life threatening and 9(5.35%) death (predicted). We observed fair degree of linear correlation between increasing age and occurrence of ME 0.99 ($r_{critical}$ value-0.878). Female sex was found to be at higher risk of MEs than male (X^2=6.73, P-value= 0.01). There was a linear correlation observed between the polypharmacy and ME 0.95 ($r_{critical}$value-0.44). It was observed that, out of total 129 drug interactions identified; only 35(27.13%) were moderate, while 72(55.81%) were severe and 22(17.05%) found mild. Significant increment in the length of stay in hospital and direct drug cost were observed among the severe, moderately severe and in mild cases. **CONCLUSIONS:** The observed finding of ME defines specific clinical domains and patient subgroups for which aggressive efforts needed to reduce MEs. Through information dissemination and education, managed health care professionals should play more active role in ME-reduction.

PDB18
ESTIMATING THE HEALTH OUTCOME OF TREATING TYPE 2 DIABETIC POPULATION TO TARGET IN LOCAL MUNICIPALITY LEVEL
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OBJECTIVES: Type 2 diabetes (T2D) and its consequences are largely studied worldwide. The number of diabetic patients is increasing and thus, a growing number of health care resources are needed to cover the treatment of this population. It is also known that in spite of the national treatment guidelines, the recommended HbA1c level (<6.5%/48 mmol/mol) is not always achieved. In order to allocate the resources effectively, local information concerning epidemiological and demographic differences across different jurisdictions must be available. **METHODS:** A national population-based study (Finriski 2007) was used to estimate the prevalence of diabetes in different geographical areas. The estimated prevalence rates and number of T2D patients were extrapolated to municipal level using demographic data from the official statistics. UKPDS risk equation was used to predict the number of cardiovascular events with and without proper treatment in each municipality. Local risk profile and different HbA1c levels (6.5% (48 mmol/mol) and 8.0% (64 mmol/mol)) were used to illustrate the importance of treating patients to target. A map-based application was built (Tableau 8) to visualize the information to be easily communicated to local authorities and clinicians. **RESULTS:** A middle-sized Finnish municipality with 74 168 inhabitants (Joensuu) was chosen as a case-example. The estimated number of diabetic patients was 2267, out of which 1678 had T2D. Within three years among patients with T2D, the predicted number of CHD events would be 73 and 57 for HbA1c levels 6.5% and 8.0%, respectively, resulting total of 16 avoidable CHD events. **CONCLUSIONS:** By bringing the understanding of epidemiology and treatment effects to local level, there is a possibility to show the positive outcomes of good diabetes care in real practice. This information may be used to help budget holders in resource allocation and to motivate authorities, clinicians (and patients) to follow the diabetes treatments guidelines.

PDB19
RESULTS FROM A TWO-STAGE DELPHI PROCESS TO IDENTIFY CARDIOMETABOLIC RISK FACTORS IN ADRENAL INSUFFICIENCY PATIENTS AND UNDERSTAND CURRENT TREATMENT IN ITALY
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OBJECTIVES: To obtain information regarding the presence of cardiometabolic risk factors among adrenal insufficiency (AI) patients in Italy. To understand treatment patterns and goals and to gain consensus regarding how effectively existing therapies meet these goals. **METHODS:** A two-stage Delphi process was conducted with four Italian key opinion leaders (KOLs). Each KOL completed an electronic survey eliciting information regarding AI management and the prevalence and importance of risk factors. To reach a consensus on the key issues, the results were discussed at a face-to-face meeting. **RESULTS:** The KOLs agreed that avoiding adrenal crisis is the main treatment goal, and that quality of life and avoiding fatigue are most important to patients. Patients typically receive 20–30 mg cortisone acetate or hydrocortisone daily in 2-3 administrations. A consensus was reached that cardiometabolic risk factors are not hallmarks of AI, but are related to its glucocorticoid replacement treatment (GC) either due to overtreatment or non-physiological replacement of serum cortisol. In agreement with the available evidence in the literature they suggested that the increase risk may be associated with the non-physiological cortisol peaks and troughs that are characteristic of the existing GC replacement therapies. They established that 50% of AI patients are over treated, often to minimise the risk of adrenal crisis and all patients currently face non-physiological cortisol replacement, given the available treatments. GC replacement–related risks included (prevalence in AI in parentheses): hypertension (10–30%), abdominal obesity (15–35%), dyslipidaemia (33%) and metabolic syndrome (30–35%). **CONCLUSIONS:** The prevalence of cardiometabolic risk factors is associated with the treatment of AI, not AI itself. Over-treatment and non-physiological cortisol replacement may explain cardiometabolic risks. A physiological alternative to existing treatments would be welcomed in Italy.

PDB20
INCIDENCE/PREVALENCE, RISK FACTORS AND COMPLICATIONS OF TYPE 2 DIABETES MELLITUS IN INDIAN PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS
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OBJECTIVES: Type 2 Diabetes mellitus (T2DM) is becoming a major chronic disease burden worldwide. Indians are known to have an increased predisposition for diabetes which has become an important health concern. The current analysis is aimed to systematically review medical literature on T2DM, its prevalence and complications in India and also explore the differential risk factors in sub-groups. **METHODS:** Studies are being retrieved from Pubmed, Cochrane and Embase databases using relevant search strategies. Search limits are: articles in English, in human adults and published since year 2001. Pre-specified inclusion/exclusion criteria will identify study types, such as randomized controlled trials (RCTs), observational and retrospective studies reporting incidence/prevalence, risk factors and complications of T2DM patients in India. Two researchers will independently extract the data and analysis of comparable outcomes will be carried out as per appropriate statistics along with critical appraisal of the studies. Meta-analysis will be done using RevMan (v5.0) **RESULTS:** Though there have been several studies assessing incidence/prevalence, complications and risk factors for T2DM, a systematic review/meta-analysis of the evidence is lacking in the Indian scenario. This study aims to provide the much-needed evidence linking incidence/prevalence, complication and risk factors in different groups of T2DM patients. This study hopes to demonstrate association of various risk factors with disease progression and with complications of T2DM. **CONCLUSIONS:** The prevalence of T2DM has been increasing over the years. The data from published studies will hopefully answer some of the prevailing variations and trends in prevalence of T2DM between different subgroups of T2DM patients and their association with risk factors.

PDB21
EARLY LIFE DETERMINANTS OF METABOLIC SYNDROME AND DIABETES MELLITUS IN SOUTH ASIAN POPULATION LIVING IN EUROPE: A SYSTEMATIC REVIEW
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OBJECTIVES: To review lifestyle and genetic factors during pregnancy and early childhood in South Asian population living in Europe that may influence later risks of insulin resistance, metabolic syndrome, T2DM and CVD **METHODS:** A systematic search, using controlled and free terms (i.e.- metabolic-syndrome, glucose-intolerance, diabetes-mellitus, pregnancy, foetal development, life-style, nutrition) was conducted in Medline, Centre for Reviews and Dissemination and Cochrane Library databases. It was completed by pearling and hand-searching. Two reviewers assessed independently the results retrieved in the search, to adopt a decision on inclusion/exclusion. The quality of included papers was appraised with STROBE checklist for

observational studies and Centre for Evidence Based Medicine checklists for any other study design. The present review is part of the GIFTS project funded by Seventh Framework Programme of European Commission. **RESULTS:** A total of 349 papers were identified, after title and abstract revision 76 full text were retrieved plus 8 identified through pearling. To date 67 full texts have been assessed, 49 excluded and 18 included. 14 (78%) were conducted in the UK. South Asian pregnant women were at higher risk of developing GDM (OR ranged 2-5.6) and intrauterine growth retardation (OR ranged 2-5) than European counterparts. These factors contributed to higher rates of stillbirth, perinatal and neonatal mortality and congenital anomalies detected in South Asian origin women. As well as higher rates of babies with vitamin D deficiency, hypocalcaemia, hyperinsulinemia, dyslipidaemia, hypoglycaemia and lower birthweight. Also higher risk of rapid weight gain between 12 to 24 months and 3 to 5 years in Asian infants was reported in two different papers. **CONCLUSIONS:** There are differences between Asian women living in Europe and European women during pregnancy, and their offspring, which as early life factors might explain higher prevalence of later metabolic syndrome and type 2 diabetes in Asian migrant population.

PDB22

PREDICTING THE FREQUENCY OF SEVERE AND NON-SEVERE HYPOGLYCAEMIA IN INSULIN TREATED TYPE-2 DIABETES SUBJECTS

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OBJECTIVES: Recent studies have quantified the resource implications associated with severe hypoglycaemia episodes (SHE) and non-severe hypoglycaemia episodes (NSHE). The objective of this study was to characterize the relationship between the frequency of SHE/NSHE and patient/therapy characteristics in insulin treated type-2 diabetes mellitus (T2DM) patients. **METHODS:** We conducted a literature review of the MEDLINE database for insulin-based T2DM clinical trials where sulfonylurea usage was also reported between June 1, 2007 and June 1, 2012. Patient demographics, treatments effects and treatment type were extracted and the SHE/NSHE rate per 100 patient years (PY) was modeled via a log-linear regression model using R. **RESULTS:** Data were extracted from 82 studies for a total of 155 trial arms meeting the search criteria; treatment regimes were categorized into basal analog (30%); bolus analog (4%); basal bolus (24%); biphasic analog (25%); biphasic human (8%) and NPH (10%). Mean (standard deviation) age was 57.9 (3.8) years; 10.2 (2.4) years duration of diabetes; 8.8% (0.7)baseline and 7.5% (0.5) end-of-study HbA1c respectively. Mean reported NSHE/100 PYs was 929.8. The final regression model was NSHE/100PY=exp(14.771 - 0.088 × age - 0.667 × baseline HbA1c + 0.427 × HbA1c reduction + 0.189 × duration diabetes + 0.007 × % study allowed sulphonylurea – 0.545 × basal analog insulin) with an R^2 goodness of fit of 0.226. Mean reported SHE/100 PYs was 5.9. The final regression model was SHE/100PY=exp(10.794 - 0.101 × age - 0.723 × baseline HbA1c + 0.638 × HbA1c reduction + 0.163 × duration diabetes + 0.768 × biphasic insulin)-1 with an $R^2$of 0.219. **CONCLUSIONS:** This study provides a basis for predicting the number of SHE and NSHE in insulin treated T2DM subjects. When linked to resource and quality life, these equations may facilitate the improved estimation of the health economic burden associated with SHEs and NSHEs.

PDB23

ANTI-DIABETIC MEDICATIONS RELATED SEVERE HYPOGLYCAEMIA RISK IN DIABETES TYPE 1 AND TYPE 2 – A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

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OBJECTIVES: Severe (requiring assistance from another individual) hypoglycaemic events (SHEs) are important from both clinical and economic perspectives. The aim was to assess treatment-related SHEs risk in different treatment regimens in type 1 and 2 diabetes. **METHODS:** Anti-diabetic treatments were stratified into six groups: basal-bolus (BB); basal in combination with oral therapy (BOT); insulin pumps; biphasic insulin; sulfonylureas; other than SU oral antidiabetic drugs (OADs). Insulin treatments were further split into analogues (IA) and human insulins (HI). The systematic review of Medline, EMBASE and Cochrane databases was conducted for recent (≤10 years), large (n ≥100), observational studies. Data on time horizon, participants number and SHEs occurrence were extracted. Using a random effects Poisson model within MCMC framework we estimated the SHEs rates. **RESULTS:** In the systematic review 5220 publications were found, 525 full texts evaluated and 101 articles included (55 trials). The following average SHE/year (No of studies; 95%CI) were estimated: Type 1: BB with IA as the basal component: 0.53 (7; 0.29–1.18); BB with HI: 1.10 (6; 0.58–2.71); pump treatment: 0.18 (14; 0.13–0.25); biphasic insulin: 1.10 (0.58–2.71). Type 2: BOT with IA as the basal component: 0.13 (11; 0.04–1.17); BOT with HI: 0.21 (7; 0.08–0.88); BB with IA: 0.01 (6; 0.003–0.25); BB with HI: 0.56 (3; 0.16–9.65); biphasic IA: 0.10 (12; 0.05–0.26); biphasic HI: 0.20 (6; 0.07–0.93); sulfonylureas: 0.05 (6; 0.02–0.14); OADs: 0.01 (0.001–0.008). The differences in the SHEs risk among regimens were significant at a 95% level. **CONCLUSIONS:** The SHEs risk differs in both type 1 and 2 diabetes across various treatment regimens. HI was found to increase the SHEs risk compared to IA. Limited availability of studies and heterogeneous data make it difficult to come up with precise rate estimation for typical anti-diabetic treatment regimens.

DIABETES/ENDOCRINE DISORDERS – Cost Studies

PDB24

ESTIMATION OF THE COST OF COMPLICATIONS RELATED TO GLYCATED HEMOGLOBIN IN THE ITALIAN DIABETES TYPE 1 POPULATION

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OBJECTIVES: In Type 1 diabetic (T1D) patients high values of glycated hemoglobin (HbA1c) have been shown to be associated with higher risk of complications leading to high costs to the National Health Care System (NHS). The aim of this analysis is to evaluate the economic impact of poor glycaemic control, and the potential savings associated with better glycemic control in the Italian T1D population. **METHODS:** A probabilistic model using published risk-curves was developed to project incidence and progression of diabetes-related complications associated with different HbA1c levels over 1-year and 5-year time-horizon in T1D patients. Associated cost of retinopathy, nephropathy, neuropathy, cardiovascular disease, diabetic ketoacidosis and severe hypoglycemia in the Italian setting were used to estimate the economic impact of complications in each HbA1c interval form the NHS perspective. Subsequently the results of the simulation were translated to the entire Italian T1D population stratified by HbA1c level accordingly to published 2012 data. **RESULTS:** Estimated cost per patients of diabetes-related complications in the first year of occurrence, stratified by HbA1c intervals, ranged from 4,463€ for HbA1c ≥10% to 2,006€ for HbA1c between 7% and 8%. A 5 year follow up analysis was also conducted. A treatment strategy able to reduce HbA1c level from ≥10% to 9% could lead to potential savings of 1,342€ per patients in the first year of treatment. Considering the total T1D Italian population, improving HbA1c to <8% in the first year would results in a potential savings of about 17 million euros. **CONCLUSIONS:** The economic impact of diabetes-related complications in the Italian setting is significant. Consequently the potential savings for the NHS derived from the implementation of strategies aimed at improving HbA1c in T1 should be considered. Moreover the greater the reduction of Hba1c obtained the greater the associated savings.

PDB25

COST-COMPARISON BETWEEN DIFFERENT TREATMENT REGIMENS IN DIABETES MELLITUS IN GERMANY BASED ON LONG ACTING INSULINS

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OBJECTIVES: Cost comparison between different basal insulin regimens (Glargine vs. Detemir vs. NPH-insulin) in diabetic patients in Germany under real-life conditions. **METHODS:** The analysis is based on IMS LRx-database (2011). This representative patient tracking tool covers nearly 60 million insurants and includes more than 500 million drug prescriptions per year (including consumables) Patients with at least two prescriptions of basal insulin (Glargine, Detemir or NPH-insulin) in 2011 (January – December) and at least one prescription of any type in 2010 and 2012 were considered eligible. Costs included basal and bolus insulin, oral antidiabetic drugs, test strips, needles and lancets and were estimated by ex pharmacy prices (Lauer Taxe) minus legally defined rebates according to §130 a of social security code (SGB V). **RESULTS:** A total of 542.438 patients were allocated to either Glargine (207.506 patients) or Detemir (90.671 patients) or NPH (244.261 patients). The mean annual treatment costs per patient are 1.211 € (Glargine), 1.224 € (NPH insulin) and 1.572 € (Detemir). A breakdown at the level of different sick funds shows a similar pattern of annual treatment costs per patient of the three basal insulin regimens. The acquisition costs of basal insulin is considerably higher for Glargine (380 €) and Detemir (448 €) compared to NPH-Insulin (253 €). The cost of bolus insulin is lower in the Glargine group (305 €) compared to NPH-insulin (419 €) and Detemir (493 €). Costs of consumables (test strips, needles, lancets) are lowest in the in the Glargine group (395 €) due fewer insulin applications compared to Detemir (509 €) and NPH insulin (461 €.) **CONCLUSIONS:** Mean annual treatment costs are lowest with Glargine followed by NPH-insulin, whereas Detemir based regimens are 30% more expensive under real life conditions. The results are in line with previous cost analyses in diabetic patients in Germany [1-3]

PDB26

A COMPARISON OF THE ECONOMIC BURDEN AND HEALTH CARE UTILIZATIONS OF VETERAN PATIENTS DIAGNOSED WITH DIABETES IN THE UNITED STATES

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OBJECTIVES: To assess the economic burden and health care utilizations of diabetes in the U.S. veteran population. **METHODS:** Adult (≥18 years of age) patients diagnosed with diabetes (International Classification of Disease 9th Revision Clinical Modification [ICD-9-CM] code 250.x0 or 250.x2) were identified from the dataset between October 1, 2009 through September 30, 2011. The first diagnosis date was designated as the index date. A comparator group was created consisting of patients without diabetes but of the same age, region, gender and index year, and matched by baseline Charlson Comorbidity Index. The index date for the comparator group was randomly selected to minimize selection bias. Continuous medical and pharmacy benefits 1 year pre- and 1 year post-index date were required for patients in both groups. One-to-one propensity score matching (PSM) was applied to compare health care costs and utilizations during the follow-up period between the diabetes and comparator groups, adjusted for baseline demographic and clinical characteristics. **RESULTS:** A total of 1,427,948 patients were identified for the diabetes and comparator cohorts. After applying 1:1 PSM matching, a total of 340,933 patients were matched from each group, ensuring well-balanced baseline characteristics. Patients diagnosed with diabetes were more likely to report inpatient (8.93% vs. 2.09%, p<0.01), emergency room (13.66% vs. 5.61%, p<0.01), outpatient (99.63% vs. 53.78%, p<0.01), and pharmacy visits (87.13% vs. 52.69%, p<0.01). They also incurred higher health care costs, including inpatient ($3,031 vs. $582, p<0.01), emergency room ($137 vs. $51, p<0.01), outpatient ($3,375 vs. $1,272, p<0.01), pharmacy ($708 vs. $293, p<0.01) and total costs ($7,113 vs. $2,148, p<0.01) than the comparator group. **CONCLUSIONS:** U.S. veteran patients diagnosed with diabetes reported a significantly higher economic burden compared to the matched controls over a 12-month period.

PDB27
COST OF INPATIENT MANAGEMENT OF HYPOGLYCAEMIA IN FRANCE
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OBJECTIVES: Severe hypoglycaemias occurring in diabetes care are associated with a major economic burden on health care systems, with a major part of the direct costs resulting from the small proportion of patients who are admitted to hospital. We assessed the inpatients costs of severe hypoglycaemic events in Type 1 and 2 diabetes (SHE) patients in France. **METHODS:** The study was done using the 2012 French National Database on hospital care (PMSI). This comprehensive database covers all hospital stays in the French population (over 20 million hospital stays per year). SHE were identified using ICD10 codes of hypoglycaemias (E160, E161, E162, T383) in combination with diabetes codes (E11, E10, E13, E14, N083) and excluding gestational diabetes. Directs costs to the health care system were estimated using the French National Costs study (2011 values). **RESULTS:** Overall, in 2012, 17,835 stays for diabetes related hypoglycaemias were identified in the database corresponding to 16,406 patients. 8.7% of patients were hospitalized twice in the year for SHE, 51% were male and aged 66.7 years on average (SD 19.7). 90% of stays occurred in public hospitals and mean length of stay was 8.1 days (median 7.0). The mean direct cost of one SHE hospital stay was €4,360. Extrapolated to the whole country the direct cost of hospitalized SHE was €77.7 million which roughly correspond to 1.2% of the overall diabetes costs for the health care system. Such value would be considered a conservative estimate due to potential underreporting of cases in the database. **CONCLUSIONS:** Our study confirmed that hypoglycaemic events lead to substantial costs for the community even it was limited to direct costs in inpatient setting. As the short-term and long term consequences of hypoglycaemia begin to be better understood, more studies have to be done to estimate the full economic burden of this disease.

PDB28
HEALTH CARE COST OF CONTROLLED VERSUS UNCONTROLLED TYPE 2 DIABETES PATIENTS IN GREECE
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OBJECTIVES: Health expenditure to treat and prevent T2DM and its complications was estimated at USD 345 million for OECD countries in 2010. These costs pose great burden to national health system's budget, which is already under pressure. In Greece there are no studies that provide information on the costs of T2DM patients including the cost of complications, hospitalizations and co-morbidities. The current study aimed to estimate the total cost of T2DM patients from a third party payer perspective. **METHODS:** A retrospective research study was performed in four major hospital diabetes centers and 211 patients with at least 10 years of T2DM from diagnosis. Patients were categorized in two groups, controlled and uncontrolled. Hospitalization and management of complications was based on DRG cost. Pharmaceutical and diagnosis cost was based on official NHS prices. Health care cost corresponds to 2012 Euros and the perspective used was of the Social Security Fund. Subgroup analysis was performed in order to evaluate the cost difference between controlled vs. uncontrolled, obese non-obese and various other subgroups. **RESULTS:** The mean age of patients was 72.9±8.1 years with mean T2DM duration 21.2±7.5 years, and mean HbA1c 7.3±1.0%. The mean average yearly cost of T2DM was €7.111 whereas only the18.8% was attributed to cost of antidiabetic drugs. Controlled patients (HbA1c $\leq$ 7) cost on average 6.366 and uncontrolled (HbA1c>7) €7.783. The mean hospitalization and complication cost was €2.456. It was found no difference of mean hospitalization and complication cost between controlled and uncontrolled patients (p=0.09). Co-morbidities cost absorbs the majority of the budget and was the differentiating factor between two groups. Few patients (21.8%) reported admission to hospital with similar hospitalization rates on number and duration between the two groups. **CONCLUSIONS:** T2DM is an expensive to treat disease with very high cost complications with economic and societal burden.

PDB29
HEALTH CARE COST OF TYPE 2 DIABETES PATIENTS IN GREECE: SUB-POPULATION ANALYSIS
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OBJECTIVES: Health expenditure to treat and prevent T2DM and its complications was estimated at USD 345 million for OECD countries in 2010. These costs pose a great burden to the national health system's budget, which is already under pressure. In Greece there are no studies that provide information on the costs of T2DM patients including the cost of complications, hospitalizations and co-morbidities. The current study aimed to estimate the total cost of T2DM patients from a third party payer perspective. **METHODS:** A retrospective research study was performed in four major hospital diabetes centers and 211 patients with at least 10 years of T2DM since diagnosis. Patients were categorized in two groups, controlled and uncontrolled. Hospitalization and management of complications was based on DRG cost. Pharmaceutical and diagnosis cost was based on official NHS prices. Health care cost corresponds to 2012 Euros and the perspective used was of the Social Security Fund. Subgroup analysis was performed in order to evaluate the cost difference between controlled vs. uncontrolled, obese non-obese and various other subgroups. **RESULTS:** The mean average yearly cost of T2DM was €7.111 whereas only 18.8% was attributed to cost of antidiabetic drugs. Diabetic men cost 2.222€ more per year in comparison to diabetic women, whereas obese diabetics cost 1.460€ more per year in comparison to overweight and normal patients. These may be explained by the higher levels of HbA1c, co-morbidities and the number of antidiabetic treatments. In addition, diabetic patients with low education level cost 2.341€ cost more on average in comparison to better educated patients. **CONCLUSIONS:** T2DM is an expensive to treat disease and in the era of limited resources and escalating costs it is critical to implement sound public health policies in order to achieve patient's good glycemic control and consequently less burden to health care budgets.

PDB30
ADRENAL INSUFFICIENCY: BURDEN OF DISEASE AND COST OF ILLNESS
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OBJECTIVES: To calculate the cost of illness (COI) associated with adrenal insufficiency (AI) in the UK. AI patients do not produce cortisol and require glucocorticoid replacement therapy (RT) to survive, which is predominantly immediate-release hydrocortisone in the UK. With current therapy, AI patients have increased morbidity and premature mortality, and suffer reduced quality-of-life. **METHODS:** The COI determines the direct and indirect costs over a 1-year period. The COI includes the cost of RT, primary and secondary care costs (GP and outpatient appointments; admissions for adrenal crises; diagnosis and management of AI) and those associated with reduced productivity (absenteeism). Direct costs were estimated using national reference costs, Payment by Results tariffs and other published data. AI prevalence and adrenal crises data were taken from published literature and activity data (hospital admissions for management of AI) from Hospital Episode Statistics (HES) data. A 2012 worldwide survey of AI patients was used to determine days taken off work and clinical expert opinion was sought to determine total outpatient appointments per year. The costs associated with premature mortality, the treatment and management of co-morbidities and the burden associated with reduced quality of life were not included due to lack of data. **RESULTS:** There are ~20,000 AI patients in the UK. Based upon the burden of disease calculations, the estimated COI associated with AI is £1,922 per patient or £39.7 million over 1 year: RT, £21.7 million; GP appointments, £1.8 million; secondary care, £4.4 million; and reduced productivity, £11.8 million. **CONCLUSIONS:** The high health care and social costs associated with AI highlight the clinical and economic need to improve RT. Indeed, as some consequences of the disease were not included in the calculations, £39.7 million is likely a considerable underestimate of the true burden of disease.

PDB31
DIRECT COST OF DIABETES MELLITUS AND ITS COMPLICATIONS IN SPAIN. SECCAID STUDY: SPAIN ESTIMATED COST CIBERDEM-CABIMER IN DIABETES
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OBJECTIVES: To assess the direct costs associated to type I and II diabetes mellitus (DM) from a health care perspective in Spain. **METHODS:** We performed a cost of illness study considering the prevalence approach. The use of resources was estimated from the existing Spanish health care databases and bibliographic references. Costs evaluated were: hospital costs (including outpatient care), primary care costs, drugs costs, consumables costs and additional tests costs. All costs were updated to 2012 euros. **RESULTS:** The total direct annual cost of DM was 5,809 million euros representing 8.2% of the total Spanish health expenditure. The total drug cost accounted for 2,232 million euros (38%) and was mainly due to the elevated contribution of non-antidiabetic drugs (24%). Hospital costs represented 1,934 million € (33%) and were mainly driven by the acute and chronic complications (17%). Cardiovascular disease cost (521 million €) and peripheral vascular disease costs (127 million €) were the most important complications cost drivers. The contribution of monitoring strips to the total cost was only 118 million € (2%). Total complications cost represented 2,143 million € (37% of the total direct cost). **CONCLUSIONS:** DM total direct costs are strongly conditioned by DM complications cost and have a considerable economic impact on Spanish health expenditure. In order to reduce the health and economic impact generated by DM, the introduction of measures and strategies focused on improving the efficiency of the treatment of the disease are crucial.

PDB32
QUANTIFYING THE DIRECT AND INDIRECT COSTS ASSOCIATED WITH SEVERE AND NON-SEVERE HYPOGLYCAEMIA IN SUBJECTS WITH TYPE-2 DIABETES WHO ARE TREATED WITH INSULIN
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OBJECTIVES: There have been a number of studies quantifying the direct and indirect resource implications associated with severe hypoglycaemia episodes (SHE) and non-severe hypoglycaemia episodes (NSHE). The objective of this study was to calculate the total direct and indirect economic burden associated with SHE and NSHE in insulin treated type 2 diabetes mellitus (T2DM) subjects. **METHODS:** We conducted two literature reviews of the MEDLINE database for studies published between June 1, 2007 and June 1, 2012. The first assessed the direct (primary and secondary care and treatment related) and indirect resource implications (lost productivity) associated with SHE and NSHE; the second established the frequency of NSHE and SHE in insulin-based clinical trials where sulfonylurea usage was also reported in T2DM. An economic model written in Microsoft Excel was developed to predict the expected annual per-patient cost (using 2011 US costs) associated with the incidence of hypoglycaemia. **RESULTS:** Resource utilisation from 6 studies and data characterising hypoglycaemia frequency were extracted from 82 studies for a total of 155 trial arms where the search criteria were met. Mean annual hypoglycaemia event rates were 16.4, 8.9, 4.8 and 2.6 for NSHE and 0.083, 0.039, 0.015 and 0.003 for SHE associated with baseline HbA1c levels of 6%, 7%, 8% and 9% respectively. Total expected annual per-patient hypoglycaemia costs were $929, $471, $237 and

$117 associated with HbA1c levls of 6%, 7%, 8% and 9% respectively. **CONCLUSIONS:** In insulin treated T2DM subjects lower HbA1c is associated with higher frequency of hypoglycaemia and associated costs. Failing to account for the cost burden associated with hypoglycaemia may underestimate the value of diabetes management strategies that minimize hypoglycaemia risk.

PDB33

COMPARATIVE ANALYSIS OF THE COST AND METABOLIC CONTROL IN DIABETIC CHILDREN USING INSULIN PUMPS

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OBJECTIVES: To assess the cost and metabolic outcomes in children with diabetes mellitus treated with CSII or with human insulin. **METHODS:** It is a cost-consequence analysis. Retrospectively were observed patients dossier and health care resources used during the period 1999 – 2012. The study sample included 34 children aged 3 to 18 years with type 1 diabetes. Seventeen of the children are using continuous subcutaneous insulin infusion (CSII) therapy and 17 using intensified dosage regime of human insulin. The duration of the disease, diabetic control, HbA1c deviation scores, height and weight were observed. Cost of pharmacotherapy, test strips were calculated and compared with the therapeutic outcomes in both studied groups. The average improvement of HbA (1c) after the CSII introduction was chosen as therapeutic outcome. **RESULTS:** Subcutaneous insulin infusion (CSII) systems are not a standard treatment for the Bulgarian children; they are of a limited usage and are not reimbursed. From the 34 children with diabetes type 1 observed 17 were on CSII (mean age 10 years, mean duration of diabetes - 7 years, average usage of CSII - 3 years). The test stripes costs 533 Euro/ year and their average cost according to the duration of the disease is 3779.45 Euro since diagnosis. The blood glucose monitoring system costs 20 Euro and for the duration of the disease - 4.96 Euro per patient per year. The CSII price is 3896 Euro and it costs 1292 euro per patient per year. The average improvement of HbA (1c) after the CSII introduction is 1.85. In the group treated while human insulin the average cost per children is 925 Euro and improvement of HbA (1c) human insulin is 0.28 for the same period. **CONCLUSIONS:** The treatment with CSII leads to significant improvement in glycemic control compared to the treatment with human insulin at the comparable costs.

PDB34

A COST ANALYSIS OF MEDICATION FOR PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) – HOW THIS VARIES ACCORDING TO BODY MASS INDEX (BMI) STATUS, AGE, GENDER AND CO-MORBIDITY

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OBJECTIVES: The rising prevalence of overweight and obesity has led to an increase in related metabolic disorders; most notably t2dm. We sought to determine how the cost of medication for this condition varies within a cohort of patients attending Galway University Hospital, according to age, gender, BMI and co-morbidity status. **METHODS:** We identified a subgroup of 185 adult type 2 diabetes patients attending our university hospital-based diabetes clinic, for whom detailed information about drug therapy and comorbidities (obesity, hypertension, dyslipidaemia) was available. We modelled the lifetime costs of medications for each patient, taking account of age, gender and comorbidity. The analysis compares the lifetime cost of medication of those patients who are obese relative to those who are overweight and of those with fewer to those with more co-morbidities; specifically obesity, hypertension and dyslipidaemia. **RESULTS:** We found that obesity is associated with a higher cost of medication relative to being overweight. Those with a BMI range of 35-39.9 had the highest mean cost of medication, costing on average €615 more than those who are overweight ($p< .01$). The highest cost of medication was associated with those aged 50-65- non-significant. Among those having all three co-morbidities compared to those having only t2dm there was a significant difference in the cost of medication costing on average an extra €418 ($p< .05$). **CONCLUSIONS:** These results suggest that the health economic costs associated with t2dm are differential with respect to the BMI status of affected individuals. These findings are of use in understanding the drug related burden of illness associated with obesity, t2dm and also the burden associated with being obese when one has t2dm compared to not being obese and having it. This study generated interesting data which will need to be replicated in larger prospective multicentre cohort studies.

PDB35

COST OF MICROVASCULAR AND MACROVASCULAR COMPLICATIONS IN PEOPLES WITH DIABETES TYPE 1 AND TYPE 2 IN BULGARIA

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OBJECTIVES: It has been shown that people with diabetes have a high prevalence of microvascular (neuropathy, nephropathy, retinopathy, diabetic angiopathy) and macrovascular (hypertension, stroke, myocardial infarction, heart failure and coronary artery disease) complications leading to hospitalizations. The objective of the present study is to evaluate the cost of hospitalizations due to micro- and macrovascular complications in an observed cohort of 433 patients with type 1 and 2 diabetes treated with insulin. **METHODS:** The evaluation is based on data from a 6 months combined retrospective and prospective observational study. People were separated in two groups depending on the type of diabetes and further into subgroups depending on the reason of hospitalization. The total costs for each subgroup of people were calculated and compared to the total costs of treatment for the observed period. **RESULTS:** In the group of people with type 2 diabetes (n=255) 128 people with complications were observed, whereas in people with type 1 diabetes it was only 70 people out of 178. The cost of hospitalizations in the type 2 diabetes group was in total 35 367 EUR for the people enrolled in the 6 months study with the following division of reported reasons: (general) diabetes- 43%, microvascular complications- 16%, and macrovascular complications- 41%. In the type 1 diabetes group the cost was equal to 15 364 EUR with the following split: 63% due to (general) diabetes, 19% due to microvascular complications, and 18% due to macrovascular complications. **CONCLUSIONS:** Type 2 diabetes is more costly than type 1 when hospitalizations occur. People with type 2 diabetes pay high cost for macrovascular complications than for microvascular probably due to high hypertension prevalence. The difference in costs between type 1 and 2 may result from different patients' characteristics.

PDB36

PHARMACOECONOMIC PECULIARITIES OF THYROID DISEASE TREATMENT IN UKRAINE

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OBJECTIVES: Due to the preparation for the transition to health insurance in Ukraine and because of the significant increase in thyroid disease it is important to assess a range of medicines included to the Ukrainian National Formulary (UNF). **METHODS:** It was compared the range of drugs for treatment of thyroid disease which are included to the Ukrainian National Formulary with the WHO Model list of Essential Medicines. Also it was calculated the annual cost of treatment by each medication considering the usual maintenance dose. **RESULTS:** In accordance to WHO Model List of Essential Medicines it was established that Ukrainian National Formulary includes thyroid hormones and antithyroid medicines for thyroid disease treatment such as: levothyroxine sodium and potassium iodide. Also it was found that there are no propylthiouracil medications in UNF. The dosage of levothyroxine sodium tablets satisfies the norms of World Health Organization, which are: 25 micrograms, 50 micrograms and 100 micrograms. Potassium iodide tablets in dose of 100 micrograms, 200 micrograms, 1 mg does not comply the norm. According to WHO Model list of Essential Medicines dosage of potassium iodide in tablets should be 60 mg. The cheapest annual cost of treatment by levothyroxine per patient is EUR 10,95 (The EUR/UAH conversion rate: 1 EUR = 10,52 UAH (Average 2013)), the most expensive is EUR 80,30. The most expensive annual cost of treatment by potassium iodide per patient is EUR 31,32, the cheapest is EUR 2,85. **CONCLUSIONS:** Propylthiouracil should be included to Ukrainian National Formulary. The cost difference of thyroid disease treatment by essential medicines caused by presence of foreign products in the pharmaceutical market of Ukraine.

PDB37

LOWER SHORT-TERM HEALTH CARE COST WITH THE ACCU-CHEK AVIVA EXPERT SYSTEM IN MULTIPLE DAILY INSULIN INJECTION (MDI) TREATED DIABETES PATIENTS - LEARNINGS FROM THE AUTOMATED BOLUS ADVISOR CONTROL AND USABILITY STUDY (ABACUS)

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OBJECTIVES: The randomized controlled ABACUS study assessed the impact of using the automated insulin bolus advisor within the Accu-Chek Aviva Expert system in combination with intensive diabetes therapy on glycemic control in patients treated with MDI therapy. This analysis assessed the potential incremental economic benefit of using this automated bolus advisor device on the short-term health care costs (SHC). **METHODS:** The study outcome parameter was "achieving the goal of an at least 0.5% reduction in HbA1c". The economic analysis was performed with a spreadsheet-model from a UK payer's direct cost perspective and based on ABACUS outcomes. Data on correlation between HbA1c change and expected cost are based on published literature. Model outputs include expected impact on SHC and sensitivity analysis. **RESULTS:** A total of 56% of patients in the intervention group (IG) achieved the goal, in the control group (CG) 34% respectively. Goal achievement led to an average HbA1c reduction of 1.2%, irrespective of group. There was no clinically relevant HbA1c effect in the remaining patients. Goal achievement correlates with an expected reduction in SHC of £189 per person / per year (PPY). The expected SHC reduction is £104 PPY in the IG and £74 PPY in the CG. The goal-achievement-rate increased by 63%, driving a comparative economic benefit of £30 PPY for an automated insulin bolus advisor supported approach. There were no significant differences in complications or in intervention cost. **CONCLUSIONS:** An MDI therapy in diabetes care that is supported by the Accu-Chek Aviva Expert systems with its automated bolus advisor leads to a 63% higher rate of goal achievement. This is expected to result in an incremental reduction in short-term health care costs of £30 PPY. Hence automated bolus calculation improved the cost-effectiveness of self-monitoring of blood glucose in this study population.

PDB38

FIRST RUSSIAN TYPE 2 DIABETES MELLITUS SIMULATION MODEL WITH DISCRETE EVENTS MODELING. HEALTH-ECONOMIC ANALYSIS

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OBJECTIVES: Type 2 diabetes mellitus (DM) is widely spread in Russia, counting about 10 million. New drugs are highly effective and carry a high cost for health care. The results of clinical trials are not enough to assess long term efficacy and safety of treatment. Modeling is a tool for making long term economic and outcome prognosis and comparing treatment strategies. The main goal of the presented study was to develop a predictive model of type 2 DM outcomes validated in Russian clinical conditions and to perform pharmacoeconomic evaluation of glucose lowering therapies. **METHODS:** Existing type 2 DM models were evaluated. Risk equations for type 2 DM complications were compiled from EAGLE and UKPDS DM models. Demographic (age, sex, height, weight, DM duration, smoking), biochemical (HbA1c, lipids) and clinical (blood pressure) patient parameters were used as inputs. Glucose lowering drug effectiveness was incorporated into

the model as to its ability to modify input parameters. The model was externally validated against epidemiological data from Russia. Mortality and complications risk equations coefficients were modified in accordance with mortality rates due to complications in Russia. Cost-effectiveness analysis was performed. **RESULTS:** The developed model allows assessing the risk of more than 15 type 2 DM complications in 5 years in patients with predefined risk factors. Among comparison of 5 strategies of type 2 DM therapies (no therapy, vildagliptin, sitagliptin, liraglutide, and exenatide) liraglutide was considered the cost-effective strategy with ICER/QALY - 470120.40 RUR, which is 51% of the willingness-to-pay threshold in Russia. With the lowest complication treatment costs inside the total direct costs, liraglutide monotherapy demonstrated the most long-term sustainable blood glucose control and HbA1c goal parameters. **CONCLUSIONS:** The developed model allows increase in compliance of therapy. Possibility of individual choice of the most cost-effective treatment regimen for each patient leads to so-called "personalized" therapies.

PDB39

HEALTH CARE RESOURCE UTILIZATION AND COSTS ASSOCIATED WITH TREATMENT OF POLISH ACROMEGALIC PATIENTS WITH LANREOTIDE AUTOGEL 120 MG – A RETROSPECTIVE OBSERVATIONAL COHORT ANALYSIS

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OBJECTIVES: To estimate the resource utilization and related costs for Polish acromegalic patients treated with lanreotide AUTOGEL 120 mg (ATG120) in routine clinical practice **METHODS:** Medical care resource (dosage regimens, diagnostic procedures, hospitalizations, out-patient visits, any treatment changes) were collected during 1-year retrospective phase of non-intreventional, observational study (Lanro-Study). The study population consisted of acromegalic patients treated for at least three injections with ATG120. The endpoints were: proportion of patients treated for acromegaly with a given pharmaceutical in a given dosing interval, resource utilization, costs per patient/month or year. Costs were calculated in PLN from the public health-care payer perspective for the year 2013 (1 EURO = 4.2 PLN). **RESULTS:** A otal of 143 patients were included in the analysis (72% women, 80% macroadenoma, 72% previous pituitary surgery). Changes in the treatment scheme were reported in 54 patients. The mean cost of treatment in patients who switched from octreotide LAR (LAR) to ATG120 (n=26) was 6060.01 PLN/patient/month with LAR and 4047.96/patient/month PLN when switched to ATG120. At the time all patients entered the prospective phase, and were receiving ATG120, the mean cost of treatment with ATG120 was estimated at 3941.84 PLN/patient/month. Most patients (n=100; 70%) received ATG120 at dosing intervals less frequent than every 4 weeks. Patients were predominantly treated in out-patient setting with 4.77 physician visits/patient/year, most common control examinations were magnetic resonance imaging of brain and brain stem (0.57/patient/year), ultrasound of neck (0.55/patient/year), and IGF-1 (1.96/patient/year), GH (1.49/patient/year), glycemia (0.91/patient/year), pituitary-thyroid axis hormones (TSH- 0.45/patient/year, T4-0.49/patient/year). Only 7.7% patients were hospitalized. The mean medical cost, excluding pharmacotherapy, was 1002 PLN/patient/year. **CONCLUSIONS:** These results represent the current use of ATG120 in the population of Polish acromegalic patients in a realistic clinical settings and indicate that this therapy may provide cost saving in comparison to octreotide LAR.

PDB40

ASSESSMENT OF REAL-WORLD USAGE OF LANREOTIDE (SOMATULINE AUTOGEL) 120 MG IN POLISH ACROMEGALIC PATIENTS – RESULTS FROM 1 YEAR PROSPECTIVE PHASE OF LANRO-STUDY

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OBJECTIVES: To assess the treatment pattern, dosage and costs of lanreotide AUTOGEL 120 (L-ATG120) administered as part of routine acromegaly care in Poland. **METHODS:** Lanro-Study is a multicenter, non-interventional, observational study on resource utilization in the population of Polish acromegalic patients treated with L-ATG120 at 4 weeks or extended (>4 weeks) dosing interval. The study recruited adult acromegalic patients treated medically for ≥ 1 year, including at least 3 injections of L-ATG120. Data on dosing interval and aspects of administration were collected prospectively during 12-months (interim analysis). Costs were calculated in PLN from the public health care payer perspective for the year 2013 (1 EURO = 4.2 PLN). **RESULTS:** A total of 139 patients were included in the analysis. Changes in dosing regimen were reported in 14 (9.4%) patients, polytherapy was used in 11 (8%) patients. 70 patients (50%) received L-ATG120 at an extended dosing interval (> 4 weeks), the mean number of days between injections was 35.56 (SD 8.4). L-ATG120 was predominantly administered in out-patient setting (77%), by health care professionalists (94%). Mean time needed for preparation and administration was 4.33 and 1.58 min., respectively, mean product wastage – 0.13 mg. The cost of L-ATG120 was estimated at 4103.87 PLN/patient/month **CONCLUSIONS:** These results represent the current use of L-ATG120 in the population of Polish acromegalic patients in a realistic clinical settings. Findings that 50% of patients could be treated with dose intervals of longer than 28 days support the potential for L-ATG120 of reducing treatment burden.

PDB41

COST-EFFECTIVENESS OF UNIVERSAL SCREENING FOR THYROID DISEASE IN PREGNANT WOMEN IN SPAIN

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OBJECTIVES: Hypothyroidism in pregnancy can lead to adverse obstetrical outcomes. Universal screening in pregnant women for thyroid disease allows diagnose and treat cases of overt and subclinical hypothyroidism that are potentially missed when screening only women at high risk. The objective of the study was to assess the cost-effectiveness of universal screening as an alternative to high risk screening and no screening for thyroid disease in pregnant women in Spain. **METHODS:** The model compared the incremental cost per quality adjusted life-year (QALY) of universal screening versus high risk screening and versus no screening. A decision analytic model was used for the pregnancy and post-partum period. Probabilities from randomized controlled trials were considered for adverse obstetrical outcomes. A Markov model was used to assess the lifetime period after the first postpartum year and accounted for the development of overt hypothyroidism. Main assumptions of the model and the use of resources were validated by local clinical experts. The analysis considered only direct health care costs (euros 2013). A 3% discount was applied to costs and QALYs for the period beyond one year. **RESULTS:** Universal screening gained 0.011 QALYs over high risk screening and 0.014 QALYS over no screening. Total direct costs per patient were €5,791 for universal screening, €5,796 for high risk screening and €5,786 for no screening. Universal screening was dominant compared to risk-based screening and highly cost-effective alternative compared to no screening with an ICER of €374 per QALY. **CONCLUSIONS:** Universal screening of pregnant women in the first trimester for thyroid disease is dominant in Spain compared to the current type of screening which is risk-based, as well as cost-effective compared to no screening.

PDB42

COST-EFFECTIVENESS OF COMBINED TREATMENT OF METFORMIN AND FENOFIBRATE ON RETINOPATHY PROGRESSION

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OBJECTIVES: To evaluate the cost-effectiveness of intensive glycemic control (metformin) combined with fenofibrate in its impact on retinopathy progression compared to the treatment with metformin only in patients with type 2 diabetes. **METHODS:** Design: Markov decision model of retinopathy progression. Population: 40-year old patient with type 2 diabetes followed for 29 years. Main outcome measures: Risk of visual impairment; incremental cost-effeciveness ratio (ICER) for the two treatment options: one combining metformin and fenofibrate, and one using solely metformin. **RESULTS:** Combined tretament of metformin and fenofibrate resulted in ICER of -133.06 GBP per QALY which means that the intervention is not only effective but is also potentially saving money to the National Health Service; tretament solely with metformin is therefore dominated. **CONCLUSIONS:** Results of our study suggest that patients suffering from type 2 diabetes will receive from additional treatment with fenofibrate substantial benefits of protection against early microvascular complications related to retinopathy, including blindness. The favorable cost-effectiveness of intensive glycemic control combined with fenofibrate will likely be further increased if other major microvascular complications (e.g., non-traumatic amputations) and macrovascular complications (e.g., total cardiovascular events) of type 2 diabetes are taken into account. Our study is one of the first to compare cost-effectiveness of combined treatment of metformin and fenofibrate with current intensive glycemic control using solely metformin in its impact on retinopathy progression. Our study also provides evidence which may be useful in shaping the current clinical practice in the UK and European Union.

PDB43

REAL WORLD OUTCOMES IN TYPE 2 DIABETES: LOWER COST OF TREATING PATIENTS TO A1C<7% WITH LIRAGLUTIDE VERSUS EXENATIDE

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OBJECTIVES: Type 2 diabetes (T2D) is characterized by progressive β-cell failure in the presence of insulin resistance. The LEAD-6 (Liraglutide Effect and Action in Diabetes) clinical trial program compared the efficacy and safety of liraglutide once-daily (LIRA) to exenatide twice-daily (EXEN). Few studies have explored the real-world effectiveness, and associated costs, of these comparators. Glycemic goal attainment of A1C<7% and total diabetes-related pharmacy costs in clinical practice were assessed over 6 months follow-up. **METHODS:** A retrospective cohort study using integrated medical and pharmacy claims and linked A1C results from the IMS Patient-Centric Integrated Data Warehouse was conducted. T2D patients ≥18 years naïve to GLP-1, DPP-IV and insulin use during a 6 months pre-index period, with evidence of ≥1 prescription for LIRA (N=234) or EXEN (N=182) between January 2010 and December 2010 were identified. Only patients who were persistent on their index treatment during a 6 months post-index period were included in the analysis. The percentage of patients achieving A1C<7% and total diabetes-related pharmacy costs were estimated using multivariable modelling to control for confounding effects. The cost per successfully treated patient was calculated as total diabetes-related pharmacy costs divided by the percentage of patients achieving A1C<7%. **RESULTS:** The percentage of patients reaching A1C<7% was 64.4% and 53.6% for LIRA and EXEN, respectively ($p<0.05$) (baseline A1C mean: 7.8% for both LIRA and EXEN). Average total diabetes-related pharmacy costs per patient at 6 months were higher for LIRA than EXEN ($2,002 vs $1,799, $p<0.001$) but when assessed as cost per patient successfully reaching A1C<7%, LIRA was cost-effective compared to EXEN ($3,108 vs $3,354, $p<0.0001$). **CONCLUSIONS:** The average cost of treating a patient to A1C<7% at 6 months follow-up was lower with LIRA than EXEN. This suggests LIRA to be a cost-effective treatment option compared to EXEN in the management of T2D.

PDB44

HEALTH-ECONOMIC COMPARISON OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION VERSUS MULTIPLE DAILY INJECTIONS FOR THE TREATMENT OF ADULT TYPE 1 DIABETES IN KAZAKHSTAN

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OBJECTIVES: To project the long-term costs and outcomes of continuous subcutaneous insulin infusion (CSII) compared with multiple daily injections (MDI) in adult patients with Type 1 diabetes in KAZAKHSTAN. **METHODS:** The CORE Diabetes Model is a peer-reviewed, validated model, which employs standard Markov techniques to describe the long-term incidence and progression of diabetes-related complications. It was used to simulate disease progression in a cohort of adult patients with baseline characteristics and costs taken from primary data collection in KAZAKHSTAN (mean age 39.7 years, duration of diabetes 10.1 years and mean HbA1c 8.5%). Clinical outcomes (HbA1c and hypoglycemic events) were taken from a published meta-analysis of CSII studies. Direct costs for 2013 were calculated from a third-party payer perspective. Discount rates of 5% *per annum* were applied to costs and 3% to clinical outcomes. **RESULTS:** Treatment with CSII was associated with an improvement in mean quality adjusted life expectancy (QALE) of 0.745 years compared with MDI and incidence of any diabetes related complication was delayed on average by 1 year with CSII. This produced an incremental cost-effectiveness ratio (ICER) of KZT 4'784'971 per quality-adjusted life year (QALY) gained with CSII vs. MDI. CSII related therapy costs were partially offset by the savings due to the reduction in long-term complications. CSII treatment also delayed the average onset of complications such as ESRD (1.9 years) and blindness (2.1 years). Extensive sensitivity analyses showed the robustness of the results. **CONCLUSIONS:** Improvements in glycemic control associated with CSII over MDI led to improved QALE owing to reduced incidence of diabetes-related complications. CSII was associated with ICERs representing good value for money by current standards in KAZAKHSTAN (using a WTP threshold of 6,330,000 KZT [3x GDP]) from a payer's perspective. CSII would be even more attractive from a societal perspective when including indirect costs.

PDB45

COST OF ACHIEVING RELEVANT COMPOSITE ENDPOINT OF HBA1C<7%, NO HYPOGLYCAEMIA AND WEIGHT LOSS OF ≥3% IN A 52 WEEK POST-HOC ANALYSIS OF DAPAGLIFLOZIN VERSUS GLIPIZIDE

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OBJECTIVES: Dapagliflozin (DAPA), a selective SGLT2 inhibitor, reduces hyperglycaemia in an insulin-independent manner by increasing urinary glucose excretion. Glipizide (sulphonylurea) reduces hyperglycemia by increasing beta cell insulin secretion. We conducted an analysis of the cost of treating patients to a clinically relevant composite endpoint of HbA1c <7%, no major or minor hypoglycaemic events and weight loss ≥3%. **METHODS:** The Cardiff Diabetes model was used to estimate the cost of treating patients to the composite endpoint of HbA1c <7%, no major or minor hypoglycaemic events and weight loss ≥3% in the UK using 52 week data from a previously published double-blind randomised clinical trial of DAPA vs glipizide (GLIP) in combination with metformin (NCT 00660907). The cost of treating one patient to the composite endpoint using DAPA or GLIP over 52 weeks was calculated as total cost per treatment arm divided by number of patients that reached the composite endpoint in that treatment arm. Calculation of costs included drug acquisition costs, cost for adverse events, and costs related to the patient's BMI level. **RESULTS:** The number needed to treat was 5 on DAPA and 54 on GLIP for one patient to achieve the composite endpoint. The overall cost of treating one patient over 52 weeks to the composite endpoint of HbA1c <7%, no major or minor hypoglycaemic events and ≥3% weight loss was £3296 on DAPA and £13620 on GLIP. **CONCLUSIONS:** The cost of treating one patient to composite endpoint of HbA1c <7%, no major/minor hypoglycaemic events and ≥3% weight loss was approximately 4 times higher with GLIP compared to DAPA. These results demonstrate that when multiple treatment goals, including weight loss and reduction of hypoglycaemic events are targeted, the cost of treating patients with DAPA is lower compared to GLIP.

PDB47

COST-EFFECTIVENESS ANALYSIS OF DAPAGLIFOZIN VERSUS OTHER T2DM TREATMENTS IN THE SPANISH CONTEXT

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OBJECTIVES: To analyse the cost-effectiveness of dapagliflozin in combination with metformin in the treatment of type 2 diabetes (T2DM) in comparison with sulfonylureas, thiazolidinediones and DPP4 inhibitors also combined with metformin in Spain. **METHODS:** The analysis was based on the results of the available clinical trials in order to estimate the quality-adjusted life years (QALY) and economic consequences of managing the disease and its complications. An economic model was used to simulate the natural history of 10,000 T2DM patients with each treatment option. The analysis was performed from the National Health System perspective considering direct costs (pharmacological costs, adverse events, T2DM complications, hypoglycaemias and costs related to weight gain) and patient's entire life as time horizon. A discount rate of 3% was applied to costs and benefits. All costs were updated to €2013. **RESULTS:** The primary analysis compared dapagliflozin with sulfonylureas resulting in 0.525 additional QALYs and €1,835 additional cost (cost-effectiveness ratio of €3,496/QALY). The higher drug cost of dapagliflozin was partially offset by lower costs of complications, hypoglycemia and the cost associated with weight gain. In the secondary analyses, dapagliflozin was a cost-effective option compared with thiazolidinediones and DPP4, resulting in a cost per QALY gained of €20,183 and €487, respectively. The univariate and probabilistic sensitivity analyses confirmed the robustness of the results. **CONCLUSIONS:** Dapagliflozin in combination with metformin proved to be a cost-effective alternative compared to sulfonylureas, thiazolidinediones and DPP4 inhibitors in the treatment of T2DM.

PDB48

A BUDGET IMPACT AND COST-EFFECTIVENESS ANALYSIS OF BLOOD GLUCOSE MONITORING SYSTEM IN ONE ITALIAN REGION

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OBJECTIVES: Diabetes is a chronic disease and associated with significant health care expenditures. Increasing costs are mainly related to long-term complications. Identifying patterns of hypoglycemia by means of a blood glucose monitoring system (BGMS) can be used to support diabetes management efficiently. **METHODS:** An economic analysis was carried out to estimate the life-time cost-effectiveness (CEA) of blood glucose monitoring system (BGMS) with pattern alert technology vs. standard BGMS for the prevention of Severe Hypoglycaemia (SH) in insulin-treated type 1 (DM1) and type 2 patients (DM2). The cost-effectiveness analysis was based on a literature review and cost data (direct and indirect) from the Emilia Romagna region; a decision tree was developed to calculate the incremental cost per additional quality of life. The BIA (Budget Impact Analysis) estimated the cost of using the new pattern alert technology in the Italian Healthcare System. **RESULTS:** For the base-case scenario, the utilization of BGMS with pattern alert technology was less costly and more effective compared to standard BGMS. Life time cost savings for the prevention of SH were 300 euro for DM1 and DM2 patients using pattern alert technology. The difference in life time QALYs was 0,17. **CONCLUSIONS:** BGMS with pattern alert technology, monitoring individual blood glucose levels are cost effective in preventing SH for DM1 and insulin-treated DM2 patients, as well as in detecting blood glucose trends and patterns. Nevertheless, empirical data on the probability of reducing Severe Hypoglycemia is necessary in order to reach any firm conclusions.

PDB49

INCRETIN THERAPY FOR PATIENTS WITH TYPE 2 DIABETES IN SPAIN: A COST-EFFECTIVENESS ANALYSIS OF LIRAGLUTIDE VERSUS SITAGLIPTIN

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OBJECTIVES: Diabetes mellitus represents a significant challenge to health care providers in Spain, with a national prevalence of over 8% and approximately 20,000 diabetes-related deaths annually. Treatment with GLP-1 receptor agonists and DPP-4 inhibitors, which target the incretin axis, has the potential to improve glycemic control without the weight gain associated with traditional therapies. To evaluate the relative cost-effectiveness of incretin therapies, the present study compared the long-term clinical and cost implications associated with liraglutide and sitagliptin in type 2 diabetes patients in Spain. **METHODS:** Data were taken from a randomized, controlled trial (NCT00700817) in which adults with type 2 diabetes (mean age 55 years, HbA1c 8.4%, BMI 33kg/m^2) failing metformin monotherapy were randomly allocated to receive either 1.2mg liraglutide or 100mg sitagliptin daily in addition to metformin. Liraglutide was associated with greater improvements from baseline HbA1c (–1.24% vs. –0.9%) and BMI (–0.99kg/m^2 vs. –0.33kg/m^2). Long-term projections of clinical outcomes and direct costs (2012 EUR) were made using a published and validated model of type 2 diabetes and assumed patients switched to insulin after five years. **RESULTS:** Liraglutide was associated with improved life expectancy (14.05 years vs. 13.91 years) and quality-adjusted life expectancy (9.04 quality-adjusted life years [QALYs] vs. 8.87 QALYs) compared to sitagliptin. Improved clinical outcomes were driven by improved glycemic control, leading to a reduced incidence of diabetes-related complications, including renal disease, cardiovascular disease, ophthalmic and diabetic foot complications. Mean cost savings as a result of avoided complications were EUR 1,827 per patient. Overall, liraglutide was associated with increased direct costs of EUR 2,297, yielding an incremental cost-effectiveness ratio of EUR 13,266 per QALY gained versus sitagliptin. **CONCLUSIONS:** Liraglutide was projected to improve life expectancy, quality-adjusted life expectancy and reduce incidence of diabetes-related complication. Liraglutide is likely to be cost-effective from a health care payer perspective in Spain.

PDB50

HEALTH-ECONOMIC COMPARISON OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION VERSUS MULTIPLE DAILY INJECTIONS FOR THE TREATMENT OF TYPE 1 DIABETES IN KAZAKHSTAN CHILDREN

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OBJECTIVES: To project the long-term costs and outcomes of continuous subcutaneous insulin infusion (CSII) compared with multiple daily injections (MDI) in children with Type 1 diabetes in KAZAKHSTAN. **METHODS:** The CORE Diabetes Model is a peer-reviewed, validated model, which employs standard Markov/Monte

Carlo simulation techniques to describe the long-term incidence and progression of diabetes-related complications. It was used to simulate disease progression in a cohort of pediatric patients with baseline characteristics taken from published KAZAKHSTAN studies (mean age 10.4 years, duration of diabetes 4.1 years, mean HbA1c >7.5%). Direct costs for 2013 were calculated from a third-party payer perspective. Discount rates of 5% per annum were applied to costs and 3% to clinical outcomes. **RESULTS:** Mean undiscounted life expectancy of patients using CSII vs. MDI was increased by 3.58 years. The Incremental-Cost-Effectiveness-Ratio (ICER) for CSII was 3,935,375KZT per Quality-Adjusted-Life-Year gained based on direct costs only. CSII related therapy costs were partially offset by the savings due to the reduction in long-term complications, i.e.638,744KZT, mainly due to cardiovascular and renal diseases. Cumulative incidences of proliferative diabetic retinopathy, blindness, ESRD, and GRP were decreased by 25.3%, 5.6%, 28.3%, and 17.7%, respectively. CSII treatment also delayed the average onset of ESRD (3.9 years), blindness (3.7 years), PVD (3.5 years), CHF (3.6 years), Neuropathy (3.4 years), first ulcer (4.0 years), amputation (3.7 years), MI (3.5 years), and stroke (3.5 years). Extensive sensitivity analyses showed the robustness of the results. **CONCLUSIONS:** Using a payer's perspective, our analysis showed that CSII is cost-effective over a lifetime horizon in children with Type 1 Diabetes in Kazakhstan (using a WTP threshold of 6,330,000 KZT [3x GDP]) and can lead to an increase in life expectancy as well as delay and reduce long-term complications. When including indirect costs, CSII would be even more attractive from a societal perspective.

PDB51

COST-EFFECTIVENESS OF INTRALESIONAL INJECTION OF RECOMBINANT HUMAN EPIDERMAL GROWTH FACTOR FOR THE TREATMENT OF SEVERE DIABETIC FOOT ULCERS IN RUSSIAN HEALTH CARE SETTING

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OBJECTIVES: To assess the cost-effectiveness of using intralesional injection of recombinant human epidermal growth factor (rhEGF) for the treatment of severe non-healing diabetic foot ulcers (DFU) in highly-specialized inpatient department in Russian setting. **METHODS:** We developed a cost-effectiveness model based on hypothesis that use of intralesional injection of rhEGF in addition to standard treatment of severe DFU (Wagner grade 3-4) would reduce the rate of amputations and related increased mortality in population of amputated DFU patients. For model inputs we used published data on the rates of amputation from retrospective study of intralesional injection of rhEGF and survival rates for patients with DFU with and without major amputations. Cost data was derived from the Russian retrospective study of real practice of inpatient treatment of severe DFU and reimbursement rates in Russian compulsory medical insurance system, cost of rhEGF treatment was provided by the manufacturer. Based on the model outputs we calculated incremental cost-effectiveness ratio (ICER) as the difference in costs to the difference in years lived during the 5-year period of observation by two cohorts of patients treated with only standard methods and with addition of rhEGF. **RESULTS:** The use of rhEGF intralesional injection treatment may prevent 52 amputations and save 29.54 years of life in a cohort of 100 patients with severe DFU during subsequent 5-year period of observation. The ICER for rhEGF is estimated at EURO 27,200 per life year saved and does not exceed the acceptable threshold of three GDP per capita as recommended by WHO. The sensitivity analysis demonstrated that the results are most sensitive to the cost of rhEGF. **CONCLUSIONS:** The model has demonstrated the acceptability of adoption of intralesional injection of rhEGF in addition to standard treatment for DFU in highly specialized inpatient departments.

PDB52

PHARMACOECONOMIC EVALUATION OF THE ORAL HYPOGLYCEMIC AGENTS IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS PATIENTS IN THE RUSSIAN FEDERATION

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OBJECTIVES: To assess the cost-effectiveness of oral hypoglycaemic agents (micronized glibenclamide, gliclazide, glimepiride and repaglinide) in the treatment of Russian patients with type 2 diabetes mellitus. **METHODS:** Based on the data from comparative studies (B. Wolffenbuttel et al., 1999; A. Holstein et al., 2001; O. Reshetko et al., 2007) the pharmacoeconomic profiles of glibenclamide and repaglinide, glibenclamide and glimepiride, glibenclamide and gliclazide were compared. It was revealed that glibenclamide and repaglinide, glibenclamide and gliclazide have equal efficacy and safety, so the cost-minimization analysis was performed. The cost-effectiveness of glibenclamide and glimepiride was measured as total costs of medicines and expenses for ambulance calls for severe hypoglycemia per one patient without hypoglycaemic events. A one-year time horizon was adopted in the models. One-way sensitivity analysis (SA) was carried out to assess the robustness of the results . **RESULTS:** Compared to repaglinide and gliclazide, treatment with glibenclamide was associated with substantial budget savings (22,699.35 RUB and 3,566.05 RUB per one patient, respectively). Costs per one patient without hypoglycaemic events were 1,137.17 RUB and 5,549.85 RUB in glibenclamide and glimepiride groups, respectively. Sensitivity analysis demonstrated that results are robust. **CONCLUSIONS:** The present study has demonstrated that administration of micronized glibenclamide is the most economically effective strategy in the treatment of Russian patients with type 2 diabetes mellitus. Treatment with micronized glibenclamide is associated with considerably lower costs as compared to repaglinide, glimepiride and gliclazide.

PDB53

IMPACT OF PATIENT WEIGHT TRAJECTORY ON COST-EFFECTIVENESS OF TREATMENTS OF TYPE 2 DIABETES MELLITUS (T2DM)

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OBJECTIVES: With new classes of T2DM medications offering weight reduction in addition to better glycaemic control, HTA agencies expect fuller accounting of the impact of post-trial weight trajectory assumptions on cost-effectiveness. Four alternative scenarios were examined using the example of the novel SGLT-2 inhibitor canagliflozin (CANA) in the UK treatment setting. **METHODS:** The importance of alternative assumptions was illustrated using CANA 300mg versus glimepiride (GLIM; 1mg titrated to 6mg or 8mg) in dual therapy with metformin simulated over 40 years using the ECHO-T2DM model loaded with patient characteristics, treatment effects, and adverse event rates from the DIA3009 trial, in which CANA 300mg reduced body weight by –5.7% versus GLIM over 52 weeks. HbA1c was assumed to drift annually by 0.14% for CANA (similar to metformin in ADOPT), 0.24% for GLIM (as sulphonylurea in ADOPT), and 0.15% for rescue therapy with insulin (initiated when HbA1c >7.5%). Upon treatment discontinuation, four alternative weight-trajectory assumptions were applied: (A) weight change maintained permanently; (B) CANA weight reduction disappears fully at treatment discontinuation, GLIM weight-gain permanent; (C) GLIM weight-gain permanent, forced convergence of weight upon CANA discontinuation; (D) weight changes disappear fully at discontinuation for both treatments. A weight increase was applied when insulin was initiated and proportional weight changes were applied when insulin dose was titrated upwards. **RESULTS:** CANA 300mg generated more QALYs at modest incremental cost, resulting in ICERs of £2,766 to £4,317 in the scenarios. Maintaining the benefits permanently (A) generated the largest QALY gain (0.243); complete elimination of benefits at discontinuation (D) offered the smallest (0.198). The proportions of incremental QALYs attributable to weight differences were 34.4%, 19.5%, 18.9% and 17.4% for Scenarios A to D, respectively. **CONCLUSIONS:** CANA 300mg was cost-effective in each of four weight scenarios following discontinuation. Further work is required to define the most clinically plausible scenarios.

PDB54

THE COST-EFFECTIVENESS OF DAPAGLIFLOZIN (FORXIGA®) VERSUS A DPP-4 INHIBITOR IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM) IN ENGLAND AND WALES

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OBJECTIVES: Dapagliflozin (Forxiga®) is the first sodium-glucose co-transporter-2 inhibitor (SGLT-2) approved by the European Medicines Association, and positively assessed by the National Institute for Health and Care Excellence (NICE) for type 2 diabetes mellitus (T2DM). This study evaluates the cost-effectiveness of dapagliflozin compared with a dipeptidyl-peptidase-IV (DPP-4) inhibitor when added to metformin in patients inadequately controlled on metformin alone. **METHODS:** The published and validated CARDIFF diabetes model was used to conduct the analysis. Clinical inputs were derived from a systematic review and network meta-analysis. Based on clinical inputs and the United Kingdom Prospective Diabetes Study (UKPDS) equations, the model predicts disease progression and the number of micro- and macro-vascular complications, along with diabetes-specific and all-cause mortality. The perspective of the National Health Service in England and Wales was adopted over a lifetime horizon. Local unit costs and utility data were assigned to the appropriate model parameters to calculate total Quality-Adjusted-Life-Years (QALYs) and costs. Univariate and probabilistic sensitivity analyses (PSA) were conducted. **RESULTS:** Compared to a DPP-4 inhibitor, dapagliflozin was associated with 0.076 incremental QALYs (95%CI: –0.028; 0.146) at an additional cost of £412 (95%CI: -£212; £853); resulting in an incremental cost-effectiveness ratio (ICER) of £5,455 per QALY gained. The univariate analyses showed that no input parameter change inflated the ICER above £15,000 per QALY. The PSA estimated that dapagliflozin has a 81% chance to increase QALYs and costs, a 9% chance to increase QALYs and save costs, a 4% chance to reduce QALYs and costs and a 6% chance to reduce QALYs and increase costs. At a willingness-to-pay threshold of £20,000 per QALY gained, dapagliflozin strategy had an 86% probability to be cost-effective in this setting. **CONCLUSIONS:** Dapagliflozin in combination with metformin was shown to be a cost-effective treatment option for T2DM patients who are inadequately controlled with metformin mono-therapy.

PDB55

SOURCES OF LONG-TERM QUALITY ADJUSTED LIFE YEAR (QALY) GAINS FOR CANAGLIFLOZIN (CANA) VERSUS SITAGLIPTIN (SITA) IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM) IN THE UK SETTING

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OBJECTIVES: The NICE reference case for T2DM requires cost-utility analysis with a lifetime horizon. The denominator in cost-utility outcomes is the incremental QALY, which is driven in most T2DM economic models by several key features, including: life extension, micro- and macrovascular events, treatment and treatment-related adverse events (AEs), and excess bodyweight. The aim of this analysis is to determine which factors most impact QALY gains in an analysis of CANA 300mg versus SITA 100mg when combined with metformin and sulphonylurea in the UK treatment setting. **METHODS:** The ECHO-T2DM model was used to simulate CANA versus SITA over 40 years. ECHO-T2DM was loaded with patient characteristics, treatment effects, and AE rates from the DIA3015 trial. HbA1c was assumed to drift upwards at an annual rate of 0.14% for CANA and SITA (similar to metformin in the ADOPT trial). CANA and SITA were discontinued and insulin initiated (annual drift 0.15% as in UKPDS) when patients failed to maintain HbA1c under 58 mmol/mol (7.5%). **RESULTS:** Hypothetical patients experienced 0.039 more QALYs when treated with CANA 300mg versus SITA 100mg. Because SITA had lower initial HbA1c lowering, it was associated with greater use of rescue medication. Patients treated initially with SITA, thus, had greater insulin-mediated HbA1c lowering over time so HbA1c values converged asymptotically (limiting differences in rates of microvascular complications). There were relatively modest QALY benefits related to macro-

vascular events, but substantial benefits attributable to weight (0.020) and especially hypoglycaemic events (0.024), related to CANA's better weight-lowering and longer time to initiation of insulin. **CONCLUSIONS:** Patients treated with CANA in triple therapy experienced an additional 0.039 QALY's over 40 years versus patients treated with SITA. The primary drivers were improved weight while on agent and fewer hypoglycaemic events.

PDB56

THE COST-EFFECTIVENESS OF DAPAGLIFLOZIN (FORXIGA®) VERSUS GLIPIZIDE IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM) IN ENGLAND AND WALES

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OBJECTIVES: Dapagliflozin (Forxiga®) is the first sodium-glucose co-transporter-2 (SGLT-2) inhibitor approved by the European Medicines Association, and positively assessed by the National Institute for Health and Care Excellence (NICE) for type 2 diabetes mellitus. This study investigates the cost-effectiveness of dapagliflozin compared with a sulphonylurea (SU) when added to metformin in patients inadequately controlled with metformin mono-therapy. **METHODS:** The published and validated CARDIFF diabetes model was used to conduct the analysis. Clinical inputs were derived from a randomized clinical trial comparing dapagliflozin and glipizide in combination with metformin. Based on these clinical inputs and the United Kingdom Prospective Diabetes Study (UKPDS) equations, the model predicts disease progression and the number of micro- and macro-vascular complications, along with diabetes-specific and all-cause mortality. The perspective of the National Health Service in England and Wales was adopted over a lifetime horizon. Local unit costs and utility data were assigned to the appropriate model parameters to calculate total Quality-Adjusted-Life-Years (QALYs) and total costs. Univariate and probabilistic sensitivity analyses (PSA) were conducted. **RESULTS:** Compared to SU added to metformin, dapagliflozin add-on to metformin was associated with an incremental benefit of 0.467 QALYs (95%CI: 0.420; 0.665) at an additional cost of £1,246 (95%CI: £613; £1,637), resulting in an ICER point estimate of £2,671 per QALY gained. The univariate analyses showed that no input parameter change inflated the ICER above £15,000 per QALY. The PSA showed that at a willingness-to-pay threshold of £20,000 per QALY gained, dapagliflozin treatment had an estimated 100% probability to be cost-effective compared to an SU treatment strategy. These findings were shown to be robust with all sensitivity analyses. **CONCLUSIONS:** Dapagliflozin in combination with metformin was shown to be a cost-effective treatment option for patients who are inadequately controlled with metformin mono-therapy within established UK cost-effectiveness thresholds.

PDB57

COST-EFFECTIVENESS OF DAPAGLIFLOZIN AS ADD-ON TO INSULIN FOR THE TREATMENT OF TYPE 2 DIABETES IN THE NETHERLANDS

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OBJECTIVES: Insulin, often combined with metformin, is usually the last therapy option for patients with type 2 diabetes Mellitus (T2DM) who are uncontrolled on oral anti-diabetic drugs. Dutch guidelines recommend up-titration of insulin until patients maintain an HbA1c <7%, yet in practice many patients never reach this target. Clinical evidence shows that dapagliflozin – a highly selective sodium-glucose cotransporter 2 (SGLT2) inhibitor – meets a need for these patients, i.e. by reducing HbA1c and weight. We studied the cost-effectiveness of dapagliflozin added to insulin (vs. not adding dapagliflozin) for patients with T2DM who have inadequate glycaemic control while on insulin. **METHODS:** We used the Cardiff Diabetes model to evaluate cost and effects of dapagliflozin added to insulin using direct comparative efficacy data from a randomized placebo-controlled trial (NCT00673231). In this trial up-titration of insulin was allowed in case of severe glycaemic imbalance. Risk factor progression and occurrence of future vascular events were estimated using the UKPDS 68 risk equations. Costs and utilities were derived from the literature. The analysis was conducted from a Dutch societal perspective using a lifetime horizon. **RESULTS:** The overall incidence of vascular complications was lower, and life expectancy was higher (19.43 LYs vs. 19.35 LYs) in those patients receiving dapagliflozin compared to patients not receiving dapagliflozin. Patients in the dapagliflozin arm obtained an incremental benefit of 0.42 QALYs. The lifetime incremental cost per patient in the dapagliflozin arm was € 2,293, resulting in an incremental cost-effectiveness ratio of €27,779 per LYG and an incremental cost-utility ratio of €5,502 per QALY gained. Sensitivity and scenario analyses showed that the results were robust to variation in modelling assumptions and input variables. **CONCLUSIONS:** This analysis shows that dapagliflozin increases the quality of life of T2DM patients compared to current practice (up-titration of insulin), and is cost-effective in a Dutch health care setting.

PDB58

THE COST-EFFECTIVENESS OF DAPAGLIFLOZIN (FORXIGA®) VERSUS INSULIN IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM) IN ENGLAND AND WALES

Charokopou M[1], McEwan P[2], Lister S[3], Callan L[4], Bergenheim K[5], Tolley K[6], Roudaut M[7]
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OBJECTIVES: Dapagliflozin (Forxiga®) is the first sodium-glucose co-transporter-2 (SGLT-2) inhibitor approved by the European Medicines Association, and positively assessed by the National Institute for Health and Care Excellence (NICE) for type 2 diabetes mellitus. This study assesses the costs-effectiveness of dapagliflozin in combination with insulin versus insulin alone for patients who are inadequately controlled despite high doses of insulin. **METHODS:** The published and validated CARDIFF diabetes model was used to conduct the analysis. Clinical inputs were derived from a randomized clinical trial comparing dapagliflozin add-on to insulin with insulin regimens. Based on clinical inputs and the United Kingdom Prospective Diabetes Study (UKPDS) equations, the model predicts disease progression and the number of micro- and macro-vascular complications, along with diabetes-specific and all-cause mortality. The perspective of the National Health Service in England and Wales was adopted over a lifetime horizon. Local unit costs and utility data were assigned to the appropriate model parameters to calculate total Quality-Adjusted-Life-Years (QALYs) and total costs. Univariate and probabilistic sensitivity analyses (PSA) were conducted. **RESULTS:** Compared to insulin, dapagliflozin added to insulin was associated with 0.342 incremental QALYs (95%CI: 0.288; 0.480) at an additional cost of £1,813 (95%CI: £1,165; £2,381), resulting in an incremental cost-effectiveness ratio (ICER) point estimate of £5,295 per QALY gained. The univariate analyses showed that no input parameter change inflated the ICER above £15,000 per QALY. At a willingness-to-pay threshold of £20,000 per QALY gained, the dapagliflozin treatment strategy was estimated to have a 100% probability of being cost-effective when compared to the insulin treatment strategy. These findings were shown to be robust with all sensitivity analyses. **CONCLUSIONS:** Dapagliflozin was shown to be a cost-effective treatment option in combination with insulin for patients who are inadequately controlled with insulin alone within established UK cost-effectiveness thresholds.

PDB59

ASSESSMENT OF THE KEY DRIVERS OF COST-EFFECTIVENESS IN THE ECONOMIC MODELLING OF CANAGLIFLOZIN (CANA) VERSUS GLIMEPIRIDE (GLIM) IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM) IN THE UK SETTING

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OBJECTIVES: To evaluate uncertainty, the NICE reference case requires estimation of cost-effectiveness using alternative parameter values. Because models of T2DM necessarily include many parameters, NICE requirements dictate a large number of simulations. This study assesses the relative importance of common sensitivity analyses by identifying key drivers of the incremental cost-effectiveness ratio (ICER) using the example of CANA 300mg versus GLIM (titrated from 1mg to 6mg or 8mg), in combination with metformin in dual therapy. **METHODS:** The ECHO-T2DM model was used to simulate CANA versus GLIM over 40 years. ECHO-T2DM was loaded with patient characteristics, treatment effects, and adverse event rates from the DIA3009 trial. HbA1c was assumed to drift annually by 0.14% for CANA (similar to metformin in ADOPT), 0.24% for GLIM (as sulphonylurea in ADOPT), and 0.15% for rescue therapy with insulin (initiated when HbA1c >7.5%). Twenty-four one-way sensitivity analyses assessed the impact of drug durability, macrovascular risk equations, utility weights, and HbA1c goals. **RESULTS:** In the base case, CANA 300mg was associated with 0.21 greater QALYs at an incremental cost of £828, generating an ICER of £4,050/QALY. QALY gains were driven by fewer hypoglycaemic events and a better weight profile. The low acquisition cost of GLIM was partially offset by a greater need for insulin rescue therapy earlier in treatment, more hypoglycaemic events, and more macrovascular complications. Assuming no difference in durability for CANA and GLIM had the greatest impact on the ICER (£49,717), followed by no disutility for hypoglycaemic events (£15,733). The only other scenario having a noticeable impact was an HbA1c goal of 9.0% (£9,718). Alternative macrovascular risk engines had little impact on the ICER. **CONCLUSIONS:** The ICER was robust under a large number of scenarios. Only the difference in assumed long-term GLIM durability reversed the interpretation of CANA as cost-effective versus GLIM using NICE criteria.

PDB60

SOURCES OF LONG-TERM QUALITY ADJUSTED LIFE YEAR (QALY) GAINS FOR CANAGLIFLOZIN (CANA) VERSUS GLIMEPIRIDE (GLIM) IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM) IN THE UK SETTING

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OBJECTIVES: The NICE reference case for T2DM requires cost-utility analysis with a lifetime horizon. The denominator in cost-utility outcomes is the incremental QALY, which is driven in most T2DM economic models by several key features, including: life extension, micro- and macrovascular events, treatment and treatment-related adverse events (AEs), and excess bodyweight. This analysis aims to determine which factors most impact QALY gains using the example of CANA 300mg versus GLIM (titrated from 1mg to 6mg or 8mg) when combined with metformin. **METHODS:** The ECHO-T2DM model was used to simulate CANA versus GLIM over 40 years. ECHO-T2DM was loaded with patient characteristics, treatment effects, and AE rates from the DIA3009 trial. HbA1c was assumed to drift upwards at an annual rate of 0.14% for CANA (similar to metformin in the ADOPT trial) and 0.24% for GLIM (as sulphonylurea in ADOPT). CANA and GLIM were discontinued and insulin initiated (annual drift 0.15% as in UKPDS) when patients failed to maintain HbA1c under 58 mmol/mol (7.5%). **RESULTS:** Hypothetical patients experienced 0.21 more QALYs when treated with CANA 300mg versus GLIM. Because GLIM was associated with greater use of rescue medication (and extra insulin-mediated HbA1c lowering) in the simulation, HbA1c values converged asymptotically limiting the differences in microvascular complications. However, lower blood pressure for patients on CANA versus GLIM was associated with reductions of 2.2% to 4.1% for the rates of macrovascular outcomes (although associated QALY gains were small due to discounting). Differences in weight and especially hypoglycaemic events, related both to GLIM and to earlier initiation of insulin, were associated with improvements in utility (0.04 and 0.16 QALYs, respec-

tively). **CONCLUSIONS:** Patients treated with CANA in dual therapy experienced an additional 0.21 QALYs over 40 years versus patients treated with GLIM. The primary drivers were improved weight while on agent and fewer hypoglycaemic events.

PDB61

COST-EFFECTIVENESS OF INSULIN DETEMIR IN T2DM PATIENTS POORLY CONTROLLED WITH NPH INSULIN IN POLAND

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OBJECTIVES: In Poland, where long acting insulin analogues (LAA) are not currently reimbursed in T2DM, it is crucial to select a group of patients for whom LAA may be particularly preferred. Based on NICE recommendation such patients are those treated with human insulin (NPH) but not achieving glycaemic control. Thus the aim of this study was to evaluate the cost-effectiveness of insulin detemir (IDet) when compared to NPH in subpopulation of poorly controlled T2DM as defined by HbA1c ≥8% and/or ≥1 episode of severe or nocturnal hypoglycemia recorded during ≥6 months of NPH treatment. **METHODS:** A validated computer simulation of diabetes model (IMS-CORE) was used to project long-term clinical and economic outcomes. Clinical effects in HbA1c improvement, BMI change and reduction in hypoglycemic episodes were modelled. Analysis was based on findings from the subgroups of the *PREDICTIVE* study – a real-world data trial – that closely reflects the defined target population. Two distinct insulin therapy regimens with IDet and NPH were evaluated: basal-supported oral therapy (BOT) and a basal-bolus (BB) regimen. Baseline cohort characteristics, disease progression and utility estimates were obtained from systematic literature review. Costs were obtained from Polish published data. The analysis was conducted from a public payer and patient perspective over a lifetime time horizon. Discount rates were 5% (costs) and 3.5% (outcomes). **RESULTS:** The mean QALY gain resulting from treatment initiation with IDet compared with NPH was 0,311 (BOT) and 0,451 (BB). Base-case incremental cost-effectiveness ratios (ICERs) were 38,136 PLN/QALY (9,113€) and 13,726 PLN/QALY (3,280€), respectively. At the current ICER threshold of 105,801 PLN/QALY (25,281€) in Poland, probability of IDet being cost-effective compared to NPH is 95% (BOT) and approaching 100% (BB). **CONCLUSIONS:** Based on generally accepted cost/QALY threshold values in the Polish settings, IDet was found to be a cost-effective option for T2DM patients with inadequately controlled diabetes.

PDB62

COST-EFFECTIVENESS ANALYSIS OF INSULIN DEGLUDEC COMPARED WITH CURRENT STANDARD OF CARE IN THE MANAGEMENT OF TYPE 1 AND TYPE 2 DIABETES MELLITUS IN THE SPANISH HEALTH SYSTEM

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OBJECTIVES: Insulin degludec (IDeg) is a basal insulin with an ultra-long duration of action for management of patients with type 1 (T1DM) and patients with type 2 (T2DM) diabetes. IDeg have demonstrated efficacious blood glucose control with less hypoglycaemic events and with an option for flexibility in dose time compared insulin glargine (IGlar). The objective was to assess the cost-effectiveness of IDeg in Spain, compared with IGlar. The analysis focused on subgroups of patients within three treatment regimens: T1DM, T2DM treated with basal insulin in combination with oral anti-diabetics (BOT) and T2DM treated with basal-bolus (BB). **METHODS:** A one-year cost-utility model driven by differences in hypoglycaemia was used. Two alternative utility approaches were used: in the first case, the utility gain was elicited from the clinical trials. In the second, published dis-utilities for hypoglycaemic events and self-monitoring blood glucose tests were used to calculate QALYs. Cost and utilities were also estimated for potential use of less blood glucose test strips. Three subgroups were analysed: those using twice daily IGlar, those with high risk of severe hypoglycaemia, and those obtaining extra utility from dosing flexibility. Unit costs pertained to public tariffs and reflected the payer perspective. Baseline incidence rates of hypoglycaemia and related resource use was derived from a Spanish observational study. **RESULTS:** IDeg was dominant for T1DM, T2DM BOT and T2DM BB switching from twice daily. T2DM BOT with high risk of hypoglycaemia was also dominant. As for patients benefiting from dosing flexibility the cost/QALY were 6,921€/QALY in T1DM, 9,244€/QALY in T2DM BOT, and 33,099€/QALY in T2DM BB. The use of the two different utility methods gave similar results. Univariate and probabilistic sensitivity analyses confirmed robust results. **CONCLUSIONS:** This analysis demonstrates that IDeg is a cost-effective option in Spain, when used in sub-groups of patients currently treated with long-acting insulin.

PDB63

EVALUATING THE COST-UTILITY OF FENOFIBRATE TREATMENT OF DIABETIC RETINOPATHY IN AUSTRALIA

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OBJECTIVES: Evidence from the landmark trials FIELD and ACCORD demonstrated that fenofibrate significantly reduces rates of diabetic retinopathy (DR) progression in type 2 diabetes patients (T2DM). This study evaluates the long-term cost-effectiveness of fenofibrate mono- and combination therapy for DR in Australia. **METHODS:** A seven-state Markov model simulated progression of DR based on data from the Blue Mountain Eye Study. Risk reductions for retinopathy progression were derived from FIELD for fenofibrate monotherapy (vs. placebo) and ACCORD for fenofibrate+statin (vs. statin alone). No additional benefits were assumed beyond 5 years (DR progression was the same with/without fenofibrate after year 5). Quality-adjusted life expectancy, direct costs and incremental cost-effectiveness ratios (ICERs) were reported over 10 years. Unit costs (2012 Australian dollars, AUD), resource use and utilities were taken from country-specific sources/expert opinion. Future costs and clinical benefits were discounted at 5% annually. Sensitivity analyses were performed. **RESULTS:** Fenofibrate monotherapy improved mean quality-adjusted life expectancy by 0.09 QALYs versus placebo due to fenofibrate patients spending more time in mild DR states. Direct medical costs were AUD 898 higher for fenofibrate monotherapy, with additional treatment costs partially offset by reduced cost associated with advanced DR (e.g. ophthalmologist time and laser treatment), leading to an ICER of AUD 10,221 per QALY gained. Similarly, fenofibrate+statin led to an improvement of 0.05 QALYs versus statin alone with an incremental direct cost of AUD 1,707. The ICER for fenofibrate+statin was AUD 33,350 per QALY gained versus statin alone. Sensitivity analysis showed that results were relatively insensitive to changes in a range of assumptions. **CONCLUSIONS:** The reduced risk of DR progression associated with fenofibrate treatment was projected to improve quality-adjusted life expectancy, with treatment costs partially offset by reduced costs of retinopathy care. ICERs indicated that fenofibrate therapy was in the range likely to be considered cost-effective in Australia.

PDB64

COST-EFFECTIVENESS OF INSULIN DEGLUDEC COMPARED WITH INSULIN GLARGINE IN A BASAL-BOLUS REGIMEN IN PATIENTS WITH TYPE 1 DIABETES MELLITUS IN THE UNITED KINGDOM

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OBJECTIVES: Insulin degludec (IDeg) is a basal insulin with an ultra-long duration of action for the management of patients with type 1 (T1DM) and patients with type 2 (T2DM) diabetes. IDeg has demonstrated effective blood glucose control with less hypoglycaemic events and with an option for flexibility in dose time compared to insulin glargine (IGlar). The aim of this analysis was to evaluate the cost-effectiveness of IDeg versus IGlar in adults with T1DM in the UK. **METHODS:** Meta-analysis data from two phase III clinical studies were used to populate a simple, transparent short-term model. The analysis was conducted from the UK National Health Service perspective and costs and benefits were calculated over a 12-month period. Sensitivity analyses were conducted to assess the degree of uncertainty around the results. In order to test the robustness of the results, two versions of the model were used. One applied disutilities derived from the SF-36 questionnaire used in the clinical trials, the other applied disutilities associated with the occurrence of hypoglycaemic events. In both approaches an additional utility gain was attributed to the benefit of dosing flexibility. Baseline incidence of hypoglycaemia was taken from a real-life study from the UK. Resource use associated with hypoglycaemia was documented in the clinical trials. Published tariffs were used as unit costs. **RESULTS:** The base-case ICERs were £12,637/QALY and £13,349/QALY in the two modelling approaches, which are below commonly accepted thresholds for cost-effectiveness. The results were robust and largely insensitive to changes in input parameters. **CONCLUSIONS:** This short-term modelling approach allows the economic evaluation of newer insulin analogues when advanced long-term modelling based on HbA_{1c} differences is inappropriate due to the treat-to-target nature of the clinical trials resulting in equivalent HbA1c levels. For patients in the UK with T1DM IDeg is a cost-effective treatment option compared with IGlar.

PDB65

COST-EFFECTIVENESS OF INSULIN DEGLUDEC COMPARED WITH INSULIN GLARGINE FOR PATIENTS WITH TYPE 2 DIABETES MELLITUS INITIATING INSULIN THERAPY IN THE UNITED KINGDOM

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OBJECTIVES: Insulin degludec (IDeg) is a basal insulin with an ultra-long duration of action for management of patients with type 1 (T1DM) and patients with type 2 (T2DM) diabetes. IDeg has demonstrated effective blood glucose control with less hypoglycaemic events and an option for flexibility in dose time compared to insulin glargine (IGlar). The aim of this analysis was to evaluate the cost-effectiveness of IDeg versus IGlar in adults with T2DM initiating insulin therapy in the UK. **METHODS:** Meta-analysis data from three clinical studies were used to populate a 1-year cost-utility model. The analysis was conducted from the UK National Health Service perspective. Sensitivity analyses were conducted to assess the robustness of results. Two versions of the model were tested, one applied disutilities derived from the SF-36 questionnaire used in the clinical trials, the other applied disutilities associated with the occurrence of hypoglycaemic events. In both approaches an additional utility gain was attributed to the benefit of dosing flexibility. Baseline incidence of hypoglycaemia was derived from a UK real-life study. Resource use associated with hypoglycaemia was documented in the clinical studies. Official tariffs were used as unit costs. **RESULTS:** Base-case ICERs were £15,705/QALY and £13,003/QALY in the two modelling approaches. Results were robust, with baseline rate of hypoglycaemia a key driver of results. Using hypoglycaemia rates from a subgroup of patients who experienced ≥1 hypoglycaemic event per year IDeg was highly cost-effective versus IGlar; with estimated ICERS of £4,706/QALY and £2,528/QALY. **CONCLUSIONS:** This short-term modelling approach allows the economic evaluation of newer insulin analogues when advanced long-term modelling based on HbA_{1c} differences is inappropriate due to treat-to-target trial design. For patients with T2DM on a basal-only insulin regimen, IDeg is cost-effective compared with IGlar and offers additional benefits to subgroups of patients, such as those suffering from recurrent hypoglycaemia.

PDB66

THE COST-UTILITY OF INSULIN DEGLUDEC COMPARED WITH CURRENT STANDARD OF CARE IN THE MANAGEMENT OF TYPE ONE AND TYPE TWO DIABETES MELLITUS IN BELGIUM

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OBJECTIVES: Insulin degludec (IDeg) is a basal insulin with an ultra-long duration of action for management of patients with type 1 (T1DM) and patients with type 2 (T2DM) diabetes. IDeg has demonstrated efficacious blood glucose control, with less hypoglycaemic events, and with an option for flexibility in dose time, compared with insulin glargine (IGlar). The objective was to assess the cost-effectiveness of IDeg in Belgium, compared with IGlar. The analysis focused on patients in three treatment regimens: T1DM, T2DM treated with basal insulin in combination with oral anti-diabetics (BOT) and T2DM treated with basal-bolus (BB). **METHODS:** A one-year cost-utility model driven by differences in hypoglycaemia was used. Published dis-utilities for hypoglycaemic events were multiplied by the rate of hypoglycaemia to calculate quality-adjusted life years (QALYs). Costs and utilities were also calculated for potential use of less blood glucose test strips. A utility gain was attributed to the additional benefit of dosing flexibility. Unit costs pertained to public tariffs and reflected the payer perspective in Belgium. Baseline incidence rates of hypoglycaemic events and related resource utilization pertained to a Belgian patient-reported outcomes study. Hospitalization costs following severe hypoglycaemia were estimated using the IMS Hospital Disease Database. **RESULTS:** IDeg was associated with an incremental cost-effectiveness ratio of 14,677€/QALY in T1DM, 4,976€/QALY in T2DM BOT, and 12,930€/QALY in T2DM BB. Univariate and probabilistic sensitivity analyses confirmed robust results. Results were most sensitive to variations in number of IGlar doses per day, and number of glucose-monitoring tests. At a willingness to pay threshold of 30,000€/QALY, IDeg would be cost-effective in 54%, 100% and 93% of the cases in the T1DM, T2DM BOT or T2DM BB treatment regimens respectively. **CONCLUSIONS:** These analyses demonstrate that IDeg is cost-effective in Belgium, when used in patients with T1DM and T2DM currently treated with long-acting insulin analogues.

PDB67

ECONOMIC EVALUATION OF LIRAGLUTIDE FOR TREATMENT OF TYPE 2 DIABETES MELLITUS IN THE RUSSIAN FEDERATION

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OBJECTIVES: The analysis goal is to determine the cost-effectiveness of liraglutide as add-on to metformin in for patients with type 2 diabetes in condition of the Russian health care system. Total medical expenses and effectiveness in terms of QALY are compared for liraglutide, glimepiride and rosiglitazone, all in combination with metformin, and metformin monotherapy. **METHODS:** Data were sourced from a clinical trial comparing liraglutide vs. glimepiride (in combination with metformin), and a clinical trial comparing liraglutide vs. rosiglitazone (as add-on to metformin). From them data on clinical effectiveness in form of impact on HbA1(c), body mass index and blood pressure are extracted. Utility values are mostly taken from the UK Prospective Diabetes Studies supplemented with other published sources. The analysis is conducted from the perspective of the Russian health care system. Respectively the cost of the following resources is accounted: comparing of alternatives, concomitant pharmacotherapy, cost of medical manipulation, cost of ambulatory visits. Both future costs and clinical benefits are discounted at 3 percent. Sensitivity analysis is performed. Results of this analysis are shown in the incremental cost-utility rate (ICUR). **RESULTS:** The data of the analysis illustrates that liraglutide therapy for type 2 diabetes patients provides a significant health improvement from the perspective of quality adjusted life-years. Simultaneously liraglutide demonstrates better cost-effectiveness than the compared alternatives. The ICUR index of 1.2 mg liraglutide in combination with metformin equal to 1 348368 rub, 1 161874 rub and 537331 rub for QALY in comparison with metformin monotherapy, glimepiride and rosiglitazone, both in combination with metformin, respectively. **CONCLUSIONS:** Liraglutide has turned to be cost-effective therapeutic alternative for treatment of type 2 diabetes in adult patients in conditions of Russian health care system over a 10-year time horizon.

PDB68

ECONOMIC EVALUATION OF SITAGLIPTIN IN DIABETES MELLITUS TREATMENT IN CHINA

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OBJECTIVES: To evaluate the long-term cost effectiveness of sitagliptin compared to glimepiride and acarbose in the treatment of type 2 diabetes mellitus in China. **METHODS:** Sitagliptin, as add-on therapy to metformin, was compared to glimepiride and acarbose, and as monotherapy was also compared to acarbose. The validated UKPDS Outcomes Model was used to estimate the direct medical costs and outcomes (life years and QALYs gained). The demographic characteristics and clinical data were taken from published literature. The quality of life data was obtained from published literature and re-confirmed through a questionnaire survey from a clinical expert panel of 20 diabetes specialists. The cost of drugs was calculated based on government guidance price or actual market price. The annual cost of complications was estimated based on expert opinions. Patients' outcomes were modeled for 40 years and incremental cost-effectiveness ratios were calculated. Both future costs and clinical benefits were discounted at 3 percent. A probabilistic sensitivity analysis was performed to understand the key drivers and general sensitivity of the model. **RESULTS:** The results showed that, compared to the treatment of glimepiride and acarbose plus metformin therapy, the add-on of sitagliptin provided a gain of 0.02 and 0.95 QALYs per patient, and the incremental cost-effectiveness ratios were USD 9,470 and USD 399, respectively. The results also showed that compared to acarbose monotherapy (100mg t.i.d and 200mg t.i.d), the sitagliptin monotherapy (100mg/d and 200mg/d) was dominant, with higher QALYs (0.58 and 0.92) and years of life (0.72 and 1.23) gained and lower cost (USD 90 and USD 185). **CONCLUSIONS:** According to the China's GDP per capita in 2011 (USD 5,674), the results demonstrate that sitagliptin is more cost-effective than glimepiride and acarbose in the treatment of diabetes mellitus in China.

PDB69

PRODUCTIVITY LOSS IN POPULATION OF INFORMAL CAREGIVERS TO DIABETIC FOOT SYNDROME PATIENTS IN POLAND

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OBJECTIVES: Foot ulceration is a major cause of disability in diabetic patients. Disability of patients with diabetic foot ulceration (DFS – Diabetic Foot Syndrome) concerns not only patients themselves, but also the informal caregivers, mainly their close relatives. The aim of this study was to estimate lost productivity in a population of family caregivers of patients with diabetic foot ulceration in Poland. **METHODS:** A survey among 189 patients with DFS (treated in ambulatory care) and their families was conducted. To assess the impact of diabetic ulceration on productivity of caregivers to DFS patients the modified questionnaire WPAI-CG was used. The PEDIS scale was used to classify severity of ulceration. **RESULTS:** A total of 116 out of 189 questionnaires were collected, and data on 93 responders (25 males) were included in the analysis (23 questionnaires were returned empty or concluded that informal care is not provided to DFS patients). Fifty-two (13 males) out of 93 caregivers were employed at the time of the survey. Mean age of the population of caregivers was 45.9±11.2 years. Most were close relatives of DFS patients (58% spouses, 27% children). Almost half caregivers were employed in private sector (46%). Most had higher (50%) or secondary (48%) education. The average weekly work time declared was 40.4±13.1 hours. Approximately 70% of caregivers were urban population. The average percentage of work time missed and the percentage of working impairment while working due to informal care of DFS patients were estimated at 11.9% and 25.0%, respectively. The percentage of overall work impairment due to informal care of DFS patients was 32.2%. This amounts to weekly average time of the absence of 13.0 hours. **CONCLUSIONS:** The lost productivity due to informal care on DFS patients is substantial and may have important implications for the economy.

PDB70

UTILISATION PATTERN OF GLP-1 AGONISTS IN COMBINATION WITH BASAL INSULIN IN PATIENTS WITH T2DM IN THE NORWEGIAN SETTING IN ONE YEAR

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OBJECTIVES: GLP-1 agonists in combination with basal insulin (BI) have demonstrated additional improvement of glycemic control in uncontrolled T2DM patients in clinical trials. It is therefore important to assess the real-world utilisation of GLP-1 agonists in combination with BI in T2DM patients. **METHODS:** Retrospective cohort analysis (2010 to 2012) to assess GLP-1 agonist utilisation in T2DM patients based on the Norwegian Institute of Public Health Prescription Database (NorPD). Both ICPC=T90 and ICD-10=E11 were applied to identify T2DM patients. Patients who had ≥2 GLP-1 dispensed within 6-month in Year-2011, with 1-year pre-Baseline/post- Follow-up GLP-1 initiation were included in the analysis. Baseline antidiabetic drug use and combination use of GLP-1 and BI at Follow-up were also assessed. **RESULTS:** Of the 1,500 GLP-1 initiators identified (mean age=57; 52% male) at Baseline, 77% were on OADs, 19% on BI, 2% on prandial insulin (no BI) and 2% on other/no anti-diabetic drug. During 1-year Follow-up of GLP-1 adding on OADs patient population, 56% used GLP-1 continuously including 50% who used GLP-1 alone and 6% added BI. In total, 15% had either combined with or switched to BI, 4 months after the first GLP-1 was dispensed. Of those GLP-adding on BI patient population, 53% continuously used GLP-1 including 26% had both GLP-1 and BI dispensed throughout the Follow-up. About 52% had either BI interrupted or discontinued approximately 2 months after the first GLP-1 was dispensed. In total, 27% had insulin bolus dispensed; of which 58% either interrupted or discontinued GLP-1. **CONCLUSIONS:** About 1/3 of GLP-1 initiators were in combination with BI. In BI treated T2DM patients >25% remained on both GLP-1 and BI, while another >25% required treatment augmentation or switched to bolus. The data suggests an unmet treatment need, particularly in T2DM patients treated with BI.

PDB71

REVIEW OF COST OF DIABETES COMPLICATIONS IN FOUR EUROPEAN COUNTRIES

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OBJECTIVES: To provide a comprehensive and coherent reference document of published cost data for diabetic complications in France, Germany, Italy and Spain for use in economic diabetes modeling. **METHODS:** A search for published cost of diabetes complications data from a health care payer perspective was performed on government websites, in peer-reviewed journals and local cost experts. All costs were inflated to 2013 Euros (€). **RESULTS:** First year costs of myocardial infarction varied between €3,041 in France and €9,690 in Germany. Heart failure costs were similar across countries: €3,104 in France; €2,791 in Germany; €4,000 in Italy and €3,316 in Spain. Costs of non-fatal stroke were higher in Germany (€16,441) than in other countries (Spain €8,016; Italy €6,073; France €5,447). Everywhere, the cost of haemodialysis was higher than peritoneal dialysis €35,972 versus €21,255 in Spain, €21,552 versus €18,485 in Italy, €34,290 versus €34,069 in Germany €71,683 versus €48,752 in France. Renal transplant cost was estimated to €84,114 in France, €34,858 in Germany, €38,528 in Italy and €26,618 in Spain. The cost of a major hypoglycemia requiring medical care was €4,275 in Spain, €2,561 in Germany, €1,391 in Italy and €1,165 in France. Neuropathy complication costs varied widely: €3,808 (France); €16,762 (Germany); €4,290 (Italy); and €5,330 (Spain) for foot ulcers and €6,056 (Italy); €7,754 (Germany); €9,578 (France); and €12,118 (Spain) for lower-extremity amputation. **CONCLUSIONS:** This study provides a coherent set of costs for diabetes complications in four European countries. Due to the differences in health care

system structure and in cost transparency, the cost estimation methodology varied among countries. One limitation of this study is that diagnostic related group (DRG) tariffs were used to estimate several costs, which may not accurately represent the burden of a specific complication nor take into account the full burden of follow-up after an acute event.

PDB72
THE COST OF SPECIALIZED HOSPITAL CARE FOR PATIENTS WITH DIABETIC FOOT ULCERS IN RUSSIA
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OBJECTIVES: To assess the direct medical costs for aggressive limb preservation treatment of diabetic foot ulcer (DFU) in a highly-specialized hospital setting in Russia **METHODS:** A retrospective data analysis of 156 admissions during 1-year period was done to get direct costs (associated with hospital stay, conservative and surgical treatment and laboratory testing) for treatment of DFU in a highly-specialized inpatient department in Russian setting (Federal Endocrinology Centre). **RESULTS:** The median cost of hospital treatment was 2270 EUR and increased with severity level, defined according to Wagner classification, ranging from 1590 EUR (grades 0-2) to 3812 EUR (grade 3) and 7683 EUR (grade 4), the difference was statistically significant. The length of stay in a hospital also correlated with the severity level starting with 14 days for grade 1 and reaching 39 days for grade 4. The costs of treatment were significantly higher for patients with inadequate vascular status requiring surgery – the median was 6185 EUR for cases with only angioplastic surgery and 8622 EUR for cases with both angioplastic and foot surgery provided. **CONCLUSIONS:** Treatment of DFU aimed at limb preservation is resource consuming, costs for treating severe stage ulcer are 4,8 times higher than are those for treating low-stage ulcer. The high costs of treating severe stages of DFU in a specialized hospital setting emphasize the value of intensive outpatient interventions designed to prevent ulcer progression.

DIABETES/ENDOCRINE DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PDB73
RISK FACTORS FOR DISCONTINUATION OF INSULIN PUMP THERAPY IN PEDIATRIC AND YOUNG ADULT PATIENT GROUPS
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OBJECTIVES: Previous studies have shown that only a small number of pediatric and young adult patients discontinue pump therapy, but risk factors for discontinuation are unclear. Aim of this study was to identify characteristics of pediatric and young adult patients with pump therapy which are associated with discontinuation of treatment. **METHODS:** Retrospective cohort study using a representative nationwide database (LRx; IMS Health) in Germany covering >80% of all prescriptions to members of statutory health insurances in 2008-2011. All patients (age groups: <6, 6-<12, 12-<18, 18-<25 years) with new prescriptions of insulin pumps or related material were identified (2009-2011) and were followed for ≥12 months. **RESULTS:** Overall, 3057 new pump users were identified, of whom 177 (5.8%) switched to other forms of insulin therapy within 12 months. Discontinuation was lowest in the age group <6 years (2.1%) and was highest in adolescents (12-<18 years: 7.5%) (p<0.01). In age-adjusted logistic regression, usage of steel needles (Odds ratio, OR, 95%CI: 1.69; 1.20-2.44) and prescriptions of antiepileptics (3.14; 1.49-6.59) were related to pump discontinuation. In younger age groups only, discontinuation was significantly higher in patients with thyroid therapy as a surrogate measure for thyroid autoimmunity (<6 years: 14.3%; 6-<12 years: 25.0%) (p<0.01). **CONCLUSIONS:** About 94% of pediatric and young adult patients maintained insulin pump therapy within 12 months. Adolescence (12-18 years), usage of steel needles and prescriptions of antiepileptic drugs are independent predictors of discontinuation. In younger age groups (<12 years) also thyroid therapy (indicating autoimmunity) was related to a higher risk of discontinuation.

PDB74
PERSISTENCE PATTERNS WITH ORAL HYPOGLYCAEMIC MEDICINES (OHM) IN NEWLY TREATED IRISH PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM)
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OBJECTIVES: To describe persistence patterns to OHM in newly treated Irish patients with T2DM. The study also investigated the effect of age, gender, reimbursement scheme and type of OHM on persistence. **METHODS:** A population based retrospective cohort study was conducted using national pharmacy claims databases, including two community drugs schemes; Long Term Illness, (LTI, non-means tested) and General Medical Services (GMS, means tested). Newly treated T2DM patients were identified for 2008-2009, having received no OHM in the previous year, and followed up until Nov-2012. Patients who subsequently switched or received additional OHM were excluded. Non-persistence was defined as a prescription gap of >12 weeks and within 1 year of initiating treatment. Logistic regression examined associations of age, gender, scheme and type of OHM with persistence with results presented as odds ratios (OR) and 95% confidence intervals (CI). **RESULTS:** A total of 15,174 persons were eligible for the study. Most patients were initiated on metformin (79.4%) and sulphonylureas (19.1%). Persistence at 1 year was 60.9%. The median overall time to non-persistence was 51.5 days. Men were slightly more likely to be persistent than women (OR=1.08; 95%CI=1.001 to1.15; p=0.0025). Patients aged 16-44 and 75+ were less likely to be persistent than patients aged 55-64 (OR= 0.18; 95%CI=0.16-0.21; p<0.0001 and OR=0.67; 95%CI=0.60-0.75; p<0.0001 respectively). Patients registered with the LTI Scheme were more likely to be persistent than from the GMS Scheme (OR=1.35; 95%CI=1.20-1.51; p<0.0001). Patients initiated on sulphonylureas were less likely to be persistent than those initiated on metformin (OR=0.50; 95%CI=0.45 to 0.54; p<.0001). **CONCLUSIONS:** Persistence amongst newly treated T2DM patients appears to be low. Type of OHM, age and scheme were all significantly associated with persistence. Prescribers should pay particular attention to newly treated patients covered under the GMS scheme, at the extremes of age and those initiated on sulphonylureas.

PDB75
THE IMPACT OF MEMORY PROBLEMS ON DIABETES TREATMENT IN CANADA
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OBJECTIVES: The impact of memory problems (MPs) on patient's insulin taking behavior, functioning, well-being and diabetes management is not well understood. **METHODS:** A 5 country web-based survey was conducted. MPs were defined as: unintentionally forgetting (UF) to take insulin, questioning whether or not insulin had been taken (QT), or questioning how much insulin dose was taken (QD). Data from Canadian respondents were analyzed and compared to the other countries (US, UK, Germany, and China). **RESULTS:** A total of 350 respondents in Canada completed the survey (74.0% Type 1, 52.0% male, mean age of 37.1 years, mean age of diabetes onset of 24.2). The prevalence of MPs was 60.6% (UF), 76.3% (QT) and 44.6% (QD) in the past month with only approximately 1/3 being confident they knew what to do when having an MP. Between 21.5% (QT) and 37.4%(UF) tested their blood glucose and 32.6% (QD) – 51.6% (QT) skipped their insulin dose and waited for next scheduled dose when experiencing a MP, requiring, on average, between 8.5 (QT)–19.1 (UF) hours for return to normal blood glucose ranges. Patients conducted between 1.9 (QT) –5.0 (UF) extra BG monitoring tests the week following the MP and reported moderate negative impacts on their ability to work, physical and emotional functioning. Up to 13.7% missed a work day (UF) and between 10.8% (QT) and 16.8% (UF) visited their health care provider as a result of MP Compared to respondents in the other countries (N=1404), Canadian respondents were reported significantly longer recovery times for returning to normal blood glucose levels following a MP and were significantly more likely to experience hyperglycemia following UF/QD than patients in other countries (p<.05). **CONCLUSIONS:** These findings suggest that MPs have economic implications, impact patients' functioning and well-being and may be serious obstacles to optimal diabetes control.

PDB76
THE IMPACT OF MEMORY PROBLEMS ON DIABETES TREATMENT IN THE UNITED KINGDOM
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OBJECTIVES: The impact of memory problems (MPs) on patient functioning, well-being and diabetes management is not well understood. The purpose of this study was to examine these impacts in the UK and compare these findings to data from US, Germany, Canada, and China). **METHODS:** A 5 country web-based survey examining MPs was conducted. MPs were defined as: unintentionally forgetting (UF) to take insulin, **q**uestioning whether or not insulin had been **t**aken (QT), or **q**uestioning amount of insulin **d**ose (QD). **RESULTS:** A total of 350 UK respondents (52.0% Type 1), 49.1% male, mean age of 40.3, mean age of diabetes onset of 25.5 completed the survey. The prevalence of MPs was 66.6% (UF) forgetting, 84.9% (QT) 56.9% (QD). MPs occurred most frequently when relaxing or doing household jobs. Between 13.7% (UF) – 32.6% (QT) of respondents skipped their insulin dose due to a MP and required between 1.4 (QD)–13.1 (UF) hours, on average, to return to normal blood glucose range. As a result of a MP, patients conducted between 1.7 (QT) –6.8 (UF) extra BG monitoring tests , reported a moderate negative impact on their physical and emotional functioning, as well as their ability to go to or function optimally at work and between 8.1% (QT) and 20.0% (UF) visited/contacted their health care provider . Economic implications include cost of additional BG strips, lost work productivity and health care resource utilization. Compared to respondents in the US, Germany, China and Canada (N=1404), UK respondents conducted significantly more BG tests during the week following a missed dose of insulin were more likely to take a dose of insulin following a MP without testing their BG. **CONCLUSIONS:** These findings suggest that MPs in the UK carry financial burden, impact patients' daily functioning and well-being and may be serious obstacles to optimal diabetes control.

PDB77
DO FIXED-DOSE COMBINATIONS IMPROVE ANTIDIABETIC TREATMENT COMPLIANCE? A STUDY BASED ON FRENCH IMS LIFELINK DISEASE ANALYZER DATABASE
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OBJECTIVES: To compare antidiabetic treatment compliance with regards to the fixed or free treatments combination. **METHODS:** A retrospective study based on the IMS LifeLink™ Diabetes Cohort linked to IMS Disease Analyzer, a longitudinal patient database containing the electronic health records of patients followed-up by a representative panel of French general practitioners. Two cohorts of patients treated both with metformin and DPPIV were constituted, the first one treated with fixed associations ("fixed cohort"), the second one treated with free associations ("free cohort"). Study investigated patients' demographic and clinical characteristics, conditions of use, persistence rates, medication possession ratio (MPR) and proportion of days covered (PDC) of the two cohorts. **RESULTS:** Respectively 2 234 and 8220 patients have been treated with free and fixed antidiabetic associations between 2007 and 2013. Patients are significantly older (66 vs. 64 years, p<0.01) in the free cohort where the proportion of men is significantly lower (56% vs. 63%, p<0.0001). Nevertheless diabetes oldness is the same (about 10 years) in both

cohorts. Daily number of prescribed tablets whatever the therapeutic classes is significantly higher in the free cohort (4.4 per day vs. 3.1, p<0.01). At the end of the first treatment year, significantly more patients of the fixed cohort are still treated by the same association regardless daily dosages or potential add-on treatments (85% vs. 72%, p<0.0001); moreover MPR is the same in both free and fixed cohort (64% and 66% without statistical difference) while PDC is significantly higher in the fixed cohort (60% vs. 54%, P<0.0001). **CONCLUSIONS:** Patients treated by fixed antidiabetic treatments associations seem to be more persistent than these treated by free ones at the end of the first year of treatment. These results will be consolidated soon by comparing two similar sub-cohorts with the same medical profile.

PDB78

IMPACT OF DOSAGE AND SEVEN OTHER FACTORS IN THE ADHERENCE TO ORAL MEDICATION IN PEOPLE WITH DIABETES TYPE 2 IN GERMANY

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OBJECTIVES: Low adherence to medications in chronic diseases is a well documented problem that diminishes drug actions. Understanding the factors that can impact adherence is a priority in order to improve it. Diabetes adherence can be influenced by the complexity of administration of some medications as well as patients' attitudes and doctor/patients interaction. This study evaluates the influence of the following variables in the adherence of people with diabetes: Dosage, patient age, gender, substance, price of drug, pack size, pack strength and doctor specialty. **METHODS:** Adherence was calculated using the medical possession ratio (MPR) = unique days of therapy/available days. A logistic regression was conducted to explore the multiple variables affecting the MPR. **RESULTS:** The analyses included 25 months (from July 2009 to July 2011) of longitudinal prescription data for Germany for the ATC class A10 (oral antidiabetic). We found significant effects on adherence for age groups 55-64 (0.0909 p<0.01), 65-74 (0.1266, p<0.0004) and > 75 (0.0868, p< 0.0155), dosage (-0.7646, p<0.0001), gender (-0.0493 p<0.001), pack size (0.0119, p <0.0001), doctor specialty (0.0251, p<0.0286) and 78% of all substances. **CONCLUSIONS:** Adherence seems to be negatively influence by dosage and younger age groups. Price does not seem to have an influence. Perhaps this is because the health care system in Germany reimbursed all oral antidiabetics. Metformin has the greater odds for poor adherence aside from the substances "glitazones". Lower adherence rate might be negatively influenced by the recent warnings for Glitazones. Gender is a weak predictor for adherence. When comparing specialists with general practitioners, the odds of adherence are not very different between them (slightly positive towards the specialist group_ coeff 0.0251, p<0.0286). This could be related to the diabetes management plan that exists in Germany since 2003, which has several aspects, from support to clinicians to training of patients.

PDB80

PSYCHOSOCIAL ADJUSTMENT IN DIABETIC PATIENTS WITH AND WITHOUT DIABETIC FOOT-ULCERS-A COMPARATIVE STUDY

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OBJECTIVES: Diabetes is a chronic illness and 15% of diabetic will develop foot ulceration at some point of their life. Poor psychosocial states have been identified as one of the major risk factors for foot ulcers. Good, regular foot care, strict metabolic control and better adjustment to illness can prevent or reduce suffering effect of the illness. The purpose of this study was to compare the psychosocial adjustment to illness between diabetic patients with and without diabetic foot ulcer (DFU). **METHODS:** A case-control study was conducted in a tertiary care teaching hospital in South India for a period of one year. Psychosocial Adjustment to Illness Scale-Self Report (PAIS-SR) were used to assess psychosocial adjustment to illness. DFU patients (Case) who admitted in the surgery units were included. Diabetic patients without foot ulcers (control) were selected from medicine units during the same period. **RESULTS:** The study participants were 84 people with diabetic foot ulceration and 84 people without diabetic foot ulceration. There were no significant differences between the two groups for gender, age and marital status. A significant difference was found between two groups for education level (p= 0.001) occupational status (p=0.045). A significant difference was found between the groups in relation to smoking (p=0.000) and drinking (p=0.000). There were a significant difference seen in PAISSR scores (lower scores means better adjustments) between the two groups (p=0.000) representing subjects without DFU had better psychosocial adjustment than subjects with DFU. **CONCLUSIONS:** The study concluded that compared to patients without DFU, patients with diabetic foot ulcer had poorer metabolic control, low educational level, bad social habits. Longer duration of diabetes, longer period of hospitalization, low level of disease knowledge and more incidence of comorbid conditions.

PDB81

DIMINISHING MARGINAL DISUTILITY OF HYPOGLYCAEMIC EVENTS

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OBJECTIVES: Hypoglycaemic events are proven to have a negative impact on the health-related quality of life (HRQoL) of patients with diabetes. The negative impact of hypoglycaemia on HRQoL may be evaluated via disutility scores. The aim of this study was to assess the marginal impact of non-severe hypoglycaemic events on HRQoL and to investigate the functional form of the disutility of hypoglycaemic events. **METHODS:** Published disutility values from a large-scale, web-based time-trade-off study (TTO) conducted in UK, USA, Canada, Germany and Sweden with 8,286 respondents, were used as a basis for the analysis of non-severe daytime and nocturnal hypoglycaemia. Non-linear regression curves were fitted to the total disutility of different frequencies of hypoglycaemic events. A weighting scheme was used to allow each data point (one event quarterly, one monthly, one weekly or three weekly) to reflect the range of hypoglycaemic frequencies the data point represented. Non-parametric bootstrapping was applied to characterise the uncertainty of the marginal disutility. **RESULTS:** Power function regression curves were estimated at $U_d=0.0141x^{0.3393}$ and $U_d=0.0221x^{0.3277}$, where U_d is disutility and x is the annual hypoglycaemic event rate, for non-severe daytime and non-severe nocturnal events. An increase from 0 to 1 hypoglycaemic events per year, produced a utility decrease of 0.0141 for non-severe daytime, and 0.0221 for non-severe nocturnal, whereas an increase of one hypoglycaemic event per year for a patient who experiences 25 hypoglycaemic events per year produces a marginal impact of 0.0006 and 0.0008 for non-severe daytime and non-severe nocturnal, respectively. **CONCLUSIONS:** If patient-level data are available, non-linear functions estimated with TTO data might improve the precision of the measured impact of hypoglycaemic events. The results seen here illustrate diminishing marginal disutility with increasing numbers of hypoglycaemic events. This fits with the phenomenon of "first being worst" with regards to hypoglycaemia.

PDB82

QUALITY OF LIFE IN PATIENTS WITH TYPE 2 DIABETES IN POLAND: COMPARISON WITH GENERAL POPULATION USING EQ-5D QUESTIONNAIRE

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OBJECTIVES: To compare the health related quality of life (HRQoL) in Polish patients with type 2 diabetes (T2D) and in matched sample from the general population. **METHODS:** Data on HRQoL came from two non-interventional studies: prospective study of patients with T2D and EQ-5D Polish general population norms study. Analysis of HRQoL was conducted in four separate age groups: 32–44, 45–54, 55–64 and above 65 years. We analyzed: an subjective and objective assessment of HRQoL (EQ VAS and EQ-5D index) and the presence of restrictions within five dimensions of the EQ-5D descriptive part. **RESULTS:** A total of 274 patients with T2D and 214 representatives from population norms study, were included. EQ VAS was systematically lower in diabetic patients compared to the general population, and decreased with age (68.2 vs 83.9, 62.4 vs 79.2; 54.9 vs 78.1, 50.2 vs. 69.8 in consecutive age groups). A similar relationship was observed with EQ-5D index. The largest mean differences were observed among subjects aged 55-64 years (EQ VAS: 23.2, EQ-5D index: 0.085). In three domains: self-care, usual activities and anxiety/depression, patients with diabetes above 45 years of age, reported significantly more problems than respondents from the general population. **CONCLUSIONS:** Both subjective and objective HRQoL in patients with T2D is lower than in respondents of similar age from the general population. Compared with type 2 diabetic populations from other countries, Polish patients characterize by a relatively high HRQoL objective assessment and very low subjective assessment.

PDB83

UTILITIES FOR TYPE 2 DIABETES MELLITUS AND ASSOCIATED COMPLICATIONS

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OBJECTIVES: The impact of Type 2 diabetes mellitus (T2DM) on health related quality of life (HRQL) is complex due to the burden of disease, lifelong treatment requirements and comorbidities. This study aimed to capture UK societal utility values for health states associated with T2DM and treatment-related adverse events (AEs) to assess the burden of the disease and common AEs. **METHODS:** Nine health state descriptions were developed (from a literature review and patient and clinician qualitative input) depicting the burden associated with T2DM and treatment related AEs. These were mild/moderate urinary tract infection (UTI); severe UTI; mycotic infection; moderate hypoglycaemic events; severe hypoglycaemic events; fear of hypoglycaemia; gastrointestinal symptoms; and hypovolaemic events. Members of the UK general public (n=100) valued these states using the time trade-off (TTO) methodology to elicit utility values (between 0= dead, 1= full health). Regression analysis was conducted to understand influence of age and gender. **RESULTS:** All treatment-related AEs were found to have a significant effect on utility. From the T2DM baseline state (0.92), the experience of AEs was associated with the following disutility: T2DM with hypovolaemic events (0.08); T2DM with mild/ moderate UTIs (0.09); T2DM with moderate hypoglycaemic events (0.11); T2DM with severe hypoglycaemic events (0.15); T2DM with fear of hypoglycaemia (0.15); T2DM with severe UTIs (0.19); T2DM with GI symptoms (0.24); andT2DM with mycotic infection (0.25); Males consistently scored the states with significantly lower utility values, but no significant age effects emerged. **CONCLUSIONS:** Findings suggest that adverse events in T2DM can be a burden for some individuals. The study indicates the potential importance of including information regarding AEs in economic evaluations. Although some states were rated severely in terms of utility, in reality, many of these only last a few days, therefore having a minimal quality adjusted life year (QALY) impact.

PDB84

HEALTH-RELATED QUALITY OF LIFE AND UTILITY IN PATIENTS WITH DIABETIC FOOT SYNDROME - AN EQ-5D SURVEY IN POLAND

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OBJECTIVES: Foot ulceration is a major cause of disability in diabetes. The aim of this study was to estimate influence of severity of diabetic foot ulceration on HRQoL. **METHODS:** A survey among DFS (Diabetic Foot Syndrome) patients with active foot ulceration treated in ambulatory care was conducted. The PEDIS scale was used to classify severity of ulceration. To assess the impact of diabetic ulceration on HRQoL in DFS patients the EQ-5D-3L questionnaire was used. Utility scores were calculated based on Polish EQ-5D value set (Golicki et al.) **RESULTS:** Between April 2012 and May 2013 185 patients were questioned directly. 179 of them (131 males) completed the EQ-5D questionnaire and had full record on ulceration severity (the PEDIS scale). The mean age of patients was 61.9±10.6 years. Diabetes type 2 was diagnosed in 150 (83.8%) patients while diabetes type 1 in 26 (14.5%). Other type of diabetes was diagnosed in 2 persons and data on one were missing. Mean time from the diagnosis of diabetes was 18.0±11.1 years. 99 (55%) and 69 (39%) patients had grade 1 and 2 perfusion, respectively. The mean ulceration size was 6.2±13.4 cm^2. 74 (41.3%), 65 (36.3%) and 40 (22.3%) patients had grade 1, 2 and 3 depth/tissue loss respectively. 84 (46.9%), 55 (30.7%) and 36 (20.1%) patients had grade 1, 2 and 3 infection, respectively. Most patients (89.4%) had loss of protective sensation (grade 2 sensation). Mean utility value in overall population was estimated at 0.618±0.320. Very week negative correlation was found between ulceration size and utility value. Despite some differences in utility value in patients with different perfusion grade no strict correlations between severity of ulceration and utility values were found. **CONCLUSIONS:** There is little or no strict correlation between severity of ulceration measured with the PEDIS scale and HRQoL measured with the EQ-5D.

PDB85

DIABETIC PATIENTS IN PRIMARY CARE: SELF-PERCEPTION AND SATISFACTION. COMPARATIVE STUDY SPAIN VERSUS EUROPE

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OBJECTIVES: EUprimecare is an European Union project aimed at analyzing the costs and quality of the different models of primary care (PC) in Europe. The aim of this study is to analyze the management of diabetic patients in PC services in Spain compared to other European countries, the satisfaction of these patients with PC services and their self-perceived health status. **METHODS:** We conducted a population survey by telephone among PC users in each of the consortium countries (Germany, Spain, Estonia, Finland, Hungary, Italy and Lithuania). The questionnaire included information on sociodemographic characteristics, health status, satisfaction, utilization of PC services, and frequency of some interventions carried out by PC professionals. The survey was conducted to 431-432 PC users in each country (Ntotal = 3020). **RESULTS:** The percentage of diabetic patients in Spain was 6.7% (N = 29), lower than the overall average (9.1%). Eighty three percent of patients living in Spain were diagnosed by their PC physicians compared with 73% of the European average. Eighty six percent of patients in Spain said that they were being treated for diabetes (EU average = 84%) and in 88% of these cases the treatment was prescribed by their PC doctor (EU average = 70%). Only 6.9% of patients said their health was poor or very poor, the lowest proportion of all countries assessed. The overall satisfaction with PC services among diabetic patients was 4.10 points on a scale of 1 to 5. Satisfaction in Spain was below the global average for all the items measured. **CONCLUSIONS:** Diabetic patients in Spain are more frequently controlled by PC professionals than in other European countries. These patients have a better self-perceived health status and the results of this study suggest a lower level of dissatisfaction with the services provided by PC.

PDB86

PATIENTS PREFERENCES REGARDING THE TREATMENT OF TYPE II DIABETES MELLITUS: COMPARISON OF BEST-WORST SCALING AND ANALYTIC HIERARCHY PROCESS

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OBJECTIVES: There is limited evidence available regarding patient preferences for treatment alternatives, including those treatment characteristics that have greatest influence on the perceived value, and how this knowledge can be used in health care decision-making. The objective of this study was to identify and elicit patient preferences for treatments in Type-II-Diabetes in different patient groups. **METHODS:** In order to elicit patient preferences this study used an explorative qualitative approach in combination with quantitative survey techniques. Literature research and semi-structured interviews (N=15) were the basis of quantitative elicitations (N=388) using Analytic-Hierarchy-Process (AHP) and Best-Worst-Scaling (BWS). The study aimed at the determination of the relative importance of patient-relevant decision criteria as well as to compare two methods of measuring preference. In total, seven therapy-related attributes (three levels each) were tested. The sample contained patients receiving oral anti-diabetics (OAD) (N=200) or insulin (N=188). **RESULTS:** The qualitative study identified 22 patient-relevant treatment-characteristics. Out of these the seven most important were included in AHP and BWS. The AHP- as well as BWS-surveys resulted in a dominance of the attribute "HbA1c-Level", for both OAD- and Insulin-patients. In the OAD-group AHP and BWS independently showed the same ranking of the three attributes: "Delay of Insulin-Therapy" (Rank 2), "Occurrence of hypoglycemia" (Rank 3) and "Weight changes" (Rank 4). In the Insulin-group "Occurrence of hypoglycemia" was ranked second using AHP and third within BWS. "Weight changes" were ranked equally in both methods. However their relevance among different patient groups changed. **CONCLUSIONS:** In both patient-groups AHP and BWS show similar results. Nonetheless both groups have different horizons of experience and differ in the ranking of decision criteria. For the first time the methods of AHP and BWS were used to assess patients' preferences for different characteristics of treatment in Type-II-Diabetes, as well as the influence of those criteria on the patient benefit.

PDB87

THE DIABETIC PERIPHERAL NEUROPATHIC PAIN IMPACT (DPNPI) MEASURE – PSYCHOMETRIC VALIDATION OF A NEW PATIENT REPORTED OUTCOME MEASURE

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OBJECTIVES: The Diabetic Peripheral Neuropathic Pain Impact (DPNPI) Measure is a patient-reported outcome (PRO) measure developed in accordance with the FDA PRO guidance for assessing the impacts of living with Diabetic Peripheral Neuropathic Pain (DPNP). A validation study was conducted to evaluate the measurement model and properties of the 27-item draft version of the DPNPI. **METHODS:** A non-interventional, observational, survey-based validation study enrolled outpatients from clinical sites in the United States. Recruitment included diagnosed DPNP patients (aged 18-80) both treated and untreated with prescription agents. Subjects completed a retest survey via mail two weeks after their in-clinic assessment. Analyses included assessment of the measurement model (factor analysis), reliability (internal consistency, test-retest) and validity (content, known-groups) of the DPNPI. IRT was utilized to evaluate item fit and function. **RESULTS:** Out of 124 subjects (56% male, mean age 62.8),105 completed the retest survey. Nine items from the draft version were deleted due to conceptual issues and/or redundancy. Factor analysis confirmed the three hypothesized domains: *Physical/Mobility Function*; *Daily Life*; *Sleep*. All domains and the total score were internally consistent (0.91 to 0.96) and reproducible (0.84 to 0.91). All *a priori* convergent validity hypotheses were confirmed ($p<.001$) with moderate-strong association between the total and/or subscale scores on the DPNPI measure and other logically related measures (range 0.43 to 0.79). Additionally, all *a priori* hypothesized associations for content and known-group validity of domains and total score were confirmed ($p<.001$) and IRT fit statistics were within acceptable range. **CONCLUSIONS:** The final 18-item version of the DPNPI can be considered a well-designed, valid and reliable measure of the impact of DPNP on patients' daily lives and physical functioning. This measure can be used as an endpoint in clinical trials to assess impacts related to DPNP. Further study is needed to understand the responsiveness of the DPNPI.

PDB88

HOW HYPOGLYCEMIA IMPACTS QUALITY OF LIFE AND TREATMENT SATISFACTION IN TYPE 2 DIABETES MELLITUS PATIENTS ON BASAL-BOLUS INSULIN THERAPY?

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OBJECTIVES: Hypoglycemia burden is the most common problem in patients with type 2 diabetes mellitus (T2DM) receiving insulin treatment. However, how hypoglycemia affects quality of life (QoL) and treatment satisfaction in this patient population is less clear. We aimed to study the QoL and treatment satisfaction in T2DM patients on basal-bolus insulin therapy with the absence and presence of different types of hypoglycemia. **METHODS:** A total of 500 T2DM patients receiving basal-bolus insulin therapy for at least 6 months were enrolled in the survey: male/female 122/378; mean (SD) age 61.8 (8.4) yrs; mean (SD) time from T2DM diagnosis 12.8 (6.9) yrs. Mean HbA1c level was 8.3%. Patients were classified as with no, non-severe, severe and nocturnal hypoglycemia events during the last month. Patients filled out SF-36 and Patient Treatment Satisfaction Questionnaire. The impact of hypoglycemia on QoL and treatment satisfaction was examined through multivariate regression, adjusting for sociodemographics and disease status. QoL and treatment satisfaction scores were analyzed using t-test, ANOVA, Chi-square test. **RESULTS:** After adjustment, QoL and treatment satisfaction decreased with the increase of hypoglycemia events ($p<0.05$). Patients with hypoglycemia had significantly lower QoL scores for 6 out of 8 SF-36 scales as compared to those without hypoglycemia ($p<0.05$). Treatment satisfaction was higher in patients without hypoglycemia than in those with hypoglycemia (mean score 7.25 vs 8.0; $p=0.01$). Patients with nocturnal and severe hypoglycemia had significant reduction of role-physical, social functioning, vitality and pain as compared to patients with non-severe hypoglycemia ($p<0.05$). The percentage of patients who were completely dissatisfied or poorly satisfied with treatment was higher in the group with severe or/and nocturnal hypoglycemia than in those with non-severe hypoglycemia (20% vs 8%; $p=0.002$). **CONCLUSIONS:** Hypoglycemia has negative impact on QoL and treatment satisfaction in T2DM patients. Severe and nocturnal hypoglycemia significantly decreases QoL and reduces treatment satisfaction.

PDB89

ASSESSING QUALITY OF LIFE IN ADULT GROWTH HORMONE DEFICIENCY: FURTHER DEVELOPMENT OF THE QOL-AGHDA

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OBJECTIVES: The QoL-AGHDA assesses quality of life (QoL) specific to adults with Growth Hormone Deficiency (GHD). Questionnaire content was derived from qualitative interviews conducted with individuals who had the condition. Since its development a number of new language adaptations have been made for Europe (9), Eastern Europe (4), and Central and South America (2). New language versions of the measure were required for use in two major new multinational clinical trials. These were for Greece, Hungary, Israel, Romania, Russia, Slovakia, Ukraine and the US (Spanish). **METHODS:** The dual-panel methodology was employed to translate each of these measures. This approach has been used in the adaptation of all needs-based QoL measures. Two panels are held. The first employs local people who are also proficient in English who agree the most appropriate translation for the instructions and items. The second panel involves lay people who ensure that the level of language is appropriate and will be understood by future respondents. Following translation, cognitive debriefing interviews were conducted with adults with GHD in each country. **RESULTS:** No major difficulties were experienced in producing

the translations. Ten to fifteen cognitive debriefing interviews were conducted in each country. Interviewees reported the measure to be easy to understand and complete and that the content was relevant without missing important issues. **CONCLUSIONS:** The standards set by the existing UK version of the QoL-AGHDA are high with internal consistency and test-retest reliability above 0.90. Construct validity was also demonstrated by the measure's ability to distinguish between patients according to self-perceived general health and by correlating scores with those on the General Well Being Index (> 0.70). Completed validations have obtained a similar psychometric quality. Similar studies are underway to evaluate the formal construct validity and reproducibility of these new language versions.

PDB90

USEFULNESS OF THE HYPOGLYCEMIA PERSPECTIVES QUESTIONNAIRE (HPQ) IN MANAGEMENT OF PATIENTS WITH TYPE 2 DIABETES

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OBJECTIVES: Assessment of patient's perspectives of hypoglycemia burden may be of value to provide adequate management of type 2 diabetes (T2D) patients. The Hypoglycemia Perspectives Questionnaire (HPQ) is a new multidimensional instrument assessing patient's experience of hypoglycemia. The goal of this study was to test the practicability and utility of HPQ-Russian version (HPQ-R) by means of its psychometric performance. **METHODS:** A total of 200 T2D patients receiving oral hypoglycemic therapy (59% – metformin; 41% – metformin plus vildagliptin or sulphonylureas, SU) were enrolled in the study: male/female 71/129; mean age – 58.7 yrs; mean disease duration – 4.1 yrs. Mean HbA1c level was 7%. All the patients completed HPQ-R at baseline and after 2-3 months of treatment. Patients and physicians were interviewed to test practicability of the instrument. Construct validity, reliability and sensitivity of the HPQ-R were assessed to provide its utility. **RESULTS:** Both patients and physicians acknowledged the comprehensiveness of the tool for revealing hypoglycemia-related problems; physicians used information from it for their decision-making. It was easily understood by, and administered to patients: 2.8% of missing values. An exploratory factor analysis revealed a strongly dimensional instrument (explained 70% of total pooled variance), with Chronbach alphas $\geq$0.9 for 6 out of 7 scales. Reproducibility of the tool was shown by comparing HPQ-R scores at two time-points for patients with effective HbA1c control receiving metformin plus vildagliptin: r=0.53–0.87 for 5 scales ($p<0.05$). HPQ-R scores were lower in patients with hypoglycemia events than in patients without hypoglycemia as well as in patients with severe hypoglycemia than in patients with non-severe hypoglycemia ($p<0.05$). Increased occurrence of hypoglycemia events and worsening of scores for 4 HPQ scales was shown after switch from monotherapy to therapy metformin plus SU ($p<0.05$). **CONCLUSIONS:** Thus, the HPQ-R is a practical and useful tool for comprehensive assessment of hypoglycemia experience in T2D patients.

PDB91

BENEFITS OF VILDAGLIPTIN PLUS METFORMIN COMBINATION THERAPY IN TYPE 2 DIABETES MELLITUS (T2DM) FROM PATIENT'S PERSPECTIVE: QUALITY OF LIFE (QOL) AND HYPOGLYCEMIA BURDEN ANALYSIS

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OBJECTIVES: Patients' preferences and evaluation of treatment benefits/risks from patient's perspective are increasingly being considered in decision-making regarding treatment option. The goal of this prospective, open, observational study was to evaluate QoL and hypoglycemia burden in T2DM patients treated with vildagliptin and metformin as compared to those treated with sulphonylureas (SU) and metformin. **METHODS:** A total of 194 T2DM patients previously on oral monotherapy were enrolled in the study. 111 patients were selected by their treating physician to receive vildagliptin and metformin (cohort 1 – mean age 58 yrs; male/female 43/68) and 83 patients – SU and metformin (cohort 2– mean age 58.6 yrs; male/female 27/56). Patient-reported outcomes were assessed at base-line and after approximately 3 mo using the SF-36 and the Hypoglycemia Perspectives Questionnaire (HPQ). For comparisons adjustment for age, sex, disease duration, complications and comorbidities was made. **RESULTS:** QoL parameters for all SF-36 scales were significantly higher in cohort 1 as compared to cohort 2 after 3 mo of therapy ($p<0.01$). Switch to vildagliptin plus metformin therapy was accompanied with remarkable increase of Integral QoL Index ($p<0.0001$) whereas no changes of Integral QoL Index were observed after switch to SU plus metformin. After 3 mo of combination therapy the number of self-reported symptomatic hypoglycemic events was 16% in cohort 1 versus 70% in cohort 2; 12% of pts had severe hypoglycemic events in cohort 2. SU plus metformin therapy was accompanied with significant hypoglycemia burden – after switching worries, awareness and symptom concern increased ($p<0.001$). No changes were observed in cohort 1. The changes in glycemic control were the same in both cohorts: DHbA1c=0.8%. **CONCLUSIONS:** Benefits of vildagliptin plus metformin combination therapy in terms of improved QoL and reduced hypoglycemia burden in T2DM patients were shown. This therapy is an effective and preferable treatment in daily medical practice from patient's perspective.

PDB92

PRELIMINARY TESTING OF THE SAGIT TOOL: A TOOL TO HELP ENDOCRINOLOGISTS IN THEIR MANAGEMENT OF PATIENTS WITH ACROMEGALY IN CLINICAL PRACTICE

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OBJECTIVES: Acromegaly is a rare, chronic, hormonal disorder caused by excessive growth hormone (GH) and insulin-like growth factor 1 (IGF-1) production resulting predominantly from pituitary adenoma. The objective was to test endocrinologist acceptability of the newly developed SAGIT tool in clinical practice. **METHODS:** SAGIT (**S**igns and symptoms - **A**ssociated comorbidities - **G**H concentration level – IGF-1 – **T**umour) is a Clinician-Reported Outcomes (ClinROs) tool developed with international experts in acromegaly; it allows patient classification and description in a standardised manner. The tool was pre-tested for acceptability, understanding and ease of use with practicing endocrinologists in France, Germany, UK, Spain, Italy and Brazil (n=2 per country) using the PRAgmatic Content and face validity Test (PRAC-Test). The endocrinologists completed the SAGIT tool prior to and following an intervention (therapeutics or surgery) for three patients each (n=36). Once completed, a one-hour phone interview was conducted with each endocrinologist to collect their feedback on the tool. **RESULTS:** The tool was well accepted and deemed concise (n=11) and informative (n=10) by the endocrinologists. Several points were raised that illustrate its usefulness in clinical practice, including the removal of the subjectivity when assessing the disease severity, the possibility of rapid evaluation of the control/progression of acromegaly or of a treatment response, and the possibility for standardisation across countries. Key recommendations for improvements were the need to include: 1) instructions to facilitate the understanding and the use of the tool; 2) definitions of rules and recommendations for patient management; and 3) addition of other signs and symptoms and further details about tumour size to better reflect their clinical cases. **CONCLUSIONS:** SAGIT is a useful tool for endocrinologists to accurately stage and classify acromegaly patients in clinical practice. It is currently being piloted in a cross-sectional study. Validation of scoring rules will confirm the utility of the tool to improve patient management.

PDB93

A DISCRETE CHOICE EXPERIMENT TO EVALUATE BLOOD GLUCOSE METER PREFERENCES IN PEOPLE WITH TYPE 1 AND TYPE 2 DIABETES IN THE UNITED KINGDOM

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OBJECTIVES: Regular self-monitoring of using a blood glucose meter helps diabetic patients to adjust their management strategies proactively, thus avoiding diabetic complications which place a burden on health care resources. The aim of this study was to elicit diabetic patients' preferences for different blood glucose meter attributes. **METHODS:** A cross-sectional, web-based survey of UK patients with Type 1 and type 2 diabetes was conducted in January 2013 and preferences for five key attributes associated with blood glucose meters were estimated using a discrete choice experiment (DCE) framework. A foldover design and optimised orthogonal differences were considered, but the final choice experiment was a Bayesian d-efficient design. Responses were analysed using a conditional logit model in STATA 12.1. **RESULTS:** Out of 447 responses, 406 (90.83%) patients were suitable for inclusion in the DCE analysis. Statistically significant differences ($p<0.05$) were found between the Type 1 and Type 2 sub-groups when comparing responder characteristics (years diagnosed, age, tests per day, number of comorbidities). Regarding glucose meter attributes, Type 1 respondents considered the 'time to test' to be the most critical factor and were willing to trade a compact device (2.61 units), or convenience (1.37 units) for a device that could produce test results in under 30 seconds. Type 2 respondents preferred the low maintenance attribute and were most willing to trade a compact device (2.72 units) or convenience (1.37 units) for this attribute. **CONCLUSIONS:** This is the first DCE to examine the impact of blood glucose meter attributes on blood glucose meter choice and adherence. Devices that provide value added features such as offline storage of data and additional data analysis will be valued by both Type 1 and Type 2 patients whereas a compact device is less valued.

PDB94

GROWTH MIXTURE MODELING (GMM) TO DETERMINE TREATMENT EFFECTS OF CANAGLIFLOZIN VERSUS SITAGLIPTIN ON WEIGHT-RELATED QUALITY OF LIFE (WRQOL) IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS (T2DM)

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OBJECTIVES: Canagliflozin is a sodium glucose co-transporter 2 inhibitor developed for T2DM. GMM was used to evaluate the effects of canagliflozin versus sitagliptin on WRQoL in subjects with T2DM. **METHODS:** Data were from 2 multinational, randomised, double-blind, Phase 3 trials: 1) subjects inadequately controlled with metformin (N=1,284) receiving canagliflozin 100 or 300 mg, sitagliptin 100 mg, or placebo for 26 weeks with a 26-week extension (placebo switched to sitagliptin; dual therapy); and 2) subjects inadequately controlled with metformin plus a sulphonylurea (N=755) receiving canagliflozin 300 mg or SITA 100 mg for 52 weeks (triple therapy). WRQoL was assessed using the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire. GMM was used to assess heterogeneity within samples to identify data-driven subgroups with differential changes in IWQOL-Lite total scores. **RESULTS:** In both trials, GMM identified 2 subgroups per treatment arm: "subgroup 1" (81% and 87% of total trial samples) started with high scores (~85 points), while "subgroup 2" (19% and 13% of total trial samples) started with low scores (44-53 points). Subgroup 1 scores remained high throughout both trials for all treatments. For the dual-therapy trial, subgroup 2 subjects treated with canagliflozin 100 or 300 mg had improvement (2.1 and 5.4 points, respectively), while those treated with sitagliptin 100 mg had declining scores (–4.0 points) over the course of the trial ($P<0.05$). For the triple therapy trial, all subgroup 2 subjects improved; improvement was significantly greater with canagliflozin 300 mg versus sitagliptin 100 mg (19.6 vs 4.8 points; $P<0.05$). In both trials, there were significant differences between the subgroups based upon baseline demographic, clinical, and patient-reported characteristics. **CONCLUSIONS:** GMM applied to these trial data enabled identification of treatment effects that were masked by standard statistical techniques. Heterogeneity should be considered when analysing WRQoL data.

PDB95
WEIGHT- AND HEALTH-RELATED QUALITY OF LIFE (WRQOL AND HRQOL) WITH CANAGLIFLOZIN (CANA) VERSUS SITAGLIPTIN (SITA) IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS (T2DM) ON BACKGROUND METFORMIN
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OBJECTIVES: CANA is a sodium glucose co-transporter 2 inhibitor developed for the treatment of T2DM. In a Phase 3 multi-national, randomised, double-blind, placebo- and active-controlled study, CANA improved glycaemia and reduced body weight and systolic blood pressure compared with placebo and SITA in subjects with T2DM on background metformin. Herein we report post-hoc analyses of the HRQoL and WRQoL data. **METHODS:** WRQoL and HRQoL were measured using the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) and the 36-item Short Form (SF-36) at baseline, Week 26, and Week 52; with both instruments, higher scores indicate better quality of life. Data were analysed for CANA 100 (n=368) and 300 mg (n=367), and SITA 100 mg (n=366). Least-squares mean changes were evaluated using ANCOVA models; gender, anti-hyperglycaemic adjustment, baseline score, and treatment as covariates. **RESULTS:** Improvements from baseline to Weeks 26 and 52 were detected for WRQoL total, physical function, and self-esteem scores in the CANA (both doses) and SITA groups (95% CI excludes zero), and for the other WRQoL domains, there was either improvement or no difference. A comparison of CANA 300 mg versus SITA at Week 26 suggests a difference in physical function (p=0.0374). Improvements from baseline to Weeks 26 and 52 were also detected for HRQoL general health scores in the CANA (both doses) and SITA groups (95% CI excludes zero), and for other domains, there was either improvement or no difference. Other HRQoL results suggest possible differences in bodily pain (Week 26, CANA 100 mg vs. SITA, p=0.0518) and the mental component summary score (Week 52, CANA 300 mg vs. SITA, p=0.0908). **CONCLUSIONS:** CANA and SITA were associated with improvements in WRQoL and HRQoL over 1 year in dual therapy. Results suggest that CANA is associated with a greater positive impact on patients versus SITA.

PDB96
ASSESSING THE RELATIONSHIP BETWEEN THE DIABETES HEALTH PROFILE AND DIABETES SPECIFIC CLINICAL INDICATORS: CASE FOR TAILORED THERAPEUTICS
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OBJECTIVES: With the increasing use of patient reported outcome measures in diabetes, it is important to understand which dimensions are most relevant to clinical indicators, and are the most predictive when assessing clinical change over time. This is important as the PROM scores can help inform the development of tailored therapeutics by highlighting the psychosocial functioning and quality of life impacts of different treatments. The aim of this study is to assess the relationship between the Diabetes Health Profile (DHP-18) and diabetes specific clinical variables to investigate how the measure can be used in the assessment of the impacts of different related complications and treatments. **METHODS:** The relationship between the DHP-18 and a number of variables, including diabetes specific and co-morbid health complications and length of time diagnosed were assessed. This was done cross-sectionally and longitudinally using a large dataset of Type 1 and Type 2 people with diabetes (n=1,802) collected in one United Kingdom health authority area. The analysis was carried out using Ordinary Least Squares and Logit regression. **RESULTS:** The Psychological distress domain is significantly associated with eye and foot related complications, and a number of co-morbid conditions including depression. The Barriers to activity domain is significantly associated with eye and foot related complications, duration of diabetes and a range of co-morbid conditions. The Disinhibited eating domain is related to duration of diabetes and co morbid conditions such as bone and lung disease. The number of associated problems was also a key predictive variable. **CONCLUSIONS:** The findings indicate that there is relationship between psychosocial functioning as measured by the DHP-18 and a range of clinical indicators. Tailored therapeutics can be used to change or reduce clinical concerns while also impacting on a patient's psychosocial functioning and quality of life, and the DHP can be used to efficiently measure this.

PDB97
A RELATIONSHIP BETWEEN BODY MASS INDEX AND HEALTH-RELATED QUALITY OF LIFE AMONG KOREANS WITH DIABETES: THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY
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OBJECTIVES: Little is known about the impact of body mass index (BMI) on health-related quality of life (HRQoL) for diabetics in the Korean population. The aim of this study was to estimate the association between BMI and HRQoL of type 2 diabetic patients in Korea. **METHODS:** This study is a cross-sectional analysis of adults who participated in 4th (2007-2009) and 5th (2010-2011) Korean National Health and Nutritional Examination Survey(total, 42,347 participants). HRQoL was measured by EuroQoL five-dimension (EQ-5D) and its association with BMI was investigated in Korean diabetic patients, especially those who did not have adequate control of blood glucose (HbA1c ≥6.5). Multivariate linear regression was performed at p-value of 0.05 with the use of SAS software, version 9.2. **RESULTS:** Out of 42,347 participants, 9.04% had diagnosed of diabetes. Among 2,726 diabetic patients in Korea, we assessed the association in 1,838 patients (median age 63) whose diabetes was not adequately controlled. We found that BMI was significantly negative associated with HRQoL(-0.0038, p-value <0.001), after adjusting for age, sex, education, income, marital status, smoking status, alcohol, HbA1c, insulin treatment status, oral anti-diabetic drug therapy, history of hypertension/high cholesterol/high triglyceride prevalence, stress level, and depression for more than two weeks. EQ-5D index decreased with rising BMI in Korean diabetic patients with HbA1c ≥6.5(-0.0038, p-value <0.001) **CONCLUSIONS:** BMI was negatively associated with HRQoL based on the multivariate regression analysis among Korean diabetic patients with HbA1c ≥6.5, after adjusting for confounding factors. This finding alerts diabetic patients to the danger of the weight gain as it is related to the lower quality of life.

PDB98
HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH TYPE 1 DIABETES AND IMPAIRED HYPOGLYCAEMIA AWARENESS: THE ROLE OF SENSOR-AUGMENTED INSULIN PUMP THERAPY WITH AUTOMATED INSULIN SUSPENSION
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INTRODUCTION: Compared with multiple daily injections, insulin pump therapy (continuous subcutaneous insulin infusion - CSII) improves glucose control in patients with type 1 diabetes mellitus (T1DM). When CSII is combined with continuous glucose monitoring (CGM) with automated low glucose insulin suspension (LGS), exposure to hypoglycaemia is significantly reduced. Patients with impaired hypoglycaemia awareness (IHA) are at increased risk of severe hypoglycaemia, so the benefits of this technology should be evident in patient reported health-related quality of life (HRQoL). **OBJECTIVES:** To compare HRQoL in T1DM patients with IHA treated with CSII alone or CSII with CGM + LGS in this 6 month, prospective, single centre RCT. **METHODS:** T1DM patients with IHA and CSII experience were randomised to either CSII alone (control, n=49) or CSII with CGM + LGS (treatment, n=46). Patients >12 years were included in this analysis (n=64, male 50%, age 23.2 ± 11.9 years, diabetes duration 13.8 ± 9.5 years, CSII duration 4.9 ± 3.6 years, Hypoglycaemia Awareness score 6.2 ± 1.4). Hypoglycaemia Fear survey (HFS) and HRQoL (EQ5D) were analysed using ANCOVA least-squares mean change from baseline to 6 months post-randomisation. **RESULTS:** Enrolled patients were not appreciably impaired at baseline (EQ5D Utility mean +SD 0.96+0.07), but overall gains in treatment group (+0.038) and decrements in control (-0.035) over 6 months produced a significant comparative utility gain for the intervention (LS mean difference 0.073, 95% CI: 0.008-0.139, p=0.028). Although not statistically significant, supporting trends were noted in EQ5D VAS and HFS (Worry subscale). **CONCLUSIONS:** Success of T1DM treatment relies upon effective and compliant self-management, so the patient perspective is relevant when evaluating treatment options and determining the impact on aspects of daily life. This analysis further supports the important role of insulin pump therapy plus CGM with automated LGS in the effective management of T1DM patients with IHA.

PDB100
QUALITY OF LIFE (QOL) AND RESOURCES CONSUMPTION IN INSULIN-DEPENDENT DIABETIC PATIENTS WITH A1CNOW+ AND CONTOUR USB. COMET STUDY
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OBJECTIVES: To analyse the quality of life in insulin-dependent patients and resource consumption due to poor metabolic control after the standarization of glycated hemoglobin measure with A1CNOW+ and the glycemia measure with CONTOUR USB. **METHODS:** An observational, prospective, multicentre study in patients with diabetes, insulin-dependent, with poor metabolic control has been conducted. Distribution of the ESDQOL questionnaire which contains the domains satisfaction, impact, social /vocational, concern regarding diabetes and degree of perception of QoL at baseline, at 3 and 6 months. The score of the domains and the full questionnaire is measured on a scale 0-100; where lower scores indicate a higher QoL. Also, Visual Analogic Scale was used to assess the patient's own perception of their quality of life. The resource consumption is analysed for urgent attention due to poor metabolic control, the use of resources included are visits to emergency department, income, length of hospital stay and additional consultations. **RESULTS:** The evolution of the domains in satisfaction goes from 35.9 at baseline to 31.5 at 6 months. The impact improves from 27.9 at baseline to 26.0 at 6 months, social/vocational concern 25, 8 to 22.4 as well as concerns related to diabetes from 37.7 to 33, 1. Also the degree of perceived improvement in VAS was 2.1 points. All analysed results were statistically significant. At baseline there were 26 patients (7.9%) who required urgent attention due to poor metabolic control in the previous 3 months versus 9 patients (2.8) who requested urgent attention on data collected at 6 months. **CONCLUSIONS:** CONTOUR USB device to measure glycemia and A1CNow device to measure HbA1C improve the quality of life of patients and reduce the use of resources due to poor control.

PDB101
IMPACT OF NOCTURNAL AND DAYTIME NON-SEVERE HYPOGLYCAEMIC EVENTS ON PEOPLE WITH DIABETES IN SOUTH AFRICA
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OBJECTIVES: Two surveys aimed to understand the impact of nocturnal and daytime non-severe hypoglycaemic events on health care system utilisation and patient quality of life. **METHODS:** People with diabetes from six countries who had experienced a non-severe hypoglycaemic event in the 4 weeks prior to the survey were eligible (n=300/survey). In South Africa, surveys were conducted online. **RESULTS:** In the South African nocturnal (N)/daytime (D) hypoglycaemia cohorts (n=50/survey), 80% and 80% (N/D) had type 2 diabetes; 30%/24% (N/D) were male; mean age 45/43 years (N/D); mean diabetes duration 11.1/9.4 years (N/D); 93/93% (N/D) insulin users. 34/40% (N/D) experienced ≥1 non-severe hypoglycaemia events/week. Most respondents (70/76% [N/D]) were unemployed, which could skew the observed impact of hypoglycaemia on productivity. Both surveys revealed that, following an event, it took 20 min (median) for acute symptoms to disappear and 60 min (median) for the respondent to function at their normal level. After an event, 11/11% (N/D) decreased insulin dose, 14/12% (N/D) modified insulin administration time

and 14/12% (N/D) contacted a health care professional. In the week after an event, respondents added an average of 2.8/3.6 (N/D) blood glucose tests to an average of 18.8/17.4 (N/D) tests in a normal week. Nocturnal events had a high impact on sleep quality (46% of respondents) and social life (24%), and 84% of respondents felt tired and/or fatigued the next day. In the daytime survey, about 26% reported the event highly impacted daily activities (outside of work). Also, 40/18% (N/D) of respondents indicated that the event had a high impact on their fear of hypoglycaemia. The majority ascribed hypoglycaemia to stress (50%/58% [N/D]) or irregular/insufficient food intake (50%/40% [N/D]). **CONCLUSIONS:** Both nocturnal and daytime hypoglycaemic events had an impact on patients' use of health care system, quality of life and daily productivity.

PDB102

CLINICAL SIGNIFICANCE OF CHANGE IN THE QUALITY OF LIFE-ASSESSMENT OF GROWTH HORMONE DEFICIENCY IN ADULTS (QOL-AGHDA) SCORE IN ADULT GROWTH HORMONE DEFICIENCY (AGHD)

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OBJECTIVES: To investigate the clinical significance of change in QoL-AGHDA score after 1 year of growth hormone (GH) replacement. **METHODS:** Observational data were obtained from KIMS (Pfizer International Metabolic Database). Minimal important differences (MID) for the QoL-AGHDA score and its five domains (memory and concentration, tenseness, tiredness, self-confidence, and social isolation) were calculated using an anchor-based approach with a rating of patient-perceived treatment benefit and patient-reported change in need for assistance. Perception of treatment benefit was measured using the KIMS Patient Life Situation Form (PLSF), a 5-point ordinal assessment of change (much improved, a little improved, no change, a little worse, much worse). The effect of baseline (BL) scores on MID was analysed using the QoL-AGHDA thresholds included in the New Zealand (≥16) and England (≥11) reimbursement criteria. **RESULTS:** Data from 1404 patients (52% female, 96% Caucasian, mean age [SD] of 45 [14] years) were included in the analysis. Mean GH dose [SD]was 0.20 [0.14] mg/day at BL and 0.32 [0.16] mg/day during Year 1. The Spearman correlation between change in QoL-AGHDA score and perception of treatment benefit was moderately positive (0.45; $p < 0.01$). The correlation was stronger for females and for patients with more impaired (higher) BL QoL-AGHDA scores. Using the anchor-based approach with patient-perceived treatment benefit, the MID for the QoL-AGHDA score was -4.61 at Year 1. Self-confidence was most sensitive and tenseness least sensitive of the domains in predicting patient-perceived treatment benefit. Patients requiring assistance at BL and not at Year 1 experienced the largest mean improvement in QoL-AGHDA score. **CONCLUSIONS:** Several national reimbursement authorities currently include the QoL-AGHDA score in eligibility criteria for access to reimbursed GH replacement. This is the first study to calculate the MID for the QoL-AGHDA score. Findings indicate that change in QoL-AGHDA score is positively correlated with patient-perceived treatment benefit.

PDB103

THE IMPACT OF DAYTIME AND NOCTURNAL NON-SEVERE HYPOGLYCAEMIC EVENTS ON PEOPLE WITH DIABETES IN BRAZIL

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OBJECTIVES: This study examined the effects of nocturnal and daytime non-severe hypoglycaemic events on utilisation of health care services and patient quality of life in Brazil. **METHODS:** People with diabetes from six different countries who had experienced a non-severe hypoglycaemic event in the past 4 weeks were asked to take part in a nocturnal and/or daytime hypoglycaemia survey. In the Brazilian subgroup, 86 people responded (50 respondents per survey). The surveys were conducted either face to face or online; hypoglycaemic events were self-reported. **RESULTS:** In the Brazilian cohort (nocturnal [N]/daytime [D] survey, respectively), 80% (N)/76% (D) had type 2 diabetes, 46%/38% (N/D) were male, mean age was 41(N)/40(D) years and mean weight was 82.4 kg(N)/81.8 kg (D). Participants received treatment with insulin (53%/70% [N/D]), oral medication (61%/60% [N/D]), GLP-1 (0%/8% [N/D]) and/or diet and exercise (32%/45% [N/D]). Approximately a quarter of respondents (26%/22% [N/D]) reported that they generally experienced a hypoglycaemic episode at least once a week. After the non-severe nocturnal (N)/daytime (D) hypoglycaemic event, 29% and 53% (N/D) decreased their insulin dose and 38% and 50%, respectively, contacted a health care professional. Participants used on average 13.0 or 11.5 (N/D) extra blood glucose tests the following week and 56%/32% (N/D) of the surveyed reported a high level of fear of a hypoglycaemic event. Among the 44/43 (N/D) respondents who worked for pay, 48%/35% (N/D) went to work late or left early; 23%/9% (N/D) missed ≥1 full days due to the non-severe event and 55%/26% (N/D) said that the event highly impacted upon their productivity at work. **CONCLUSIONS:** In Brazil, nocturnal and daytime non-severe hypoglycaemic events severely impact upon patients' quality of life and work productivity, with half of patients surveyed decreasing their insulin dose and/or contacting their health care provider after a non-severe event.

DIABETES/ENDOCRINE DISORDERS – Health Care Use & Policy Studies

PDB105

HEALTH ECONOMICS ASSESSMENT OF THE CNAMTS SOPHIA DIABETIC PATIENT SUPPORT PROGRAMME: RESULTS OF THE FIRST 4 YEARS

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OBJECTIVES: Since 2008, the *Caisse Nationale d'Assurance Maladie des Travailleurs Salariés*has set up a diabetic patient support programme in ten pilot departments in France. In addition to written advice, programme members also have access to telephone support from health education nurses. In 2010, the sophia programme was extended to another nine departments and, at the beginning of 2013, it was generalized to all French departments. The present study evaluated the health economics impact of the programme after a follow-up of 3 years. This analysis follows a preliminary assessment that demonstrated positive results after 1 year. **METHODS:** The variation of various health care use indicators as well as outpatient and inpatient costs was compared between three cohorts: members of pilot departments, non-members, and a control group of diabetic patients living in departments in which sophia was not available. Results are adjusted for between-group differences observed at the beginning of the programme. **RESULTS:** Adjusted analysis showed that, after matching for all other characteristics, compliance with recommended examinations improved to a much greater extent among programme members than among control subjects and non-members. Although all health care costs continued to increase in each cohort, outpatient and inpatient expenditure was €226 lower for programme members than for controls for the period 2009-2011: -€54 for outpatient care and -€172 for inpatient care. Although the outpatient expenditure of programme members was higher (+€40) for outpatient visits and medical procedures, their paramedical expenditure was lower (-€89). Hospitalization rates for diabetes were significantly lower among members than among controls. **CONCLUSIONS:** These results confirm the significant impact of the sophia programme on compliance with clinical practice guidelines in diabetology, hospitalization rates, and the 3-year growth of outpatient and inpatient costs. An assessment of the impact of the sophia programme on clinical parameters will be conducted in the near future.

PDB106

CONSISTENCY OF CURRENT TYPE 2 DIABETES (T2DM) TREATMENT PATTERNS IN GENERAL PRACTICE VERSUS THE 2013 FRENCH HAS T2DM GUIDELINES: A TRANSVERSAL STUDY BASED ON THE FRENCH IMS LIFELINKTM PROSPECTIVE DIABETES COHORT

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OBJECTIVES: To evaluate the consistency of T2DM management by French GPs in 2012 versus 2013 HAS guidelines that recommend modulating glycaemic objectives depending on patient's profile. To assess current treatment need for T2DM patients. **METHODS:** A transversal study, based on the IMS LifeLink™ prospective Diabetes Cohort linked to Electronic Medical Records database (Disease Analyzer) was used to investigate patients' profiles (age, disease history and complications, renal impairment, cardiovascular events, co-morbidities), HbA1c, hypoglycaemic risk, self monitoring of blood glucose (SMBG), and BMI evolution, linked to the current treatment. **RESULTS:** A total of 6680 T2DM patients (56% men) were included in the 2012 study cohort. The mean age was 66.6 years (25% of patients above 75 years); 19% had moderate to severe renal impairment and 56% had cardiovascular history. The new HAS guidelines split patients into several categories with associated HbA1c objectives varying from 6.5% to 9% based on age, frailty, diabetes history, and co-morbidities. 4%, 35%, 43%, and 18% of diabetic patients were eligible for the 6.5%, 7%, 8%, and 9% HbA1c objectives respectively. It appears that 55% of the diabetic population were at risk of hypoglycaemia, age and long diabetes history being the major risk factors. Given the modulation of glycaemic objectives more patients reached the new HbA1c objectives (74% of patients) vs. previous guidelines (about 55%). In this representative cohort, SU were prescribed with no dosage adjustment to all patients and even more frequently to patients at risk of hypoglycaemia (60.6%) while DDP4i were prescribed to "healthy patients" mostly not at risk of hypoglycaemia (51.5%). **CONCLUSIONS:** A minority of T2DM patients (39%) are eligible for an HbA1c objective of 7% or below, highlighting their frailty. This survey also shows that more patients are reaching their HbA1c target. However many of them are receiving treatments they should not due to high risk of hypoglycaemia.

PDB107

THE IMPACT OF MEMORY PROBLEMS ON DIABETES TREATMENT IN GERMANY

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OBJECTIVES: The impact of memory problems (MPs) on patient functioning, well-being and diabetes management is not well understood. This study examines these impacts in Germany and compares findings to data from US, UK, Canada and China. **METHODS:** A 5 country web-based survey was conducted. MPs were defined as: **u**nintentionally **f**orgetting to take insulin (UF), **q**uestioning if insulin had been **t**aken (QT), or **q**uestioning amount of **d**ose (QD). **RESULTS:** A total of 350 German respondents (60.0% Type 1) completed the survey, 61.1% male, mean age of 39.5 (±13.3) and mean age of diabetes onset 30.2 (±12.6). The prevalence of MPs in the past month was: 74.0% UF, 82.0% QT and 68.3% QD. MPs occurred most frequently when waking in the morning or when relaxing. Between 27.9% (UF) – 48.3% (QD) of respondents skipped their insulin dose and waited for next scheduled dose when experiencing a MP. Patients experiencing MPs required between 2.0 (QT)–8.7 (UF) hours, on average, to return to normal blood glucose range, conducted between 1.2 (QT) –4.4 (UF) extra BG monitoring tests, reported a moderate negative impact on their physical and emotional functioning, work absenteeism or reduced ability to function optimally when at work and between 3.6% (QT) and 13.8% (QD) visited/contacted their health care provider due to MPs. Compared to the total sample (N=1404), German respondents were more likely to report that their diabetes was very well/well controlled and that they were very/extremely confident in knowing what to do when they had an MP compared to respondents and were less likely than patients in other countries to have contact with a physician or other health care professional following a MP. **CONCLUSIONS:** These findings suggest that MPs

carry financial burden, impact patients' daily functioning and well-being and may be serious obstacles to optimal diabetes control. This burden may be some lower in Germany than other countries.

PDB108

TREATMENT PATTERNS AND HEALTH CARE RESOURCE UTILIZATION OF PATIENTS WITH ACROMEGALY IN THE UNITED STATES

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OBJECTIVES: To examine patient characteristics, treatment patterns, and health care resource utilization of patients with acromegaly in the US. **METHODS:** Using a large US claims database, adult individuals with commercial insurance newly diagnosed with acromegaly (ICD-9-CM: 253.0) between 07/01/2007 and 12/31/2010 were identified (the first observed diagnosis was the index date). Patients were required to have 6-month pre-index and 12-month post-index continuous enrollment. Descriptive analysis was performed to describe demographic and clinical characteristics, treatment patterns of acromegaly, and health care resource utilization during the post-index period. Similar analysis was conducted for Medicare-eligible patients with supplemental private insurance. **RESULTS:** This study included 930 commercially-insured patients (mean age: 47.2 years; 52.0% female) and 104 Medicare-eligible patients (mean age: 72.8 years; 36.5% female) with acromegaly. For the commercial population, of the comorbidities evaluated, hypertension (38.2%), diabetes (25.9%), and anthropathy/arthralgia/synovitis (23.7%) had the highest prevalence. More than half of the patients (57.3%) received no treatment; 21.7% received tumor resection surgery and 21.0% received medical therapy as the first-line treatment. During the 12-month post-index period, one-third had inpatient hospitalization and 23.2% had emergency room visit; the mean physician office visit was 17.1. For the Medicare population, hypertension (67.3%), diabetes (36.5%), and anthropathy/arthralgia/synovitis (29.8%) were most prevalent comorbidities. About two-thirds (63.5%) received no treatment; 8.7% received tumor resection surgery and 27.9% received medical therapy as the first-line treatment. More than one-third (34.6%) had inpatient hospitalization and 26.9% had emergency room visit during the 12-month post-index period; the mean physician office visit was 21.1. **CONCLUSIONS:** Our findings suggest high unmet needs in the population with more than half of patients with acromegaly being untreated. Efforts should be made to understand this untreated population to provide better care. Future research should investigate different treatment options as well as their impact on health care costs and health care resource utilization.

PDB109

UK QUALITY OUTCOMES FRAMEWORK (QOF) THRESHOLDS AND ELEVATED HBA1C LEVELS AMONG PATIENTS WITH TYPE II DIABETES - A LONGITUDINAL STUDY USING THE CLINICAL PRACTICE RESEARCH DATALINK (CPRD)

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OBJECTIVES: HbA1c concentrations predict the risk of complications in patients with type 2 diabetes mellitus (T2DM). This study assessed temporal trends in elevated HbA1c levels in the UK primary care setting. **METHODS:** T2DM was identified by medical diagnosis, prescribing, elevated blood glucose and/or prescribing of monitoring devices. Patients had ≥12 months of CPRD history, with data available for the entire year of observation. T2DM patients prescribed insulin were excluded. Mean HbA1c levels and proportion of patients with elevated HbA1c were assessed across six years (01/04/2006–31/03/2012). Elevated HbA1c was defined according to the UK Quality and Outcomes Framework (QOF) threshold: >7.5% for all years except 2009/2010 (>7.0%). Estimates were stratified by age-band, gender, T2DM-status and treatment categories. **RESULTS:** Mean HbA1c levels among 176,428 patients were relatively stable and below threshold across the study period (2006/2007: 7.05%; 2011/2012: 7.16%), with the exception of 2009/2010 (7.09%). Nonetheless, >20% of patients had a record of elevated HbA1c in each year (36.7% in 2009/2010). Elevations were more common among males than females (20%-25.0% vs. 18%-20%) and among patients 40-59 years (27.2%-33.7 %) vs. those ≥60 years (15.9%-23.3%). Although elevations were similar among prevalent (20%-23%) and incident-T2DM (22%-23%), prevalent-T2DM showed an increasing trend in the proportions with an elevation over time, whilst incident-T2DM showed a decreasing trend. The proportion with elevated HbA1c varied by treatment: diet and exercise 4.8%-6.1%; monotherapy 24%; dual therapy 32.7%-38.0%, and; triple therapy 42%-50%. Over 80% of patients with elevated HbA1c were overweight or obese, >20% had a 10-year Framingham Risk score >20% (patients without existing CVD) and 17%-21% of patients had history of chronic renal failure. **CONCLUSIONS:** Although mean HbA1c concentrations were below target (apart from 2009/2010), elevated HbA1c was present in >20% patients across all years. Further efforts are needed to help patients to achieve adequate glycaemic control.

PDB110

SELF-MONITORING OF BLOOD GLUCOSE WITH INSULIN ANALOGUES: NICE TO HAVE OR NEED TO HAVE? ANALYSIS OF PHASE III REGISTRATION TRIALS AND EUROPEAN PUBLIC ASSESSMENT REPORTS OF INSULIN ANALOGUES

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OBJECTIVES: Registration trials' purpose is to show safety and efficacy of insulin therapy. They are the basis of subsequent insulin reimbursement decisions. Insulin dosing is typically individualized: a safe and efficacious insulin therapy requires upfront dose finding and regular dose adjustments. These adjustments are based on data from Self-Monitoring of Blood Glucose (SMBG). However, some countries reimburse insulin analogues, but not blood glucose test strips. This analysis investigates the use of SMBG in Phase III registration trials of selected insulin analogues and if consequently the European Public Assessment Reports (EPARs) recommend the use of SMBG as part of the insulin therapy. **METHODS:** Systematic search and analysis of phase III registration trials (full-publication if available, and Clinical Trial report/study Synopsis) and EPARs of commonly used short-acting (Insulin Aspart and Insulin Glulisine) and pre-mix (Biphasic Insulin Aspart) insulin analogues. **RESULTS:** Therapy adjustments based on SMBG data were documented in 5/24 Insulin Aspart-, 3/18 Insulin Glulisine- and 4/15 Biphasic Insulin Aspart phase III registration trials. The EPARs of all three insulin analogues recommend the use of SMBG to adjust the insulin doses, repeatedly and throughout all sections in EPAR. **CONCLUSIONS:** Overall, in 12/57 phase III registration trials the dose of insulin analogues was regularly adjusted based on SMBG data, and the EPARs of all insulin analogues explicitly recommend the use of SMBG to adjust the insulin doses. Therefore, the demonstrated safety and efficacy of these insulin analogues are the result of a complex intervention including insulin analogues, their dose adjustments based on SMBG data as well as training rather than the insulin analogues alone. This is not consequently reflected in reimbursement schemes, in particular in emerging countries. Full study reports were not available for further analysis. These potentially would have provided deeper insights on how SMBG was used in the remaining 45/57 trials.

PDB111

DIFFERENT INJECTION FREQUENCIES OF BASAL INSULINS IN TYPE 2 DIABETES PATIENTS UNDER REAL-LIFE CONDITIONS: A RETROSPECTIVE DATABASE ANALYSIS

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OBJECTIVES: Little is known about routine use of basal insulins (Glargine, Detemir, NPH) in primary care patients with type 2 diabetes. The aim was to compare injection frequencies of basal insulins in type 2 diabetes (T2D) in primary care practices, both for basal-supported oral (BOT) and basal-bolus (ICT) treatment regimens. **METHODS:** Primary care data from 4,503 Glargine (BOT/ICT: 2,247/1,964), 1,373 Detemir (490/800), and 4,072 NPH-insulin (1,331/2,425) users were retrospectively analysed (05/2009-04/2012). The Disease Analyzer database (IMS HEALTH) assembles drug prescriptions, diagnoses, basic medical and demographic data obtained from the practice computer system of general practitioners and specialists throughout Germany. The Charlson Comorbidity Index was used as generic marker of comorbidity. Logistic regression (>1 daily injection) and propensitiy scores were used to adjust for various confounders (age, sex, type of physician, dosage, BMI, HbA1c). **RESULTS:** Overall, more than one daily injections were observed in 7.5% of Glargine users (BOT: 6.2%, ICT: 9.0%), which was lower than for Detemir (overall: 25.4%; BOT: 22.0%, ICT: 27.4%) and NPH-insulin (25.4%; BOT: 23.9%, ICT: 27.2%) (all $p<0.001$). The adjusted odds of having more than one injection was lower for Glargine compared to Detemir (OR; 95% CI: 0.26; 0.22-0.32) and NPH-insulin (0.20; 0.17-0.23). Similar results were found for BOT (Glargine vs. Detemir: 0.23; 0.17-0.32; Glargine vs. NPH-insulin: 0.16; 0.13-0.21) and for ICT (Glargine vs. Detemir: 0.27; 0.21-0.35; Glargine vs. NPH-insulin: 0.22; 0.18-0.27). Finally, after matching the groups for the propensity score, the odds for more than one daily injection was also significantly reduced in the Glargine group both compared to Detemir (OR; 95%CI: 0.30; 0.24-0.37) and NPH insulin (0.25; 0.22-0.29). **CONCLUSIONS:** Glargine is associated with significant lower injection frequencies than other basal insulins. These findings might impact treatment satisfaction and as a consequence quality of life, persistence and economic aspects of diabetes treatment.

PDB112

ORAL HYPOGLYCAEMIC MEDICINE (OHM) INITIATION IN NEWLY TREATED TYPE 2 DIABETES MELLITUS (T2DM) IN IRELAND: AN ANALYSIS OF TREATMENT INTENSIFICATION AND SWITCHING PATTERNS

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OBJECTIVES: To examine treatment intensification and switching patterns of individuals with T2DM initiating OHM. The results are compared to international guidelines issued in 2009. **METHODS:** Data were analysed using a population-based pharmacy claims database from January 2008 to November 2012. Incident users of OHM were identified for 2008-2009 as not having received OHM in the previous 12 months. Patients dispensed insulin, >one OHM, or <16 years were excluded from the study. Patients were followed until Nov-2012. Treatment intensification was defined as receiving an additional one, or two hypoglycaemic medicines (double or triple-therapy respectively). Treatment switching was defined as OHM monotherapy discontinuation with initiation on alternative monotherapy. **RESULTS:** A total of 24,869 patients were included in the study. Most were initiated on metformin (76.4%) or sulphonylureas (21.6%). Treatment intensification: 25.8% of patients initiated on metformin progressed to double-therapy. Sulphonylureas (61.5%), DPP-4 inhibitors (23.9%) and GLP-1 agonists (6.2%) were the most frequently prescribed add-on treatment (median time to add-on OHM=424days). Of those initiated on sulphonylureas 32.4% progressed to double-therapy; metformin (78.4%), DPP-4 inhibitors (9.3%) and long-acting insulin (5%) were the most frequently prescribed (median time to add-on=295days). 14.3% of patients on double-therapy progressed to triple-therapy (median time to add-on=434days). 26.6% of patients did not receive the recommended double-therapy and 64.3% received agents in their triple-therapy that were not recommended. Treatment Switching: Overall 7.1% switched medication. The most frequent switches were metformin to sulphonylureas (46.5%, median time to switch=226days), sulphonylureas to metformin (22.5%, median time to switch=330days) and metformin to DPP-4 inhibitors (6.9%, median time to switch=577days). Initial OHM was significantly associated with time to switch ($p<.0001$). **CONCLUSIONS:** Initial drug treatment followed guidelines. However, evidence-based practice was not closely followed for treatment intensification suggesting prescribers may be unaware of treatment guidelines. This data may be useful for assessing the potential place in therapy, and cost-effectiveness of new hypoglycaemic medicines.

PDB113

THREE-YEAR HEALTH CARE EXPENDITURES IN DIABETIC PATIENTS RECEIVING RAPID-ACTING INSULIN ANALOGUES VERSUS THOSE ON HUMAN REGULAR INSULIN

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OBJECTIVES: To compare health care expenditures following rapid-acting insulin analogues or human regular insulin utilization in a cohort of diabetic patients through the analysis of administrative databases. **METHODS:** A population-based cohort study was conducted using administrative data from four local health authorities in the Abruzzo Region (900,000 inhabitants). Diabetic patients free of macrovascular disease at baseline and treated either with human regular insulin or rapid-acting insulin analogues were followed for a maximum of 3 years. Propensity score matching was used to adjust for significant differences in the baseline characteristics between the two treatment groups. The direct cost was calculated as the sum of drug use, financial compensation by hospital DRG and outpatient activities (laboratory tests, services use and specialistic consultations), all regulated by government contracts. Generalised linear mixed models under gamma distribution were used to evaluate the costs. In case of cost variables with a large proportion of zeros, a two part model (logistic regression and glm with gamma distribution) was employed. **RESULTS:** After PS approach, 566 patients treated with human regular insulin were matched with an equal number of patients receiving rapid-acting insulin analogues. During the 3-year follow-up, the average number of hospitalizations was higher (0.54 vs. 0.47; P=0.028), and the average length of stay was 4,7 days longer (P < 0.004), among patients receiving human regular insulin in comparison with those receiving rapid-acting insulin analogues. The annualized total health care costs were significantly lower in the rapid-acting insulin analogues group than human regular insulin group with an estimated difference between the two groups of 1336.7 € per patient per year (P=0.001) . **CONCLUSIONS:** This analysis from real-world clinical practice suggests that rapid-acting insulin analogue is associated with lower rates of hospitalizations and lower overall health care costs in diabetic patients.

PDB114

HEALTH CARE COST AVOIDANCE DUE TO INSULIN GLARGINE FOR TYPE 2 DIABETIC PATIENTS IN HONG KONG AS COMPARED TO NPH INSULIN

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OBJECTIVES: Many studies have shown that insulin glargine (IG) is associated with a better glycemic control and less incidents of hypoglycemia. The objective of this study is to examine the potential cost avoidance arising from reduced hypoglycemic episodes by IG vs NPH insulin in T2DM patients receiving insulin in Hong Kong. The findings will fill a knowledge gap as no data is available before. **METHODS:** A decision analytic model was developed using local and international data to evaluate the potential health and economic impact of routine use of IG over a 1-year horizon. The study was conducted from a payer perspective. Probability of IG and NPH causing severe hypoglycemia was derived from the LEAD (LANTUS Evaluation in Asian Diabetics) study. Disease epidemiology and costs were all Hong Kong-specific. One-way sensitivity analysis was performed to test the robustness of model assumptions. **RESULTS:** The use of IG over a 1-year period is estimated to result in a substantial 81.9% reduction of hospitalization cost (HKD313,572,521) and a 29% reduction of emergency room cost (HKD1,184,312) which together accounts for about 0.7% of the overall annual public hospital budget of HK. In addition, IG is expected to prevent 23,755 cases of severe hypoglycemia events and to avert 95,022 hospitalization-days over 1 year. The overall incremental cost using IG vs. NPH is HKD126,843,257. **CONCLUSIONS:** The use of IG in T2DM patients receiving insulin in Hong Kong is likely to substantially reduce health care costs in hospitalization and emergency room visits due to severe hypoglycemia compared with NPH. The results of this study are considered as conservative because if improvement in clinical outcomes of IG over NPH is included, the additional clinical benefit will translate into larger long term health savings.

PDB115

HEALTH CARE UTILIZATION FOLLOWING NEWLY-DIAGNOSED TYPE-2 DIABETES IN SWEDEN: A FOLLOW-UP OF 38,956 PATIENTS IN A REAL CLINICAL SETTING

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OBJECTIVES: The growing prevalence of diabetes leads to increased pressure on national health care budgets. Despite the high prevalence the long-term health care costs of diabetes patients are not widely studied in a clinical practice setting. The study objective was to quantify and describe health care resource utilization following newly-diagnosed type-2 diabetes mellitus (T2DM) patients over time. **METHODS:** Newly diagnosed T2DM patients were identified from 84 primary care centers in Sweden between 1999 and 2009, and followed for a maximum of 9 years. Resource use data were extracted from electronic patient records (primary care contacts and laboratory tests) and a national patient register (hospitalizations). Data were linked using unique social security numbers. Resource use patterns are reported for the full study period and by partitioned time periods to investigate trends in resource use over time. The relationship between weight and resource use was also investigated. **RESULTS:** The study included 38,956 T2DM patients (women, 45%; mean age, 64 years; HbA1c, 5.7%; mean BMI, 29.8) with a total number of 183,614 observation years. Over a mean follow-up of 4.7 years there were 2,134,870 (per patient mean 55) primary care contacts; 1,200,142 (31) laboratory tests and 24,656 (0.63) hospitalizations. Mean annual resource use almost doubled the first year after diagnosis and remained on a higher level than before diagnosis throughout the study period. This pattern was seen in primary care as well as for hospitalizations. Furthermore, obesity at baseline appeared to be correlated with a higher level of resource use. The relationship between resource use, baseline weight and weight changes appears complex. **CONCLUSIONS:** Data from 183,614 patient years of follow-up show that T2DM diagnosis is associated with increased long-term resource use. Quantifying resource utilization using data from clinical practice setting may provide an important input to diabetes cost-effectiveness modeling and resource allocation decisions.

PDB116

THE IMPACT OF THE POLISH HUMAN INSULIN (GENSULIN) ON PUBLIC PAYER'S EXPENDITURE IN 2001-2013

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OBJECTIVES: Reference pricing (RP) – an approach where a payer sets payment for a group of similar drugs using benchmark based on a lower-priced option is a strategy commonly used to control drug expenditures. The aim of this study was to determine the impact of Polish human insulin (Gensulin, BIOTON) on public payer's expenditure in 2001-2013. **METHODS:** We analyse published data on insulin consumption and changes in reimbursement limits between October 2001 and February 2013. An Excel-based model was developed to compare scenario with (1) and without (2) Gensulin on the Polish pharmaceutical market. The reimbursement limit for insulin in (1) was determined by Gensulin (the lowest priced product within a group of human insulins), in (2) was fixed at 151 PLN/1500 i.u (A) or decreased to 134.99 from April 2002 (B). In the calculation all products containing 1500 i.u.insulin/pack or only pen were considered. Cost was adjusted for inflation and reported in PLN at 2013 prices (1 Euro=4.2 PLN). Results were presented as total and incremental cost in subsequent years and over the entire period. **RESULTS:** Between 2002-2012 the consumption of human insulins in Poland increased from 3.8 mln to 5.6 mln pack a 1500 i.u. The reimbursement limit in PLN/pack decreased gradually from 151 in 2001 to 98.57 in 2013 (scenario 1). Overall for the 12.5-year period the total public payer savings resulting from setting the reimbursement limit by Gensulin were 3 157 114 474 and 2 039 163 591 PLN in A and B, respectively. If only pens were considered RP policy led to a saving of 2 719 053 565 PLN in (A) and 1 777 711 973 PLN in (B) over 12.5 years. **CONCLUSIONS:** The launch of Gensulin and RP resulted in considerable reduction of public resources spent on human insulin in Poland

PDB117

WHO KNOWS BETTER? A KNOWLEDGE, ATTITUDE AND PRACTICE SURVEY OF OSTEOPOROSIS PRESCREENING TOOLS AMONG PHARMACISTS AND PHYSICIANS

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OBJECTIVES: Although osteoporosis is preventable, still its prevalence is escalating to endemic proportions. The reason for this massive incidence of osteoporosis is lack of identification of high risk individuals. In order to overcome this scenario and to cut cost associated with bone scanning; various prescreening tools were developed in 1990's. The purpose of such tools is to select high risk individuals for bone densitometry. The objective of current study is to analyze knowledge, attitude and practices of both physicians and pharmacist towards prescreening tool and to evaluate possible reasons for non-implementation of existing prescreening tools. **METHODS:** Using convenience sampling method, an explorative cross sectional survey was conducted in Penang, Malaysia. A pre-validated self- administered questionnaire was used to carry out the study among community pharmacists (n=83) and physicians (n=87). **RESULTS:** There was a statistically significant difference between mean rank score of pharmacist (137.55) and physicians (78.05). Although, pharmacists scored higher than physicians in all three domains of questionnaire but still both showed poor knowledge and practices regarding prescreening tools. Pharmacists considered low awareness regarding availability of such tools as the main factor that pose hindrance in implementation of such tools while physician suggested lack of time ,on their part, as the main reason. **CONCLUSIONS:** Participants showed general lack of awareness regarding osteoporosis pre-screening tools but in order to save cost associated with bone densitometry majority showed willingness to utilize such tools in future.

PDB118

REAL LIFE APPLICATIONS OF SOCIAL SECURITY INSTITUTION (SSI) REGULATIONS; A CASE STUDY OF DPP4 INHIBITORS IN TREATMENT OF DIABETES IN TURKISH HEALTH CARE SYSTEM

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OBJECTIVES: Analyze real life applications of SSI regulations via a case study: patient access to DPP4 inhibitors (ProductA*&Product B**) for Diabetes treatment, in Turkish health care system (2010-2012). **METHODS:** Regulation analysis is completed to define access conditions to DPP4 inhibitors. IMS Medical Index is used for prescription data analysis (patient age, sex, diagnosis, localization, medications, etc.). Calculations and process modelling are completed by Microsoft Excel-2007. **RESULTS:** Patient access to DPP4 inhibitors is possible if glycemic control cannot be sustained after use of maximum tolerable doses of metformin and/or sulphonylurea. This new requirement is being applied since April 2011. This study evaluates two comparable timeframes T1 and T2 (before and after regulation update); T1: 2010 (Q1/Q2/Q3/Q4) & 2011 (Q1) and T2: 2011 (Q2/Q3/Q4) & 2012 (Q1/Q2). From T1 to T2, Product A percentages of monotherapy, w-biguanides and w-sulphonylurea prescriptions changed from 32% to 35% (+3%), 51% to 42% (-9%) and 17% to 23% (+6%), whereas for Product B presciptions changed from 10% to 37% (+27%), 68% to

47% (-21%) and 22% to 16% (-6%), respectively. **CONCLUSIONS:** For Product A, after the regulation update, prescription rate for w-biguanides is decreased, while that for w-sulphonylurea and monotherapy options are increased. However, for Product B, prescription rate for w-sulphonylurea is decreased, while those for w-biguanides and monotherapy options are increased. For both products, prescription rate for monotherapy is increased. Limitation of this study is level of comprehensiveness for the system variables (market dynamics, patient profiles, etc.) This study concludes that, regardless regulation updates, there is an unmet need, which results in physicians' preference of innovative treatment options in clinical practice for treatment of Diabetes. *ProductA=Sitagliptin, **ProductB=Vildagliptin

PDB119
THE POTENTIAL IMPACT OF AMNOG-TRIGGERED INTERNATIONAL REFERENC PRICING: A SCENARIO FROM DPP-IV INHIBITORS
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OBJECTIVES: 1) International reference pricing (IRP) is a complex cost containment policy which has an often unclearly defined ripple effect across countries; 2) The aim of this study was to quantify by simulation what the ripple effect through IRP would be if prices of DPP-IV inhibitors in Germany dropped post-AMNOG benefit assessment because of either internal referencing or subject to the specific AMNOG provisions under which the IRP process can be deployed; and 3) A secondary objective was to draw initial conclusions over the evolution of IRP. **METHODS:** 1) The IRP landscape was studied using primary and secondary payer research on the basket of countries formally or informally employed in 40 countries, specifying a) those which reference Germany directly and b) identifying a cascading "indirect wave" of those which reference the countries that reference Germany, and 2) We examined current pharmaceutical pricing data and employed an industry validated proprietary simulation model for assessing the impact of selected AMNOG-triggered price decline scenarios. **RESULTS:** 1) In the universe of 32 countries where the 2 DPP-IV inhibitors studied are on the market, 25 countries are potentially affected by a price decrease in Germany: 16 countries that reference Germany directly and 9 via a secondary phase of IRP, and 2) The resulting interdependent price impact - solely from IRP - in the diverse afflicted countries is quantified for each model scenario. **CONCLUSIONS:** 1) As more countries explore the possibility or already deploy IRP as a pricing policies, it will become increasingly crucial for pharmaceutical companies to gauge the full impact of evolving international referencing and cross-referencing – and integrate this early on in their pricing strategy; 2) The results demonstrate that he composition itself of the basket of reference countries is driving the pricing impact; and 3) IRP and value-based or market pricing could be complementary and need not necessarily be diametrically opposed.

PDB120
TREATMENT PATTERNS AND BURDEN OF ILLNESS OF ACROMEGALY IN THE UNITED KINGDOM: REAL WORLD (RW) DATA FROM CLINICAL PRACTICE RESEARCH DATALINK (CPRD)
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OBJECTIVES: Acromegaly is a rare slowly progressing endocrine disorder characterized by abnormally elevated levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Acromegaly has a significant impact on patients' health, as well as on their physical, cognitive, emotional, and social well-being. Treatment of acromegaly is complex involving surgery, radiotherapy and medication; however, there are limited published real world data on treatment patterns. **METHODS:** A retrospective database analysis study using CPRD linked with Hospital Episode Statistics (HES) was conducted. Patient population included patients enrolled between January 1956 and March 2012 with Acromegaly diagnosis at two timepoints or Acromegaly diagnosis and either GH or IGF-1 test. Data was collected from 500 general practitioners (GPs). Patients' characteristics, treatment history, comorbidities and disease control were analysed. Biochemical control was defined as an age/gender adjusted IGF-1≤ULN and GH≤2.5mg/l. Standardized Mortality Ratio (SMR) was calculated and compared to general age/gender matched UK population. **RESULTS:** A total of 822 patients with Acromegaly were identified (580 alive and 242 dead at March 2012). Among alive patients, mean age (SD) was 63(15) years old, 52% male, mean age at diagnosis was 48(14). Comorbidities included: hypertension (46%), osteoporosis (31%), arthralgia/synovitis (21%), diabetes (18%), carpal tunnel (13%) and sleep apnea (11%); 31% of patients had no treatment records. Among treated patients: 38% received TSS, 29% radiotherapy, 45% somatostatin analogs (SSAs), and 45% dopamine agonists (DAs). A total of 45% of TSS 1st line and 52% of radiotherapy 1st line patients received further treatment; 22% of SSAs patients and 34% of DAs patients switched to/added 2nd line medical therapy. 64% of patients with GH+IGF-1 data (n=109) were not controlled. SMR was 4.6, 3.4 and 2.5 at 5, 10 and 15 years after diagnosis respectively. **CONCLUSIONS:** This study demonstrated significant mortality and morbidity burden of Acromegaly in the UK GP practice.

PDB121
HOW DOES HOSPITALIZATION IMPACT INSULIN TREATMENT IN DIABETES MELLITUS? RESULTS OF A RETROSPECTIVE GERMAN DATABASE ANALYSIS
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OBJECTIVES: One important aspect for patients suffering from diabetes is an appropriate metabolic control to avoid micro- and macrovascular complications. There is a lack of information about adjustment of antidiabetic treatment during hospitalization. **METHODS:** To identify a change in medication in patients suffering from diabetes, treatment regimens before and after hospitalization were investigated retrospectively. Information was taken from 2006 to 2010 German claims data. Data of about 25,000 hospitalizations from 180,000 diabetic patients were analyzed over a five year period. **RESULTS:** Study population of statutorily insured diabetic patients is representative as it is comparable to the overall German population by age, gender, mortality and morbidity. Treatment of most diabetic patients on oral anti-diabetic drugs remained unchanged before and after a hospital stay (55.8%). A smaller part of diabetic patients (37.6%) is admitted and discharged with the same insulin regimen. In 15% of the cases where patients are discharged with insulin, insulin treatment was initiated or changed during hospitalization. 53% of these patients received a first prescription of insulin. Basal supported oral therapy (BOT) and conventional insulin treatment (CT) regimens made up the largest fraction of all insulin initiations (62%). If a BOT was initiated, insulin glargine was favored (60%) compared to all other long acting insulin formulations such as human insulin (30%) and insulin detemir (10%). In 21% of the cases initiation results in a basal-bolus regimen (ICT) and in 17% in a prandial insulin therapy (SIT). **CONCLUSIONS:** Insulin treatment was first prescribed or switched during hospitalization in 15% of the cases where patients are discharged with insulin. Initiation of BOT and CT regimens turned out to be the overall preferred therapies in the underlying analysis. Given the fact that 26.7% of the German diabetic population has suboptimal HbA1c-values more of them should receive an adequate adjustment of antidiabetic therapy during hospitalization.

PDB122
TREATMENT PATTERNS AND BURDEN OF ILLNESS OF CUSHING'S DISEASE IN THE UNITED KINGDOM: REAL WORLD (RW) DATA FROM CLINICAL PRACTICE RESEARCH DATALINK (CPRD)
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OBJECTIVES: Cushing's disease (CD) is an extremely debilitating endocrine condition caused by an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma. CD has a significant impact on patients' health, as well as on their physical, cognitive, emotional, and social well-being. Treatment of CD is complex involving surgery, radiotherapy and medication; however, there are limited published real world data on treatment patterns. **METHODS:** A retrospective database analysis study using CPRD linked with Hospital Episode Statistics (HES) was conducted. Patient population included patients enrolled after January 1956 up to March 2012 with at least two CD diagnosis or Cushing's Syndrome diagnosis and one of the following: transsphenoidal surgery, benign pituitary neoplasm or pituitary disorder. Data was collected from 510 general practitioners (GPs). Patients' characteristics, treatment history, and comorbidities were analysed. Cortisol values (urinary free or serum) were expressed as ULN-fold based on patient specific lab norms. Standardized Mortality Ratio (SMR) was calculated and compared to general age/gender matched UK population. **RESULTS:** A total of 258 patients with CD were identified (227 alive and 31 dead)). Among alive patients, mean age (SD) was 54(15) years old, 76% female, mean age at diagnosis was 38(15). Comorbidities were: infections (63%), hypertension (47%), fractures (30%), depression (25%), diabetes mellitus (22%), osteoporosis (22%) and obesity (18%); 65% of patients had treatment records. Among those: 48% received TSS, 41% adrenalectomy, 24% radiotherapy and 42% oral medications. A total of 32% of 1st line TSS and 34% of 1st line radiotherapy patients received further treatment; 26% of adrenalectomy patients were treated with radiotherapy and/or surgery for Nelson's syndrome. Among patients on oral medications, majority received metyrapone (79%) or ketoconazole (32%). 69% of patients with cortisol measurements (n=92) were not controlled. SMR was 7.4, 5.1 and 3.1 at 5, 10 and 15 years respectively. **CONCLUSIONS:** This study demonstrated significant mortality and morbidity burden of CD in the UK primary practice.

PDB123
SYSTEMATIC REVIEW ON THE COST-EFFECTIVENESS OF THERAPEUTIC EDUCATION TO PREVENT THE DEVELOPMENT AND PROGRESSION OF TYPE 2 DIABETES
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OBJECTIVES: To critically appraise current evidence on the cost-effectiveness (CE) of therapeutic education for people with type 2 diabetes (T2D) and prediabetes compared to usual care. **METHODS:** We conducted a systematic review of economic evaluations of educational programs for people with T2D or prediabetes which were based on randomized controlled trials and published between 2002 and 2012. The quality of the clinical and the health economic evidence was ranked high, moderate, low or very low after critical appraisal by means of the Cochrane Collaboration's tool for assessing risk of bias and the Consensus Health Economic Criteria List. Interventions were classified based on the reported incremental cost-effectiveness ratios (ICERs). **RESULTS:** The search yielded 1.886 publications. Fourteen met the inclusion criteria. In prediabetes, patient education was found to be cost-saving in two out of five studies. The reported ICERs were €850; €24.400; €110.850 per quality adjusted life-year (QALY) gained from the payer's perspective and €6.800; €40.000; €48.500 per QALY gained from the societal perspective. In T2D, the CE of patient education varied from cost-saving to not cost-effective and had a mean ICER of €44.500 (range: €6.380; €83.000) per QALY gained from the payer's perspective. The quality of the health economic evidence was mainly moderate or low in studies on prediabetes, and very low in studies on T2D. The uncertainty analysis were not exhaustive in most studies. In the modeling studies (n = 10), the models' structural assumptions and validation methods were in general not properly reported. **CONCLUSIONS:** Current evidence on CE of therapeutic education of people with prediabetes and T2D is limited in volume and quality but consistently suggests that investing in patient education may offer good value for money. Studies of better quality are needed to reconfirm these findings. Commonly accepted methodologies for performance and assessment of health economic evaluations should guide further research.

PDB124

IMPACT OF VALUE COMMUNICATION IN DECISION MAKING: AN APPROACH TO THE TREATMENT OF TYPE 2 DIABETES IN PORTUGAL

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The increasing budgetary constraints faced by health care payers have made the access decision increasingly complex and decentralized processes a growing trend. Thus, demonstration of new health technologies value has become critical to ensure patients' access to innovation.**OBJECTIVES:** To identify the most important value messages within decision making process in the treatment of Type 2 Diabetes *Mellitus* (T2DM) among General Practitioners (GP) coordinating Primary Care Centers. **METHODS:** Regional meetings based on Health Economics training held (during 2013) with GPs, including the presentation of a cost-effectiveness analysis of vildagliptin vs sulphonilureas (SU) and a budget impact tool that enables the estimation of meaningful impacts of T2DM. Two surveys were developed to be applied at beginning and end of training to characterize the learning insights and identify the factors considered in the decision process. **RESULTS:** Partial results based on a 51 GPs sample are presented. The positive impact of the training in HE concepts was statistically significant (p=0.000) with an 89.4% average rate of correct answers. More than 50% of GPs considered the increasing prevalence of T2DM, cost of macrovascular and microvascular complications and the impact of hipoglycaemias in patients' quality of life (QoL) and costs, as the most important factors in the decision process. The key decision factor to use vildagliptin is the improvement of patients' QoL. The use of SU is explained due to its fast response, mainly in patients with Hb1Ac level above 7.5%. Majority of GPs (87.5%) chose vildagliptin as the preferred therapeutic for T2DM patients not controlled with metformin. **CONCLUSIONS:** This analysis demonstrated that both epidemiological and economic factors are important at local decision process. Clinically, patients' QoL is the most relevant achievement. Most GPs prefer vildagliptin to control T2DM, considering QoL improvements its greatest benefit.

PDB125

QUALITY OF CARE FOR TYPE 2 DIABETES MELLITUS PATIENTS IN DUBAI

Donato BMK[1], Osenenko KM[2], Korol EE[2], Szabo SM[2], Qatami L[3], Al Madani A[4], Al Awadi F[4], Al Ansari J[4], Maclean R[5], Levy AR[2]
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OBJECTIVES: Despite the high prevalence (25%) of type 2 diabetes mellitus (T2DM) in the United Arab Emirates (UAE), few data are available on the types and quality of care administered. Quality of care is an important determinant of whether clinical targets can be met, and serious complications avoided. The objective was to estimate the proportion of T2DM patients receiving recommended monitoring of clinical measures in Dubai, over one year. **METHODS:** Charts from T2DM patients aged ≥18 years that visited the Dubai Hospital between October 2009 and March 2010 (enrolment period) were systematically sampled until the target (n=250) was reached. Quality of care was assessed from April 2010 to March 2011, adapted from the United States (US) Healthcare Effectiveness Data and Information Set (HEDIS) Comprehensive Diabetes Care measures. Measures included: glycosylated haemoglobin (HbA1c) screening, control (<8%) and poor control (>9%); low-density lipoprotein (LDL) screening and control (<100mg/dL); blood pressure (BP) control (<140/90mmHg); retinopathy screening; and medical attention for nephropathy. Patients were classified as having control based on their latest test in the period. **RESULTS:** Mean age at enrolment was 58 years (standard deviation (SD): 12 years), 33% were male, and mean T2DM duration was 14 years (SD: 8 years). Over the 12-month period, 98% underwent HbA1c screening (54% had control and 26% displayed poor control); 90% underwent LDL screening (64% had control); 43% had BP control; 32% had retinopathy screening; and 16% attention for nephropathy. Two-hundred and eleven patients (84%) were screened for BP, LDL and HbA1c measures over the period. **CONCLUSIONS:** Guideline monitoring was conducted for most patients; rates of compliance were comparable to or higher than US benchmarks for HbA1c and LDL monitoring. Greater understanding of the factors leading to high adherence to the guidelines would be useful for other areas of preventive care, and other hospitals and jurisdictions.

PDB126

USING A "STANDARDS OF CARE ECONOMIC MODEL" TO QUANTIFY BARRIERS AND POTENTIAL SOLUTIONS TO PROVIDING OPTIMAL GUIDELINE-DRIVEN CARE TO PATIENTS WITH DIABETES MELLITUS IN THE UNITED STATES

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OBJECTIVES: 1) Build economic model to estimate resources to deliver current standards of care to US diabetes patients, and 2) Evaluate provider costs to meet standards, assess patient outcomes specified in guidelines relative to reimbursement. **METHODS:** Build model: 1) Integrate 3 national standard sets (ADA, AACE, and TES) into 28 consolidated standards of optimal care; 2) Develop provider matrix for rendering care; 3) Draft 6 clinical vignettes: 3 each T1DM and T2DM; 4) Convene 3 multidisciplinary panels of 4-7 care professionals; with facilitator, estimate minimum/maximum time to achieve care standards/patient type – baseline/best cases; 5) Convene separate panel estimating time to start/follow patients using CSII or CGM; 6) Multiply provider time by average wage and overhead amounts to determine visit cost; 7) Map activities to CPT and HCPCS billing codes and payment rates; 8) Compute reimbursement per expected payer mix; and 9) Note gaps in reimbursement compared to costs on unit and total basis. Populate model; perform analytics: Repeat Steps 4-9 with data from national provider survey and national database. **RESULTS:** 1) Baseline scenarios show provider costs exceed reimbursements for all type patients; best case indicates same in 5 of 6 scenarios; 2) In different scenarios costs of treating adults exceed reimbursement by >$750,000 per year; practices would require 19%-64% increase to breakeven; 3) In pediatric practice, costs exceed reimbursement by >$471,000 per year; 4) Gaps are increased for patients using CSII and CGM; and 5)Results are more sensitive to reimbursement for routine physician care and lifestyle modification services. **CONCLUSIONS:** 1) Seven American professional societies comprising the Diabetes Working Group (DWG) concur delivering high-quality, guideline-based diabetes care unrealistic given current care and payment paradigms; 2) DWG recommends alternative approaches in 3 areas: care management, payment reform, and workforce supply, to mitigate increasing medical and financial impact of this epidemic chronic illness; 3) Model can be used internationally to support public policy efforts.

PDB127

GLP1 AND INSULIN GLARGINE TREATMENT PATTERNS AMONG TYPE 2 DIABETES PATIENTS IN MAJOR EU MARKETS

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OBJECTIVES: Evaluate treatment patterns of Type 2 diabetes (T2D) patients initiating glucagon-like peptide-1 receptor agonists (GLP1) or insulin glargine in Germany (GE) and UK. **METHODS:** Adult T2D patients initiating exenatide twice-daily (exBID), liraglutide (LIRA) or glargine (1/10-12/11), or exenatide once-weekly (exQW) (1/10-6/12), were identified using the IMS LifeLink™ EMR-EU databases (exQW in GE only). Therapy initiation date was termed '*index date*'. Eligible patients were naïve to index therapy class and had ≥180 days pre- and ≥360 days post-index data (180 post-index exQW only). Treatment modification was evaluated over 180-day and total post-index period. Patients were required to have non-missing prescription data. **RESULTS:** 6,171 GE (300 exBID/174 exQW/906 LIRA/4,791 glargine) and 1,042 UK (249 exBID/306 LIRA/487 glargine) patients were included. Approximately half were male (GE/UK% 53.9/51.9). At index, mean age in GE/UK was 57.6/57.6 among GLP1 initiators; 67.4/63.1 among glargine initiators. Incidence of treatment modification (discontinuation, switch or augmentation) over 180-day post-index varied by treatment and country (GE/UK,%): exBID (58.0/41.4), LIRA (54.1/39.2), exQW (40.8/NA), glargine (13.7/29.2). Augmentation as first modification was rare among exBID and LIRA patients (GE/UK,% of those with modification); 11.5/6.8 and 10.0/7.5, respectively, compared to exQW (26.8/NA) and glargine (66.1/45.1). Discontinuation rates (i.e., stopping index therapy without switch to a new therapy) were higher than switching rates throughout the 180-day period for GLP1 and glargine users (GE/UK,% of those with modification): GLP1 74.4/75.3 discontinuation & 13.6/17.5 switch; glargine 32.9/52.8 discontinuation and 1.1/2.1 switch. Using all available post-index data, mean follow-up was (GE/UK, months): exBID 24.5/25.6, LIRA 24.0/21.8, exQW 10.6/NA, and glargine 24.4/25.4; proportions with treatment modification were (GE/UK,%): exBID 91.0/81.5, LIRA 80.1/71.6, exQW 57.5/NA, glargine 69.8/72.1. **CONCLUSIONS:** Treatment patterns varied among GLP1 and glargine patients. Longer-term data would be useful to further elucidate practice patterns associated with these medicines, particularly exQW.

PDB128

TREATMENT PATTERNS AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN DUBAI

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OBJECTIVES: The United Arab Emirates (UAE) has among the highest prevalence (25%) of type 2 diabetes mellitus (T2DM) globally; however, few data are available on how patients are managed in clinical practice. The objective was to characterize recent treatment patterns among T2DM patients in Dubai. **METHODS:** Charts from T2DM patients aged ≥18 years that visited the Dubai Hospital between October 2009 and March 2010 (enrolment period) were systematically sampled until the target (n=250) was reached. Treatment data from enrolment to September 2011 were abstracted from patient charts, as well as treatments received before enrolment. Treatment regimens, their frequency of use, and the number of switches (drug replacement/removal/addition) over the study period were calculated. Analyses were stratified by T2DM duration, and data for those recently-diagnosed (<5 years; n=29) and with longstanding disease (≥20 years; n=67) are presented. **RESULTS:** Mean age at enrolment was 58 years (SD: 12 years), 33% were male, and mean T2DM duration was 14 years (SD: 8 years). At enrolment, 74% of patients had received prior insulin treatment (recently-diagnosed: 55%; longstanding disease: 84%). During the study period, the most common regimens were insulin+oral combination therapy (55%) and oral combination therapy (39%). Overall, 67% received any insulin therapy during the study period (recently-diagnosed: 45%; longstanding disease: 87%). By study end, 78% had received insulin therapy at any time (recently-diagnosed: 62%; longstanding disease: 88%). On average, T2DM patients had two treatment switches; little variation was seen by T2DM duration. **CONCLUSIONS:** Most patients had longstanding T2DM and received treatment with insulin. Patients had an average of two treatment switches over the relatively short study period, indicating modification was attempted to improve T2DM control. Novel therapies may improve clinical outcomes among T2DM patients and this study provides valuable baseline data with which to compare the effectiveness of new T2DM treatments in Dubai.

RESEARCH POSTER PRESENTATIONS – SESSION III
HEALTH CARE USE & POLICY STUDIES

HEALTH CARE USE & POLICY STUDIES – Consumer Role in Health Care

PHP1

HOW CO-PAYMENT MECHANISM HAS CHANGED PATIENTS' PERCEPTION TOWARDS OTC-TYPE PRODUCTS?

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OBJECTIVES: Turkish health care system has developed in terms of quality, access, equity and efficiency with the introduction of a number of reforms under "Health Transformation Program" since 2003. However, these have created significant financial burden to the government. In order to contain expenditures, avoid overuse, misuse and abuse; government has implemented certain cost sharing tools. Our objective is to define how co-payment mechanism has affected patients' purchasing behavior regarding OTC-type products. **METHODS:** Regulations and reports published by Ministry of Health and Social Security Institution, "Health Systems in Transition Turkey 2011" and "IMS Market Prognosis 2012-2016" reports are examined. **RESULTS:** In Turkey, family physicians do not act like gatekeepers since a formal referral system does not exist. Therefore, patients could directly apply to secondary/tertiary health care services without co-pay. At secondary/tertiary health care levels, co-payment rate is 5 TL and 12 TL for outpatient care in public and private hospitals respectively, 3 TL for prescription fee and extra 1 TL for each product exceeding 3 products per prescription. All active workers pay 20% while retirees pay 10% of total amount of the prescriptions as co-pay. Patients with chronic conditions requiring medical report are exempt from co-pay. Considering different co-payment rates and number of visits/prescriptions recorded in hospitals, it is calculated that patients paid approximately 3 billion TL in total outpatient care as co-payment in 2012. **CONCLUSIONS:** Minimum 9 TL in total is required as a co-payment for outpatient care and prescription, if patient visits a public hospital. Therefore, for products with a lower price than 10 TL, patients rather go directly to pharmacies. This behavioral change of out-of-pocket payments might be explained by improved purchasing power and increased co-pay rates.

PHP2

METHODOLOGICAL CHALLENGES IN MULTI-CRITERIA DECISION ANALYSIS (MCDA) FOR HEALTH POLICY DECISION-MAKING: A SYSTEMATIC REVIEW

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OBJECTIVES: Decision making about health technologies from research and development to reimbursement is affected by heterogeneous opinion and criteria of participating stakeholders. There is a lack of systematic consideration of stakeholders' preferences in current health policy. Multi-criteria decision analysis (MCDA) offers a solution to take preferences into account. This study gives an overview about the applications of MCDA methods in health economic decision-making. **METHODS:** A systematic review of the health care literature was performed to identify original research articles. Using predefined categories, data was systematically extracted for the type of policy applications, MCDA methodology, criteria used and how they were defined. **RESULTS:** Twenty-one studies were included in the analysis. 12 studies (67%) used indirect approaches and nine studies (43%) used direct MCDA approaches. Four studies (19%) focused on technologies in the early innovation process. The majority of 17 studies (81%) examined a technology on the level of reimbursement decision. Eight studies (38%) resulted into implementation, which means that an official committee considered the MCDA results. Other studies were conducted in an explorative manner. MCDA decision criteria used were obtained from literature research and context-specific studies, expert opinions, and group discussions. The number of criteria ranged from three up to 15. The most prominent criteria described health outcomes (71%), disease impact (62%), and implementation of the intervention (38%). **CONCLUSIONS:** MCDA is used at different levels of medical innovation and can increase transparency for involved stakeholders by explicitly structuring decision criteria. Further research is needed to understand existing variability of the number of criteria used and ensure that models are robust regarding potential criteria overlaps, performance scales and operationalizability aligned with evidence needs.

PHP3

SUPPLEMENTARY HEALTH INSURANCE IN TURKEY

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OBJECTIVES: In Turkey, almost everyone is covered by General Health Insurance Scheme (GHIS) under Social Security Institution (SSI). GHIS provides a Basic Benefit Package (BBP) for patients to benefit from both public and private health care providers contracted with SSI. Patients are obliged to pay certain level co-pays for extra services as defined in the regulation. Besides GHIS, patients could benefit from private health insurances(PHI) by paying relatively high level of premiums for different types of PHI packages. Supplementary Health Insurance(SHI) law has been enacted in June 2012 and patients started to benefit from SHI by paying relatively lower premiums for health care services that are not covered or partially covered by BBP. The objective is to evaluate the significance and potential of SHI in Turkey. **METHODS:** Regulations of SSI, OECD publications, International Investors Association's Turkey Report and database of Insurance Association of Turkey are examined. **RESULTS:** Number of private hospitals has increased by 50% over 5 years and reached out 500 by 2012. Parallel with this growth, PHI sector market share has also increased. By 2012, number of people covered by PHI has reached out more than 2 million and the PHI market is expected to reach nearly USD 2 billion in 2015. Meanwhile, approximately 20 thousand people has covered by SHI since November 2012 and SHI is expected to reach 5 million people next 5 years. **CONCLUSIONS:** Public health care expenditure is continuously rising due to increased health demand, increased coverage and demographic changes. In order to assure a financially sustainable health care system, PHI could be an option and create source of funding for the health care expenditure. In this context, SHI will reduce the pressure on public health budget, create an area of growth for the private health insurance sector, allowing health care providers supplying both public and private health care to become more effective.

PHP4

THE ROLE OF COMMUNICATION AND HEALTH LITERACY ON PATIENT SAFETY IN PUBLIC PHARMACIES IN THE REPUBLIC OF SRPSKA

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Health literacy is the skill (social and cognitive) that determines the motivation and ability of the person to receive, understand and use information in order to improve and maintain good health. Communication between patients and pharmacist is essential for optimal patient safety.**OBJECTIVES:** To highlight the importance and present the results of conducted research and to give recommendations for improving the health literacy among patients and pharmacists' communication skills. **METHODS:** The study was conducted in June 2013 in 5 selected branches of pharmacy-chain "Zdravlje Pharm" in Bijeljina, Republic of Srpska, Bosnia and Herzegovina. The sample consisted of 219 patients selected randomly, of whom 195 accepted the survey, and 24 rejected to participate. The instrument was previously validated and adjusted questionnaire of Pharmacy Zrenjanin, Serbia, related to patient satisfaction with pharmacy services, but also conceived needs of the thesis, with 32 close-type questions, except one. Health literacy of patients and communication with pharmacists were followed. The analysis was done in Excel, and the results are given in tables and graphs. **RESULTS:** About 90% of patients reported that pharmacists give clear information during consultations and the advices helped them. A total of 65% reported to easily remember the information from the pharmacists, which shows a good level of patient health literacy; but the rest can have uncertain outcomes of the therapy and be exposed to greater safety risks. **CONCLUSIONS:** There is a place for improvement of aspects which can contribute to better patient safety. That can be achieved by applying certification standards throughout the health care system in the Republic of Srpska.

PHP5

ARE THE BIOTECHNOLOGY AND PHARMACEUTICAL SECTORS DEFENSIVE RELATIVE TO THE S&P 500?

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OBJECTIVES: The health care sector is widely regarded as a defensive play in the stock market. We analyzed the performance of a pharmaceutical and a biotechnology index from March 2000 through April 2013 alongside the S&P 500. **METHODS:** We categorized the S&P 500 from March 2000 through April 2013 into bull and bear markets. During this time there were three bull markets and three bear markets. Bull and bear markets were defined as changes in the S&P 500 of more than 20%. We followed the AMEX Pharmaceutical (^DRG) and Biotechnology (^BTK) Indices to represent their sectors. We compared the returns of the sectors with the overall market and also calculated their correlated volatility (beta) with the S&P 500. **RESULTS:** For the entire analysis period, the S&P 500 returned 4.59% while ^DRG and ^BTK returned 25.43% and 252.83%, respectively. During the bear markets, the S&P 500 lost at an average annual rate of 27.17%, while ^DRG and ^BTK lost at annual rates of 12.16% and 21.99%, respectively. Though ^DRG performed best during the bear markets, it was a laggard in the bull market gaining 8.15% annually, while the S&P 500 and ^BTK had 22.04% and 31.97% annual returns, respectively. The overall beta during our analysis period was 0.63 for ^DRG and 1.07 for ^BTK. **CONCLUSIONS:** Both the AMEX Pharmaceutical and Biotechnology Indices fell at a lesser rate than the S&P 500 during bear markets. The Pharmaceutical Index may be the more defensive play as it lost at an average annual rate of more than two times less than the S&P 500. However, the Biotechnology Index gained almost four times more than the Pharmaceutical Index in bull markets and also outperformed the S&P 500 by almost 10 percentage points during bull markets.

HEALTH CARE USE & POLICY STUDIES – Diagnosis Related Group

PHP6

COMPARISON OF DEVELOPMENT DIAGNOSIS RELATED GROUPS BASE RATE IN HUNGARY AND GERMANY

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OBJECTIVES: Diagnosis Related Groups (DRG) based methods was introduced for acute hospital care reimbursement in 1993 in Hungary (H-DRG) and in 2003 in Germany (G-DRG). The aim of our study is to compare the development of DRG base rate in Germany and Hungary. **METHODS:** The Hungarian data derive from the financial database of the Hungarian National Health Insurance Fund Administration (NHIFA), the only health care financing agency in Hungary. German data derive from German DRG Institute. We analyzed how the uniform, nationwide DRG base rate has been introduced in both countries. **RESULTS:** The German DRG system consists of 1200 disease groups, while the Hungarian contains ca. 736 groups. The German DRG base rate was hospital specific between 2003-2004. From 2005 to 2009 hospital-specific base rates converged to a state-wide base rate. From 2010 to 2014, the state-wide base rates should converge to a nationwide base rate. The German hospital specific base rate varied between EUR2200-3200. In Hungary, a hospital groups specific base rate was applied for 16 groups of hospitals between 1993-1998 with a gradual converge of base rates. Middle level (county or regional) base rate was not introduced in Hungary. The nationwide uniform DRG base rate was set up in 1998 in Hungary. The Hungarian uniform DRG base rate was EUR518 in 2012. **CONCLUSIONS:** Both Hungary and Germany applied a gradual implementation of uniform DRG base rate. Germany took three steps (hospital, Lander and nationwide), while Hungary took two steps (hospital group, nationwide) in reaching the nationwide uniform DRG base rate.

HEALTH CARE USE & POLICY STUDIES – Drug/Device/Diagnostic Use & Policy

PHP8

THE ASSOCIATION BETWEEN EUROPEAN MEDICINES AGENCY APPROVAL AND HEALTH TECHNOLOGY ASSESSMENT RECOMMENDATION

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OBJECTIVES: To find the association between duration of the process of marketing authorization (MA) approval at European Medicines Agency (EMA) and health technology assessment (HTA) recommendations in European Union (EU) countries. **METHODS:** EMA MA timing for new active substances (NASs) during 2007-2009 were analyzed based on publicly available information. HTA recommendations (positive, positive with restrictions, negative, not assessed) issued for the same medications in 6 EU countries (SMC, Scotland; AOTM Poland; CVZ, The Netherlands; HAS, France; NICE, UK; INFARMED, Portugal) were also analyzed based on public information. Hypothesizing that EMA approval process timing might be an indicator of complexity and potential issues in the dossier, the potential for longer EMA approval times being associated with less beneficial HTA recommendation was investigated. Analyses were performed per country as EMA decisions are centralized but HTA recommendations are taken independently by member states. **RESULTS:** A total of 86 NAS were approved by EMA in 2007-2009; mean time of approval was 460 days (median 423 days). In total, we expected 516 HTA recommendations (86 drugs assessed by 6 organizations). We found in total 138 positive, 77 positive with restrictions, 67 negative recommendations. 234 expected recommendations for 6 HTA included in this study were not assessed (45,3% of all expected recommendations). The association between HTA recommendation and approval time (in days) was analyzed using Spearman's rho rank correlation. There was statistically significant negative correlation between approval time and HTA recommendation in The Netherlands. More time needed for EMA approval was associated with less beneficial HTA recommendations. Correlations in other countries were not statistically significant. **CONCLUSIONS:** Our research indicates that a longer EMA approval process is associated with a less beneficial HTA recommendation in The Netherlands. Further research is required whether this indicates that the same issues that cause delays at EMA are reconsidered at HTA authorities.

PHP9

THE IMPACT OF INDICATION EXTENSIONS ON PHARMACEUTICAL PRICES

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OBJECTIVES: To assess the impact of an indication extension on pharmaceutical prices in 9 markets: Australia, Brazil, France, Germany, Italy, Japan, Spain, Turkey, and the UK. **METHODS:** Websites of the EMA and national regulatory agencies were surveyed to indentify medicines granted an indication extension between 2007 and 2013. Eight case studies (bevacizumab, trastuzumab, sunitinib, ivabradine, telmisartan, aripiprazole, paliperidone, and omalizumab) were selected based on market share and availability across the geographies of interest. The list prices, at ex-manufacturer levels, of these eight drugs and those of the medicines belonging to their therapeutic class (at ATC level 3) were collected for the period 2007-13. Price movements for these eight medicines were compared to the price evolution within their therapeutic class over the period. **RESULTS:** Based on the selected case studies, there is ambivalent synchrony between indication extensions and pharmaceutical list price movements in the countries analysed. The data show that list prices tend to remain stable following an indication extension. When list prices changed subsequent to an indication extension, the movements could not directly be linked to the indication extension, as external factors such as a class trend or a wider pricing and reimbursement process (e.g. blanket price cuts) could also play a role. **CONCLUSIONS:** There is inconclusive evidence that indication extensions lead to list price changes in the countries analysed. Moreover, the impact of commercial agreements and discounts should be taken into account as secondary indications may be subject to separate pricing arrangements (e.g., patient access schemes). As such, the selection of the indication for the first marketing-authorisation filing (such as a high medical need, niche indication, commanding a premium price) is pivotal for the commercial success of a medicine, as its launch price seems unlikely to be reviewed following subsequent approvals in broader patient populations.

PHP10

ECONOMIC ANALYSIS OF THE PREVENTION OF MEDICAL SHARPS INJURIES WITH SAFETY-ENGINEERED DEVICES: A SYSTEMATIC REVIEW

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OBJECTIVES: To protect health care workers from risk of needlestick injury, preventive safety measures are increasingly mandated in the health care environment, which may include the use of safety-engineered medical sharp devices (SEDs) specifically designed to prevent sharps injuries. We undertook a systematic review of the literature to understand the economic impact of replacing conventional sharps devices with SEDs. **METHODS:** We conducted searches of electronic databases including Embase/MEDLINE, PubMed, CINAHL Plus, HEED, NHS EED, the Cochrane Library, ProQuest Nursing and Allied Health Source, and the Tufts CEA Registry. Databases of the WHO and HTA agencies, reference lists of identified studies, conference abstract books and the internet were also searched. The time horizon covered January 1990 to March 2013. Two reviewers independently screened titles and abstracts, applied inclusion criteria to full text papers and extracted data from identified studies according to an a priori defined data set. Differences were resolved by consensus. Study quality was assessed using a published 10-point checklist. **RESULTS:** From 19621 records, 21 studies met the review criteria and were selected. Most studies (16) were budget impact analyses (BIAs). Reductions in sharps injuries with SEDs ranging from 12% to 100% were reported. Just 4 studies were assessed as providing the best quality evidence: a cost benefit analysis and 3 BIAs. Key assessment criteria that the other studies did not meet were consideration of all relevant costs and execution of a sensitivity analysis. Of the best quality studies, 3 reported net economic benefits from implementing SEDs, at least in the base case analysis. **CONCLUSIONS:** Investment in SEDs generates economic benefits from savings in managing medical sharps injuries and their sequelae. Future economic evaluations need to carefully assess all important and pertinent costs to enable well-informed decision making about the implementation of SEDs in the health care workplace.

PHP12

A PRICE COMPARISON STUDY OF RECENT DRUGS IN EU5, 2008-2012

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OBJECTIVES: To compare prices of new drugs between France and the other EU4. **METHODS:** Study used IMS MIDAS database for economic data such as prices and sales volume and LEEM database (French association of the pharmaceutical manufacturers) for the ASMR scale (HAS assessment of the drug's added value/innovation). All the products applying for the first time for reimbursement by the French Public health insurance between January 2008 and June 2012 were included in the study (except those restricted to hospital use in France) and having an ASMR rating and an official price in June 2012. Paasche and Laspeyres price-index were calculated for drugs with: a) high ASMR, b) ASMR IV, c) ASMR V and d) all drugs. A sensitivity analysis was conducted to measure the effect of different weighting options. **RESULTS:** A total of 107 products (245 dosages) were included in this study. Fifty-one (48%) have been found available in the community pharmacies of all the 5 countries. The availability analysis by pair of countries (France + another) is higher: 94 for Germany, 79 for UK, 71 for Spain and 69 for Italy (Italy often restricts drug's access to hospitals only). French prices are generally equal to or lower than prices in the four other markets, which shows a relative price index decrease for France since 2008 studies. The only significant exception are UK prices for products ranked in France ASMR 1-2-3 (20% less expensive). Prices are regularly and significantly higher in Germany than in all other countries. Interestingly, the highest disparities in prices occur for the ones ranked as most innovative in France – while ASMR IV have surprisingly consistent prices across EU5. **CONCLUSIONS:** European patients don't have consistent access to the same drugs in retail market, and the drugs considered innovative in France show a large price index disparity across EU5, with UK prices being 20% lower.

PHP13

TO WHAT EXTENT CAN BIOSIMILARS COMPETE WITH BRAND NAME BIOLOGICS? A EU-5 GRANULOCYTE-COLONY STIMULATING FACTORS MARKETS ANALYSIS

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OBJECTIVES: To determine the ability of biosimilars (copies of branded biologics) to compete with brand name biologics within the same therapeutic class by analyzing EU-5 G-CSF (Granulocyte-Colony Stimulating Factors) markets and the factors affecting the G-CSF biosimilar uptakes, particularly that of biosimilar prices relative to reference G-CSFs. **METHODS:** Data on medicine volumes, values and ex-manufacturer prices for all G-CSF categories were provided by IMS Health. Volumes were calculated in DDD (Defined Daily Doses) and prices in euros per DDD. In the EU-5 countries biosimilar G-CSFs benefit from a 5-year experience. Data were available from 2007 until 2011. **RESULTS:** There are two G-CSF market profiles: i) countries with a high retail market distribution which are the largest G-CSF markets with low global G-CSF biosimilar uptakes (5.4% in France and 8.5% in Germany in 2011); ii) countries with a dominant hospital channel which are the smallest markets with higher G-CSF biosimilar uptakes (12.4% in Spain and 20.4% in the UK). The G-CSF biosimilar uptakes depend critically on their market access at a local/regional level. The more the decisions are decentralized (hospitals, local purchasing structures) the more their uptakes are high (28.3% of the hospital market in France in 2011 and 20.4% in the UK). The price difference between G-CSF biosimilars and their reference plays a marginal role at a global level (+13.3% in the UK and -20.4% in France). **CONCLUSIONS:** The competition with G-CSF biosimilars varies significantly between EU-5 countries due to distribution channel differences. Currently, this competition is not mainly based on prices, but on local political options to stimulate tendering between them and other most recently branded products. In countries with dominant retail markets, a prerequisite for the success of biosimilar G-CSFs is that governments approve their substitution in the same way generics are authorized by introducing them case-by-case.

PHP14

CHARACTERISING PRELIMINARY PROFILE PARAMATERS FOR FDA BREAKTHROUGH THERAPY CANDIDATES

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OBJECTIVES: Since the new Breakthrough Therapy (BT) designation was introduced with the new Food and Drug Administration Safety and Innovation Act (FDASIA) on 9 July 2012, the FDA has received over 50 requests, and has issued over 20 such designations to various candidates in various indications based on preliminary evidence that the investigational drugs fulfill a highly unmet medical need where no alternatives exist, or demonstrate a significant improvement over existing therapies. We have set out to examine the key parameters that characterise a "Breakthrough" candidate, and to determine the likelihood of an investigational therapy being granted the status. **METHODS:** Using the FDA listing of BT designation statistics, publicly available information, as well as IHS Global Insight data, we identified a list of currently approved BT candidates between 9 July 2012 and 14 June 2013 and determined their preliminary profile characteristics. **RESULTS:** To date, nearly 75% of the designations have been publicly announced by the pharmaceuticals firms

developing the candidates, with investigational oncology drugs representing the largest proportion (53%). Orphan diseases make up the second largest group with over a third of publicly disclosed BT therapies. In therapeutic areas with already available treatment options, such as Hepatitis C Virus infections and advanced melanoma, there is still potential for drug candidates to gain BT designation if they can be shown to provide an alternative to effectively treat patients that fail to respond to the current standard of care. **CONCLUSIONS:** Our investigation has highlighted the FDA's focus on finding breakthrough candidates within oncology as well as rare genetic or orphan diseases that do not currently have adequate treatment options. Additionally, candidates offering alternative options to non-responders have also secured a place on the list, which is likely to grow as increased interest and awareness is generated.

PHP16

MEDICO-ECONOMIC EVALUATION IN FRANCE: METHODOLOGY AND IMPACT ON THE PRICING AND REIMBURSEMENT SYSTEM

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OBJECTIVES: From October 2013, some pharmaceutical products will be required to undergo a medico-economic evaluation in France. The aim of this study was to interview key stakeholders involved in this conceptual change in order to understand how this reform will be implemented and how it will affect market access in France. **METHODS:** Primary research was conducted between April and June 2013 with stakeholders from the French National Authority for Health (HAS), the Economic and Public Health Evaluation Commission (CEESP), the Transparency Commission (TC) and relevant French ministries. Interviews lasted between 45 and 75 minutes and focused on the methodology for medico-economic assessment and its implications on the French pharmaceutical pricing and reimbursement (P&R) process. **RESULTS:** Medico-economic evaluation in France will be based on cost-utility or cost-effectiveness analyses, depending on whether or not quality of life is an important outcome. Cost-utility analyses will rely on QALYs (quality-adjusted life years), whereas cost-effectiveness analyses will rely on survival. The medico-economic assessments will inform pricing negotiations, on the one hand, and potentially the development of prescribing guidelines, on the other. Medicines will be subjected to a medico-economic assessment based on their level of innovation and/or on their financial impact on the health care budget. **CONCLUSIONS:** France is formally introducing the QALY into its P&R system; however, this reform will come with a twist on the Anglo-Saxon approach, as there will be no associated ICER (incremental cost-effectiveness ratio) above which the medicine will not be reimbursed. While there is still some level of uncertainty with regards to the medicines that will be subjected to this assessment (as stakeholders have yet to put a quantitative value on a "significant impact" on the health care budget), the direction of travel is toward greater pressure on pharmaceutical prices.

PHP17

OVERCOMING THE HTA HURDLE IN GERMANY: KEY CONSIDERATIONS FOR A MANUFACTURER'S PRICING AND MARKET ACCESS STRATEGY

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OBJECTIVES: In 2011, we saw the introduction of an evidence-based pricing approach to new branded pharmaceuticals in Germany. The process arose from the Act of the Reform of the Market for Medicinal Products (AMNOG) and all new drugs must undergo clinical benefit assessment by the Federal Joint Committee (GBA) followed by price negotiation with the German sick fund (GKV-SV) heads depending on whether additional benefit has been demonstrated. A review of the final GBA assessments published to date was undertaken and the aim was to evaluate the implications for manufacturers considering Germany as a launch country. **METHODS:** The GBA and IQWIG websites were searched for AMNOG evaluations performed between January 2011 to May 2013. Where appropriate the approach taken in the GBA assessment was compared with that of other HTA groups in Europe. **RESULTS:** The most important consideration for a manufacturer is choosing the right comparator in their submission, the core evidence document in this process. A number of drugs have been compared to the wrong treatment and subsequently were found to have no additional benefit. Some submissions chose the appropriate comparator but only for certain subgroups, leading to a reduced overall benefit for the new drug. Like most HTA groups, the preference is for mortality, morbidity and side effects evidence from head-to-head trials, however GBA appear to give little consideration to quality of life evidence. The review also revealed that GBA make decisions that are independent of other HTA bodies and sometimes reject recommendations of its own evidence review group, IQWIG. **CONCLUSIONS:** Early engagement with GBA to agree an appropriate comparator, patient population and clinical outcome measures is very important to improve chances of a positive assessment. However, the requirements of the GBA process should be balanced with those of other key markets as part of the drug's global PRA strategy.

PHP18

TROIKA IN PORTUGAL: PHARMACEUTICAL SECTOR FROM PAPER TO REALITY

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OBJECTIVES: The Memorandum of Understanding signed in May 2011, between the Portuguese Government and the International Authorities, increased requirements to reduce the public expenditure with medicines. These measures included the major change in margins distribution system. This study aims to: 1) describe the MoU measures related to medicines; 2) analyze public expenditure and impact of distribution margins reductions on medicines public expenditure, due to MoU and legislative changes in Portugal. **METHODS:** Descriptive study with updates to the MoU and published legislation. Market analysis and simulations were computed based on the Pharmacy Sales Information System (a nationwide database with representative drug dispensing data from ambulatory care). The statistical analysis was performed using SAS Enterprise Guide 4.1. **RESULTS:** The average price of medicines in the NHS market reduced significantly. Until March 2013, the average price of generics reduced 59.0% and brands 12.9%. The margins of pharmacies and wholesalers decreased in 2012. As a consequence, the outpatient pharmaceutical market decreased € 752 million and the NHS expenditure € 468.1 million, between 2010 and 2012. However, hospital market in 2012 remains at the same level observed in 2010. In the first quarter of 2013, outpatient market reduced another 90.3 million € and NHS expenditure € 49.7 M, of which 21% is due to the reduction of distribution margins. **CONCLUSIONS:** Even before the MoU, several changes led to a great reduction of the public expenditure in 2011. This impact worsened after the MoU, with direct effects on the reduction of the remuneration of pharmacies and wholesalers. Urgent strategies that ensure the access of patients to medicines while preserving the sustainability of both the NHS and the network of pharmacies are required, as well as policies to monitor the prescribing, dispensing and utilization of medicines and concrete changes in the inpatient NHS expenditure.

PHP19

UTILIZING STORYTELLING TO PROMOTE RATIONAL ANTIBIOTIC USE IN 9-11 YEARS OLD SCHOOL CHILDREN IN IRAN

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OBJECTIVES: Antimicrobial resistance is still a growing health problem which increases morbidity, mortality, and health costs and has been associated with inappropriate antibiotic use. In Iran antibiotic prescription rates are high in children and antibiotics are the most common medication prescribed. Teaching children about the different types of microbes and the increasing problems of antibiotic resistance with unnecessary and inappropriate use of antibiotics should not only raise awareness in our future generation of antibiotic users but also in the family environment. This study aimed to evaluate the effectiveness of the story telling in improving children's knowledge about rational antibiotic use. **METHODS:** Junior (9–11 years) school classes were divided into either control or intervention groups for evaluation of the story telling. Students were required to complete identical knowledge questionnaires at three time points (before, immediately after and 4 weeks after teaching), to assess knowledge change and retention. Teaching, using story books which provided by National Committee on Rational Drug Use (NCRUD), was given by junior school teachers. **RESULTS:** A total of 164 junior students, 95 were intervention and 69 control groups, were studied. The junior story telling demonstrated a significant improvement in student's knowledge (34.5% of change) and there was no significant decrease in student knowledge observed after a 4 week period. **CONCLUSIONS:** Availability of information on the effectiveness of intervention for improving and promoting appropriate antibiotics use can facilitate implementation of strategies in this field. Regarding the effectiveness of storytelling, it is therefore recommended that decison-maker place greater emphasis on the use of such interventions.

PHP20

RELEVANT DECISION-MAKING CRITERIA IN GERMAN HOSPITAL FORMULARIES

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OBJECTIVES: Hospital formularies are usually the gatekeepers for pharmaceutical drugs. Typical majority members of hospital formularies are physicians, although most of the time the formulary is chaired by a pharmacist. As German hospitals are struggling with a difficult economic environment the question arises: what kind of decision-making criteria are applied when pharmaceutical drugs should be added to the formulary list? Information regarding this topic is scarce due to the sensitive topic of decision-making. Only one study (Thürmann et al., 1997) is looking into this for Germany. **METHODS:** a total of 588 public, private and ecclesiastic hospitals in Germany have been contacted to participate in an online-survey regarding the structure of their hospital formulary, roles of members and applied decision-making criteria. **RESULTS:** Thirty-five of 588 hospitals (6%) have finally participated and filled out the complete questionnaire. Out of the 35 participants, 29 were pharmacists (82.9%) and 6 were physicians (17.1%). 34.3% of the hospitals have no guidelines for their decision-making and 65.7% of the hospitals with guidelines have written (48.6%) or verbal (17.1%) guidelines. Out of these, 78.3% discuss decision-making criteria, but only 47.8% talk about the relative importance of the discussed decision-making criteria. Budget impact (82.6%), clinical studies (69.6%) and price (65.2%) are the most often mentioned decision-making criteria in the guidelines. **CONCLUSIONS:** A third of the participating hospitals do not have guidelines for their decision-making process and only half of the guidelines discussing decision-making criteria also talk about the relative importance. Hospital formularies in Germany do not seem to be transparent in their decision-making process. In addition the top 3 decision criteria in the existing guidelines include 2 economical criteria which lead to the question of dominance of economical versus medical or other criteria. Further research needs to look at the real applied decision-making criteria and how much impact economical criteria have on decision-making in German hospital formularies.

PHP21

2.5 YEARS OF AMNOG IN GERMANY – AN ANALYSIS OF BENEFIT ASSESSMENT AND NET PRICE NEGOTIATION TRENDS

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OBJECTIVES: In 2011, the AMNOG law changed the price-setting procedure for drugs in Germany. Manufacturers are now required to submit a dossier to the Federal Joint Committee (GBA) for newly launched or, upon specific request, already market products. The GBA decides on the level of additional benefit which impacts the reimbursement price negotiations with German sick funds. The objectives of this study were thus to: 1) identify ways in which manufacturers can optimize the benefit

assessment outcomes, 2) analyze correlations between additional benefit, budget impact and negotiated rebate. **METHODS:** To achieve objective 1, assessments by the GBA and the IQWiG (Institute for Quality and Efficiency in Healthcare) (source: GBA website) were scanned for key trends. To achieve objective 2, list and post-negotiation prices were extracted from the Lauer-Taxe (German price database). For the 10 agents that had so far completed price negotiations, these were mapped against additional benefit and the budget impact (annual therapy costs as stated in GBA assessment). **RESULTS:** The results linked to objective 1, which were more qualitative in nature, allowed for the extraction of 5 key learnings for manufacturers to keep in mind. The results associated with objective 2 showed no link between additional benefits granted and negotiated rebate but did reveal price impacting parameters apart from budget impact. **CONCLUSIONS:** Concerning objective 1, the ways in which manufacturers can attempt to optimize benefit outcomes include: 1. Focus on comparator choice, 2. Focus on hard endpoints, 3. Make patient segmentation more solid, 4. Expect independent action of GBA and IQWiG and 5. Accept that there is no methodological standard for the definition of an additional benefit. Regarding objective 2, we concluded that budget impact, influenced primarily by target population size, annual therapy costs and drug price, is an – if not the most important driver in the negotiation.

PHP22

IS DRUG INNOVATION STILL REWARDED IN THE TOP 5 EUROPEAN PHARMACEUTIAL MARKETS?

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OBJECTIVES: To assess how drug innovation is rewarded and how it is impacted by cost-containment policies. **METHODS:** Manufacturer prices per unit of package and strengths were compared and assessed in a basket of 97 innovative drugs approved by the European Medicines Agency (EMA) since 2000. The products were still patent protected, and available in each of the top 5 European pharmaceutical markets. **RESULTS:** Prices of innovative drugs in Germany were still the highest and had a benchmark price index of 100. In France, when drugs were deemed innovative, premium prices were granted – resulting in a price index of 94 – but significantly decreased over time. While prices at launch in Italy, Spain and the UK were commonly lower – with price indexes of 89, 88 and 86 respectively - they tended to remain constant over time. **CONCLUSIONS:** Despite the fact that governments in developed markets are attempting to lower prices, differences still exist across the largest markets, enabling pharmaceutical companies to implement differential and protective pricing strategies. In Germany, time to market is comparatively fast and premium prices at launch have been granted. In future, the AMNOG reform will complicate this picture, although pricing premiums have still been achieved for drugs deemed innovative that have gone through the full AMNOG process. In France, although prices are relatively high at launch, they drop at time of renewal and innovation is granted to a limited number of drugs. Prices have been comparatively low at launch but remain constant in Italy and Spain, reflecting the fact that price cuts in those countries have often been directed towards generics, although these are still considered high-risk markets. In the UK, it remains to be seen how the value-based pricing reform will impact prices.

PHP23

ACCESSIBILITY OF ORPHAN DRUGS IN FRANCE, UNITED KINGDOM AND GERMANY: DIFFERENT APPROACHES WITH REGARD TO HTA AND PRICES

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OBJECTIVES: To describe availability of orphan drugs in France, UK and Germany and to compare agencies' assessments and prices. **METHODS:** All the products designated as orphan drugs by the European Commission and commercialized at least in one of the three countries were included in the study. Comparison of prices is made per dosage and is based on prices per standard unit, using IMS MIDAS database. Comparison of assessments is based on Transparency Committee opinions, NICE guidances and IQWIG benefit assessments. **RESULTS:** Sixty-two products (103 dosages/forms) were included in this study; 47 (76%; 84 dosages/forms) are commercialized in the 3 countries, 8 (13%) products in only 2 countries (6 both in Germany and UK and 2 both in Germany and France) and 7 (11%) only in 1 country (6 in Germany only and 1 in France only). Among the 84 products/dosage/forms available in the three countries, most of them are available at hospital (respectively 68, 70 and 77 in Germany, France and UK) but those available through retail pharmacists are much numerous in Germany (72 of them) than in France (29) or UK (30). German and UK manufacturer March 2013 retail prices more often higher than French one, despite the fact that among the 49 orphan drugs commercialized in France, 31 are innovative products (ASMR rate I to III). For instance, French assessment of pirfenidone was less favorable than the Germans'one, and German price is thus +65.2% higher than French price. French and UK HTA assessments for azacitidine were both positive and led to similar prices. **CONCLUSIONS:** Most orphan drugs are available in the three studied countries but accessibility to them seems to be different and depends on HTA results.

PHP24

COMPARISON RETAIL PRICES OF DRUG PRICES BETWEEN TURKEY AND EUROPEAN COUNTRIES

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OBJECTIVES: The reference pricing system is used for setting drug prices in Turkey since 2006. There are 5 reference countries following; Spain, Italy, Germany, France and Greece. Except those countries, manufactured or imported countries may be used as reference countries. Reference prices are reviewed time by time and may be subject to certain alterations, but evaluation of box prices may be different if evaluation made based on milligram. The aim of this study is to evaluate differences of average milligram sales prices of some generic medicines between Turkey and European countries. **METHODS:** Comparison of miligram based prices analysis between European countries done by Intelligent Health System(IHS) was used. The analysis of IHS included Germany, France, United Kingdom(UK), Spain and Italy(EU5). Comparison was done with taken row data of analysis EU5 and Turkey average milligram retail prices of Ceftriaxone, Clopidogrel, Esomeprazole, Fentanyl, Lamotrigine, Levofloxacin, Metformin, Venlafaxine, Letrozole and Olanzapine molecules. **RESULTS:** It has been reported that compared 10 molecules highest average miligram based prices of Esomeprazole(0,043 €), Levofloxacin(0,058 €) and Clopidogrel(0,0083 €) molecules belong to Turkey, Lamotrigine(0,01 €) belongs to Germany. The highest average miligram based prices of other 6 molecules belong to UK with following; Ceftriaxone(0,0196 €), Fentanyl(0,186 €), Letrozole(1,24 €), Metformine(0,00013 €), Venlafaxine(0,0074 €), Olanzapine(0,261 €). **CONCLUSIONS:** It has known that because of UK used free pricing mechanism on drugs, prices of drugs are higher than other compared countries. This sitiuation established on the anaylsis. But despite of Turkish Government policy decisions; it is important indiciation that 3 drugs represents highest prices out 10 drugs. Reference pricing system applied based on box price. Better control mechanism may achievable if miligram based pricing apply in Turkey. On the other hand because of the study only consist retail sales prices the evaluation should be done from point of reimbursement prices on future studies.

PHP25

CONSUMPTION OF BIOSIMILAR DRUGS IN CAMPANIA REGION IN THE YEARS 2009-2012

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OBJECTIVES: The expiration of biotech drugs patent has led to the creation of drugs copies of originator products, defined 'biosimilars'. No European country allows automatic substitution between the originator and the biosimilar. In Italy, due to the lack of a national legislation, some Regions have issued directives to encourage the use of biosimilars, recognizing a potential saving of resources. Campania Region was the first region to legislate on the matter, (decree no. 15 of 11.30.2009) supporting the prescription of biosimilars to the naive patient. The aim of our study is to describe trends in biosimilars consumption in Campania region and evaluate how biosimilar products are replacing the originators in the respective markets. **METHODS:** IMS Health regional database was used to analyze biosimilar drugs consumption patterns (erythropoietins, G-CSF, somatropin) in the years 2009- 2012. Information was retrieved about different distribution channels (retail, direct distribution, hospital). Consumptions are expressed in Counting Units (CU) and trends have been calculated using Compound Average Grow Rate (CAGR). The study especially focused on consumption trends of erythropoietin (ATC B03XA) in the years 2009-2012. **RESULTS:** In 2012 the penetration rate of biosimilars was 40.1% (evaluated as the biosimilars share of the total erythropoietins, G-CSF, somatropin market). These values are double than those at national level, that are estimated to be 19.7% of consumption. Focus on erythropoietin trends showed a strong increase in biosimilars consumption (451 CU in 2009 vs 140,327 CU in 2012) after the introduction of regional measures to promote the prescription of biosimilars to the naive patient. In 2012, biosimilar erythropoietins and reference drugs show similar market shares (37.0% and 33.7% of the total erythropietins market respectively) showing a high substitution effect. **CONCLUSIONS:** Our analysis outlines the significant effects of regional measures on market penetration rates of biosimilars.

PHP26

INDIRECT AND DIRECT SAVINGS RESULTED FROM PARALLEL TRADE OF PHARMACEUTICALS IN POLAND – RESULTS OF VALUATION SALES DATA FROM PUBLIC PHARMACIES

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OBJECTIVES: Estimation of the direct and indirect savings generated by parallel importing (PI) of pharmaceutical products in public pharmacies in Poland, and estimation of the savings for the payer in the case of reimbursed drugs. **METHODS:** IMS Health Poland National Sales Data (2005-2012) and data from respective reimbursement lists were used for all calculations. Direct savings were estimated considering all PI products sold in public pharmacies(433 products, 1550 SKUs). To avoid overestimation, only 18 products that passed restrictive criteria were used for calculations of indirect savings. Twenty-seven reimbursed products were used for the payer savings calculations. Direct savings were calculated as a difference between PI and reference product prices multiplied by the number of packs of PI product. Indirect savings were calculated as a difference between the reference product price and the theoretical reference product price (i.e. prices in a hypothetical situation where there is no price pressure caused by PI – calculated using linear regression). Indirect savings considered only those products which met the criteria of the reference product's price decrease of at least 5% within 3 months prior to, or after, the appearance of the PI product. **RESULTS:** Study revealed that the savings generated by the PI of pharmaceuticals in Poland between 2005-2012 may be estimated at the level of EUR 146m (direct savings EUR 46m and indirect savings EUR 100m). Savings for the payer calculated for reimbursed products between 2008-2012 reached the level of EUR 0.06m. **CONCLUSIONS:** This is the first study estimating direct and indirect savings coming from PI phenomena covering all years since PI was reinforced by Poland's accession to the EU. It has been found very interesting that indirect savings tend to be substantially higher that direct ones. This indicates that high price pressure is created by PI, and affects the prices of reference products.

PHP27

PRICING OF "FOLLOW-ON" DRUGS AND COMPETITION WITHIN PHARMACEUTICAL CLASSES: EVIDENCE FROM GERMANY 1993-2008

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OBJECTIVES: Competition within therapeutic drug classes from "follow-on" drugs has been a highly controversial issue. Manufacturers launching new molecules in existing drug classes have often been criticized for inflating health systems' expenses, but it has been argued that such drugs increase therapeutic options. Economic theory suggests that follow-on drugs induce price competition. We contribute to this discussion by addressing the topic of pricing at market entry and price development in the German market with the distinct focus on competition within already existing drug classes. **METHODS:** We measure determinants of price strategies of follow-on drugs using regression analyses, considering all new molecules launched in the German market in the period from 1993-2008. Prices of products are standardized on Defined Daily Dosages controlling for sales volumes based on data from the IMS Health DPM database, a census audit of pharmaceutical sales in Germany, and for the therapeutic quality of a new product using ratings by Fricke/Klaus as a proxy for innovation. **RESULTS:** We identify prices correlating with therapeutic value at market entry. While the first two molecules engage in quality competition by offering more therapeutic options, price discounts below the market price can be observed from the third entrant on. Price discounts are even more distinct in development races with several drugs entering the market within two years and in classes with a low degree of therapeutic differentiation. Prices remain relatively constant over time. **CONCLUSIONS:** This study contributes to assessments of competition in pharmaceutical markets focusing on price strategies of new market entrants. After an initial phase of market building, further follow-on products induce price competition. Largely unchanged prices after 4 years may be interpreted as quality competition and can be attributed to prices in Germany being anchor point for international price referencing.

PHP28

THE IMPACT OF GENERIC SUBSTITUTION ON HEALTH OUTCOMES AND COSTS: A SYSTEMATIC REVIEW

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OBJECTIVES: Although generic drugs are considered to be therapeutically equivalent to their off-patent (branded) counterparts, the overall impact of generic substitution on clinical and economic outcomes has not been comprehensively evaluated. The goal of this study was to test whether 1) generics and branded products yield the same health outcomes; and 2) generic therapies save economic resources versus branded therapies for de-novo patients and patients on maintenance therapy. **METHODS:** We performed a systematic literature review in Medline, Cochrane Database of Systematic Reviews and Embase (2000-2012) to identify original research studies on clinical or economic outcomes with either independent or pre-post comparator groups. Data were aggregated using a standardized extraction form. For each included study, outcomes were categorized as favoring or opposing generic drug substitution. As we compared different outcomes, one publication could contribute to multiple outcome comparisons. **RESULTS:** We included 40 studies that led to 121 outcome comparisons. Similar clinical effects were found in 74% of all studies in which patients were initiating therapy (de novo) and 64% of all studies involving maintenance therapy comparisons. 100% of the economic analyses of de novo patients and 56% of comparisons of maintenance therapy patients showed lower costs associated with the use of original brand. Overall, 66% of the outcome comparisons reported similar clinical outcomes and 64% suggested that brand products lower costs compared to generic substitution. **CONCLUSIONS:** Our analyses suggested that clinical effects were mainly similar, whereas economic savings of brand to generic drug substitution may be overstated, particularly in sensitive therapeutic areas such as anti-epileptic drugs or immunosuppressives. More systematic research comparing clinical and cost outcomes with or without generic substitution is needed to inform policy on the use of generic substitution. **ACKNOWLEDGEMENTS:** We would like to thank Anke-Peggy Holtorf and Zoltán Kaló for their scientific input.

PHP29

PRICING AND REIMBURSEMENT ANALYSIS OF LIFESTYLE MEDICINES IN SERBIA

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OBJECTIVES: To determine whether there was a difference between wholesale prices, utilization and market share, as well as to explain Rx-OTC switches and reimbursement possibilities of "lifestyle-medicines", in 2009 and 2010, before and after the adoption of new Medicines Law, in Serbia. **METHODS:** We investigated how many potential "lifestyle-medicines", satisfying the previously determined criteria, were authorised for sale. Utilization, price changes and reimbursement status were monitored. Price index and margin index were calculated using the formula: I=QxP (index(I),quantity(Q),price(P)). To compare the differences in prices and utilization, non-parametric Mann-Whitney test was used. To test difference in market shares, T-test of proportion was used. **RESULTS:** There were 21 registered "lifestyle-medicines". Five medicines (oral contraceptives) were listed. In 2009, there were 1,763,030 units dispensed worth 16,074,922€. In 2010, 1,814,405 units were dispensed while total value was 14,129,792€. The average sales(€) were higher in 2009, which is not in line with the expected growth trend, but observed difference was not statistically significant. The wholesale price-index 2009/2010 was -13%. This means that prices were 13% lower in 2010. In fact, during 2010, prices remained the same in national currency, which weakened against euro. The margin index was 21% in 2009 and 20% in 2010. Since all drugs were Rx (margin was set up to 12%, VAT was fixed to 8%), this was completely expected. At the end of 2010, two medicines: levonorgestrel (1,5mg) and orlistat (60mg), were authorised as OTC medicines (free pricing, margin:25%, VAT:18%). **CONCLUSIONS:** "Lifestyle-medicines" are difficult to define. Market success depends on product characteristics, effectiveness, tolerability, convenient drug-delivery format, simple dosing regimen, good safety profile, first-to-market position, premium prices, sustained media attention, Rx-OTC switch potential and reimbursement potential. Although more new "lifestyle-medicines" will be authorised in Serbia, market share is expected to decrease because of low purchasing power and low reimbursement potential.

PHP30

IS EXTERNAL PRICE REFERENCING AN APPROPRIATE DRUG POLICY FROM AN EFFICIENCY, EQUITY, AND QUALITY PERSPECTIVE?

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OBJECTIVES: Different external price referencing (EPR) configurations are applied by countries worldwide. Depending on how EPR schemes are implemented, they may have varying effects on short- and long-run prices, market dynamics, key stakeholders, and other relevant endpoints. This research evaluated the merits and demerits of EPR from an efficiency, equity, and quality perspective. **METHODS:** A theoretical and empirical analysis of the effectiveness of EPR was conducted, based on a systematic review of the literature and stakeholder interviews. As EPR has been most common in Europe, the study focused on this region. **RESULTS:** The systematic review identified 100 relevant articles. The articles were categorised according to study characteristics and four major themes were identified; these findings were confirmed by the interviewees. The evidence suggests that EPR schemes often generate disproportionate price levels in relation to national abilities to pay; this is likely due to the reliance on foreign list prices which do not reflect negotiated discounts. If manufacturers apply launch strategies to exert upward pressure on prices (e.g. launch delays or product withdrawals), it may also limit patient access to life-saving medicines. In addition, the bureaucratic complexity of many EPR schemes may undermine the objectives of EPR use (i.e. cost containment and macroeconomic efficiency). Finally, widespread EPR application may stifle pharmaceutical and biomedical innovation. **CONCLUSIONS:** A national pricing policy should provide an effective, predictable, transparent, and stable pricing environment for pharmaceutical products. It should internalise national priorities for health and industrial policy, including cost containment, employment, innovation, and trade promotion. EPR is associated with important short- and long-term issues. If EPR is going to continue to be applied by EU Member States and other countries, then it is necessary to establish guiding principles to govern EPR use across jurisdictions. Still, differential pricing and risk-sharing agreements may represent more sustainable policy options.

PHP31

DOES EUROPE REWARD REFORMULATIONS? A DATA DRIVEN ANALYSIS OF VALUE PRESERVATION THROUGH REFORMULATION

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OBJECTIVES: Reformulating existing drugs can improve patient convenience, compliance and create new uses for the product. However, reformulations cost millions of Euros - a risky investment without guaranteed exclusivity or returns. This study assessed whether markets reward incremental value creation through reformulation by comparing sales performance close to patent expiry for reformulated and non-reformulated products. **METHODS:** IMS MIDAS data was interrogated to identify 829 small molecule, non-generic products which had peak sales above €5M and lost patent protection between 2001 and 2010 in EU-5 (France, Germany, Italy, Spain and UK). Ex-manufacturer sales value (€) 2 years after patent expiry was compared with sales value 4 years earlier to calculate percentage value erosion for each of the 829 products. A subset of 133 products which launched at least 1 reformulation close to patent protection expiry (launch between 3 years before and 1 year after patent protection expiry) were analysed to assess whether value erosion varied across countries or therapy areas. **RESULTS:** Mean ex-manufacturer sales value erosion of reformulated products (24%) was significantly less than non-reformulated products (37%, $P<0.01$). Reformulated product value erosion varied with country and therapy area. Germany saw highest number of reformulations launched yet only reformulations launched in Italy showed significantly less value erosion than non-reformulated products ($P<0.01$). Across therapy areas, reformulations were most common in nervous system, metabolism and anti-infective categories. However, reformulated anti-infective product value erosion was pronounced while musculoskeletal and nervous system products experienced significantly less value erosion than for non-reformulated products (both $P<0.05$). **CONCLUSIONS:** Overall, reformulated products do maintain more value than non-reformulated products following loss of patent protection. Chronic disorders e.g. nervous and musculoskeletal system disorders appear to be the most promising areas for reformulating. Future reformulation potential is tightly linked to country-specific pricing and market access policy decisions to recognise incremental value products.

PHP32

CONSTRUCTING AN INDEX OF INTERNATIONAL PHARMACEUTICAL PRICES. A COMPARISON OF PHARMACEUTICAL PRICES IN 56 COUNTRIES

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OBJECTIVES: To construct a number of pharmaceutical price indices for a broad set of countries, covering a range of regions, including countries with different levels

of economic development and a representative sample of medicines. **METHODS:** The indices were developed using the Fisher EKS method. In order to construct an index the products needed to be defined as like. The definition of like in this study was based on molecules which are deemed to deliver equivalent health outcomes. This is a very broad definition and allows a large number of countries and molecules to be included in the indices. Two price indices have been constructed. The first compares prices of mostly off-patent medicines across 56 countries over the period from 2005 to 2011 and included 42 molecules which were sold in each country for the period. The second examined on-patent medicines across 17 countries and 9 molecules. **RESULTS:** The results showed prices varied significantly between regions and that prices of genericised medicines both fell and converged over time. For the mostly generic drugs index the regions from lowest to highest price were - Region of the Americas A; South-East Asian Region D; South-East Asian Region B; European Region B; Western Pacific Region A; European Region A; African Region E; European Region C; Western Pacific Region B; Eastern Mediterranean Region D; Region of the Americas D; Region of the Americas B and Eastern Mediterranean Region B. Prices tended to be similar within each region. These results will be presented in detail. **CONCLUSIONS:** This research makes a unique contribution to our understanding of drug prices. It is the largest international comparison of pharmaceutical prices ever undertaken; employs new method to pharmaceutical pricing indices through the Fisher EKS method and outcomes based definitions of equivalence and examines genericised and on-patent markets separately.

PHP33

TRANSPARENCY OF THE MEDICINES REIMBURSEMENT SYSTEM IN IRELAND: A QUANTATIVE ANALYSIS OF THE INFLUENCES ON REIMBURSEMENT DECISIONS [2006-2013]

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OBJECTIVES: To identify what process and technology related characteristics influence reimbursement decisions in Ireland. **METHODS:** Using publically available data compiled from the NCPE and HSE websites from 2006 to 2013, we examined several variables (disease area; transparency; and, assessment and judgement of effect and CE), as defined in Fischer (2013), to identify what influences reimbursement decisions made through the community drugs schemes (i.e. GMS, and High Tech schemes). Analyses included, Spearman's Rank Correlation (SRC), Kruskal-Wallis and Fishers exact tests in the univariate analyses, and a step-wise multivariate regression. **RESULTS:** For technology features most disease areas were found not to have a significant influence on reimbursement decisions (SRC: max 0.30, Fishers Exact: $p>0.10$; and, regression analysis $p>0.10$). However, treatments for endocrine conditions were significant ($p<0.10$). For process features the availability, quantity, and type of assessment information were strongly correlated with reimbursement decision (SRC: ≥ 0.73). Judgement of effect and cost-effectiveness were significant ($p<0.05$), and the multivariate regression showed "transparency", "judgement of effect" and "judgement of CE" to be statistically significant (odds ratios: 0.095, 2.752, and 3.657 respectively; $p<0.10$). **CONCLUSIONS:** Overall, increased transparency (i.e. publically available documentation of the decision rationale) has a negative influence on the likelihood of reimbursement. This can be explained by the Rapid Review process, whereby products are initially screened and selected for further HTA analysis. As expected, those not selected for HTA are more likely to be reimbursed, but have less documentation supporting the decision, introducing less transparency overall. Where a HTA has been conducted, judgement of effectiveness and cost-effectiveness has strong positive influence on reimbursement, with cost-effectiveness being the strongest positive influence. Fisher (2013) found stakeholder involvement to be an important influence; this could not be tested in the Irish context as the numbers of stakeholders known to be involved are constant across all observations.

PHP34

RELEVANCE OF A NATIONAL FORECAST GROWTH RATE, AS A REGULATION TOOL OF THE EXPENSIVE HOSPITAL DRUG SPENDING, IN FRANCE

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OBJECTIVES: In France, a forecast growth rate in spending related to the list of expensive hospital drugs, funded in addition to DRG-based payment, is determined annually (2% in 2012). If hospitals exceed the rate, they will be controlled, based on the proper use of drugs. The objective is to question the relevance of this national growth rate as a regulation tool. **METHODS:** This study used 2011/2012 data from "medicalized information system program". Expensive drug expenditures are aggregated by each type of French hospitals (without private sector): cancer centers (CC=19), university hospitals (UH=32), hospitals centers (HC=415) and private non-profit hospitals (PNPH=104). In order to identify their specificities, we analyzed the expenditures of the first therapeutic class in value by hospital type and how much the top 3 drugs, that drive the overall growth, contribute to their respective growth. **RESULTS:** Overall spending grew by 4.95% in 2012. Antineoplastic drugs (1% of decrease) represent 48% of overall expenditures. Their market share varies from 34% in UH expenditures to 95% in CC, the only hospital type that meet the forecast rate. The top 3 drugs (2 immunosuppressant drugs and 1 replacement enzyme; 17% of overall expenditures) contribute to 3.93 points of the total growth. Their contribution to the growth of each hospital types is uneven: from -0.02 point out of -6% in CC to 5.35 points out of 9.03% in UH. **CONCLUSIONS:** There is a divergence in the growth of spending for the different hospital types because of their specific characteristics leading to different consumption profiles. Therefore, some hospitals are more impacted by changes in the spending structure, as CC for antineoplastic drugs. A regulation by an annual growth rate is useful because of its flexibility. But relevance of a single national rate does not reflect the care's offer heterogeneity and needs local analyses.

PHP35

INTRODUCTION OF INNOVATIONS INTO THE GERMAN STATUTATORY REIMBRUSMENT SYSTEM – FACTORS FOR SUCCESS

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OBJECTIVES: Innovations are fundamental for progress and improvement in health care and medicine. In German hospitals provision of all kind of services is allowed, since it is not forbidden explicitly. But it is paid only if it is represented in the reimbursement system. For integration of innovations into this system applications must be addressed by each hospital which wants to provide a special innovative service in each year separately to the German institute for reimbursement in hospitals which decides about (additional) payments. The objective is to determine which factors influence the chance for innovations being incorporated. Results can be used by hospitals to assess if certain innovations have good chances to be afforded. **METHODS:** Data about applications, their approval and assessment, number of hospitals and years in which approvals were made were obtained from the German institute for reimbursement systems in hospitals from 2005 to 2011. Innovations have been classified into types of methods. Applications made by medical associations and for orphan drugs were identified. Associations between each variable and success of application were calculated. In all analyses Bonferroni correction was conducted. Finally intercorrelation of variables was assessed. **RESULTS:** Chance of integration was best for innovations with the following characteristics: Applications were made by medical associations, innovations were applied over a period of 6 years and by more than 100 hospitals, subjects were drugs (especially orphan drugs) and they belong to gynecology, oncology or cardiology and vascular medicine. Intercorrelation between these independent variables is also a predictor of success in some constellations. **CONCLUSIONS:** The success of integration of a new method depends on all analyzed variables. Therefor all of them have to be taken into account when decision is made about what innovation should be applied.

PHP36

THE IMPACT OF AMNOG ON DRUG REIMBURSEMENT IN GERMANY

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OBJECTIVES: There are three main governmental stakeholders in the German AMNOG process: The IQWiG assesses the AMNOG drug manufacturer's submission and provides advice on any additional benefit to the GBA who makes the final decision. Following confirmation of additional benefit, manufacturers start price negotiations with the GKV-Spitzenverband (association of German sickness funds). The aim of this research is to assess the AMNOG-decisions so far. **METHODS:** All AMNOG decisions up to December 2012 were analyzed in terms of additional benefit decision, reason for additional benefit decision, reimbursed price versus manufacturer set price, and consistency in IQWiG-recommendation and GBA-decision. **RESULTS:** In total AMNOG decisions of 41 drugs (60 subgroups) were identified. IQWiG recommendations were as follows: 22 cases demonstrated no additional benefit, 2 unquantifiable benefit, 3 slight benefit, 7 significant benefit, and 7 additional benefit due to orphan-drug status. In 6 cases, the GBA upgraded IQWIG's recommendations. In 3 cases it downgraded it. The following reasons were identified for GBA "additional benefit decisions" (multiple reasons apply for some decisions): No or non-quantifiable additional benefit (18 cases); no reliable clinical data (14 cases; 3 cases no submission), wrong comparator (5 cases); additional benefit in any form (23 cases): mortality advantages (7 cases), orphan drug status (7 cases), morbidity advantages (8 cases), and QoL advantages (3 cases). The negotiated price rebates varied from 4.7% to 70.7% based on manufacturer set price; the rebates show limited correlation to the degree of additional benefit so far. **CONCLUSIONS:** Key factors for positive AMNOG decisions are conducting superiority trials on mortality or at least morbidity/QoL against active comparators. If benefits are based on soft end-points, it is crucial to demonstrate these on high quality, preferably German data. Indirect comparisons seem to be challenged as proof of additional benefits.

PHP37

EU PAYER AND DECISION MAKER USE OF OBSERVATIONAL STUDIES FOR HEALTH CARE REIMBURSEMENT DECISIONS

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OBJECTIVES: As cost-containment pressures across Europe intensify, evidentiary hurdles to justify new drugs will continue to grow. Data from clinical trials alone are no longer adequate to meet the needs of all health care decision makers (e.g., payers and health technology assessment [HTA] agencies, physicians and patients), driving a need for robust, complementary data. However, perceived need to collect real-world clinical, patient-centered, and/or economic outcomes through observational studies varies across countries, stakeholders and organizations. The objective was to better understand how decision makers use observational studies to inform reimbursement and/or market access decisions for new products. **METHODS:** Desktop research identified the types of observational studies most valuable for reimbursement decision making. This project extends a United States (US) payer study by conducting qualitative one-on-one interviews with decision makers across Europe to review the need for real-world evidence. Participants represented national and regional decision makers from several European countries, to identify specific evidence requirements and design attributes most accepted by payers/ HTA advisors and to understand how real-world evidence contributes to the value of a new drug from the decison-makers' perspectives. **RESULTS:** Data from observational studies are used to describe patient segments, understand treatment patterns, resource utilization, and provide effectiveness data that supplement clinical trial data as well as inform risk sharing schemes. Observational studies help inform payer decision making but the validity and robustness of the results is often scrutinized. Publication of observational data in a Tier 1, peer-reviewed journal lends critical credibility to real-world study

results. **CONCLUSIONS:** The current study extends the evaluation into Europe to confirm that as reimbursement decision makers continue to rigorously review new drug therapies, accurate, robust, peer-reviewed published and generalisable real-world data will become particularly important for outcomes- or performance-based access schemes and health care budget management both in the US and Europe.

PHP38

THE SURVEY OF THE JAPAN-STYLE PREMIUM SCHEME IN PHARMACEUTICAL PRICING DECISIONS

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OBJECTIVES: To review the new drugs which were listed in the past on the Medical Fee Schedule of Japan, and to clarify the profile of the quasi value-based pricing in the Japan-style premium scheme. **METHODS:** The information on pricing decisions with premium was searched, extracted, and analyzed from the government documents open to public on the website of the Ministry of Health, Labour and Welfare in Japan. The four drug categories were focused due to data availability: 1) antihypertensive; 2) antidiabetic; 3) antibiotic; and 4) psychotropic, listed from April 1998 through April 2013. The information relevant to the premium decision included listing dates, drug prices, premium categories, premium rates, and also clinical evidence that could be associated with the premium decision. **RESULTS:** Among total 106 of new drugs, 27 have been identified with premium, whilst 79 with no premium. For each category, there existed 12 antihypertensive (single agent), 25 antidiabetic, 52 antibiotic, 17 psychotropic. That is, the acquisition rate of premium for each category was 17%, 20%, 31% and 24%, respectively. The high proportion, 85%,of the rewarded premium categories was recognized in the category of "Usefulness II", i.e., the 3rd ranked premium, while only one drug obtained the premium of innovativeness, the highest ranked premium. Regarding the benefit associated with the premium, both of clinical and humanistic outcomes seemed to be accepted for decision-making although the criteria for the decisions were not clearly indicated. **CONCLUSIONS:** The profile of the Japan-style premium scheme was clarified based on the survey over the new drugs listed in 1998 to 2013. The information extracted in our study will be useful for further investigations to improve the Japanese quasi value-based pricing methods.

PHP39

THE STRUCTURE AND PROCESS OF WORK OF SPANISH REGIONAL COMITTEES ASSESSING MEDICINES: PRELIMINARY RESULTS

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OBJECTIVES: Spain has a decentralized health care systems with several levels of decision-making. After a drug is approved by the Spanish Agencia del Medicamento, regional committees (RC) conduct evaluate and assess those drugs for their use in ambulatory settings making recommendations to health professionals within its territory. The objective of this study is to analyze the structure and process of work of those RC. **METHODS:** RC were contacted by phone and informed about this study. A web based questionnaire was ellabored including questions on: 1) General information of the RC; 2) Procedure of work of RC; and 3) Criteria used for the selection of medicines to asess and the procedures followed to. A link was sent by email to contact persons of the RC of the Spanish 17 Autonomous Comunities (AC). **RESULTS:** To this date 10 RC (59%) have submitted their answers and 3 regions (18%) have responded indicating the absence of this type of structure or process in their region. These 3 regions, though, make recommendations usually conducting their own assessments or using assessments conducted by other regions. 7 RC have a normalized process of work (5 is open to the public). 8 RC have more than 8 members. All RC evaluate medicines prescribed for outpatients purchased through pharmacies (5 of them exclusively), and 5 conduct also assessments of drugs used in hospitals. 9 RC use as comparator the standard treatment for a given indication. Economic evaluation is performed through budget impact (6 RC), cost-effectiveness (5 RC); and cost-minimization (2 RC). 6 RC make public their assessments through public web pages and 2 using electronic bullletins. **CONCLUSIONS:** Preliminary data indicate that the majority of Spanish regions conduct their own drug assessments, and most of them have established RC, whose structure and process of work show some variability and indicate certain degree of duplication.

PHP40

CROATIA'S EU ACCESSION IN THE CONTEXT OF INTERNATIONAL REFERENCE PRICING: WHAT WILL BE THE WIDER IMPACT FOR PRICING AND REIMBURSEMENT?

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OBJECTIVES: To assess the implications of Croatia's accession to the European Union for the pricing and reimbursement landscape both in Croatia and other EU member states, focusing on international reference pricing. **METHODS:** Changes to Croatia's laws governing drug pricing and reimbursement were examined in detail, in relation to their likely effects on drug prices in Croatia and in other EU member states through international reference pricing. The IHS International Reference Pricing Matrix was used to determine impact of Croatian prices on other markets likely to include Croatia in their reference pricing basket. Interviews were conducted with representatives of the pharmaceutical industry in Croatia, and regulators in Croatia and other EU member states, to gauge their views. **RESULTS:** The existence of comparatively low prices of medicines in Croatia is likely to result in some downward pressure on pricing in countries which include all EU countries in the IRP basket of countries. However, this impact is not likely to be felt immediately, and only for the few therapeutic areas where Croatia's prices are among the lowest in Europe. Changes to Croatia's international reference pricing basket are unlikely to result in any great changes, although in certain areas, price reductions can be expected. **CONCLUSIONS:** Some downward pressure on prices in other EU markets is likely as Croatia becomes a reference market for IRP, although this is likely to be limited in scope in the short term, with only particular products and therapeutic groups affected. Over the longer term, as more markets add Croatia to their reference-pricing baskets, this pressure is likely to intensify.

PHP41

GENERIC SUBSTITUTION IN IRELAND – THE VIEWS OF KEY STAKEHOLDERS

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OBJECTIVES: The Health (Pricing and Supply of Medical Goods) Act 2013 passed in June 2013 provides for generic substitution in Ireland. The aim of the study was to ascertain the views of the stakeholders i.e. patients, pharmacists and prescribers on generic substitution,prior to the Act's introduction. **METHODS:** Three stakeholder specific surveys were developed to assess knowledge of and attitudes to generic substitution. Convenience samples of health care professionals and patients were gathered until data saturation was achieved. Descriptive quantitative and qualitative analysis was undertaken. **RESULTS:** A total of 742 health care professionals and 330 patients responded. The study highlighted 4 areas where prescribers and pharmacists differed; (1) Prescribers ranked cost-savings as the most important information to impart to patients while pharmacists advocated therapeutic equivalence as highest. (2) Pharmacists considered that more patients would be agreeable to generic substitution (52%) as compared to 41% of prescribers. (3) Prescribers considered that generic substitution would have a greater effect (25%) on patient care than pharmacists (14%). (4) 19% of prescribers supported generic substitution in all cases and 76% with some exceptions, compared to 16% and 84% for pharmacists respectively. More than 80% of patients were on between 1 and 8 medicines daily, and of these >50% reported that they were on generic medicines. More than 80% would be happy with generic substitution, while more 75% of those interviewed considered generic drugs to contain the same drug, to be as effective and as safe as branded medicines. **CONCLUSIONS:** To prevent possible confusion and concern among patients it is important that health care professionals acquire the necessary tools and knowledge to manage transition into and rollout of this new system, so that they can work together to ensure the obvious benefits of the new system are maximised.

PHP42

AN ANALYSIS OF PRISCRIPTION AND REIMBURSEMENT OF POTENTIALLY INAPPROPRIATE MEDICATION (PIM) IN A GERMAN PRACTICE NETWORK

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OBJECTIVES: Potentially inappropriate medication (PIM) in the elderly increases the risk of adverse drug reactions (ADR) and consequently has an impact on both patients' quality of life and health care costs. In 2010, the PRISCUS list was published in Germany to identify PIM and to propose adequate substitution medication. The objective of the study was to assess both the prevalence and reimbursement of PIM in a German practice network applying the PRISCUS list. Moreover, costs for proposed surrogates were evaluated. **METHODS:** Patients fulfilling the following criteria were included: (1) insured at the local health fund AOK Bavaria, (2) treated by physicians of the practice network, and (3) aged ≥65. Data was provided from AOK Bavaria and contained 214,177 anonymized prescriptions between Q1/2009 and Q4/2011. Information included age, gender, date of prescription and ATC-Code. Since no information on dosage or package size was given, medication and its application duration were differentiated in acute and long-term medication by expert opinion. Costs were calculated by applying the concept of DDD. **RESULTS:** On average, 16.0% of the patients received at least one PIM prescription each quarter. 13,736 prescriptions were classified as PIM (6.4%; 68.7% to women). Out of these, psycholeptics such as Zopiclon (11.8%) and calcium antagonists such as Nifedipin (7.9%) were prescribed most frequently. Total costs of PIM-prescriptions were calculated to be 446,430€ (mean 40,585€ per quarter; min. 32,869€; max. 50,024€). When assuming prescription of surrogates, costs varied between 267,990€ and 935,826€. **CONCLUSIONS:** PIM represents both a medical and economic burden to the German health care system. From an economic perspective, substitution of PIM may result in cost disadvantages. Thus, there is little economic incentive for health insurances to further promote the substitution of PIM. Future research should take a broader perspective and include costs of PIM-related ADR to fully evaluate the economic impact of PIM in the elderly.

PHP44

HOW DOES PRESCRIPTION OF GENERIC DRUGS SPREAD OUT?: DATA MINING AND VISUALIZATION BY USING PRESCRIPTION DATA FORM ACUTE CARE HOSPITALS NATIONWIDE

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OBJECTIVES: To clarify the spread with prescription of generic drugs and the shift from brand drug market by using nationwide administrative data. **METHODS:** For the sample, out of 30 drugs seen as the parameter for generic drugs in France, 27 have been selected after considering their availability in Japan. For those drugs unapproved in Japan, they were replaced by other drugs with the same effects, and anticancer agents as well as radio contrast agents were added. New drugs listed to National Health Insurance list around the same time were also included for comparison. Database was created by extracting the data of patients who were

prescribed those drugs from DPC/PDPS data collected between 1st April 2010 and 31st March 2012 at 1139 of acute care hospitals in Japan. Hospitals were classified into five categories (university, private, publi, social insurance group, and others). SQL Server 2008 R2 was used for data handling, R for data analysis, and ArcGIS for statistical analysis of geography. **RESULTS:** Generic drugs were least used amongst almost all types of drugs in university hospital and social insurance group. For prescription of generic drugs, private hospital was the most proactive, followed by public hospital. It was revealed, thorough comparison between 20% of medical care institutions that are the most proactive towards introduction of generic drugs and 20% of the least proactive, that the shifting progress was slower in bigger size medical care institutions. **CONCLUSIONS:** This study indicated that for effective promotion of generic drugs, it is important to establish plans for changing the policy of medical care institutes, which are amongst the bottom 20% of introduction rate, where a policy maker does not shift to generic drugs even in the area of expensive drugs such as anti anticancer agents and radio contrast agents.

PHP45

HEALTH TRANSFORMATION PROGRAM IMPACT ON IMPORT AND LOCAL PHARMACEUTICAL CONSUMPTION IN TURKEY

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OBJECTIVES: Health Transformation Program(HTP) started in year 2003 by MoH of Turkey. All health system changed dramatically. It had impact on all health consumptions and expenditures. The aim of this study is to show the impact of HTP on the imported pharmaceuticals(IP) and local manufactured pharmaceutical(LMS) sales in Turkey. **METHODS:** Pharmaceutical retail sales data in units and volume(US$) from year 1998 to 2012 were retrieved from IMS Dataview. Local and import consumption trends were reviewed. The data was analyzed with Microsoft Excel 2010. **RESULTS:** Total unit sales were 689M in 1998, 698M in 2002 and 1768 M in 2012; after 10 years of HTP. Total sales were 1937M, 2526M and 8000 M USD for the same years, respectively. Between 1998 and 2012, CAGR(Cumulative Annual Growth Rate) of unit sales was 7%, while the majority of this growth came from HTP(9,7% after HTP vs 0,3% before HTP). There was no significant change in unit sales between 1998 and 2002; total CAGR was 0,3%. Sales between 1998 and 2012 in USD had an average growth rate of 10,7%. Comparing CAGR for before and after HTP; LMP was 1,5% before and 7% after while IP showed an inverse ratio with the total and LMP values and was 23,5% and 13,1% before and after. In the beginning of the 15 years period market share for local manufacturing 92,6% in units and 80,8% in USD; in 2002 dropped down to 88,8% in units and 65,7% in USD, and finally in 2012 to 75,2% in units and 49,8% in USD. **CONCLUSIONS:** The percentage of IP both in units and volume increased in years. This increase may be caused by different reasons, particularly new oncology and biotechnology molecules. It was observed that the volume increase in IP or decrease in LMP was limited by the HTP.

PHP46

UNDERSTANDING PATTERNS OF MONITORING OF APPROPRIATE PRESCRIBING IN EUROPE

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OBJECTIVES: To analyse the current requirements and patterns for drug use monitoring in Europe and highlight new ways for pharmaceutical companies to meet these requirements **METHODS:** We combined three methods of data collection to characterise current requirements and patterns for drug use monitoring: 1) review of official reports by European agencies; 2) analysis of data elements on the European Medicines Agency (EMA) website; and 3) interviews with experts from pharmaceutical companies, facing requirements for conducting drug utilisation studies (DUS). **RESULTS:** The recent Good Vigilance Practice (GVP) established a clear regulatory framework for drug safety monitoring and calls for the assessment of the effectiveness of risk minimisation measures (RMMs). This should include the evaluation of their implementation and outcome. DUS provide simple metrics for monitoring of appropriate drug use, and thus the implementation of RMMs. We identified 28 drugs with DUS in their risk management plan and an additional 23 DUS requested by EMA. We observed a top total number of requests for DUS in the fields of contraception (n=10), infectious diseases (mainly HIV and hepatitis) (n=8) and diseases of the metabolism (mainly diabetes) (n=6) and less for other therapeutic areas. The main reasons for DUS requests were monitoring of off-label use (n=30) and new safety concerns (n=27). Experts confirmed an increasing demand for DUS. In order to optimise the RMMs, repetitive DUS in different points in time are necessary. This study analyses DUS' critical data elements allowing for the automation of such measurements. **CONCLUSIONS:** Current and future EMA practice for DUS seems to focus on new active substances, particularly in diseases of high public health relevance and infectious diseases. To meet this demand, pharmaceutical companies are required to propose more repetitive measurements of the drug use. This study identifies data elements allowing for the automation of such measurements.

PHP47

CATCHING THE LOW-HANGING FRUIT IN MEDICINES OPTIMISATION

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OBJECTIVES: The medicines bill in high income countries accounts for approximately 17% of total health care expenditure. However, around $500 million could be saved a year worldwide by optimising medicines use. This study aims to scope the evidence on the effectiveness and cost-effectiveness of interventions to address suboptimal use of medicines and pinpoint the evidence gaps to prioritise future research. **METHODS:** Systematic searches (up to February 2013) of the NHS Economic Evaluation Database, the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects for systematic reviews on effectiveness or cost-effectiveness and for primary research on cost-effectiveness of interventions. Studies in English set in any country were included. **RESULTS:** Of the 646 records found, 108 studies met the inclusion criteria (29 cost-effectiveness studies (CES) and 81 systematic reviews on effectiveness (SRE)). The majority of CES addressed adherence (55%), followed by inappropriate prescribing (31%) and prescribing errors (28%). No studies addressed the full medicines pathway. A similar picture emerged for SRE at 67%, 15 and 11 respectively. Among the 15 types of outcomes used in CES, the top three were clinical (31%) measures of adherence (21%) and quality-adjusted life years (17%). In SRE, hospitalisations (43%), measures of adherence (23%) and mortality (21%) were the most frequent. **CONCLUSIONS:** Interventions to improve suboptimal use of medicines tend to be specific to a particular aspect of the pathway and/or to a particular disease area. Little consideration is made on how to improve medicines use in patients with co-morbidities and poly-medication. The medicines pathway is rarely examined holistically but in a fragmented manner, making it difficult to draw conclusions on which aspect of suboptimal use of medicines should be prioritised for investment.

PHP48

THE EFFECT OF REDUCED OR REMOVED COPAYMENTS FOR PRESCRIPTION MEDICINES ON ADHERENCE – A SYSTEMATIC REVIEW

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OBJECTIVES: To examine the effect of removal or reduction in prescription copayments, in the absence of disease management plans, on adherence to prescription medications. **METHODS:** Six electronic databases were systematically searched for relevant articles, along with hand searches of references in review articles and the included studies. Studies were included if they involved an intervention which reduced or removed copayments and if the outcome was objectively measured adherence. Study designs permitted were randomised controlled trials, time series analyses, controlled before/after studies and cohort studies. Studies were excluded if the intervention was part of a disease management plan. Study exclusion, data extraction and quality appraisal were carried out by two independent reviewers. Data were qualitatively synthesised. **RESULTS:** Nine out of 40 studies were included. One study was an RCT; the remainder were all controlled before/after studies. There were 144,991 cases and 125,057 controls in this review. The mean age was 54.39yrs and 55.21yrs for the cases and controls respectively. 44.79% of the cases were female, whereas 49.54% of the controls were female. Four studies analysed the effect of reduced copayment, 4 studies analysed the effect of a removed copayment and 1 study analysed both. Only one study received a strong quality assessment, one study was rated as moderate, and the remainder were rated as weak. Seven studies showed a significant improvement in adherence. Two studies did not show an improvement in adherence. **CONCLUSIONS:** This review concludes that there is some evidence of small increases in adherence on the removal or reduction of copayments. However, confounders and biases between the included studies were variable. Future studies should concentrate on establishing associations between reduced cost-sharing and clinical and economic outcomes.

PHP49

PREVALENCE OF PHYSICIANS CAUSING POTENTIAL DRUG INTERACTIONS IN AMBULATORY CARE IN SWITZERLAND: A REPRESENTATIVE NATIONAL SURVEY

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OBJECTIVES: No representative data on the quality of drug prescription exist in Switzerland. We analysed potential drug interactions (PDI) in primary care based on prescription data from 2010 from three large health insurers. **METHODS:** In our study population we identified based on the national drug formulary 494 drug-drug interactions (DDI) classes. Of those, 41 were from drug interaction severity classes I (contraindicated) and II (potentially contraindicated) and classified as PDI. PDI were calculated for two indicators with different denominators, 1) the total number of DDI and 2) the total number of patients potentially exposed to a PDI. For each physician we calculated the probability that the number of caused PDI was unlikely (p-value between 0.05 and 0.01; 'problematic prescription behaviour') and very unlikely (p-value <0.01; 'likely problematic prescription behaviour') to be explained by chance. **RESULTS:** Of 3.13 million individuals 1.34% were exposed to at least one PDI; figures increased to 3.78% and 4.40% in females and males aged ≥70 years. Of 20,710 physicians 42% caused at least one PDI. With DDI being the denominator 6.2% und 3.4% of general practitioners and 0.9% und 0.5% of specialists were classified with a 'problematic' and 'likely problematic prescription behaviour'. With the patient population being the denominator between 0.96% and 6.22% of physicians from all specialty groups had caused a PDI that was classified as 'likely problematic' (p-value <0.01). When combining both indicators 457 of 20'720 physicians (2.2%) had a prescription behaviour causing a PDI that in comparison to peers was highly unlikely to be explained by chance (p-value <0.01). **CONCLUSIONS:** A total of 2.2% of physicians in primary care prescribe during one year at least one drug combination that is classified as PDI. A linkage to other data sources would be needed to further classify PDI that put patients at serious risk for adverse drug reactions.

PHP50

A SYSTEMATIC EVALUATION OF DRUG-DRUG INTERACTIONS IN PRESCRIPTIONS; FACTS AND COMPARISONS

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OBJECTIVES: The study focus was to evaluate and compare the prescriptions for the encountered potential drug-drug interactions (pDDIs) and their different levels on the basis of onset, severity and documentation status, in a tertiary care hospital and community pharmacies in Bahawalpur, Pakistan. **METHODS:** Total 800 prescriptions, 400 from a tertiary care teaching hospital and 400 from community pharmacies, fulfilling inclusion criteria were collected thrice a week during a period of three months and were analyzed for potential drug-drug interactions using dug digest database, drug interaction checker of www.drugs.com and reference text

Drug Interaction Facts. **RESULTS:** A highly significant difference was observed between the prevalence of pDDIs in prescriptions from hospital (45%; 180 out of 400 prescriptions with at least 1 pDDI) and community pharmacies (29.25%; 117 out of 400 prescriptions with atleast 1 pDDI). On the whole, out of total 543 pDDIs (hospital = 337; community = 206) majority of them were of delayed onset (hospital = 50.44%, community = 44.66%), moderate severity (hospital = 57.87%, community = 42.72%), suspected type (hospital = 27.6%) and possible documentation (community = 14.08%). Most of the prescriptions (hospital = 80%; community = 83%) contained 2-4 medicines. The interacting combinations such as aspirin-clopidogrel omeprazole-clopidogrel and digoxin-furosemide (in hospital); isoniazid-rifampin and tramadol-escitalopram were found to be frequently involved in major interactions. The findings showed that cardiovascular drugs were involved in most of the rapid pDDIs (in hospital = 32.46%; in community = 33.33%) and respiratory system drugs were associated with majority of established documented pDDIs (in hospital = 16.67%; in community = 42.86%). **CONCLUSIONS:** Drug-drug interactions in prescription medicines were observed in high percentage both in hospitals and community pharmacies. Clinical practices must be standardized as rational prescribing practices.

HEALTH CARE USE & POLICY STUDIES – Equity and Access

PHP51
UNMET HEALTH NEEDS OF IMMIGRANTS LIVING IN GREECE DURING THE ECONOMIC CRISIS: THE LONG-TERM IMPACT FOR THE HEALTH CARE SYSTEM

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OBJECTIVES: To examine access of migrants in health care services, their unmet health needs, and the factors associated with these. **METHODS:** A cross-sectional pilot study was conducted from January to May 2013. The study population consisted of 231 recent immigrants living in Greece. A questionnaire was developed including information about demographics, health status, difficulties in health services access etc. Statistical analysis included Pearson's x^2 test, x^2test for trend, student's t-test, analysis of variance and Pearson's correlation coefficient. **RESULTS:** Almost half of the participants (n=115, 49.7%) used public health services in the last 12 months in Greece. Among them, 56.8% (n=131) used emergency department services. A considerable proportion of the participants (n=144,62.3%), during the last year, needed at least one time to use health services but they could not afford it. The most important reasons for that were high cost of health care (n=80, 34.5%) and the long waiting lists (n=29, 12.6%). More than half of the participants (n=122, 52.9%) reported that they had major difficulties in accessing health services. Increased family monthly income was associated with decreased difficulties in access in health services (x2 test for trend=32.1, p<0.001). The use of preventive services has been limited since more than 60% of the women 40+ reported not having conducted a pap test or a mammography, while more than 30% of the respondents were not subjected to a blood test or a cholesterol examination. **CONCLUSIONS:** Barriers to health services access for migrants may lead to decreased use of health services, especially primary, and thus lead to increased hospitalizations and higher cost in the longer-run. Formulation of policies to improve access and use of health care services are necessary.

PHP52
IMPORTANCE OF SUBGROUP ANALYSES FOR HEALTH TECHNOLOGY ASSESSMENTS

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OBJECTIVES: Cost effectiveness analyses play a critical role in determining coverage of novel drugs and devices. Increasingly, payers are demanding subgroup analyses to determine indications which would be covered by the national health system or insurance agency. **METHODS:** To understand and review trends in the use of subgroup cost effectiveness analysis, we analyzed NICE HTAs for products approved between 2011-2012. Manufacturer submissions for CEA were compared to final review and decision by HTA agency. Analogs were identified and case studies were developed to further understand the use of subgroup analyses and cost effectiveness models. **RESULTS:** Decisions made by NICE in 2011-2012 show increasing trends towards the use of subgroup analysis for determining indications for coverage by national payer bodies. Between 2011-2012, 80% of the assessments included subgroup analyses. Approximately half of them included cost effectiveness analyses for various subgroups. Interestingly, the ICER values estimated by NICE for the same subgroups showed a large variation (1X-3X fold difference) compared to ICER values estimated by manufacturers. Selected case studies highlighted that for several products, NICE is recommending treatments only for subgroups whose ICER values are within the cost effectiveness threshold. **CONCLUSIONS:** New products need robust broader population and subgroup analyses for insurance coverage.

PHP53
CHRONIC PATIENTS' ACCESS TO PHYSICIANS SERVICES IN TIMES OF ECONOMIC CRISIS

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OBJECTIVES: To explore the magnitude of certain access barriers to physician services that chronic patients are in front of as well as which patients are more vulnerable to such restrictions. **METHODS:** A cross-sectional study was conducted in 1600 chronic patients suffering from diabetes, hypertension, COPD and Alzheimer. Logistic regression analysis was carried out in order to explore the factors related to economic and geographical barriers in access, as well as the determinants of barriers imposed by waiting lists. **RESULTS:** A total of 25% of chronic patients face geographical barriers while 63.5% and 58.5 % of them are in front of economic and waiting list barriers, respectively. More likely to face economic barriers in access are unemployed patients [coef.0.55; 95% CI (0.1, 1)] and patients with low income [-0.2; 95% CI (-0.26,-0.13)] and lower educational level [-0.04; 95% CI (-0.08, 0)]. Women [0.22; 95% CI(0.02,0.42)], low-income patients [-0.13 ; 95% CI(-0.2, -0.06)], and patients with lower health status [-0.02 ; 95% CI(-0.02,-0.01)] are more likely to be in front of geographical barriers in access. Moreover, all occupational categories examined, demonstrate a statistically significant positive relationship with the probability of geographical barriers occurrence. In addition, unemployed patients [0.51; 95% CI (0.06, 1)], public or private sector employees [0.45; 95% CI (0.09, 0.81)] and low income patients [-0.086; 95% CI (-0.15, 0.02)] are more likely to deal with barriers attributed to waiting lists. **CONCLUSIONS:** Chronic patients face extensive barriers in access, which can mainly be explained by the fall of income, the rise of unemployment and the policy of decreasing the supply of certain health services in order to reduce health expenditure. If such barriers won't be minimized inequalities will be enlarged and chronic patients' health status will be worsened which might lead to increased future costs and adverse effects on health expenditures.

PHP54
QUALITY ASSURANCE OF FOURTH HURDLE CONCERNING TO DRUGS AND MEDICAL DEVICES

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OBJECTIVES: From 2011, there are basic thresholds (λ1=24 x average monthly salary € / QALY and λ2 = 35 x average monthly salary € / QALY) defined directly in the Slovak legislation reflecting the benefits displaced elsewhere in the Slovak health care system when funds are allocated to new medicines and medical devices. The objective of this study was to analyse the quality of submitted economic studies, related critical appraisals process and impacts of the new legislation on the access to medicines and medical devices. **METHODS:** We created a working group to review previously submitted economic evaluations and related critical appraisals in order to identify potential technical and methodological problems. The working group scrutinized previous submissions and critical appraisals, concerning to chosen ATC groups of drugs and groups of medical devices, published between June 2012 and June 2013 at the webside of MoH. **RESULTS:** Pharmacoeconomic evaluations of drugs and medical devices within decision making process concerning to reimbursement are mandatory but the quality of studies are very often rather poor. The concept "the QALY is a tool not a rule" was slightly modified in Slovakia. Our analysis shows that implicit thresholds included into the Slovak legislation have influenced decision-making process concerning to drugs and medical devices. In the defined time period 4 drugs exceeded the basic thresholds described in the Slovak legislation, however 108 drugs and medical devices were refused to include into the reimbursement list, because of the poor quality of provided pharmacoeconomic studies from the side of applicants. **CONCLUSIONS:** The transparent method of HTA can improve the consistency of reimbursement decisions making related to drugs and medical devices in Slovakia. However significant improvements in the quality of submitted pharmacoeconomic dossiers have to be the first step towards the better access to drugs and medical devices for the Slovak patients.

PHP55
THE HYBRID PURCHASER-PROVIDER SPLIT IN ENGLAND: SHOULD EUROPE FOLLOW SUIT?

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OBJECTIVES: Developed countries have embraced the purchaser-provider split as a mechanism to improve health resource allocation and outcomes. With the emergence of Clinical Commissioning Groups (CCGs) as both buyers and providers of health services a hybrid purchaser-provider model is being explored. This research explored the opportunities and challenges of this model and analysed the implications for NHS England and Europe. **METHODS:** Eighty influential regional and national payers involved in the NHS England reforms took part in 1-hour tele-depth interviews to better understand the changes and uncertainties before the reforms were implemented. This research was re-visited three months post implementation in an advisory board setting to externally validate our findings and identify case studies for further analysis. **RESULTS:** NHS payers stated that they were still 'broadly optimistic' about the re-allocation of purchaser responsibilities to CCGs. One case study illustrated that greater clinician involvement provided opportunities to redesign services like respiratory care and allocate funding more efficiently between acute and primary care. Initial success stories include the creation of primary care diabetes clinics and Pharma-NHS local partnerships to help reduce hospital activity. Within the advisory board, payers voiced concerns with this hybrid model. Questions raised from the meeting included: 1) How do we equip GP commissioners with the right skill set to draft and negotiate hospital contracts? 2) How can we help GP commissioners and GP providers to help minimise potential conflicts of interest? **CONCLUSIONS:** The purchaser-provider model implemented in England presents a new way to tackle reduced financial budgets and need to improve health outcomes. The results of this research suggest that the purchaser-provider model has the potential to make a difference for patient care. A number of challenges appear to still be present and it will be important to address these in order for the UK and other countries to further explore its benefits.

PHP56
CURRENT STATUS AND EVIDENCE OF EFFECTS OF E-PRESCRIBING IMPLEMENTATION IN UNITED KINGDOM, ITALY, GERMANY, DENMARK, POLAND AND UNITED STATES

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OBJECTIVES: Electronic-prescribing (E-prescribing) in comparison to manual ("by hand") generation, transmission and filling of prescriptions is thought to substantially lower the risks of inaccuracy and therefore reduce associated health care resource use and costs. The purpose of this work is to describe the current state of e-prescribing systems implementation in Denmark, Germany, Italy, Poland, United Kingdom (UK) and United States (USA), and to assess present evidence of its influence on health care. **METHODS:** A systematic review supplemented by additional hand-search was conducted to find relevant articles. Medline, Embase, The Cochrane Library and Scopus were searched. Quality was assessed on the basis of PRISMA, MOOSE and STROBE checklists and West 2002 recommendations. **RESULTS:** Thirty-one relevant full texts were identified during systematic review, and then as a result of hand-search, 5 publications were added. E-prescribing varies considerably across these countries. It is currently voluntary in Germany, Italy and United States. In United Kingdom the system is implemented except for electronic signature. In Denmark e-prescribing is mandatory for primary care providers. Model implementation in Poland is expected to take place in 2014. Of these 36 sources, 4 articles assessing e-prescribing were of the highest quality, as judged using the assessment methods. Positive influence on medical visits frequency, quality of care, patient satisfaction, prescription errors frequency, and prescriber-pharmacy-patient communication was described in literature; most studies were conducted in the UK and USA. No data about effects of implementation for Germany, Italy, Denmark and Poland were found. **CONCLUSIONS:** Implementation of e-prescribing is in process in the majority of described countries. Although few studies exist that definitely demonstrate positive impact of e-prescribing on health care, gathered papers do indicate positive effects. More comprehensive assessments would be valuable in showing the attributes of e-prescribing that are most valuable, and those that may be strengthened.

PHP57

MODELS OF DRUG SAFETY MONITORING IN ENGLAND, POLAND, ITALY, GERMANY, DENMARK AND UNITED STATES

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OBJECTIVES: To review, describe and assess models of drug safety monitoring in England, Poland, Italy, Germany, Denmark and in the United States and prepare recommendations useful in health authorities decision-making process. **METHODS:** A review of documents, materials and information published on national medicines agencies as well as WHO's statements was conducted, supplemented by hand-search of literature. **RESULTS:** The advantages and disadvantages of described pharmacovigilance schemes in selected countries has been discussed. The gathered data, related i.a. to the level of adverse drug reaction reporting in different countries, was used to assess the efficacy of national reporting process. Moreover our research allowed us to value the formula of pharmacovigilance schemes as well as the attitudes of health care professionals and patients towards it. **CONCLUSIONS:** Although the majority of compared countries are European Union members bound to respect the same acts of European law, there are still many significant differences met in Pharmacovigilance practice reflecting in the level of adverse reaction reporting. These differences may be found as the treatment of newly registered medicines, data availability and transparency of procedures within the agencies or the relationship between health authorities and potential reporters. A set of recommendations has been prepared related to special treatment of new medicines, creating awareness of importance of pharmacovigilance in health care (hospitals, pharmacies), changing the attitude to risk aspects, transparency of safety monitoring practice and patients' enrollment. The implication of our proposals could help to amend the pharmacovigilance systems in all discussed countries.

PHP58

SPECIFIC ATTRIBUTES OF PHARMACEUTICAL CARE IN ENGLAND, POLAND, GERMANY, DENMARK, ITALY AND UNITED STATES

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OBJECTIVES: To describe existing models of pharmaceutical care (PC) in England, Poland, Germany, Denmark, Italy and United States and to indicate similarities and specific attributes meant as differences (from the whole system point of view), identifying possibly promising solutions (promising means having preliminary or probably positive results described in found literature). **METHODS:** A systematic and non-systematic literature review in Medline, Embase, Scopus and the Cochrane Library was performed. Quality of publications was critically appraised. **RESULTS:** The review identified 48 full texts. The majority of papers were of moderate quality (PRISMA, MOOSE or STROBE checklists) and intermediate consistency, coherence and strength (West 2002). In chosen countries differences in the definition of PC have been noticed and therefore often it is difficult to find similarities. Although in some countries like England and the US, PC is firmly established and comparable with one another, in other it is very heterogeneous. Mainly in Central and Eastern Europe (CEE), especially in Poland, it is offered to a very limited extent or only pilot implementations exist. Four types of PC models have been distinguished: Anglo-Saxon, Scandinavian, German and Italian. Specific attribute of English PC is division into essential, advanced and enhanced services. American pharmacists providing this service must be highly specialized. Danish system focuses on identifying, solving and prevention of drug-related problems. In Germany family pharmacy concept emerged. Pivotal point of Italian system is hospital PC. Identified promising solutions found in some countries were i.a. Drug Utilization Review, disease management programs or medicines use review. **CONCLUSIONS:** Identical PC concept may be difficult to introduce in all EU Member States, due to differences in health systems. However, some identified, promising actions should be considered by decision makers and providers, as well as implementing PC to a sufficient extent in CEE countries.

PHP59

WHICH ARE THE ATTITUDES OF PRIMARY HEALTH SERVICES USERS CONCERNING COST SHARING MEASURES IN A PERIOD OF ECONOMIC CRISIS IN GREECE?

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OBJECTIVES: To identify the extent to which patients accept the measure of cost sharing fee (5€) in public primary health care units (health centers and hospitals' outpatient departments) as well as to investigate whether patients perceive the potential benefits of the measure for the quality improvement of provided health care. **METHODS:** The study population consisted of 1260 people, who used public primary health care units. A structured questionnaire was used, including questions for patients' demographic characteristics, their attitude regarding the cost sharing mechanism (compliance, perception of the benefits for health services upgrade etc), and their level of satisfaction with the provided services. **RESULTS:** The implementation of cost sharing mechanism was positively accepted by 30% of respondents. Approximately 90% of the respondents, who expressed positive opinion for the implementation of the mechanism, considered that it would provide financial support to health units. Among the respondents who expressed negative opinion for the measure, 95% believed that health services should be public and free for everyone, 83% expressed lack of confidence that the measure aims at upgrading the provided services, 78% believed that the insurance contributions they already pay are high and 67% stated no financial comfort. The negative opinions were more frequent among people with lower socio-economic profile and those who have used health centers ($p<0.06$). Respondents with higher socio-economic profile, coming from urban areas and respondents who were very satisfied with health services had statistically significantly greater possibility to express positive opinion for the measure. **CONCLUSIONS:** Low socio-economic profile is negatively associated with the acceptance of the implementation of cost sharing mechanism, while high satisfaction with services is positively associated with the acceptance of the mechanism. The majority of those, who expressed positive opinion for the measure, consider it as a contribution to the enhancement of health services.

PHP60

FINANCIAL INCENTIVES IN HEALTH CARE: EVIDENCE OF UNINTENDED CONSEQUENCES

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OBJECTIVES: Financial incentives or Pay-for-Performance (P4P) have become a common approach to improve the quality in health care. Although the effectiveness is mixed, more and more P4P initiatives are implemented. Besides the desired effects of quality improvement, a growing number of evaluations show that financial incentives lead to unintended consequences. Therefore this study analyses negative effects of P4P. **METHODS:** On the basis of a systematic review of systematic reviews regarding P4P in health care (nine systematic reviews included that evaluate 75 different primary studies; Methodological quality assessment using the AMSTAR checklist) an additional hand search was conducted to identify evidence of unintended consequences of P4P. **RESULTS:** Both theory and evidence of financial incentives demonstrate the potential of negative effects. Risk selection is identified in six reviews: Patients could get selected due to their severity of illness in order to achieve quality targets with minimum effort (cherry picking); Physicians will focus on indicators or aspects of care that are linked to payments (teaching to the test). Focussing on incentivized indicators could lead to quality decrease in non-incentivized indicators (negative spillover effects), assessed in four reviews. Five reviews show that physicians could game the P4P program by reporting incorrect results and therefore increase their payments (gaming). Furthermore, improvements can be the result of better documentation and not actual quality improvements (four reviews). Finally one review identified crowding out of intrinsic motivation due to financial incentives. **CONCLUSIONS:** The available evidence shows that P4P can result in unintended consequences. Evaluations of P4P should include these effects in order to assess an overall effect and thereby determine the effectiveness of P4P. To avoid negative effects it is important to consider the potential of unintended consequences and develop appropriate solutions.

PHP61

GEOGRAPHICAL INEQUALITIES IN THE ACCESS TO AND UTILIZATION OF HOME CARE (NURSING) SERVICES IN HUNGARY

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OBJECTIVES: Home care (nursing) was introduced into the Hungarian basic health insurance package in 1996. The aim of our study is to analyze the geographical inequalities in the access to and utilization of that services in Hungary. **METHODS:** Data were derived from the nationwide administrative dataset of the National Health Insurance Fund Administration (OEP), the only health care financing agency in Hungary. The geographical inequalities in home care (nursing) services were measured by the number patients, visits and reimbursement according to 20 Hungarian counties. We analyzed the year 2011. **RESULTS:** The national average number of patients was 51 patients / 10000 population. We found the highest patient number in county Zala (67), Jász-Nagykun-Szolnok (63) and Baranya (62), while the lowest number in county Békés (43), Somogy (43) and Szabolcs-Szatmár-Bereg (28). The national average number of home visits was 1193 visits / 10000 population. We found the highest number of visits in county Nógrád (1494), Tolna (1385) and Fejér (1377), while the lowest number in county Somogy (1138), Csongrád (1106) and Szabolcs-Szatmár-Bereg (678). The national average of reimbursement per patient was 65345

Hungarian Forint (HUF) or 234 Euro (EUR) / patient. We found the highest reimbursement per patient in county Nógrád (87879 HUF, 315 EUR), Fejér (80851 HUF, 290 EUR) and Békés (77643 HUF, 278 EUR), while the lowest reimbursement county Budapest (58859 HUF, 211 EUR), Jász-Nagykun-Szolnok (55757 HUF, 200 EUR) and Zala (54924 HUF, 197 EUR). **CONCLUSIONS:** We found significant differences measured by all the three indicators in home care (nursing) services in Hungary. Our results revealed that there are important inequalities both in the access to and utilization of home care services.

PHP62

SELF-REPORTED POPULATION HEALTH: AN INTERNATIONAL PERSPECTIVE BASED ON EQ-5D

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OBJECTIVES: General population EQ-5D health surveys have been accumulated in the EuroQol Group's archive over the past two decades. Using the database as a source of standardized measure of self-reported health, the objective was to estimate the level of health (EQ-5D population norms) and the distribution of health within populations along socio-demographic characteristics. **METHODS:** Analyses captured EQ-5D data on 163,838 individuals from 18 countries with nationally representative population surveys. Descriptive statistics were used to provide EQ-5D-3L population norms by age and gender categories for EQ VAS, EQ-5D index values, and for the 5 dimensions for each country. Odds ratios and the health concentration index methodology were used in the socio-demographic analysis of EQ-5D data. **RESULTS:** The mean EQ-VAS rating varied from 71.1 to 83.7 and from 70.4 to 83.3 across countries without and with age standardization, respectively. Statistically significant inequalities existed in all samples ($p<0.01$) with the EQ-VAS based health concentration index varying from 0.090 to 0.157 across countries. Among the socio-demographic factors, age had generally the largest contributing share, while education also had a consistent role in explaining lower levels of self-reported health. Among the 5 dimensions, usual activities and pain/discomfort were the highest contributors to overall inequalities in most countries. **CONCLUSIONS:** EQ-5D norms can be used as reference data to compare patients with specific conditions and to assess the burden of the disease in question. Inequalities in self-assessed health exist in all countries with different social and cultural backgrounds, deserving the attention of policy makers within each country.

HEALTH CARE USE & POLICY STUDIES – Formulary Development

PHP63

ANALYSIS OF ADVERSE REACTIONS OF MEDICINE IN UKRAINE

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OBJECTIVES: In Ukraine the pharmacovigilance system for adverse reactions is working. In 2008 was received 7,115, 2009 – 8291, 2010 – 8673, 2012- 11674 card-reports of adverse reactions (AR) drugs. MoH conducted a detailed analysis of these reports found that 13% of them experienced serious adverse events, and 0.7% of the cards with the unexpected AR. **METHODS:** We analyzed the side effects depending on the ATC-group drugs. **RESULTS:** We found that antimicrobial agents for systemic use the largest number of reports received on AR (75.4%), which in most cases manifested anaphylactic AR. Further analysis showed that AR often were drugs (by INN): ceftriaxone (12.6%), amoxicillin in combination with clavulanic acid (8.0%), levofloxacin (6.3%). Among the cardiovascular drugs, reports AR often came on enalapril (10.0%), pentoxifylline (9.7%) and amlodipine (8.1%).Among the drugs affecting the nervous system, haloperidol (7.4%), metamizol sodium (7.4%) and paracetamol (7.0%). The analysis showed that the ratio of serious not serious AR under anti-neoplastic drugs and antiretroviral drugs is 1:2, anti-TB drugs - 1:3, and those affecting the cardiovascular system, gastrointestinal tract, respiratory system - under 1:9, 1 : 6, 1:6. Thus, the frequency of serious AR is much higher in the application of anti-neoplastic, anti-HIV and anti-TB drugs.The greatest risk AR was for children aged 28 days - 11 years, especially boys, and adults, especially women aged 46-60 years. **CONCLUSIONS:** Results of the analysis of AR indicate that needed pharmaceutical care when dispensing antiretrovirals, anti-tuberculosis, anti-neoplastic drugs that meet the requirements of Good pharmacy practice in Ukraine. Implementation of training courses and programs for pharmacists on the subject of safe use of drugs to treat infectious diseases, tuberculosis and HIV / AIDS is essential. As well as acquiring skills pharmaceutical care and prevent AR in dispensing drugs to children and women 45-60 years.

PHP64

A 10-YEAR REVIEW OF THE CANADIAN COMMON DRUG REVIEW: PHARMACEUTICAL MANUFACTURERS' SUCCESS RATE

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OBJECTIVES: The Canadian Common Drug Review (CDR) is a national HTA agency that has been in existence for 10 years. During this, the CDR has reviewed the clinical and cost-effectiveness of 188 drugs and provided 269 recommendations to the publically funded drug plans. Of all the drugs reviewed over the past 10 years, 50.4% have received a positive recommendation and 49.6% have received a negative recommendation. The objective of this analysis was to describe the success rate of each pharmaceutical manufacturer in terms of type of recommendation, time to recommendation, and time to listing in the provincial formularies. **METHODS:** The CDR Tracker database was used to analyze all CDR drug reviews from 2003 to the end of 2012. There were a total of 189 reviews during this 10 year period. All manufacturers that had three or more submissions with CDR were included in the analysis; 29 companies met this criterion. **RESULTS:** Of the 189 reviews and 29 companies analyzed, the positive recommendation rates ranged from 100% to 17%. The top 5 most successful manufactures in terms of positive recommendations were Roche (100%), Abbott (100%), Bayer (83%), Gilead (80%), and Boehringer-Ingelheim (80%). The average time to receive a CDR recommendation varied from 170 days to 248 days. The manufacturers with the fastest time to recommendation are GSK, Abbott, Roche, Boehringer-Ingelheim, and Watson. Time to reimbursement / formulary listings in all provinces ranged from 123 days to 593 days. **CONCLUSIONS:** This is the first analysis to describe the success rate of pharmaceutical manufacturers through the CDR. There appears to high variability in all the metrics that were measured and further research into the determinants of variability is warranted.

HEALTH CARE USE & POLICY STUDIES – Health Care Costs & Management

PHP65

IMPACT OF MEDICARE PART D ON PRESCRIPTION USE, HEALTH CARE EXPENDITURES, AND HEALTH SERVICES UTILIZATION: NATIONAL ESTIMATES FOR MEDICARE BENEFICIARIES, 2002 TO 2009

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OBJECTIVES: To investigate the impact of Medicare Part D on prescription utilization, health services utilization, and health care expenditures in the general Medicare population. **METHODS:** A retrospective analysis of Medicare beneficiaries (N=32,228) was conducted using the Medical Expenditure Panel Survey 2002 to 2009 data. Multivariable quantile regression was used to estimate the following outcomes at the 25th, 50th, 75th, and 90th percentiles, adjusting for socio-demographic characteristics: 1) number of prescription fills; 2) out-of-pocket (OOP) drug expenditures; 3) total drug expenditures; 4) OOP health care expenditures; 5) total health care expenditures; 6) number of hospitalizations; and 7) number of emergency department (ED) visits between the pre-Part D (2002-2005) and post-Part D (2006-2009) periods. All expenditures were inflation-adjusted to 2009 dollars. **RESULTS:** In the general Medicare population, Part D was associated with decreases in OOP drug expenditures (-25.7% to -33.6%; $p<0.0001$) and OOP health care expenditures (-22.1% to -24.3%; $p<0.0001$) across all percentiles. Part D was associated with increases in the number of prescription fills across all percentiles (5.8% to 8.4%; $p<0.0001$) but only at the 75th and 90th percentiles for increases in total drug expenditures (75th percentile: 5.5%; 90th percentile: 10.2%; $p<0.0001$). Part D was not associated with changes in total health care expenditures, hospitalizations, or ED visits in the general Medicare population. **CONCLUSIONS:** Part D resulted in increases in medication utilization and reductions in OOP drug and OOP health care expenditures among Medicare beneficiaries, but was not associated with differences in total health care spending, hospitalizations, or ED visits.

PHP66

THE IMPLICATIONS OF DEMOGRAPHIC CHANGES FOR GMS COSTS IN IRELAND THROUGH TO 2026

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OBJECTIVES: The General Medical Services (GMS) scheme presently covers around 40% of the Irish population and entitles them, inter alia, to free prescription drugs and appliances. This paper projects the effects of future changes in population, coverage, claims rates and average claims cost on GMS costs in Ireland. **METHODS:** Data on GMS coverage, claims rates and average cost per claim are drawn from the Primary Care Reimbursement Service (PCRS) and combined with Central Statistics Office (CSO) (Regional and National Population Projections through to 2026). A Monte Carlo Model is used to simulate the effects demographic change (by region, age, gender, coverage, claims rates and average claims cost) will have on GMS prescribing costs in 2016, 2021 and 2026 under different scenarios. **RESULTS:** A total of 100,000 Monte Carlo simulations indicate that GMS medicines costs could rise to €1.9bn by 2026 and will likely fall in the €1.7bn to €2.3bn region. Population is projected to grow by 32% by 2026 and by 96% for the over 70s. The Eastern region is estimated to grow by 3% over the lifetime of the projections at the expense of most other regions. The Monte Carlo simulations project that females will be a bigger driver of GMS costs than males. Those aged 70 and over and children under 12 will be significant drivers of GMS costs with the impending demographic changes. **CONCLUSIONS:** GMS coverage is increasing in tandem with falling public health budgets and poses a threat going forward to the sustainability and funding of the GMS scheme. Our projections and simulations map the likely evolution of GMS cost, given existing policies and demographic trends.

PHP68

VARIABILITY IN PUBLICALLY-PRESCRIBED DRUG COSTS: THE ROLE OF REGION, AGE AND GENDER

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OBJECTIVES: Ireland currently has one of the highest levels of public drug spending per capita in Europe. As budget retrenchment efforts continue, publically-funded drug schemes such as the General Medical Scheme have been the subject of several initiatives to reduce costs in recent years. However, little is known about the regional and socio-demographic factors that may influence variations in prescribing across the state. The objective of this study was to identify these factors. **METHODS:** Using a 192,000-strong sample of PCRS data drawn from monthly GMS returns for 2007, we constructed an ANOVA model that included the main effects of age, gender and region together with their second order and third order interactive terms in an interactive effects regression model examining the role of gender, age category and region of residence in explaining variation in prescribing costs for Ireland. **RESULTS:** Mean cost per person per month was €102. Men were on average more expensive than women (€109 vs. €94) and cost increased with age group (€34 for those 0-12yrs and €169 for those over 75). The most expensive region was the Midlands HSE region (€103) while the North West (€90) was the least costly. Most of the variation in prescribing costs was explained by age, though the relationship between prescribing cost and age category was not constant. A significant three-way interaction was found between age category, gender and region. **CONCLUSIONS:** The regional and

demographic factors underlying the cost of GMS prescribing in Ireland are complex and inter-related. Alternative solutions to the question GMS coverage in the elderly may need to be found soon that prove fiscally and economically sustainable. The large gap in GMS prescribing costs between men and women in early adulthood requires further investigation.

PHP69

THE TRANSPARENCY OF NATIONAL HEALTH CARE COSTS IN THE 'EUROPEAN UNION FIVE (EU-5)'

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OBJECTIVES: Cost-effectiveness analyses play a key role in the reimbursement of health care technologies and require health care resource use (HRU) cost inputs. Inaccuracies in inputs can lead to potentially significant differences in results. Thus, the availability of HRU costs is vital for decision-making. This study's objective is to assess the transparency and ease of access to HRU costs in France, Germany, Italy, Spain and the UK. **METHODS:** A targeted search and contact with country-specific representatives highlighted existing national documentation. A cross-sectional selection of costs were searched for including GP and nurse costs; hospital bed and overhead costs; drug prices; follow-up/out-patient visit costs; and the availability of Diagnosis-Related Group (DRG) codes and tariffs. The transparency and availability of costs were assessed using the following criteria: the date, access restrictions and the need for assumptions to generate cost estimates. **RESULTS:** DRG tariffs were identified for all countries, but the availability of other data varied. Drug prices were obtainable online (such as the website MedicPrix, France), but others required paid registration (Giofil, Italy). The UK had the most accessible primary and secondary care HRU cost data through PSSRU. Italy was the least transparent however AIFA informed us a website reform will increase access to data in 2014. Where not explicit, HRU costs can be indirectly derived from total procedure codes (for example through ATIH, France). Spain and Italy's regional structure made sourcing national cost data challenging, resulting in wide ranges in input costs in published cost-effectiveness analyses. **CONCLUSIONS:** Whilst some nations provided transparent HRU cost data, others did not, causing inconsistent inputs across cost-effectiveness analyses. To minimise inconsistency we propose a hierarchy of evidence for use when sourcing costs: 1) Govt/health service official sources; 2) Official international websites (OECD/WHO); 3) Published economic studies; 4) Published non-economic studies; 5) National expert opinion; and 6) Unofficial websites/sources.

PHP70

A RETROSPECTIVE ANALYSIS OF DRUG REIMBURSEMENT DECISIONS IN IRELAND: A MULTI CRITERIA DECISION ANALYSIS APPROACH

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OBJECTIVES: Standard approaches to economic evaluations based on cost utility analysis are increasingly considered inadequate. While simple and intuitive, it is acknowledged that the QALY alone does not capture all aspects of health benefit. Multi Criteria Decision Analysis (MCDA) has been proposed as a way of incorporating multiple factors influencing the value of a health technology. The objective of this study was to analyse past reimbursement recommendations by the National Centre for Pharmacoeconomics (NCPE) in Ireland in order to identify factors which have influenced decisions in the past. **METHODS:** Based on published literature, national guidelines and experience, a list of potentially influencing criteria was identified. Information on each criterion was extracted for each full pharmacoeconomic assessment conducted by the NCPE. Logistic regression was used to estimate the impact each of these criteria has had on past recommendations. Model fit was assessed using the Deviance Information Criterion and the best fit model was chosen using backwards stepwise regression. **RESULTS:** Between 2006 and May 2013 the NCPE conducted 54 full pharmacoeconomic assessments. Each of these was scored against 14 criteria, which can be grouped into clinical utility, consumer demand, economic incentives, societal perspective and efficiency/affordability. The model of choice identified criteria of each group which impact on reimbursement recommendations. **CONCLUSIONS:** This analysis shows that factors other than cost per QALY have impacted on past valuations of health technologies in Ireland. Since the analysis was carried out retrospectively, these factors have influenced decisions in an informal manner and do not necessary represent the factors which should influence future reimbursement decisions. This approach contrasts with methods used elsewhere to estimate weights for the criteria. The results of this analysis provide a basis for the development of a MCDA approach to HTA in Ireland, which has the potential to improve consistent and transparent decision making.

PHP71

MEDICAL CARDS DURING RECESSION: HOW MANY, FOR WHOM AND HOW MUCH?

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OBJECTIVES: To model the age, gender and regional pattern of GMS coverage rates as they are key determinants of public spending on GMS medicines. **METHODS:** We used PCRS (Primary Care Reimbursement Service) and CSO (Central Statistics Office) databases to estimate GMS coverage rates by age, gender and region in 2010 and 2011. Assuming log-normally distributed incomes we used CSO SILC data to estimate GMS coverage semi-elasticities in 2010. We estimated how much GMS male and female coverage rates in 7 adult age categories and 8 Irish regions in 2010 responded to changing average income levels, income inequality and income thresholds. We tracked how well our predicted GMS coverage rates fitted actual rates in 2011. We simulated the 2011 GMS medicines cost burden of a ceteris paribus repeat of the 2010 changes in income and income-inequality. **RESULTS:** Our modelled coverage rates have high goodness of fit compared to conventional econometric estimates. Coverage income-semi-elasticity ranges from .7 to 2.3, is highest for elderly age cohorts and in the South-East and South-West regions and is similar for males and females. Growing inequality generally increases GMS coverage but pushes some persons aged over 70 above the qualifying income threshold. Repeating 2010 average income in 2011 would increase the 2011 GMS medicines cost by around €110m; repeating the 2010 inequality changes would increase it by a further €105m, ceteris paribus. **CONCLUSIONS:** Fiscal cutbacks during recession induce countervailing increases in the medical card population and the public cost of its medicines. These are the first systematic and detailed estimates – by age, gender and region – of whose medical access is affected and how much the offsetting public cost will increase.

PHP72

THE BURDEN OF DISEASE ATTRIBUTABLE TO PHYSICAL INACTIVITY IN THE AUSTRIAN REGION OF BURGENLAND

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OBJECTIVES: About 52.6% or 125,434 people of the population in Burgenland is physical inactive. As a risk factor for several chronic diseases like cardiovascular diseases, type 2 diabetes, osteoporosis, depression, back-pain, hypertension, breast cancer and colorectal carcinoma physical inactivity can potentially be a substantial public health burden. Furthermore, it is one of the greatest risk factors for global mortality. Hence, the aim of the analysis was to estimate the direct health-care costs saved, the number of diseases and premature death saved each year attributable to a health promotion program focusing on walking ("3,000 steps" more). **METHODS:** The evaluation of the health-economic impact was performed using a cost-of-illness analysis. We have used relative risk (RR) estimates from the literature to evaluate the effects of physical inactivity on the above mentioned diseases. Afterwards, the population-attributable fraction (PAF) for each illness to estimate the risk factor on the given disease was computed. Direct medical costs were considered from the health care system perspective. Costs were calculated bottom-up for the year 2012. We have calculated effects of a reduction in inactivity level by 10,000 physical inactive people in Burgenland. **RESULTS:** Results show that physical inactivity causes 27,542 cases of illness as well as 50 premature deaths in population of Burgenland, leading to a total cost-of-illness of 58.9 million Euro (6.3% of total health expenditure). Reducing the inactive group by 10,000 people, 2,221 cases of illness and cases of death will be reduced by four. Moreover the cost of illness could be reduced by 6.40 million Euro each year of which 5.03 million Euro are directly related to diminish physical inactivity. **CONCLUSIONS:** Physical inactivity represents an important public health burden in Austria. Even modest reductions in inactivity levels could result in substantial cost savings.

PHP73

THE IMPACT OF THE BLIND BID PROCEDURE IN HUNGARY

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OBJECTIVES: The modified reference price procedure, which was introduced in October 2011, caused significant savings in the Health Insurance Fund's Pharmaceutical budget. In our analysis we aim to give an insight into the effects of this measure on the drug consumption and on the sales of the pharmaceutical companies as well as measure the generated savings and losses on the side of the industry. In the course of the analysis we examine the change in the demand of the related drugs and in their composition, from the aspect of industry, financer and patients. We explore which are the price strategies of the companies and are they managed to increase the sales or decrease the losses with them. The proper knowledge of the effects of blind bid will support the decision making of the concerned market actors as well as the further rulemaking. **METHODS:** A retrospective data analysis was conducted on the official NHIFA (national Health Insurance Fund) monthly data-base between October 2011 and March 2013. **RESULTS:** In the blind bid procedure 90 companies, 169 active substances and more than 2100 product were involved. The relevant products market share is almost 30% of the total Hungarian Pharmaceutical budget, which is almost 1 billion € annually. As we found, the blind bid process has a significant saving effect for the financer. The cumulative savings on the 18 months period reached 113 millions € for the financer. It means 24% reduction on the average reimbursement level, whilst the average manufacturer price decreased 16% and a minimal 3% savings was realized on the co-payment side. **CONCLUSIONS:** Huge savings were realized with this new reference pricing method, where the financer realized the most of the savings.

PHP74

COST-EFFECTIVENESS OF AN INTERFACE GERIATRIC INTERVENTION: ACUTE MEDICAL UNIT COMPREHENSIVE GERIATRIC ASSESSMENT INTERVENTION STUDY (AMIGOS)

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OBJECTIVES: Older people (>70) with high risk of future health problems discharged from acute medical units (AMU) within 72 hours, in Nottingham and Leicester, England, were included in an RCT of an interface geriatric intervention (IGI) comprising geriatrician assessment and further specialist management. The objective was to assess cost-effectiveness of IGI compared to standard care. **METHODS:** In the trial-based economic evaluation, 417 participants (IGI: 205) were analysed at 90-day follow-up. Health (inpatient, day-case, outpatient), social care and IGI resource-use data were collected and combined with unit costs to estimate total cost. Quality-adjusted life years (QALY), based on EQ-5D valuations at baseline and follow-up, were obtained for 254 (60.9%) participants. Multiple imputation by chained equations was applied to deal with missing QALY values. Cost and QALYs were adjusted by baseline characteristics using regression methods, and probabilistic incremental cost-effectiveness ratios (ICER) were constructed. Sub-group analysis was carried

out for patients who had not been hospitalized within six months prior to index AMU admission. **RESULTS:** In the whole group, total cost for IGI was higher (£207.4, 95%CI: £94.8-£331.2) with no QALY gain (-0.001, 95%CI: -0.009-0.007); IGI was dominated by standard care (3%-probability of ICER<£30,000/QALY). In the sub-group of 209 patients (IGI: 106) without a hospital stay in the previous six months, total cost for IGI was lower (-£274.2, 95%CI: -£480.4--£46.3) with non-significant QALY gain (0.001, 95%CI: -0.011-0.013), and 49%-probability of IGI being dominant (90%-probability of ICER≤£30,000/QALY). In the whole group (sub-group), inpatient cost was lower by £212 (£778), and social care cost was higher (lower) by £220 (£141), comparing IGI to standard care. **CONCLUSIONS:** The IGI for high-risk older people discharged from AMU was not cost-effective for all patients, but was cost-effective in patients without a hospital stay in the previous six months. This suggests targeting the intervention is required.

PHP75

ANALYSIS OF TOTAL TREATMENT COSTS OF ORGANOPHOSPHOROUS POISONING IN A TERTIARY CARE HOSPITAL

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OBJECTIVES: . To establish the correlation of log mean cost with respect to APACHE II score, pre-hospitalization and length of hospital stay, and to determine the intra-group variance of log mean treatment costs in different parameters. **METHODS:** Categorical data was presented as frequencies with percentages and was analyzed by Chi-square test, log regression and Pearson correlation. A logarithmic transformation was used for total cost to convert into normal distribution. Geometric mean and Geometric SD was used to summarize total cost. One way ANOVA was used to compare the mean of log (total cost) across various categorical variables. Multiple linear regression was used to find the factors associated with total cost of hospitalization of OPP. Correlations was used for measuring the strength of linear relationship between total cost and APACHE II score. **RESULTS:** A significant variance in log mean treatment costs was observed in different parameters like pseudocholinesterase levels, type of poison consumed, anticholinergics administered and incidence of intermediate syndrome. A high mean cost was observed in patients with a pseudocholinesterase level of less than 2000 and those who consumed WHO class Ib pesticide. A cost difference of INR 25,000 was noted in patients who developed intermediate syndrome. The APACHE II Score, pre-hospitalization period and length of hospital stay had significant correlation with log cost. Among the variables, length of hospitalization had strong correlation with log cost ($r=0.673$, $p<0.001$). For every one-unit increase in pre-hospitalization period, APACHE II score and length of hospital stay, the log cost increases by INR 1.01, 1.27 and 1.5 respectively. **CONCLUSIONS:** High costs of treatment coupled with a proportionately great loss of man-days, make OPP an extremely important area for pharmacoeconomic evaluation and for framing appropriate policies for remedial measures. Hence studies evaluating treatment regimens with respect to costs and outcome are highly desirable.

PHP76

COST OF INTENSIVE CARE STAY IN TURKEY: IN THE VIEW OF PAYER AND HEALTH CARE PROVIDER

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OBJECTIVES: The demand for intensive care units has risen in the recent years as the increasing aged population in all countries and in Turkey. The aim of the study is to calculate the average cost of intensive care stay(ICS) and to compare the cost with the reimbursement amount depending on a public hospital data in Turkey. **METHODS:** The records of ICSed patients from a public hospital in Ankara were evaluated retrospectively between November 2011 and January 2012. The hospital cost and reimbursement amount were calculated depending on the data. **RESULTS:** A total of 104 patients stayed in the given time line. Four patients excluded due to the missing data in files. The average cost of pharmaceuticals, medical devices, laboratory, health care and total cost per patient were calculated as 1209.16 TL± 492.46, 137.48 TL± 41.08, 422.35 TL± 108.70, 873.10 TL± 247.82 and 2992.43 TL± 994.06, respectively. The average reimbursement amount per patient was calculated as 2846.59 TL± 842.60. The average profit or deficit of the hospital were calculated for the 1st,2nd,3rd,4th, 5th,6th, 7th,8th,9-15th,16-29th and 30-51st days as 34.90 TL± 49.69, -75.48 TL± 671.39, -23.25 TL± 315.41, 382.80 TL± 368.58, 283.09 TL± 628.57, -266.13 TL± 612.81, 312.45 TL± 416.11, 118.99 TL± 729.00, -916.58 TL± 1430.94, -1500.57 TL± 3217.87 and -2054.55 TL± 3204.79, respectively. The profit and deficit trend line was calculated with the number of ICS days as "y = -51,889x2 + 446,98x - 631,73" (y=profit or deficit, x=hospital stay days). **CONCLUSIONS:** It was concluded that the average daily cost of ICS increased depending on the length of stay. The patients in critical state who needed more ICS days may have caused this. On the other hand, it was observed that the fixed daily reimbursement amount is inadequate for prolonged ICS. As a result this leads to the deficits of the hospitals in the prolonged ICS.

PHP77

REVIEW OF THE USE OF RESOURCE USE INSTRUMENTS BASED ON PATIENT RECALL IN RELATION TO OTHER METHODS OF COST ESTIMATION

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OBJECTIVES: Instruments for resource use measurement based on patient-recall (e.g. questionnaires, logs and diaries) are used extensively in trial-based economic evaluations; sometimes on their own and sometimes alongside other methods for estimating costs. The aims were to assess: 1) how resource use instruments are used in practice; 2) which items of resource use are based most frequently on patient-recall; and 3) how estimates compare if more than one method of data collection is used for the same resource items. **METHODS:** Articles citing 38 trial-based resource use instruments catalogued in the MRC-funded Database of Instruments for Resource Use Measurement (www.DIRUM.org) were identified using Google Scholar, ISI Web of Science and Scopus, and screened according to resource use measure usage. Data were extracted on: the method of administration, resources measured, rates of return and the nature of the other methods of resource use measurement. **RESULTS:** A total of 146/1503 citations met the screening criteria. Nearly all (143/146) used resource use instruments derived from Beecham and Knapp's Client Service Receipt Inventory. Most instruments relied on patient- or proxy-recall (126/146) generally administered during researcher interviews. Primary and secondary care usage were the most widely asked items (136/146) with 75 using no supplementary supporting data such as from hospital notes. Twelve studies compared one or more method of data collection for the same resource items with 8 indicating good agreement between medical records and patient/carer recall, 1 indicating the greater reliability of case notes and 3 were not evaluable. **CONCLUSIONS:** Resource use instruments based on patient recall are valuable complements to other methods and essential for certain items (e.g. out of pocket costs, non-medical costs). However, there remains inappropriate use in circumstances where more objective measures are available.

PHP78

BEYOND PATENT EXPIRY: DEVELOPMENT OF A MODEL FOR PRICING GENERIC DRUGS IN SOUTH AFRICA

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OBJECTIVES: Generic drugs provide a safe, effective and affordable alternative to medicines whose patent protection has expired. Generics have to meet the same quality standards as the innovator drugs; the only substantive difference is the price. Generic manufacturers compete 'on a knife-edge' of narrow margins of profitability. The generic pharmaceutical industry is risky and complex, success depends on the number of other generic drug manufacturers on the market, which affects the profit margins and volumes that each company could realize. The objective of the current study was to develop a model that explains the effect of generic drug entry on price competition after patent expiration in the pharmaceutical industry. **METHODS:** Innovators and their generics selected from all the chemical entities whose patents expired from 1999 through 2009. Data were obtained from IMS Health (Market Segmentation Report) and National Department of Health (Database of Medicine Prices) for the patents' expiration dates, prices, sales volume, therapeutic group, schedule, and dosage forms of drugs in the sample. **RESULTS:** A year after patent expiration, the innovators' products retained an average of 59% of the market share; the generic-to-innovator price ratio was at an average of 65%. By the end of the first year after patent expiration, an average of 2 generics was registered per innovators' product. **CONCLUSIONS:** Generic entry is commercially driven; it is influenced by the market size of the innovator product prior to the expiry of the patent protection. Generic penetration is slow, only intensifies after 5 years since the loss of patent protection. The price erosion of the innovator product is strongly influenced by generic penetration. The cost of drugs in South Africa is not coming down fast enough.

PHP79

HOSPITAL RESOURCE USE IN CHRONIC DISEASE COMBINATIONS: IS IT ENOUGH TO JUST ADD THEM UP?

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OBJECTIVES: Economic evaluations often ignore the possibility of non-linear health care costs when chronic diseases occur in combination. This paper aims to quantify the comparative effect of single and multiple chronic diseases on hospital resource use. **METHODS:** Using records of all admissions to public hospitals in the state of Victoria, Australia in 2010-2011 we estimate multiple regression models of hospital length of stay (and total annual discharges) for combinations of 11 chronic diseases. For length of stay we run separate models for same-day and overnight stays, adjusting for observed and unobserved characteristics of patients. **RESULTS:** A higher chronic disease count decreases the odds of a same-day hospitalization (day-case) exponentially while some disease combinations increased these odds. Having ischemic heart disease (IHD) & dementia doubled the odds of a day-case compared to a patient with dementia only. Among overnight stays, having a mental disease had the highest single disease effect on length of stay (LOS) – increasing LOS by 3-4 days. Some disease combinations had non-additive effects (i.e. their combined effect was greater/less than the sum of their single disease effects) on LOS while others were additive. The interaction effect in a depression-renal failure combination added 3 days to its single disease effects, while in cancer-osteoporosis it was -2 days. Disease combinations that produced a positive interaction effect were usually unrelated diseases. We found disease count to be positively correlated with number of admissions. Having a combination of diseases was generally found to have a less-than-additive effect on the number of admissions. **CONCLUSIONS:** Patients with chronic diseases have a resource use pattern that includes longer lengths of stays and more admissions. Combinations of unrelated diseases are particularly correlated with longer lengths of stay therefore it is the disease and combination type that is associated with higher lengths of stay and admitted episodes.

PHP80

PHARMACEUTICAL EXPENDITURE, CLINICAL OUTCOMES AND EXPENDITURES ON OTHER HEALTH SERVICES

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OBJECTIVES: The study examined: a) the relationship between pharma care and health outcomes, b) the influence of expenditure on drugs to the level of expenditure on other forms of care c) the impact of providers on the level of pharma expenditure. **METHODS:** We conducted linear multiple regression analysis with pharma expenditure as independent variable, and dependent variables such as clinical indicators and expenditure of other categories. Also, we conducted analyses with number of physicians and pharmacists as independent variables and pharma expenditure as dependent. Analyses were conducted for all Eurozone countries (2003-2011). All tests of statistical significance were two-tailed, and p-values of less than 0.05 were considered significant. **RESULTS:** Increased total per capita outpatient pharma expenditure (in US $ PPP's) by 10% was related to increase in life expectancy: a) at birth for men by 0.41% (p=0.07), b) for men 65+ by 2.35% (p=0.004), and c) at birth for women by 0.37% (p=0.03). Moreover, increased public pharma expenditure as a % of total current public expenditure by 10% was related to a reduction of public current health expenditure (as a % of GDP) by 2.8% (p<0.001). A 10% increase of total pharma expenditure as a % of total current health expenditure as a % of GDP, was related to a reduction of total current health expenditure as a % of GDP by 3.3% (p=0.045). Finally, an increase in the number of pharmacists/100,000 population by 10% was related to an increase of total per capita pharmaceutical expenditure by 0.93% (p=0.07). **CONCLUSIONS:** Overall drug expenditure is positively related to population health and negatively connected with the level of total health expenditure, a finding that should influence political decisions on public insurance coverage. The accuracy of our results will be further enhanced by similar research in the future, when longer time series data are available.

PHP81

BIOSIMILAR AND ORIGINATOR BIOLOGIC PRICING DYNAMICS IN EMERGING MARKETS

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OBJECTIVES: To characterise pricing dynamics between originator biologics and biosimilar products in a number of emerging markets, namely Brazil, China, India, Mexico, Russia, South Korea and Turkey. **METHODS:** Prices for the products concerned were based on calculations of ex-manufacturing prices. Prices at time of biosimilar launch and from the most recent time point available were selected for the respective biosimilar and originator products, and converted to a price-per-unit basis. Average prices were then calculated per brand name, where more than one strength or formulation of a product existed. In addition, primary and secondary research were utilised to obtain further manufacturer and/or retail-level price data where possible. **RESULTS:** At the time of launch, biosimilar products in emerging markets exhibit a manufacturer-level price representing an approximately 30% discount, on average, over that of the originator biologic. There are a number of exceptions, with evidence that some biosimilar products are priced at a mere 40% of the originator at time of launch. The more typical 30% differential appears to narrow significantly with time, as evidenced across a number of markets that have seen activity in the first generation of biosimilar products (e.g., erythropoietins, granulocyte colony-stimulating factor, etc). **CONCLUSIONS:** At time of launch, the pricing dynamic between originator biologics and their respective biosimilars in emerging markets appears to mimic the scenario which has thus far been observed in Europe. However, there are exceptions, with some products associated with significantly larger discounts at time of launch in certain emerging markets. Over time, there tends to be dramatic price erosion for both originators and biosimilars as a function of the original originator price. This erosion is driven by competitive entry into the market of subsequent biosimilars, coupled with widespread use of tendering in the public markets.

PHP82

EVALUATION OF THE POLICIES IMPLEMENTED TO MONITOR PRESCRIPTION AND REDUCE PHARMACEUTICAL EXPENDITURE AT THE UNIVERSITY GENERAL HOSPITAL OF PATRAS, GREECE

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OBJECTIVES: The University Hospital of Patras (GPNP) has implemented a series of prescription monitoring measures that aim at reducing the hospital's pharmaceutical expenditure. The objective of this study was to evaluate the results of those policies. **METHODS:** Analysis of the 2011 and 2012 economic data of the GPNP on purchase and consumption (in terms of quantity and value) of pharmaceutical products, both in the inpatient and outpatient settings, was conducted. Data on the total number of outpatient prescriptions and high-cost drugs were also analyzed. The subgroup of high-cost drugs was further investigated, by performing a breakdown analysis of the expenditure of high-cost drugs by disease area. **RESULTS:** The cost containment measures implemented by the GPNP (which include, among others, the development of guidelines on rationalizing the use of pharmaceutical products, and a hospital formulary, which took into consideration both clinical and cost data), have resulted in a reduction of the total pharmaceutical consumption by 11.5% in 2012 (€29.4 million) compared to 2011(€33.2 million). Although total outpatient prescriptions and the related quantity of pharmaceutical products prescribed were increased by 8.1% and 10.5%, respectively, the pharmaceutical cost of outpatient care was reduced by almost 28%, indicating a significant increase in the prescription of lower cost pharmaceuticals. Indeed, the high-cost hospital medicines prescribed to outpatients was reduced by almost 21% in 2012. In the inpatient setting, the total expenditure on high-cost hospital medicines was reduced by 12.9%. The expenditure on cytostatic drugs, which accounts for more than 70% of the total expenditure for high-cost drugs in the inpatient setting, was reduced by almost 10%, while the number of patients hospitalized was reduced by only 1.6%. **CONCLUSIONS:** The policies implemented by the GPNP were successful in reallocating pharmaceutical budget towards more innovative medicines in order to ensure patients' access to new therapies.

PHP83

COST-OUTCOME DESCRIPTION OF CLINICAL PHARMACIST INTERVENTIONS IN A UNIVERSITY TEACHING HOSPITAL

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OBJECTIVES: Clinical pharmacist interventions are actions which aim to improve a patient's pharmaceutical care. The primary objective of this study is to estimate the cost savings achieved by clinical pharmacists through the prevention of adverse drug events (ADE) in a hospital setting. Previous studies have estimated the benefit of these interventions over shorter periods of time and in specific hospital areas. This study will encompass a longer time period and a complete hospital system. **METHODS:** This study was a retrospective analysis of a database detailing pharmacist interventions on patient therapies at Cork University Hospital. Period examined was from January 2012 to December 2012 inclusive. Cost savings were calculated based on the probability that an ADE would have occurred in the absence of the proposed pharmacist intervention (Average cost of ADE = €970). Input costs were calculated based on the time required for pharmacists (n = 17) to enact interventions. One way sensitivity analysis incorporated published ranges for intervention time, pharmacist salary and probability an ADE would have occurred. Alternative costs for an ADE were also included in analysis. Cost savings are from the perspective of the health care institution. Costs are presented in 2012 € values. **RESULTS:** A total of 4,247 interventions were documented. Base case analysis resulted in net cost benefit of €590,000 per annum and a cost benefit ratio of 10.4:1. Cost savings of €650,000 were generated and the cost of providing the service was estimated at €60,000. Sensitivity analysis resulted in cost benefit ratio varying from 5.2 – 64.8 (minimum – maximum). The most prevalent pharmacist intervention was the identification of drug omissions (n=1820, 42.9%). **CONCLUSIONS:** Cost benefit ratio remained positive in all situations examined. This study has added to the body of evidence that clinical pharmacist interventions are cost effective over extended time periods and entire hospital settings.

PHP84

DIFFERENTIAL DISCOUTING: CAPTURING THE VALUE OF LIVING LONGER AND BETTER

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OBJECTIVES: Discounting future cost and health benefits is standard in pharmacoeconomic evaluations. Using different discount rates for costs and benefits remains controversial, although there is a case for lowering the health effect discount rate as the general population benefits from better health over a longer period of time. The implications of differential discounting on the likely duration of health benefits was assessed. **METHODS:** An extensive literature review sourced current discount rates for European countries, including the justification for those rates where available. Using a specific example (mifamurtide [Mepact, Takeda] for the treatment of osteosarcoma) the time to loss of health benefits for equal and differential discount rates using a UK reference case was assessed. **RESULTS:** Like most of Europe, the UK National Institute for Clinical Excellence (NICE) has been using a discount rate of 3.5% for both costs and health effects. However, it has recently adopted a differential reference case where health effects are sustained over a period of 30 years or more: 1.5% for health effects and 3.5% for costs. Taking the example of mifamurtide and using the original rate of 3.5% for health effects, all benefit would be discounted away after just 22 years. By adopting the lower rate, the effects will not be discounted away until 49 years after treatment. In this case, the discount rates used to for mifamurtide are particularly sensitive because all costs are borne in the first year, yet benefits of treatment can be over a patient's lifetime. **CONCLUSIONS:** Adopting differential discounting rates reflects the potential long-term benefits of new health care technologies. However, most European countries, with the exceptions of Belgium, The Netherlands and now the UK in specific circumstances, continue to use the same discount rate for costs and health effects, thereby potentially undervaluing the long-term benefits current and new treatments.

PHP85

ADVANCED BUDGET NOTIFICATION (ABN): IS THERE A WIN:WIN FOR MANUFACTURERS AND PAYERS GIVEN THE CURRENT AUSTERITY MEASURES ACROSS THE EU

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OBJECTIVES: The mature health economies across the EU are severely fiscally challenged, and yet manufacturers of innovative medicines are where the legislation permits expected to give a notifiable 'warning' of expected budget impact. A survey was undertaken amongst payers to ascertain their real world expectations in terms of advanced warning and how realistically a collaborative approach to access could be achieved. **METHODS:** Manufacturers of innovative technologies are where legislation permits advised to supply payers and budget holders with information that will assist the aforesaid bodies with sufficient information to decide on the managed entry of that technology; historically manufacturers are in two minds about the value of this process. A study was undertaken with payers as to their perceived interest and interaction with manufacturers who willingly entered into ABN. Payers at a regional and national level were interviewed to gauge their opinions. **RESULTS:** There appears to be a dichotomy of opinion amongst payers as to the value of the legislation; 'damned if you do, damned if you don't', however it clearly is in the interest of both parties to work together. Payers value the contact and information provision from Manufacturers, Manufactures seek to garner the approval of payers. **CONCLUSIONS:** The EU is in the worst economic depression since the 1930's, affordability is the key watchword. New technologies need to continue to be presented to payers in a manner which allows them to plan for fiscal pressure and service redesign.

PHP87

PHARMACOECONOMIC ANALYSIS OF IOVERSOL VERSUS IOHEXOL FOR DIAGNOSTIC PROCEDURES

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Contrast-induced nephropathy (CIN) is a clinically significant and costly complication related to the use of iodine-based contrast media (CM). The hypothesis regarding the advantages of isoosmolar CM compared to low-osmolar CM was not confirmed in recent meta-analyses; still, there may be safety differences between individual CM. **OBJECTIVES:** To perform a pharmacoeconomic comparison of the CM ioversol and iohexol used for x-ray procedures in Russia. **METHODS:** We calculated the costs for using ioversol and iohexol taking into account the risk of the occurrence of CIN and CIN-associated complications. Data for the model were extracted from published clinical trials and reviews. We performed an indirect comparison of both CM to calculate the relative risk (RR) of CIN (via the CM iodixanol as a mutual control). This RR value was used in the model to simulate the impact of potential safety differences between both CM on the costs. Direct medical costs were calculated based on the Russian health care system setting. Related costs for CM and for CIN-associated complications (e.g. cardiovascular complications, respiratory distress syndrome and hemodialysis for acute kidney injury) were also taken into account. Cost calculations were performed separately for patients with low, medium and high risk for CIN. One-way sensitivity analysis was performed. **RESULTS:** RR of CIN was 0.26 (95% confidence interval 0.12-0.58) for ioversol vs iohexol in the indirect comparison. Direct medical costs were higher for iohexol than for ioversol due to the slightly higher rate of CIN, thus, CIN-associated complications: net benefits were 469.16; 752.88 and 3313.13 rubles (~11.03; 17.70; 77.91 Euros) per patient with low, medium and high risk of CIN correspondingly. Still, results were sensitive to the price of both CM. **CONCLUSIONS:** In the Russian health care setting, the use of ioversol seems to be more cost efficient than iohexol due to slightly favorable renal safety.

PHP88

ECONOMIC EVALUATION OF INTRAVENOUS IODINATED CONTRAST MEDIA IN ITALY

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OBJECTIVES: Contrast-induced acute kidney injury (CI-AKI) is defined as a deterioration in renal function after administration of radiologic iodinated contrast media (CM). Iodixanol, showed a lower CI-AKI incidence than low-osmolar contract media (LOCM). A cost-effectiveness analysis was performed comparing iodixanol and LOCM in intravenous (IV) setting in Italy. **METHODS:** A Markov model was developed. Patients moved across four health states, CI-AKI free, CI-AKI, myocardial infarction and death. The simulation horizon was lifetime with one-month cycles. Costs and outcomes were discounted at 3.5% rate. CI-AKI incidence was considered from published literature across different definitions. Cost-effectiveness of iodixanol was assessed in terms of incremental cost per life year gained. Net monetary benefit (NMB) was also calculated. Both deterministic and probabilistic sensitivity analysis were performed. **RESULTS:** Base-case results showed an average survival increase of 0.51 LYs and a saving of €7.25 for iodixanol vs. LOCM. The cost-effectiveness of iodixanol was confirmed when other scenarios were explored, such as varying CI-AKI definition, sub-populations with specified risk factors, CM hospital bids prices and inclusion of adverse drug reactions of allergic nature. A NMB ranging between €6,007.25 and €30,007.25 was calculated. **CONCLUSIONS:** base-case results are showing that IV iodixanol is cost-effective compared to LOCM in the Italian clinical setting of hospital CT radiology practice. However, some caution is due, mainly linked to inherent limitations of the modelling technique and to the lack of agreement on CI-AKI incidence data in the clinical literature.

PHP89

A DETERMINISTIC MODEL TO EVALUATE THE COSTS FOR SURGICAL PROCEDURES: THE WIN-WIN MODEL

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OBJECTIVES: The Italian National Health Service (*Servizio Sanitario Nazionale-SSN*)is financed at hospital level by DRG (Diagnosis Related Group): the classification is defined at national level and the tariffs at regional level. Each region could define different tariffs for different types of hospital, choosing different criteria to identify them. The aim of this study is to analyze the incidence of the different types of costs for different surgical procedures and to evaluate the impact of the case mix on the total hospital costs. **METHODS:** We developed an excel model, the Win-Win, in order to analyze the incidence of different types of costs using the hospital perspective: length of stay, operating room time, personnel, materials. We identified 8 surgical procedures, based on the International Classification of Disease 9-Clinical Modification, and for each one, we collected all the data from a survey based on different clinical practices in different types of hospitals. The model has been set up with the possibility to customize each type of data, consumptions and unit costs. **RESULTS:** We calculated the average (AVG) and the confidence interval (IC) for the incidence of each type of cost among the different surgical procedures. For the length of stay we observed the highest average incidence (35,1%; IC95% 24,4-39,9), followed by the cost of materials with an average of 34,9% (IC95% 30,1-43,1), the operating room cost (avg 20,6%; IC95% 18,8-22,8), and the personnel (avg 9,4%; IC95% 7,2-11,1). **CONCLUSIONS:** Through the Win-Win Model it is possible to analyze the costs of each type of surgical procedure and evaluate the economic impact of the case mix of the hospital activity. As a consequence, it could be a useful model to increase the awareness of the economic impact and to allow a more informed management at hospital and regional level.

PHP90

COST ANALYSIS OF AN INTENSIVE CARE UNIT

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OBJECTIVES: The aim of our study is to analyze the costs incurred by hospitalized patients in 2010, in the intensive care unit (ICU) of San Leonardo Hospital (Southern-Italy). **METHODS:** A retrospective cost analysis was performed on patients with a length of stay longer than 24 hours. Direct medical costs were estimated (hospitalization, surgical procedures, devices). The costs of hospitalizations and surgical procedures were calculated based on the 24.0 version of the tariff system DRG (Diagnosis Related Group). The data on the costs of the devices were provided by the management of the hospital pharmacy. To evaluate the burden of the diagnostic groups two indicators were used: cost per surviving patient (total resources used / total survivors) and money loss per patient (total resources used for dead patients / total patients) [Rossi et al. Intensive Care Med. 2006]. **RESULTS:** A total of 201 patients hospitalized in the ICU in 2010 were selected and analyzed depending on their diagnostic group. Hospitalized patients who had a hospital stay longer than or equal to 24 hours, were 95% of the sample. Most frequent diagnostic groups have been: edema (16.4%), left heart failure (13.9%) and COPD (9.0%). There is a wide variation between the average costs per patient probably due to the difference in the duration of hospitalization (from a minimum of € 2,777 in stroke, to a maximum of 7,227 euros in nephro-urological disease). Intracranial bleeding is the disease causing the highest costs per dead or survived patient. The nephro-urological and neurological diseases are characterized by the lowest costs, for dead and survived patients, indicating a better efficiency. **CONCLUSIONS:** The results are a starting point for further investigations aimed at the exploitation of resources absorbed by ICU opposed to the need to provide patients with the best possible health care.

PHP91

HEALTH ECONOMIC EVIDENCE FOR MEDICAL NUTRITIONS: ARE THESE INTERVENTIONS VALUE FOR MONEY?

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OBJECTIVES: Medical nutrition (MN) targets patients with malnutrition or with specific disease such as Crohn's disease (CD) to support their recovery. Efficacy of MN has been demonstrated in malnutrition, as well as in paediatric CD or gastrointestinal (GI) cancer surgery. However, its health economic evidence is less known. This article summarizes the findings of a systematic literature search on health economics evidence of MN in order to understand what the value for money of MN interventions is. **METHODS:** A systematic literature search was performed to identify publications related to health economics evidence of MN. The result of it was communicated elsewhere. For selected articles, the clinical background, basis of the analysis, health economic design and results were extracted and summarized by relevant disease areas. **RESULTS:** Among the 32 articles found, 11 covered malnutrition, 9 related to GI surgery, 6 studied cow milk allergies (CMA), whereas the remaining focused on various diseases. When targeting malnutrition, MN was accepted as being cost-effective and/or cost-savings from budget impact analyses. In GI surgery, when taking into account the full episode of care, oral and enteral nutrition was assessed as good value-for-money. In CMA, there was a significant health care budget impact of using MN to treat symptoms of this allergy. In the remaining indications, the use of enteral tube feeding was demonstrated as being cost-saving compared to parenteral nutrition. **CONCLUSIONS:** Based on a systematic literature search, MN interventions showed value for money in different health care settings. Although few studies calculated an incremental cost-effectiveness ratio (ICER), those calculated were all below thresholds applied in medical settings. In addition, most of the times MN was more effective and cost saving, thus a dominant option. However, more research is needed to strengthen economic modelling for medical nutrition interventions.

PHP92

IMPACT OF PHARMACOECONOMICS MODELLING ON REIMBURSEMENT OF MEDICINES IN SERBIA

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OBJECTIVES: To assess the impact of recently published (2011) Guidelines for Pharmacoeconomic Evaluations for Serbia and ISPOR Guidelines (2013) on the methods and the conduct of budget impact analysis (BIA) during reimbursement submission. **METHODS:** We investigated how many reimbursement submissions were made with an accompanying BIA to the Health Insurance Fund in Serbia from 2012 till June 2013. **RESULTS:** There were 306 submissions in 2012 and 2013 and none of those had a thorough and complete BIA submitted. There were 65 new drugs (international non-proprietary names (INNs)) added to the Reimbursement list in 2012 and 5 new drugs (INNs) in April 2013. Possible reason for a non-complete BIAs was that it is not an obligatory part of the submission dossier. It is recommended at this moment, but the plan is to make it an obligatory part. BIA simply quantifies the financial consequences of using health-care services, comparing reference with anticipated scenario. Currently there is no template for the BIA, just recommendations how to address time horizon, target population, costing, scenarios and discounting. This could be one of the reasons why most of the submissions had almost complete pharmacoeconomics evaluation. **CONCLUSIONS:** The availability of a template for BIA would increase transparency, the quality of submissions and pro-

mote its use. The audience includes those who develop, submit or use budget impact models and committees who evaluate reimbursement submissions. With a use of Guidelines for Pharmacoeconomic Evaluations, ISPOR Guidelines and proposed BIA template (which will be published in the updated version of the Guidelines for Pharmacoeconomic Evaluations) the quality of submissions to the HIF in Serbia would be raised and the decision time could be reduced.

PHP93

THE SUSTAINABILITY OF IRISH PHARMACEUTICAL EXPENDITURE

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OBJECTIVES: The recent economic crisis has threatened the sustainability of many international economies as well as their health care systems. The objective of this paper was to quantify recent cost containment measures used to reduce Irish public pharmaceutical expenditure in light of the ongoing fiscal restrain. **METHODS:** Pharmaceutical expenditure across the EU was briefly examined using the most current OECD data. The main pharmaceutical cost containment measures recently adopted in Ireland were identified under the headings of drug prices, fees/mark-ups and coverage/co-payments with full year 2011 public savings estimated. **RESULTS:** EU pharmaceutical expenditure was estimated at €190 billion in 2010, almost one fifth of all health expenditure. At €528, Ireland spent more on pharmaceuticals than any other European country on a per capita basis and 50% more than the average across EU member states. Governments under pressure to maintain a sustainable national health system and reduce deficits, while still preserving acute care levels, are cutting pharmaceutical expenditure. Many European countries, including Ireland, have increased the use of cost containment measures including a mix of price and volume controls. Collectively, these measures were estimated to have reduced Irish public pharmaceutical expenditure by €380m in 2011. The main cost containment measures used involved addressing; 1) the ex-factory price of drugs including price cuts of up to 40% on off-patent and generic drugs leading to an estimated €200m saving, 2) pharmacy dispensing fees and mark-ups via a new dispensing fee structure and reducing both retail and wholesale mark-ups with a €100m saving, and 3) scheme coverage and patient co-payments including restricting scheme coverage for persons over 70 years and increasing the level of co-payments with savings of €80m. **CONCLUSIONS:** There use of pharmaceutical cost containment measures to decrease health expenditure is a trend that is likely to continue for some time yet.

PHP94

BASIC ATTITUDE TOWARDS HEALTH CARE RESOURCE ALLOCATION DECISION MAKING IN JAPANESE PEOPLE -UTILITARIANISM OR EGALITARIANISM?

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OBJECTIVES: Japan is now confronting budget constraints and trying to introduce economic evaluation into health care resource allocation. To clarify the basic attitude towards health care resource allocation in Japanese people, a national survey was conducted. **METHODS:** A survey was carried out in a face-to-face manner with random sampling on the 50 municipalities in Japan, adjusting for age and sex, between March and April 2013. The questionnaire consisted of two scenarios; question 1:"Imagine that there are two clinical examinations (A: less expensive with low power; B: more expensive with high power) and choose from the following two options: option 1: all subjects receive examination A and subsequently the death of 1,000 people is prevented; option 2: a half of the subjects is selected by lottery and receives examination B, preventing the death of 1,100 people as a consequence." ; question 2:" Imagine that two types of diseases differing the treatment cost(A: 10 million per patient; B: 2 million per patient), and allocate 100 million yens to these diseases." **RESULTS:** Out of 1143 respondents, 601 chose the option 1 in question 1. In question 2, 217 chose the least utilitarian combination(A;8, B;10), 139 chose 2nd combination(A;6, B;20), 289 chose 3rd one(A;4, B;30), 67 chose 4th one(A;2, B;40), and 379 chose the most utilitarian option(A;0, B;50). The weak correlation was observed in the utilitarian trend and age ($r=0.29$, $p<0.01$). Utilitarian tendency to maximize the health benefit varied among respondents with different educational backgrounds. **CONCLUSIONS:** We investigated the basic attitude towards health care resource allocation in Japanese people by answering to specific scenarios, which revealed fairly extreme utilitarian selection was the most popular. This utilitarian tendency correlated with age and education. It seems that the discussion on the priority setting in health care resource allocation in Japan based on this kind of empirical data become important.

PHP95

RESOURCES SAVED BY THE INTRODUCTION OF DAY SURGERY IN THE GREEK NATIONAL HEALTH SYSTEM

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OBJECTIVES: Day surgery has been introduced in numerous heath care systems and has been proved able to save resources and promote efficiency and effectiveness. The aim of this study is to estimate the savings that can be realized by the adoption of day surgery by the Greek National Health System. **METHODS:** Surgery procedures were classified according to the type of anesthesia and the post-operative care they require. The procedures identified as suitable for day surgery, according to the above criteria, were matched to the Greek Diagnostics Related Groups (DRGs). The possible savings were calculated on the basis of the marginal cost these procedures impose to hospitals when treating them as inpatient surgeries. Savings were estimated for both the social insurance(SI) and for the government budget due to the fact that SI reimburses the capital production factor of each DRG while the labor cost is funded by the government budget. **RESULTS:** Sixty-two DRGs were identified as suitable for day cases. The majority of these were procedures of the eye (16%), the ear, nose and throat (11.3%), the myoskeletal system (9.7%), the kidney and the urinary tract (9.7%) and the female reproductive system (9.7%). The hospital marginal cost of an increase in the length of stay by one day was estimated at 563.32 euros (95%CI: 541.6–585.1). The annual savings were estimated at 93.7 million euros for the SI and when labor opportunity cost is included the amount saved exceeds 225 million. **CONCLUSIONS:** In light of the economic crisis and the continuously reduced health care budget, the health system should adopt cost-effective intervention in order to preserve a satisfactory level of health services output. As this study concludes, day surgery can save a great amount of resources and according to the international literature can also guarantee patients' safety and satisfaction.

PHP96

CHRONIC PATIENTS' PERCEPTIONS ABOUT GENERIC MEDICINES IN GREECE: FINDINGS FROM A CROSS SECTIONAL SURVEY

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OBJECTIVES: The Greek authorities implemented mandatory generic substitution trying to expand the use of generics, due to reasons of cost-containment. However, Greece lacks a strong, established generics culture. This study aims to investigate chronic patients' perceptions on generics in Greece. **METHODS:** We carried out a cross-sectional study among 1600 patients from four chronic illness groups (HTN, Diabetes, COPD and Alzheimer mild to moderate stage). Logistic regression analysis was used to determine the factors associated with chronic patients' perceptions. **RESULTS:** Of 1600 patients, 1594 responded to the survey (99.6%). Only 67% has used generics in the past. 39.3% considers them safe, 34.3% thinks that the generics have the same quality standards as the originals and 37.3% believes that they have the same treatment outcomes. 63% expressed concern on potential adverse effects from generics. 58% argues that the drug's country of origin affects its safety. Statistical analysis revealed that generics quality has a statistical significant relationship with patient's income (OR 1.24; 95% CI 1.00-1.19), age (OR 0.99; 95% CI 0.98-1.00), gender (OR 0.73; 95% CI 0.57-0.94) and health status (OR 1.00; 95% CI 1.00-1.02) while generics effectiveness was positively related with the patient's income (OR 1.10; 95% CI 1.02-1.20), gender (OR 0.70, 95% CI 0.55-0.90) and health (OR 1.00, 95% CI 1.00-1.01). Women and the elderly are less likely to consider that the generics have the same standards as the originals. **CONCLUSIONS:** Our findings reveal that chronic patients express reservations towards generic medicines which in an extent can probably explain the low generic market share in Greece. Perceptions about generics were found significant related mostly with patients' demographic characteristic. The latter can be considered as useful information as it assists stakeholders to identify on which chronic patients groups should direct campaigns in order to encourage generic drug use as a means to control expenditures and to save resources for innovative drugs.

PHP97

ANALYSIS OF SPANISH GENERIC MEDICINES MARKET: RECOMMENDATIONS TO ENHANCE LONG-TERM SUSTAINABILITY

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OBJECTIVES: To provide an overview of the Spanish generic medicines retail market and to identify policy measures which impede its development. Finally, recommendations to increase both the efficiency of health care with regards to pharmaceuticals in general and the sustainability of the Spanish generic medicines retail market are put forwards. **METHODS:** A literature review has been carried out to explore the current situation of the Spanish generic medicines market. In addition, a survey has been developed and interviews have been conducted to validate the information obtained from the literature review. **RESULTS:** The Spanish government's focus on the price level of generic medicines in the past has decreased prices of generic medicines drastically. The current reference pricing system (since 2011) has eroded price differentials between originator and generic medicines in more than 90% of the reference groups. Differing policies at the demand-side have resulted in differing generic market shares between the autonomous communities. Policies are needed to increase both the efficiency of the health care system with regards to pharmaceuticals (e.g. electronic prescribing, prescribing by international non-proprietary name, etc.) and the sustainability of the Spanish generic medicines retail market (e.g. creating price difference between originator and generic medicines, accelerating market entrance, building and improving trust for generic medicines in patients and physicians, etc.). **CONCLUSIONS:** The low volume of generic medicines used in Spain combined with the continuous pressure on the price level of generic medicines threatens the sustainability of the generic medicines industry. The reduced price difference between originator and generic medicines tends to be an important barrier for the development of a generic medicines market. The unique experience in the Spanish market shows the importance of demand-side policies on the use of generic medicines.

PHP98

ACCEPTABILITY OF INDIRECT EVIDENCE TO SUPPORT DRUG REIMBURSEMENT IN AUSTRALIA

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OBJECTIVES: When there are no direct head-to-head trials versus an appropriate comparator, indirect comparisons are commonly performed to support a clinical claim and relative pricing. In Australia, Public Summary Documents (PSDs), reporting on the Pharmaceutical Benefits Advisory Committee's (PBAC) decision-making process relating to government reimbursement of medicines, have been published since July 2005. A review of PSDs specific to drugs where the primary claim was based on indirect evidence was undertaken to assess the success of the approach and

identify the PBAC's main concerns relating to the methodology. **METHODS:** All PSDs published between July 2005 and November 2012 where the primary evidence was based on an indirect comparison, either as simple or a mixed treatment comparison, were reviewed. Data relating to comparator, clinical claim, economic analysis, and PBAC concerns were extracted and analysed. **RESULTS:** PSDs relating to 105 products using an indirect comparison as the primary analysis were reviewed. A total of 70 (67%) submissions were recommended; the remaining submissions were rejected (32, 30%) or deferred (3, 3%). An indirect comparison was used to support a non-inferiority claim in 84 (80%) submissions and superiority claim in 21 (20%) submissions. Of those claiming non-inferiority, 60 (71%) submissions were recommended by the PBAC. Of those claiming superiority, the PBAC accepted the clinical claim for 10 (48%) submissions; 6 (29%) received a price premium. The PBAC expressed concerns relating to the indirect comparisons in 56 (53%) PSDs. The key issues related to the exchangeability of the trials as a consequence of different patient populations (25%), quality of trials (24%), and dosing (18%). **CONCLUSIONS:** Clinical comparisons based on indirect evidence are associated with increased uncertainty related to the exchangeability of the trials. The PBAC usually accepts evidence to support a claim of non–inferiority, but rarely the same in regards to superiority.

PHP99

INVESTIGATING THE ECONOMIC IMPACTS OF NEW PUBLIC PHARMACEUTICAL POLICIES IN GREECE

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OBJECTIVES: Since 2010, cost contaiment efforts in Greece focused on the reduction of public pharmaceutical expenditure. Changes in cost sharing levels (dementia/alzheimer & epilepsy 0%-10%, osteoporosis & copd: 10-25% etc.), reductions in prices and generics substitution are some of the measures implemented after the second quarter of 2012. The aim of the study is to investigate the economic impact of the above measures for public funds and households. **METHODS:** Data on volume and values for prescribed drugs for each therapeutic category and cost sharing level were derived from EOPYY, the main reimbursement agency (95% of population). The periods compared were January to February 2012 vs. January to February 2013. **RESULTS:** During 2009-2011, public pharmaceutical expenditure in Greece declined by 23%, while for 2009-2014 the decline is projected at 61%.During 2013, 2014 targets are €2.44billion or 1.3% of GDP and 1.935 billion or 1% of GDP. In 2013, only 8.2% of prescribed drugs boxes were provided free of charge, vs 13.6% in 2012 A 25% cost sharing level was imposed to 76.4% of prescribed medicines in 2013 compared to 51.4% in 2012. Consequently, the mean cost-sharing burden for pharmaceuticals in 2013 was estimated at 18% vs 13.1% in 2012. Monthly savings in public expenditures from changes of cost–sharing patterns was estimated at €18-€20 mil. Average price per package declined in 2013 by 23%, from €18 in 2012 to €14 in 2013. Public funds savings, because of consumption of cheaper drugs, were estimated at €55-€60 mil.per month. Major savings for public funds were achieved through cardiovascular diseases drugs **CONCLUSIONS:** The economic results of the measures for third party payers are positive. However, the measures should be reconsidered and examined more closely also taking in mind social effects, in terms of accessibility of users and especially for vulnerable groups who in need of essential pharmaceutical care.

PHP100

CHRONIC PATIENTS RESPONSE TO THE IMPLEMENTATION OF INTERNATIONAL NON-PROPRIETARY NAME (INN) PRESCRIBING IN GREECE

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OBJECTIVES: Under the pressure of fiscal consolidation and pharmaceutical spending decrease in Greece, mandatory generic substitution and compulsory prescription by international non-proprietary name (INN)were recently introduced as reimbursement drivers in Greece. This study aims to investigate the implications of INN implementation regarding chronic patients' choices and their willingness to switch to an alternative pharmaceutical treatment. **METHODS:** A cross-sectional study was carried out among 1600 patients from four chronic disease groups(HTN, Diabetes,COPD and Alzheimer). Logistic regression analysis was used to investigate the factors associated with chronic patients' choices. **RESULTS:** Out of 1600 patients approached, 1594responded to the survey(99.6%). 69% of them stated that they were aware of the new reimbursement system. After the implementation of INN prescribing, only few(11%) have changed their usual drug. 43% were totally certain that an original drug is more effective than a generic, while 67% have never used generics in the past. Most patients(82%) preferred to be prescribed their usual medicine, despite of the extra cost they had to bear. This choice was a co-decision with their physician as 58% of them stated. The average additional amount that they would be willing to spend in order not to switch to another medicine was estimated at €17.8. These results showed a significant statistical correlation with patients' income, educational level and occupation category. **CONCLUSIONS:** According to this study chronic patients are not willing to change their usual drug and switch to a generic, despite the cost this choice imposes. Consequently INN prescribing may decrease public expenditures on pharmaceuticals but it will lead to higher private expenditure. Given that due to economic crisis incomes are continuously decreasing and unemployment rate is rising, the measure might eventually result in lower adherence to medication and consequently in adverse effects on patients health status and future public expenditure for treating possible complications.

PHP101

MARKET ACCESS RISK SCORING: A UNIFIED FRAMEWORK FOR CROSS COUNTRY COMPARISON OF DIVERSE MARKET ACCESS SYSTEMS AND PROCESSES

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OBJECTIVES: To define and develop risk - and more specifically market access risk– as a framework towards understanding and evaluating stability in market access systems at an individual country level. **METHODS:** We created a combination model of rating quantitative and qualitative variables which affect a country's ability and willingness to pay for new drugs. The criterion for selection of variables is based on relevance, availability and uniformity in our model. We included a total of 42 variables categorised under three verticals - quantitative, qualitative and measures of stability. In order to derive a non-recursive model of ratings, we fit the regression equation for quantitative and qualitative variables as: $Y(1) = \alpha_i + \sum\beta_i{}^*X_i + \varepsilon$ (Equation 1.1) $Y(2) = \alpha_j + \sum\beta_j{}^*X_j + \varepsilon$ (Equation 1.2) where Y(1) and Y(2) are the market access risk ratings for quantitative and qualitative variables, X_i and X_j are vectors of independent quantitative and qualitative variables, and ε is the error term. The final score was derived by taking the geometric mean of the two ratings together with ratings for the measures of stability and is described as below: Total Risk Score = √Y(1)^2* Weight of Y(1) + Y(2)^2*Weight of Y(2) + Risk Rating (Measures of Stability)^2*Weight of (Measures of Stability). **RESULTS:** We decided to aggregate risk scores from different countries into defined clusters – such as BRICS (Brazil, Russia, India, China and South Africa), BRICS-MT (Brazil, Russia, India, China, South Africa, Mexico and Turkey), and Emerging Europe (Czech Republic, Hungary and Poland) - for easier comparison. Their respective risk scores were 4.17, 4.96 and 3.30. **CONCLUSIONS:** Market Access Risk ratings could serve as a starting point for crafting tailored strategies to fully capitalise new opportunities. These ratings could also serve as a benchmark for a country to improve its overall access to pharmaceutical products and improve quality of care.

PHP103

CAN VARIATION IN HOSPITAL PROCEDURE RATES IDENTIFY CANDIDATES FOR HEALTH TECHNOLOGY REASSESSMENT AND DISINVESTMENT?

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OBJECTIVES: The process of disinvestment from inefficient health care involves identification and prioritisation of candidates, a health technology reassessment (HTR)of evidence, implementation and monitoring of discontinuance. We evaluate whether variation in procedure rates is a useful tool for identifying potential candidates for HTR and disinvestment. **METHODS:** We used English Hospital Episode Statistics (HES) data to identify inpatient procedures. We selected the 181 most frequent interventional procedures for analysis. For each procedure we used Poisson regression to estimate the variance in procedure rates, adjusting for age, gender and other proxies of clinical need, between Primary Care Trusts in England. We conducted multivariate regression analyses to examine factors that might be associated with high variation in procedure rates (e.g. coding uncertainty, evolving evidence). **RESULTS:** The degree of inter-PCT variation in procedure rates differed vastly from procedure to procedure. Among the five procedures with the highest inter-PCT variance, the procedure rate was more than thirty times higher in the PCT at the ninetieth percentile than the PCT at the tenth percentile. The multivariable analysis provided strong evidence that large increases in procedure use, large decreases in procedure use, the presence of a substitute procedure, and shorter length of stay were all associated with higher inter-PCT variation in procedure rates. **CONCLUSIONS:** The widespread geographic variation in hospital procedure rates in England are not solely due to variance in clinical need and are likely to reflect clinical uncertainty about appropriate procedure use which might be reduced by HTR. The relevant HTR questions often concern the appropriate procedure setting and patient subgroups or the relative value of two alternative procedures rather than the value of a single procedure per se. In some circumstances knowledge of geographic variation might lead to NHS savings and disinvestment or discontinuation of inefficiently used procedures.

PHP104

INFERENCE ON INCREMENTAL COST EFFECTIVENESS THRESHOLDS INFLUENCING NICE DECISIONS: A BAYESIAN ANALYSIS

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OBJECTIVES: NICE has been issuing health technology guidance based on cost-effectiveness evidence alongside other factors since 2000. Previous studies have shown that technologies with higher incremental cost-effectiveness ratio (ICER) were more likely to be rejected; however none drew direct inference on the ICER threshold(s). Our aim is to directly estimate the ICER threshold(s) as well as the possible range. **METHODS:** Data were abstracted from the technology appraisals (TA) published from 03/2000 to 12/2012. For each decision to 'recommend' or 'reject' a technology we collected: ICER, publish date, disease area, technology type, comparator, reason for rejection if rejected, population and end of life (EOL) criteria (applies only to TAs after January 2009). Cancer related technologies which had been evaluated for EOL criteria were classified as satisfying or not satisfying the criteria. A Bayesian hierarchical model was implemented to estimate the overall threshold as well as the thresholds in different technology categories. **RESULTS:** A total of 270 TA's were evaluated. After excluding those updated or terminated, a total of 187 appraisals with 323 decisions entered the final analysis. Non-informative priors were given to all the model parameters. The unadjusted estimate of the ICER threshold was £46,850 (95% CI: £40,420-£55,570). After adjusting for disease area, cancer related technologies had an estimated threshold of £48,550, (95% CI: £36,550-£63,200) compared to non-cancer related technologies' estimated threshold of £43,430, (95% CI: £35,440-£52,300). Among the 37 technologies evaluated for end of life criteria, the estimated ICER threshold was £56,160, (95% CI: £39,020-£79,970) and £33,100, (95% CI: £19,180-£49,620) for those satisfying and not satisfying the criteria respectively. **CONCLUSIONS:** Preliminary assessment of NICE appraisals and associated ICER indicates that a likely ICER threshold exceeds the £20K-£30K quoted in the NICE Methods Guide. Additional analyses are needed to assess the impact of other factors on the likely variability of ICER thresholds.

PHP105

DRIVERS OF CLINICIAN PRESCRIBING DECISIONS AND THE ECONOMICS OF INFORMATION

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OBJECTIVES: Policy decision makers require accurate forecasts of the financial implications of funding a new drug. They may also wish to influence adoption to ensure the most cost-effective pattern of care. The seminal theory regarding the adoption of innovations was published by Rogers in 1962; but there are several reasons why health care may be a special case. This paper assesses the applicability of Rogers's theory to the adoption of new drugs, and identifies how it could be extended using economic theories of information. **METHODS:** The empirical literature on drug adoption was reviewed to determine the consistency of findings with Rogers's theory and the economic theories of information. **RESULTS:** Overall 74 empirical studies were reviewed. Clinicians consider a broad range of attributes when adopting a new drug, with their relative importance dependent on the patient and therapeutic area. Consistent with Rogers's theory, interpersonal communication channels are the most important information source, with clinicians, especially GPs, more likely to rely on advice from specialists or pharmaceutical representatives than peer-reviewed publications. Moreover, clinicians are influenced by 'norm' prescribing behaviour. These findings can be further explained using economic theories of information. Obtaining information via peer-reviewed publications requires more effort compared to specialists and pharmaceutical representatives. As patients cannot observe the effort expended, there is a potential for moral hazard in terms of reduced effort and thus an increased reliance on pharmaceutical representatives. Clinical evidence is often uncertain and not always directly applicable to current practice, which can lead to following 'norm' prescribing behaviour and persistent prescribing when combined with risk-aversion. **CONCLUSIONS:** Rogers's theory only partially explains drug adoption. An expanded framework regarding drug adoption is proposed, incorporating agency relationships, moral hazard, uncertainty and risk-aversion.

PHP106

HEALTH ECONOMIC ANALYSES IN MEDICAL NUTRITION: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: Medical nutrition is dedicated to patients with some nutritional deficiencies or inability to eat normally. When used on top of normal diet in patients or in Crohn's disease, medical nutrition can improve patient's recovery or have a therapeutic effect. Although efficacy studies of medical nutrition exist, it is unclear regarding health economic analysis. This research assessed the current health economic evidence published on medical nutrition. **METHODS:** A systematic literature search was performed using PubMed, the Health Technology Assessment Database, and the NHS Economic Evaluation Database. For selected articles, the clinical background and basis of the analysis, health economic design and results were extracted. Finally for health economic modeling studies, the Drummond checklist was applied to validate their quality; whereas for systematic reviews the AMSTAR checklist was used. **RESULTS:** Fifty-three articles were identified and obtained via PubMed. Among them, 32 articles have been included in a thorough data extraction procedure. Among these articles, only few health economic models have been found: Most of the articles were modelling analyses and economic trials. Overall only 8 health economic models were validated applying the Drummond checklist. Anyhow, most included models have been carried out with a quite high quality standard even though some areas were identified for further improvement. Within the two identified reviews of health economic studies one review achieved the highest quality scores applying the AMSTAR checklist. **CONCLUSIONS:** Reasons for finding only few modeling studies but quite a large number of clinical trials with health economic endpoints might have different reasons. Until recently, health economics wasn't required in reimbursement or coverage decisions for medical nutrition interventions; and there might be specificities of medical nutrition which might not allow easy modeling. Further research is warranted to understand the specifics of medical nutrition and its applicability for health economic modelling.

PHP107

PREFERENCE STRUCTURE OF CLINICIANS IN THE USE OF ELECTRONIC MEDICAL RECORDS; QUANTIFYING THE RELATIVE IMPORTANCE OF BARRIERS AND FACILITATORS OF AN INNOVATION

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OBJECTIVES: Electronic medical records (EMRs) in hospitals are potentially beneficial for quality and safety of care, but diffuse slowly. Many of the barriers and facilitators of the adoption of EMRs are identified, but the relative importance of these factors is still undetermined. This paper quantifies the relative importance of known barriers and facilitators of EMR, experienced by the users (i.e., nurses and physicians in hospitals). **METHODS:** A d-efficiently designed discrete choice experiment (DCE) was conducted among physicians and nurses. Participants answered ten choice sets containing two scenarios. Each scenario included attributes that were based on previously identified barriers in the literature and the model of the Unified Theory of Acceptance and Use of Technology (UTAUT), namely : data entry hardware, technical support, supervisor attitude, performance feedback, flexibility of interface and decision support. Panel Mixed Multinomial Logit analysis was used to determine the relative importance of the attributes. **RESULTS:** Data on 148 nurses and 150 physicians showed that high flexibility of the interface was the most important factor for the intention to use the EMR. For nurses this attribute was followed by support from supervisor, presence of performance feedback from the EMR and presence o f decisions support. While for physicians this ordering differed since presence of decision support was relatively more important than performance feedback and support from the supervisor. **CONCLUSIONS:** Considering the prominent wish of all the intended users for a flexible interface, currently used EMRs only partially comply with the needs of the users, indicating the need for closer incorporation of user needs during development stages of EMRs. The differences in priorities amongst nurses and physicians show that different users have different needs during the implementation of innovations. Hospital management may use this information to design implementation trajectories to fit the needs of various user groups.

PHP108

EVALUATE THE STATUS OF PHARMACOECONOMIC RESEARCH DEVELOPMENT IN CHINA FROM 2002 TO 2013

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OBJECTIVES: To describe the current status of Pharmacoeconomic (PE) research in China from Jan 2002 through June 2013. **METHODS:** We conducted a review of pharmacoeconomic studies performed in China during Jan 2002 to June 2013. Using the Wanfang Chinese Database, we identified a total of 1338 articles. Keywords used are 'Pharmacoeconomics' or 'Cost-Effectiveness Analysis' or 'Cost-Benefit Analysis' or 'Cost-Utility Analysis' or 'Cost' or 'Cost Study' or 'Economics Analysis' all following by '(Healthcare and Medical Care)' to exclude animal and other studies. Through a manual review, we excluded another 52 articles that did not align with study objectives. Article types selected are Journals, Academic Essays and Conference Essays. Descriptive analyses were performed to identify current trends, including number of articles by year, type of studies, and type of studies by year. **RESULTS:** A total of 1286 articles were conducted in China from 2002 to 2013. In general, the number of articles per year has been on the rise since 2002and appears to approach a steady state after 2007. Numbers of articles by year are 91 in 2002, 84 in 2003, 107 in 2004, 110 in 2005, 136 in 2006, 132 in 2007, 121 in 2008, 120 in 2009, 130 in 2010, 116 in 2011, 112 in 2012 and 27 during first half of 2013. The most common type of studies found were economic analyses (n=908/1286), of which cost-benefit analyses (n=395) were most commonly conducted. Two other common research types included treatment use (n=48) and application of PE (n=146), namely the role of PE to help determine price and inform health care management decisions. **CONCLUSIONS:** The development of Pharmacoeconomic research in China has been on a steady rise since 2002 with most output focused on economic modeling, followed by application of PE and treatment use.

PHP110

LONG-TERM SURVIVAL AFTER INTENSIVE CARE UNIT DISCHARGE IN THAILAND: A RETROSPECTIVE STUDY

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OBJECTIVES: Economic evaluations of interventions in the hospital setting often rely on the estimated long-term impact on patient survival. Estimates of mortality rates and long-term outcomes among patients discharged alive from the intensive care unit (ICU) are lacking from lower and middle-income countries. This study aimed to assess the long-term survival, life expectancy (LE) and the quality-adjusted life expectancy (QALE) amongst post-ICU patients in a middle-income country. **METHODS:** In this retrospective cohort study, data from a regional tertiary hospital in northeast Thailand and the regional death registry were linked and used to assess patient survival time after ICU discharge. Adult ICU patients aged at least 15 years who had been discharged alive from an ICU between 1anuary 1, 2004 and December 31, 2005 were included in the study, and the death registry was used to determine deaths occurring in this cohort up to December 31, 2010. These data were used in conjunction with standard mortality life tables to estimate annual mortality and LE. **RESULTS:** A total of 10,321 ICU patients were included in this analysis; 3,251 patients (31.5%) died during ICU admission. Of 7,070 patients discharged alive, 2,527 (35.7%) were known to have died within the five-year follow-up period, a mortality rate 2.5 times higher than that in the Thai general population (age- and sex-matched). The mean LE was estimated as 18.3 years compared with 25.2 years in the general population. Given the range of the Health Related Quality of Life (HRQOL) from the published literature, the mean QALE of post-ICU patients would range from 10.2 to 16.1. **CONCLUSIONS:** Post-ICU patients experienced much higher rates of mortality than members of the general population over the five-year follow-up period, particularly in the first year after discharge. Further work assessing HRQOL in both post-ICU patients and in the general population in developing countries is needed.

PHP111

INVESTIGATING SAFETY-APPRAOCH IN SAUDI ARABIA MINISTRY OF HEALTH HOSPITALS

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Joint commission (JCI) International Patient centered standards-2011 promotes improvements in patient safety(ISPG) & Medication Management Use (MMU). **OBJECTIVES:** To investigate historical changes of patient-safety approach in Saudi Arabia, create comparison baseline for future studies. **METHODS:** Cross-sectional 2003 survey sent to pharmacy managers of 127 hospitals of Ministry of Health(MOH); 67.7% responded; data of 63.7% hospitals were valid for analysis. 19 hospitals were chosen deliberately according to their level of development, their data was tested against selected criteria. Due to limitations of data; only 2 criteria were selected:

IPSG.1; identify patients correctly (criteria 1) and MMU.1& MMU.7; identify medication use & monitoring (criteria 2) Average for conforming to both criteria was calculated for each hospital. Correlation was tested between compliance to both criteria and hospital characteristics which were hospital type; general/tertiary & hospital geographical location; urban/rural. For each criterion; several measurables were selected from literature; and their average was calculated accordingly. Criteria 1; 1 measurable, composed of 2 components of which there average was calculated. Criteria 2; 2 measurables; measurable for MMU.1 composed of 3 components, while measurable for MMU.7 composed of 2 components. Average of averages was calculated. **RESULTS:** A total of 89.47% were complying to criteria 1 &10.53% non-complying with 10 hospitals 100% conforming. 52.63% were complying to criteria 2& 47.37% non-complying. Average compliance percentage with criteria 1 was 97.75, 85.91& 98.25 for general rural, general urban and tertiary urban hospitals respectively. In case of criteria 2, it was 28.75, 27.18& 20.5 for general rural, general urban and tertiary urban hospitals respectively. Correlations could not be established, no significant difference in means of compliance between or within criteria for different geographical locations or different hospital types; this can be contributed to the small sample size. **CONCLUSIONS:** A baseline for comparison of compliance to safety-related approach in Saudi Arabia was established which can be used for comparison in future studies.

PHP112

PHARMACISTS' SATISFACTION WITH DIFFERENT PHARMACEUTICAL DISTRIBUTION MODELS IN FIVE EUROPEAN COUNTRIES

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OBJECTIVES: Serving 172,709 dispensing points, the pharmaceutical wholesale-industry is a vital branch. One of the major business-objectives is total-customer-satisfaction. Thus, a questionnaire aimed to draw a comprehensive picture of the level of satisfaction (including delivery-times and country-specific-issues) of pharmacists with pharmaceutical-full-line and short-line wholesalers, Direct-sales from manufacturers, Direct-to-Pharmacies (DTP) and Reduced-Wholesale-Arrangements (RWA) in Europe, focusing on Germany, UK., France, Spain and The Netherlands. **METHODS:** The necessary data was obtained from an online-questionnaire (March 2011-October 2011) which was directed to pharmacies (n=473). **RESULTS:** The majority of the observed countries (99% in Spain to 72% in the UK) of the respondent pharmacists were satisfied with the distribution through pharmaceutical-full-line-wholesalers. With regard to the delivery-time offered by pharmaceutical-full-line wholesalers the satisfaction ranged from 97% in Spain to 76% in the UK. With regard to the distribution through short-line-wholesalers 62.50% of the German pharmacists were satisfied. With their delivery-time 56.30% of the pharmacists were satisfied, whereas 50.00% (distribution) and 38.90% (delivery-time) of the Dutch-participants showed satisfaction. Less than half of the respondents (58% in Spain to 12% in the UK) in four out of the five countries observed showed satisfaction with the distribution through Direct-sales from manufactures. 80% of the pharmacists in the UK were unsatisfied with this kind of distribution-system. Concerning the delivery-time pharmacists in the majority of the observed countries answered with neutral. Pharmacists in the UK (76%) were unsatisfied with Direct-sales from manufacturer. Pharmacists in the UK were unsatisfied with Direct-to-Pharmacy and the Reduced-Wholesale-Arrangements (DTP: 89.70% distribution vs. 75.90% delivery-time; RWA: 90.80% distribution vs. 58.50% delivery-time). Country-specific-issues mentioned were lack-of-availability of medicinal-products, stock-problems (UK), out-of-stocks problems (NL), shortages, supply-problems (ES) and decrease in discount-rates (DE). **CONCLUSIONS:** The satisfaction of pharmacists varies greatly between different distribution-models. Responding pharmacists in the countries observed receiving their medicinal-products through pharmaceutical full-line-wholesalers showed overall-satisfaction with this kind of distribution-system.

PHP113

THE FUTURE OF INDIVIDUAL FUNDING REQUESTS IN CLINICAL COMMISSIONING GROUPS ERA

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OBJECTIVES: Until March 2013,decisions on Individual funding requests (IFRs) had been the job of the primary care trusts to decide upon such requests. It has been widely acknowledged that IFRs to fund particular treatments have caused PCTs some thorny problems (with the rate of acceptance of IFRs having fallen from 59% in 2008/09 to 46% in 2010/11). However, with the Clinical Commissioning Groups (CCGs) formally assuming commissioning responsibilities for their local populations since April 2013, it is expected that health services and care pathways will become more patient focussed. The objective of this study was to assess whether IFRs will enjoy better success under the so-called 'patient centred' CCG leadership. **METHODS:** This research was based on a combination of secondary and primary research to assess the CCGs attitudes and expertise to cope with IFRs. Secondary research of published data such as current IFR policies and overall CCG health care priorities contributed towards a framework to understand the key factors affecting successful management of IFRs, which was then validated through a telephone survey of health care stakeholders. **RESULTS:** CCGs understand the importance and the value of having a clear and robust IFR policy. Learning from PCTs, CCGs also realise that having a clear IFR standard operating procedures and clear timeframes would mean spending significantly less time considering and defending decisions on IFRs. Some CCGs also believe that public conversation may be required IFRs are to be managed effectively. **CONCLUSIONS:** While CCGs realise that IFRs would be one of complicated bit of commissioning responsibilities, their real challenge is avoid making the same mistakes as PCTs. Early engagement with local populations about commissioning priorities is perceived to be crucial. Also the success of IFRs depends on organisations such as NHS Clinical Commissioners due to their dual role as CCG supporter and a body accountable to government.

PHP114

PRE-FINANCING FUNCTION OF THE PHARMACEUTICAL FULL-LINE WHOLESALE SECTOR IN THE EUROPEAN UNION

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OBJECTIVES: Pharmaceutical full-line wholesalers carry out a variety of main functions. One of these is the financing function. Pharmaceutical full-line wholesalers stock and distribute the complete assortment of products in range and depth. Moreover, they acquire ownership over the medicinal products when purchasing them from the manufacturers and pass on ownership to pharmacies when they are delivered. Thus, the analysis aims to draw a comprehensive picture of the pre-financing function, expressed in terms of working capital, of the pharmaceutical wholesale sector in Europe. **METHODS:** The necessary data was provided by the European Association of Pharmaceutical Full-line Wholesalers (GIRP). The study analysed core indicators representative for all countries of the European Union plus Croatia, Norway and Switzerland (EU-25 + 3), with the exception of Malta and Cyprus as no full-line wholesalers are operating in the latter. **RESULTS:** In the analysed countries, 935 pharmaceutical full-line wholesalers operate 1,220 warehouses, serving 171,767 retail and hospital pharmacies and dispensing doctors and supply 520 million people. In 2012, pharmaceutical full-line wholesalers generated a total turnover of €130 billion in the EU-25 + 3. Pharmaceutical full-line wholesalers assume a pre-financing function towards manufacturers and pharmacies that is not offered by other distribution models. In the EU-25 + 3 alone they pre-financed on average €12.2 billion over a period of 35 days. In total, this sum is pre-financed approximately ten times per year. **CONCLUSIONS:** Pharmaceutical full-line wholesalers pre-finance the entire retail market of medicinal products, guarantee the continuous supply of all medicinal products and secure the cash flow of social insurers. The funding and holding of buffer stocks, the resulting working capital and ownership that goes with wholesaling services are vital for an effective and efficient functioning of the health care industry in Europe.

PHP115

ESTIMATING MARKET POTENTIAL FOR BIOSIMILAR INTRODUCTION

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OBJECTIVES: The global biopharmaceutical industry is facing a biologics "patent cliff" between 2013 and 2020, which will leave approximately $54 billion in drug revenue, without patent protection. In order to achieve success with these biosimilar agents, it is critical that manufacturers/marketers target the highest potential global markets. The objective of this research is to provide a framework for identifying the markets with the highest potential for biosimilar adoption and utilization. **METHODS:** A review of literature, research reports, and review articles was conducted, along with a panel discussion of industry thought leaders in biosimilars. Key indicators of biosimilar market potential were identified, evaluated, and prioritized. A systematic approach was developed to score each key indicator, and a mathematical approach adopted to aggregate the market scores. A series of 20 country markets were evaluated and ranked in order of biosimilar market potential. **RESULTS:** Key indicators of biosimilar market potential were separated into three categories: 1.) Originator-drug indicators including originator sales, reimbursement level, and reimbursement status. 2.) Market indicators including rate of uptake of currently available biosimilars, payer cost-containment mechanisms, and future biosimilar outlook. 3.) Regulatory indicators including barriers to marketing authorization based on the complexity of required data packages, and the risks associated with the development of clinical programs. Secondary research of public domain information was conducted on each of 20 countries, in order to obtain the data to populate the key indicators for market potential. Each country achieved a score based on the data, and was ranked based on biosimilar market potential. **CONCLUSIONS:** The process demonstrates a rational approach to identifying and sequencing of biosimilar market potential, which can be used to inform clinical-development and market-access plans. Also, in practical application for a manufacturer/marketer, "resource indicators" of market-specific assets should be included.

PHP116

CONFIDENTIAL PATIENT ACCESS SCHEMES IN THE UNITED KINGDOM – DO THEY AFFECT PRICES IN OTHER MARKETS?

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OBJECTIVES: To investigate whether trends exist in drug prices of products approved by the UK NICE with a Patient Access Scheme in other key EU countries in the last 2 years. **METHODS:** Expensive new pharmaceuticals that are not deemed cost-effective by NICE in the first instance, can often still become recommended with a Patient Access Scheme. It is a trend that the type of scheme offered is becoming purely financial-based, with the last 17 schemes approved offering a simple discount. Although these discounts are 'commercial in confidence', the company's willingness to negotiate is obvious. To investigate if NICE recommended drugs with simple discount schemes affect pricing elsewhere in Europe, we compared their list prices in France, Germany, Italy and the UK. The analysis focused on pharmaceuticals recommended after 1 January 2011. **RESULTS:** Since 2011, 20 therapies were recommended by NICE with a PAS based on a simple discount. In all except one case, the UK list price was the lowest among available list prices in all countries analysed. Where an Italian list price was available it was usually the highest. When comparing the prices on an ex-manufactory level, the UK prices remain the lowest, but the German prices are generally the most expensive in this scenario. Of the countries analysed, only Italy has a risk sharing framework in place besides the UK. Out of the 20 therapies analysed here, only 3 were under an Italian scheme. **CONCLUSIONS:** The analysis shows that even before a PAS discount is applied, the UK price is already low, usually the lowest in the 4 EU countries analysed. There were no clear

signs that a potential discount had lowered a list price in one of the other countries, but is it clear that despite the external reference price systems in Europe prices of high-priced therapies vary considerably.

PHP118

PUBLIC PREFERENCE ELICITATION IN DRUG REIMBURSEMENT USING MULTI-CRITERIA DECISION ANALYSIS (MCDA) FOR UNIVERSAL HEALTH INSURANCE SYSTEM IN SOUTH KOREA

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OBJECTIVES: To elicit public preference for drug reimbursement criteria in Korea's universal health insurance system using three commonly used weighting methods in Multi-Criteria Decision-Analysis (MCDA). **METHODS:** Based on literature review, we established five criteria in drugs reimbursement decision-making: disease impacts, context of reimbursement, improvement of health outcomes, economics and quality of evidence. We evaluated the relative importance of five criteria using three weighting methods of direct rating (DR), SWING and analytic hierarchy process (AHP). 283 people were selected across the country by quota sampling and asked to assess the weights of five criteria with all three weighting methods repeatedly. The survey was self-administered by the participants with help of the trained interviewers. **RESULTS:** It was revealed that improvement of health outcomes and disease impacts have relatively higher weights than other three criteria in all weighting methods. Survey participants considered improvement of health outcomes the most important with DR (Mean [SD]: 0.210 [0.033]) and AHP (0.271 [0.127]), whereas disease impacts with SWING (0.231 [0.050]). Meanwhile, no coherence was shown in the low-ranked three criteria (context of reimbursement, economics, and quality of evidence) over three weighting methods. Quality of evidence ranked the third with DR (0.200 [0.035]), the fifth with SWING (0.165 [0.041]) and the fourth with AHP (0.160 [0.121]). Economics ranked the fourth with DR (0.197 [0.035]) and the third with SWING (0.192 [0.045]) and AHP (0.207 [0.118]). Lastly, context of reimbursement ranked the fifth with DR (0.188 [0.035]) and AHP (0.112 [0.090]) and the fourth with SWING (0.189 [0.045]). **CONCLUSIONS:** In this study, it was discovered that the survey participants considered improvement of health outcomes and disease impacts relatively more important than economics, context of reimbursement and quality of evidence in drug reimbursement decision making.

PHP120

DIFFUSION OF THE EFFICIENCY FRONTIER APPROACH WITHIN HEALTH ECONOMIC EVALUATION: CURRENT AND FUTURE APPLICATIONS

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OBJECTIVES: This study explores current applications (and potential future use) of the Efficiency Frontier (EF) in health economic evaluation. **METHODS:** We performed desk research on pharmacoeconomic guidelines for current usage of the EF and investigated possibilities for future use. **RESULTS:** Currently, the EF is officially used in 3 European countries. In Germany, since the enforcement of the 'Act on the Reform of the Market for Medicinal Products' (AMNOG) in January 2011, IQWiG applies the EF to determine non-arbitrary flexible thresholds across disease areas to ultimately determine an appropriate reimbursement price of new drugs (including interquartile-range to display uncertainty) in negotiations on request of the decision maker or manufacturer. In Belgium, the updated KCE guidelines dated July 2012 request the EF to identify the appropriate comparator among all relevant alternatives. In France, the updated HAS guidelines dated October 2012 require health interventions to be plotted on the EF to inform decision-making. In the future, the EF-approach could also be used to check on prices of national reference pricing clusters. Furthermore, the EF could help with priority setting (as suggested by the World Health Organization guide to cost-effectiveness analysis in 2003) and guiding or informing potential future (dis)investment decisions. The EF may also be combined with other approaches (e.g. making reimbursement decisions up to an ex ante fixed cost/outcome-threshold but setting prices beyond that level with the flexible EF). Lastly, it should not be overlooked that the EF can be applied for multiple purposes simultaneously. **CONCLUSIONS:** Since its first use to measure hospital efficiency, the EF is a valuable tool in health economics. Currently, its use diffuses within health economic evaluation and reimbursement decision-making. Yet, the full potential of the approach has not been exploited so far and the EF-approach remains under-researched by the scientific community.

PHP122

IMPACT OF THE GERMAN AMNOG EVALUATION ON DRUG PRICES: CORRELATION OF REBATE?

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OBJECTIVES: In January 2011 the new German law on the reorganization of the pharmaceutical market (AMNOG) came into force with the intention to reduce drug prices in Germany. Up to June 2013 44 dossiers completely evaluated and for 16 drugs (excluding orphan drugs) a price has been negotiated between the manufacturer and the National Association of Statutory Health Insurance Funds (GKV-SV). Since previous analyses have shown no correlation of negotiated price and the extent of clinical benefit, the underlying analysis aims to identify further parameters potentially influencing the reimbursed price of a new drug. **METHODS:** Evaluated drugs with completed price negotiation between manufacturers and the GKV-SV were selected from the website of the Federal Joint Committee (G-BA). The manufacturer free price was analyzed for potential interactions with following parameters extracted from module 3 of the AMNOG dossier: number of eligible patients, annual drug cost of the evaluated intervention and appropriate comparator, and the final price as listed in the Lauer-Taxe (official German drug price index). **RESULTS:** The 16 drugs, for which a negotiated reimbursement price was available, showed a minor (n=8), considerable (n=5), not quantifiable (n=2) or no additional clinical benefit (n=1).The investigated drug price was between 0,73 and 71 times the price of its appropriate comparator before entering negotiations. The negotiated price was between 0% and 56% lower compared to the price listed in the AMNOG dossier, regardless of the level of additional benefit. The number of eligible patients for each drug (141 - 214,000) tends to correlate with the negotiated rebate. **CONCLUSIONS:** An additional benefit is necessary for a reimbursement beyond the reference group price. Despite the small number of observations it might be concluded, that the reimbursed price inversely correlates with disease incidence. The highest rebate on reimbursement price resulted from the decision of the arbitration board.

PHP123

INFORMING THE AFFORDABILITY OF VACCINES WITH DIFFERENT HEALTH CARE FINANCING MECHANISMS

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OBJECTIVES: Budget impact analysis is the traditional approach of assessing the affordability of new interventions. While vaccination has been shown to be one of the most cost-effective means to improve health, budget requirements can be a barrier. This study aims at comparing an affordability indicator of a new vaccine in countries with similar Gross Domestic Product (GDP) per capita, but different health care financing mechanisms. **METHODS:** Based on National Health Accounts data, analyses of Total Health Expenditures (THE) and share of Public Health Expenditures (PHE) of various middle income countries were performed. Brazil and Turkey were selected for in-depth analysis as they had comparable GDPs and health care expenditures per capita. Health care access and financing data were also obtained from various government sources for a quantitative analysis. The budget requirements for a new vaccine costing $40 Purchasing Power Parity (PPP) per immunized child covering 80% of the birth cohort were calculated and expressed as a share of PHE. **RESULTS:** THE per capita doubled over 10 years in both countries since 2001, reaching $1,037 (PPP) for Brazil and $1,160 for Turkey in 2011. However, the share of PHE is vastly different; 46% in Brazil compared to 75% in Turkey. Implementing the new vaccine would require an additional budget of $97Million and $42Million. While large in absolute values they represent only 0.11% of the PHE in Brazil and 0.07% in Turkey. The higher affordability in Turkey can be explained by a different financing mechanism. **CONCLUSIONS:** While the implementation of a new vaccine in comparable countries in terms of wealth and THE per capita would require significant additional national spending in absolute terms, it represents only a small fraction of the PHE. The underlying health care financing mechanisms is an important factor affecting the affordability of a new vaccination program.

PHP124

IQWIG'S EFFICIENCY FRONTIER APPROACH: FIT FOR PURPOSE!

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OBJECTIVES: Since its adoption by the Institute for Quality and Efficiency in Health Care (IQWiG) in 2009, the Efficiency Frontier (EF) approach is criticized by the pharmaceutical industry, key opinion leaders and national organizations. In a German context, we aim to verify the accuracy of those concerns. **METHODS:** Review of the most commonly stated arguments against the EF-approach published within the scientific community and given as stakeholders' response on IQWiG's first cost-effectiveness analysis of antidepressants. **RESULTS:** Often stated objections against the EF include: 1) no international health economic standard, 2) merely disease specific without prioritization across disease areas, 3) no fixed threshold, and 4) avoiding the quality-adjusted life year (QALY). Ad 1): IQWiG adopted the EF-approach to inform setting appropriate reimbursement caps (since 2011 to inform negotiations for appropriate reimbursement caps with an interquartile-range as basis). In other jurisdictions, an appropriate price need not be determined; decisions (or recommendations) are made regarding whether or not the cost-effectiveness of a drug supports (restricted) reimbursement. Ad 2+3): Although prioritizing funds is no primary aim in Germany, the EF can still be applied equally across indications. Within indications, the reimbursement cap may not distort competition by disadvantaging a manufacturer unfairly and needs to be appropriate when compared with other available interventions. Contrary to the EF-approach, determining prices based on arbitrary fixed thresholds may not stand up in court. Ad 4): Despite methodological doubts concerning QALYs, they are not antecedently excluded as possible patient-relevant outcome measure when using the EF in Germany. Only a fixed cost/QALY-threshold was rejected. **CONCLUSIONS:** The EF fits the purpose of decision-making in Germany. Most objections are flawed or originate from a profound misunderstanding of the concept or the German (legal) context, where the EF is necessary and viable. The EF's prime distinction remains: Deriving flexible, non-arbitrary thresholds for disease areas.

PHP125

A SYSTEMATIC COMPARISON OF MARKET ACCESS AND REIMBURSEMENT PATHWAYS FOR DIAGNOSTIC TESTS IN GERMANY, UNITED KINGDOM AND THE UNITED STATES

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OBJECTIVES: A diagnostic test is any kind of medical test performed to aid in the diagnosis or detection of disease and is becoming a key component of Personalized Health Care (PHC). The market access and reimbursement pathways for pharmaceuticals are well described however such pathways are missing for diagnostics in many countries and similarities between countries are not well understood. **METHODS:** A targeted literature review has been executed on top of reviews from market access and reimbursement authorities in Germany, the UK and the US. Existing pathways were plotted and key decision criteria have been evaluated in terms of comparability and health care decison-maker impact. **RESULTS:** In Germany inpatient reimbursement is being differentiated from outpatient with inpatient access being easier to be achieved (DRG, OPS coding). The outpatient pathway includes a full evidence pack-

age including clinical and health economic data and takes on average more than two years. In the UK the process is largely based on three different PCT payment and the various NHS value for money mechanisms combined with procurement systems. The value-based pricing system might change the current situation. Finally, in the US CPT codes are similarly being applied as DRG codes in Germany with a different pathway of application. In comparison the health economic evidence plays a larger role in the UK, even though (still) not in a systematic manner as for pharmaceuticals. The clinical evidence plays an important role in all countries, however it was identified that for diagnostic tests the access routes and especially the coding process is more dependent on consistency on applicability of existing codes and technology argumentation. **CONCLUSIONS:** In the different countries the evidence base for market access and reimbursement pathways for diagnostics differs significantly. Instead, having a unified approach might ease a value based market access argumentation for diagnostics.

PHP126

A COMPARATIVE STUDY OF THE ROLE OF DISEASE SEVERITY IN DRUG REIMBURSEMENT DECISION MAKING IN BELGIUM, FRANCE, THE NETHERLANDS AND SWEDEN

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OBJECTIVES: Considerations beyond (cost-) effectiveness are increasingly important in reimbursement decision-making. We investigated the importance of disease severity relatively to other decision criteria in drug reimbursement decision-making in four European countries. **METHODS:** The importance of disease severity and its operationalization was assessed in Belgium, France, The Netherlands and Sweden. We investigated scientific literature, policy documents, reimbursement reports, and conducted three interviews in each country (four in The Netherlands) with policymakers involved in drug reimbursement. **RESULTS:** All interviewees acknowledged that disease severity is, especially in case of high severity, an important criterion while considering a drug's (cost-) effectiveness. However, its relative importance compared to other decision criteria remains implicit in the decision-making process. Although rarity of the disease is not a criterion as such, interviewees indicated difficulties in separating rarity from severity and the availability of alternative treatments. Only Belgium and France explicitly show societal willingness to pay by using reimbursement levels depending on the severity of the disease. In Sweden, 'need and solidarity' is one of the three prioritizing principles. The Netherlands is the only country that quantitatively operationalized disease severity using the proportional shortfall method and suggesting a cost-effectiveness threshold range depending on disease severity (which was never formalised by the minister). Although interviewees acknowledged that quantitative information, besides a qualitative description of the disease, may provide additional decision information, none of them considered such information to be of decisive importance. **CONCLUSIONS:** Disease severity is, especially in case of high severity, an important decision criterion in all four countries. However, all countries seem to struggle in making its actual role explicit. The operationalization differs across countries. While Belgium and France are most explicit by using the severity of the disease in setting reimbursement levels, all countries could improve transparency of its actual importance relatively to other decision criteria.

PHP127

CLINICAL AND HEALTH ECONOMIC EVIDENCE REQUIREMENTS FOR OBTAINING HEALTH INSURANCE COVERAGE FOR INNOVATIVE MEDICAL DEVICES IN GERMANY

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OBJECTIVES: To evaluate the clinical and health economic evidence requirements for obtaining statutory health insurance coverage for innovative medical devices (MDs) in Germany. **METHODS:** We have assessed the requirements for innovative MDs in Germany according to the available reimbursement pathways and grouped them by the application setting as this had a significant impact on the research question. **RESULTS:** According to the German statutory rules in the inpatient care setting (reservation of prohibition; 'Verbotsvorbehalt') all innovative MDs can be applied once they have received marketing approval for Germany (CE mark) whereas a positive voting from the federal joint committee is required before MDs can be applied in the outpatient setting (reservation of authorization; ‚Erlaubnisvorbehalt'). The reimbursement coverage in the inpatient setting depends on the available coding and grouping mechanisms that define specific diagnoses related groups and their reimbursement value. If this value is not adequate or an adequate coding/grouping is not possible specific applications can be made, that require no specific clinical and health economic evidence; only a detailed (additional) cost estimation of the new procedure and a rationale of the innovative character are required. In contrast the outpatient reimbursement of the statutory health insurance shows very strict requirements as a detailed clinical evidence reporting (e.g. randomized-controlled trials) and a full health economic evaluation (e.g. cost-effectiveness and budget impact assessment) need to be provided for obtaining reimbursement coverage. There are recent political streams that claim that the regulatory and reimbursement process of MDs should be adapted comparable to the more restrictive regulations for pharmaceuticals which might have a major impact on the evidence requirements for the inpatient sector. **CONCLUSIONS:** Currently MDs applied in the inpatient setting require no specific evidence whereas strong clinical and health economic evidence is required for MDs applied in the outpatient setting.

PHP128

IMPACT OF REIMBURSEMENT OF MEDICINES ON ECONOMIC ACCESSIBILITY LEVEL FOR WORKING POPULATION IN REPUBLIC OF MOLDOVA

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OBJECTIVES: Moldova is a country where expenditure on pharmaceuticals is already very high and exceeds several times the prices in the region. Drugs expenditure represents 70% of direct health expenditure of a household and is the main factor that reduces the financial protection of health care services. The objective of the study was to assess affordability of reimbursement medicines and to evaluate the National Health Insurance Company (NHIC) impact on ensuring economic accessibility. **METHODS:** To determine the affordability of medicines was used the methodology recommended by the World Health Organization. Have been analyzed data concerning price of drugs, the amounts paid by patients and the amounts paid by the NHIC for partially reimbursed drugs for 5 years (2008-2012). Was calculated: the median price for each drug international common name dependent's on strength; duration of treatment and number of units needed for treatment (for chronic disease); number of working days required for a treatment cure depending on minimum wage and average wage in economy. Available treatment is considered, the cost of which is 1 or less than the cost of one working day. Based on these results has been also determined the impact of the NHIC. **RESULTS:** Number of economically accessible reimbursed drugs depending on minimum wage was: 2008-24 (42%), 2009-34 (60%), 2010-43 (53%), 2011-48 (58%), and 2012-71 (86%); depending on average wage in economy: 2008-50 (87%), 2009-50 (87%), 2010-66 (81%), 2011-73 (88%), and 2012-77(94%). The average number of working days compensated by NHIC based on the minimum wage: 2008-6.23, 2009-3.5, 2010-3.7, 2011-2.92, and 2012-1.03; based on average wage in economy: 2008-0.98, 2009-0.76, 2010-0.75, 2011-0.55, and 2012-0.38. **CONCLUSIONS:** Compensation of drugs by NHIC, doesn't significantly affect the affordability of reimbursement medicines. Patients feels no real benefit from NHIC, drugs expenditure within the households practically remain unchanged even if it get reimbursed medicines.

PHP129

ASSESSMENT OF METHODOLOGICAL QUALITY OF ECONOMIC EVALUATIONS IN BELGIAN DRUG REIMBURSEMENT APPLICATIONS

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OBJECTIVES: To assess the methodological quality of economic evaluations included in Belgian reimbursement applications for Class 1 drugs. **METHODS:** For 19 reimbursement applications submitted during 2011 and Spring 2012, a descriptive analysis assessed the methodological quality of the economic evaluation, evaluated the assessment of that economic evaluation by the Drug Reimbursement Committee and the response to that assessment by the company. Compliance with methodological guidelines issued by the Belgian Healthcare Knowledge Centre was assessed using a detailed checklist of 23 methodological items. The rate of compliance was calculated based on the number of economic evaluations for which the item was applicable. **RESULTS:** Economic evaluations tended to comply with guidelines regarding perspective, target population, subgroup analyses, comparator, use of comparative clinical data and final outcome measures, calculation of costs, incremental analysis, discounting and time horizon. However, more attention needs to be paid to the description of limitations of indirect comparisons, the choice of an appropriate analytic technique, the expression of unit costs in values for the current year, the estimation and valuation of outcomes, the presentation of results of sensitivity analyses, and testing the face validity of model inputs and outputs. Also, a large variation was observed in the scope and depth of the quality assessment by the Drug Reimbursement Committee. **CONCLUSIONS:** Although general guidelines exist, pharmaceutical companies and the Drug Reimbursement Committee would benefit from the existence of a more detailed checklist of methodological items that need to be reported in an economic evaluation.

PHP130

PRICING AND REIMBURSEMENT SYSTEM OF ORPHAN DRUGS IN THE CZECH REPUBLIC

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OBJECTIVES: In the CZ, orphan drugs so-called highly innovative drugs first enter a temporary reimbursement period of three years. Having proven their cost-effectiveness they later become permanently reimbursed. The objective of the study was to determine how successfully orphan drugs enter the database of reimbursed drugs. **METHODS:** The EMA list of orphan drugs was compared to the Czech database of reimbursed drugs to the date of 1-Jul-2013. For each detected drug the date of entering the database was found. In drugs reimbursed after 2008, submissions of cost effectiveness analyses were recorded. Although CZ has no willingness to pay threshold, interpretation of cost effectiveness analyses results could improve the process of HTA of drugs. **RESULTS:** To the date of 1-Apr-2013 the EMA has registered 65 orphan drugs. Out of these, 28 have been assigned a maximum and reimbursement price in the CZ. To this date, 27 drugs have not applied for reimbursement price. Starting from 2008, 30 drugs have applied: in 20 products the decision is legally effective, in 2 cases only hospital use has been approved, in 7 cases (3 appeals, 4 unfinished proceedings) the proceedings are still in process and in one case the application was withdrawn. In about a third of cases a cost effectiveness analysis was submitted and accepted by SUKL. The upper limit of the ICER of the submitted analyses exceeds by far the cost-effectiveness level recommended by the WHO. **CONCLUSIONS:** The results imply that in almost in all cases the submitted applications for maximum and reimbursement price are approved by SUKL. In some cases, however, the health insurance companies hinder reimbursement of drugs by filing an appeal. However, the assessment of cost effectiveness of drugs should be performed at an earlier level – during the administrative proceedings. This calls for necessary emphasis on health technology assessment.

PHP131

PRICING AND REIMBURSMENT OF PHARMACEUTICALS IN IRAN

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OBJECTIVES: To investigate the problem of pricing and reimbursement of pharmaceuticals in Iran. A large amount of country's Health care expenditures, including insurance organizations' expenses, are spent for pharmaceutical products. However, the high amount of capital spent by the users for purchasing pharmaceuticals indicates a serious flaw in the system. As will be shown, this flaw is due to the structures, policies, and regulations of Iranian medical insurance system. **METHODS:** This is a descriptive study and, therefore, ethnographic site and fieldwork were used as the main source of information. Furthermore, information on the Internet and several Iranian online databases has been used for comparison purposes. **RESULTS:** Ministry of Health and Medical Education (MOHME) is the main responsible body for pharmaceuticals in Iran. However, different government organizations such as Ministry of Commerce, the Central Bank of Iran, and National Industries Organizations are involved in policy-making in this sector. MOHME decides how to allocate governmental supports and foreign currency quotas, to various related industries. This is done due to the fact that MOHME decides which pharmaceuticals should be covered and distributed in the country. However, prices are set by insurance organizations due to their bargaining power over MOHME. Insurance companies pay approximately 70-90% of the final price of a product. However, for purchasing expensive products, confirmation from insurance companies is needed. The reimbursed price is set at the level of the lowest priced equivalent on the market. **CONCLUSIONS:** These flaws and loopholes arise because of system's negligence on research and development methods and, therefore, lack of standard regulations on reimbursement decisions and priority settings. Inflexible profit margins for different products with different unit costs, incomplete support for vulnerable groups and patients with chronic diseases, and absence of rational pharmaceutical usage campaigns can be named as other major problems.

PHP132

PERSONALIZED HEALTH CARE IN FRANCE, GERMANY AND THE UNITED KINGDOM: ARE HEALTH TECHNOLOGY ASSESSMENT AGENCIES READY?

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OBJECTIVES: Personalized health care (PHC) is a treatment model that customizes health care based on biomarker-based prediction of likely response. It is increasingly being prioritized by politicians and payers—one recent example is the published strategy plan by the German Federal Ministry of Education and Research. A key policy question remains whether health care systems and health technology assessment (HTA) bodies are adequately prepared evaluating these new treatment options. **METHODS:** Existing HTA evaluation methods for therapies in France, Germany, and the UK were reviewed with respect to the applicability to PHC products based on information provided by decision-making bodies and the literature. **RESULTS:** Current HTA evaluation methods being applied to medical therapies, in general, need to be modified when applied to PHC. For example, traditional benefit evaluations that require randomized clinical trials are standard but cannot always be fulfilled in PHC. Furthermore, combined benefit assessments for typical PHC treatment—e.g., a pharmaceutical combined with a diagnostic test—lack experience about appropriate evaluation methods to use. Today, decison makers and manufacturers rarely make use of the opportunity to re-assess or for joint evidence generation. Finally, reimbursement for PHC is inflexible and does not fully reflect the value of targeting, including the reduction in uncertainty and greater appropriate use. Among these three, the UK seems the most open to PHC funding. HTA in France and Germany does not recognize the special economic and evidence features of PHC, though the French system is more open to innovative market access. **CONCLUSIONS:** If the largest EU health care systems are to secure the full benefits of PHC, they will need to provide for full and flexible reimbursement for innovative technologies and services based on value. Currently, the importance of PHC by health care politicians is not being reflected in the evaluation tools or reimbursement methods being applied.

PHP133

TRENDS IN REIMBURSEMENT DECISIONS IN IRELAND: AN ANALYSIS OF THE NCPE DATABASE FROM AN INDUSTRY PERSPECTIVE

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OBJECTIVES: To analyse trends in reimbursement in Ireland to help in the planning of HTAs from an industry perspective. **METHODS:** A database of all NCPE decisions and reimbursement for drugs from 2006 to April 2013 was developed from publically available NCPE reports and HSE websites. A descriptive analysis of the database was undertaken. **RESULTS:** From 2006 to April 2013 37% of drugs were reimbursed without a HTA and 63% were recommended for HTA (N=126). There were three HTAs undertaken in 2006 compared to 26 in 2012. High Tech (HT) drugs were more likely to attract a HTA compared to General Medical Services (GMS) drugs (83% vs. 51%). Of the HTAs completed, 57% resulted in a positive reimbursement recommendation within a median time from HTA submission to reimbursement of 7.9 months (min 3.9, max 16.3). The median time was 7.1 and 9.8 months for GMS and HT drugs respectively. Dominance almost perfectly predicted reimbursement; 83% reimbursed. Of the ICERs in the north-east quadrant, 54% resulted in a positive reimbursement recommendation (average ICER around €60,000/QALY). The cost per QALY for those not reimbursed in this quadrant was almost twice this at around €110,000. Finally, the average probability of cost effectiveness for reimbursed and non-reimbursed drugs were 60% and 30% respectively. **CONCLUSIONS:** Companies can expect more requests for HTAs especially for HT drugs. When HTAs are requested the probability of success is around 60% with an expected timeline of 8 months from submission to launch. Budget impact does have an important role to play as dominance is a strong predictor of reimbursement. The average cost per QALY for reimbursed drugs is above the €45,000/QALY threshold but does not take into account confidential discounts under patient access schemes. Finally, the threshold probability of cost effectiveness seems to lie between 30% and 60%.

PHP134

PARAMETER UNCERTAINTY IN VALUE BASED MULTI CRITERIA DECISION ANALYSIS: A SYSTEMATIC REVIEW OF METHODS

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OBJECTIVES: Multi criteria decision analysis (MCDA) aims to support decision-making where decisions are based on multiple criteria. In disciplines like engineering and environmental policy, MCDA is widely accepted and routinely used. The use of MCDA in HTA priority setting and reimbursement decisions is growing, but mostly limited to research projects. A factor that might influence acceptance is a perceived difficulty to value an MCDA's outcome when its inputs and outputs contain uncertainties. When this is the case, decision makers might not feel confident in accepting or rejecting its outcome. The objective of this study is to systematically review how parameter uncertainty is taken into account in value-based MCDA methods in general, and to discuss which of the approaches is appropriate for the setting of reimbursement decision making in health care. **METHODS:** A systematic literature review was conducted using the Scopus database. Found abstracts were categorized by MCDA method used. Then, themes and families of methods were identified by two independent reviewers. Selected full text articles were read to identify methodological details. **RESULTS:** The search strategy identified 635 abstracts, mostly from engineering and environmental journals and only 1.6% in health journals. Identified themes were fuzzy set theory (n=223), probabilistic framework (n=68), deterministic sensitivity analysis (n=140), Dempster-Shafer theory (n=14), Bayesian framework (n=7) and Grey theory (n=8). A large number of papers considered the Analytic Hierarchy Process in combination with fuzzy set theory (n=155). **CONCLUSIONS:** In the health literature there is little attention for parameter uncertainty. Methods to deal with parameter uncertainty in MCDA must strike a balance between comprehensibility and understandability. Several complex methods are developed for parameter uncertainty, but there seems to be a gap between the theory and the implementation of those methods. For simple applications, methods like deterministic sensitivity analysis are likely to be sufficient.

PHP135

AMNOG BENEFIT ASSESSMENT: TIME DELAY OF MARKET ACCESS FOR PHARMACEUTICALS IN GERMANY?

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OBJECTIVES: To investigate quantitatively, if and to which extent the German Arzneimittelmarkt-Neuordnungs-Gesetz (AMNOG) delays market access of pharmaceuticals. Secondary objective was to potentially identify predictors for access delay. **METHODS:** All AMNOG assessment procedures that were completed at the level of the joint federal committee (G-BA) by May 15 2013 were included (website www.g-ba.de). Time delay to dossier submission was calculated between the approval date of the European Medicines Agency (EMA) and the mandatory AMNOG dossier submission date. Submission date usually occurs when pharmaceuticals are made available and is decided upon by the manufacturer. We also included in the analysis the ordinal level classification and evidence certainty level for each product as assessed by Institute for Quality and Efficiency in Health Care (IQWiG) and G-BA as well as the ATC code. **RESULTS:** In n=17 (49%) of N=35 investigated pharmaceuticals a small time delay greater than 1.1 months (which is usually feasible) after EMA approval was observed, but only 20% had a delay >2 months. A negative correlation existed between the amount of time delay to dossier submission and the benefit level outcome as assessed by IQWIG (r=-0.258, n.s.) and the final result by G-BA (r=-0.484, p=0.003). Benefit assessment outcomes between IQWiG and G-BA were correlated moderately with r=0.442 (p<0.008). For both, IQWiG (r=0.841) and G-BA (r=0.773) certainty of evidence correlated highly with the benefit level outcome. **CONCLUSIONS:** This analysis highlights the impact of AMNOG on the market access of pharmaceuticals in Germany. Overall, only small time delays existed for most products. Time delay in market access correlated significantly with a negative assessment of additional benefit by G-BA. Evidence certainty clearly correlated with benefit outcomes.

PHP136

A COMPARISON OF COVERAGE AND REIMBURSEMENT DECISIONS IN GERMANY (AMNOG) AND SCOTLAND (SMC)

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OBJECTIVES: In Scotland, drug reimbursement is predominantly based on cost-effectiveness in contrast to the corresponding German AMNOG process. The study compares the reimbursement and pricing process in Germany (AMNOG), as reformed in 2011, and Scotland (SMC) based on reimbursement assessments. **METHODS:** All AMNOG and SMC appraisal decisions made in 2011-2012 were identified. Matching AMNOG-SMC cases were found and compared in terms of final appraisal decision and rationale. **RESULTS:** For 2011-2012, forty-one AMNOG cases over 60 subgroups and 193 SMC cases were identified; twenty five matching cases were compared as these were assessed by both organizations. Regarding these 25 cases, AMNOG deemed ten cases demonstrated no additional benefit, in two cases the additional benefit was unquantifiable, slight benefit was acknowledged in seven cases and in six there were significant benefits. Based on the benefit assessment the negotiated price rebates ranged from 4.7% to 70.7% based on manufacturer set price. No restrictions to subgroups were opposed to any reimbursement decision. The SMC reimbursed 18 products (72%), of which four were restricted to a certain population due to cost-effectiveness. SMC rejected 7 cases (28%) based on weak economic evi-

dence. Both organizations reached the same assessment regarding clinical benefit in only 13 cases (52%). **CONCLUSIONS:** AMNOG implements a more rigorous process with respect to clinical evidence assessment compared to SMC. All AMNOG decisions are positive; however final prices may resemble generic prices for products that demonstrate low additional benefit ("Festbetragsgruppen"). In comparison, a negative decision by SMC warrants re-submission and re-assessment of the set price for successful drug reimbursement. Orphan drugs are assessed as normal products in Scotland and may be rejected on the grounds of economic evidence, while in Germany the additional benefit is presumed and price negotiation starts automatically. Furthermore, the SMC assessment process starts later than the AMNOG process.

PHP137

ACCESSING THE PHARMACEUTICAL MARKETS OF BRAZIL, RUSSIA, INDIA AND CHINA

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While pharmaceutical sales in mature economies are declining, in emerging markets they have been expanding rapidly, with growth rates in double figures. Here we focus on market access in BRIC (Brazil, Russia, India and China) which together represent just over 40% of the world population.**OBJECTIVES:** To identify the processes and key stakeholders involved in gaining market access in BRIC; to assess the importance of health technology assessment (HTA) in gaining reimbursement in these countries; to identify opportunities and challenges to market access. **METHODS:** A review was conducted to identify the current processes and key stakeholders in market access in the BRIC countries and to identify favourable and unfavourable factors to market access. **RESULTS:** The licensing and reimbursement processes vary in the BRIC countries. Brazil follows processes similar to those in Western Europe, including HTA and public consultation as part of the reimbursement application. In China, the licensing process can take 4-6 years, though fast-tracking for innovative drugs has recently been introduced. Russia, China and India do not yet rely on HTA for reimbursement decisions. In India plans to use "pharmacoeconomic principles" in setting prices of new molecules have been announced. Opportunities in all these countries result from increasing affluence and life expectancy and the diseases associated with these. Some challenges to market access are: poor IP protection; protectionist measures; compulsory licensing; drive to use generics or biosimilars, often produced locally; price controls; variable health insurance/NHS coverage; and limited budgets for prescription drugs. **CONCLUSIONS:** HTA is now common practice in Brazil, but not yet in Russia, India or China. Although demand for new drugs is increasing in these markets, protectionism measures, competition from generics and budget constraints due to the increased burden and requirement for new high priced drugs present a challenge when accessing the pharmaceutical market in BRIC countries.

PHP138

PLACEBO-CONTROLLED TRIALS: ARE THEY ACCEPTABLE TO HEALTH TECHNOLOGY ASSESSMENT BODIES?

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OBJECTIVES: The gold-standard pivotal trial design has three arms with experimental medicine, placebo and active control however, often marketing authorisation is granted on placebo controlled (PLAc) trial(s). While PLAc trials are often still acceptable to the European Clinical Trials Directive and European Medicines Agency (EMA), they are less acceptable to Health Technology Assessment (HTA) bodies. The latter request an (in)direct comparison vs. the relevant active comparator(s) (AC) to demonstrate the added value of existing standard of care. We have investigated the hurdles encountered during HTA assessments for those drugs with marketing authorization based solely on PLAc studies. **METHODS:** We identified those drugs approved since 2010 by EMA based only on PLAc trials. We then reviewed the HTA assessments for these drugs in France (HAS), Germany (G-BA) and the UK (NICE and SMC) and compared these HTA assessments to others where the trial included an AC. **RESULTS:** Applications for 41 (45 indications) of the 220 drugs approved by EMA between 2010 and end of 2012 were based exclusively on PLAc trials. The number of indications already assessed and recommended (percentage) by HTA bodies are 19 and 11 (58%) for NICE, 33 and 18 (55%) for SMC, 24 and 20 (83%) for HAS, and 18 and 12 (67%) for G-BA. When compared to all HTAs irrespective of comparator being placebo or AC assessed since 2010, lack of an AC seemed to have no impact in HAS (83% vs 75% favorable opinion among all assessments) and G-BA (67% vs 58%) assessments but had a negative impact on SMC (55% vs 85%) and NICE (58% vs 64%) recommendations. **CONCLUSIONS:** The impact of no direct comparison with an AC varies across countries. The analysis seems to indicate that in absence of head-to-head data HTA agencies will accept indirect evidence against the right AC.

PHP139

THE IMPACT OF THE ECONOMIC RECESSION AND PHARMACEUTICAL-HEALTH SERVICE AGREEMENT ON THE PROBABILITY AND TIME OF REIMBURSEMENT OF NEW MEDICINES IN IRELAND

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OBJECTIVES: To assess the impact of the Irish economic recession (September, 2008) and the Irish Pharmaceutical Healthcare Association agreement (IPHA; November, 2012) on the probability of reimbursement decided by the National Centre for Pharmacoeconomic Evaluation (NCPE). We also aim to test whether the new IPHA agreement reduced the time-to-reimbursement for new medicines in the General Medical Services (GMS) and High Tech Drug Scheme (HTDS). **METHODS:** A database of all NCPE decisions since 2006 to present was compiled from publically available NCPE decision reports and a logistic model was used to test the occurrence of the recession and the IPHA agreement on the rate of positive reimbursement made by the NCPE. We also tested whether the new agreement had an impact on the time-to-reimbursement using a linear regression model. **RESULTS:** The results of the logit model suggest that neither the economic recession nor the agreement had any statistically significant impact on the probability of reimbursement. However, there was some evidence that the time-to-reimbursement was reduced after the agreement ($p<0.10$). **CONCLUSIONS:** Although the analysis suggests that these two events had no impact on the rate of reimbursement it is possible that the reimbursement price of new drugs may have decreased over this period which could have facilitated reimbursement. Unfortunately, details of the final price of medicines are not always known in the Irish system and it is therefore not possible to test this hypothesis using currently available data. Our analysis of time-to-reimbursement suggests that the new agreement may have satisfied one of its main objectives in getting new medicines onto the market sooner.

PHP140

MODELLING THE HEALTH TECHNOLOGY ASSESSMENT (HTA) PROCESS FOR INNOVATIVE DRUG TECHNOLOGIES (IDTS) IN THE TURKISH HEALTH CARE SYSTEM

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OBJECTIVES: Offering a standardized HTA process model through economic evaluation of IDTs in the Turkish health care system. **METHODS:** Current regulations on evaluation of innovative drug technologies through the reimbursement process are defined via a process flow scheme. A stepwise model is proposed to cover a standardized HTA system within the economic evaluation through an independent HTA body (Model HTA Authority). **RESULTS:** In the current system, economic evaluation content of a reimbursement application dossier is evaluated by Social Security Institution (SSI) through Technical and Main Commissions respectively. However this evaluation process is not standardized with respect to main variables such as scientific methodologies, timelines and responsibilities. This study offers a model, which initiates a re-defined application step for economic evaluation content of a IDT reimbursement dossier; parallel application to SSI and an independent HTA body (Model HTA Authority). Therefore, the Main Commission in SSI will be able to combine a general evaluation from the Technical Commission and an HTA report of the IDT by an independent HTA body. These reports will be available to owners of reimbursement applications until announcement of a final decision of SSI, and will become publicly available afterwards. **CONCLUSIONS:** IDTs are not involved in a standardized HTA process in the current Turkish health care system. However, pharmacoeconomic analysis reports are requested by SSI for reimbursement applications of IDTs. This study offers a model, which includes a standardized HTA process for IDT in the Turkish health care system. Applicability of this model may be tested through pilot projects and further steps may be defined for further excellence.

PHP141

CANADIAN PRIVATE PAYERS' PERCEPTIONS AND EXPECTATIONS OF SUBMISSION REQUESTS FOR DRUG REIMBURSEMENT SUBMITTED BY THE PHARMACEUTICAL INDUSTRY

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OBJECTIVES: To identify, from a private payer's perspective, the required elements to include in a pharmacoeconomic model and a budget impact analysis and compare them to that of the public payers' requirements. The secondary objective was to determine the preferred components to present in a submission regarding private payers. **METHODS:** A survey was sent to 21 submission reviewers from 14 private insurance companies offering drug reimbursement, using an online survey builder, *KwikSurveys*. The survey included 15 questions divided in 5 sections: General information, Clinical information, Pharmacoeconomic evaluation, Budget impact analysis and General appreciations. **RESULTS:** Nine reviewers from eight different companies, which represent 80% of the Canadian private payer market shares, responded to the survey. Results showed that 67% of participants follow the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines for economic evaluations. 88% of participants prefer a cost-effectiveness evaluation, while 75% prefer a cost-benefit evaluation. 100% of the participants would like direct drug costs and the indirect costs related to loss of productivity due to reduced working capacity to be included in the pharmacoeconomic model. 75% would like the costs to employer to hire and train replacement worker, the costs of premiums paid to, as well as benefits received from, private insurers to also be included in the model. 63% of the participants would like to see a population data-based model for their budget impact analysis. Similarly, 63% of the participants prefer a time horizon of 3 years for the budget impact analysis. **CONCLUSIONS:** The parameters to be considered in a submission sent to private payers are different from public payers' requirements. The perspective of the pharmacoeconomic model should be that of a private payer and the budget impact analysis should only consider a population covered by private payers.

PHP142

POINT OF CARE TESTS: THE LONG AND WINDING ROAD TO REIMBURSEMENT

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OBJECTIVES: Market access for innovative new technologies can be complex and time consuming. As cost-containment pressures in the European Union (EU) intensify, evidentiary hurdles to justify new point-of-care (POC) tests continue to grow. Decentralized health care decision making can also be a significant hurdle. This study aimed to characterize the process and identify challenges for Health Technology Assessment (HTA), pricing, reimbursement, and market access for a new POC test in the EU-5 countries. **METHODS:** We conducted desktop research of

published literature, HTA reports, and third-party websites, to identify the critical path and data most valuable to reimbursement decision making. We conducted 26 qualitative one-on-one interviews with payer decision makers in the EU-5: 12 key opinion leaders, 4 laboratory directors, and 10 academic health economists and HTA advisors. **RESULTS:** Reimbursement is critical to rapid adoption of new technologies. There are multiple appropriate access pathways for various theatres of care (e.g., outpatient office/clinic, inpatient, emergency), all with varying requirements and value drivers. Payment for new diagnostic tests typically is handled regionally or locally; treating physicians and medical societies can influence these budget decisions. Shared financial agreements or risk-sharing scenarios may speed introduction of a new POC test. Test reimbursement processes may differ for inpatient versus outpatient use. Currently, the evidence hurdle for a POC test is not as high as for prescription medicines. **CONCLUSIONS:** Market access for a POC test varies across and within countries; adequate data to meet decision makers' needs is not well understood. No roadmap exists for navigation of the critical path for POC tests, and evidence requirements in the EU are not well established. Access for a POC test will be complex; regardless of pathway, decisions regarding reimbursement and adoption of new technology are diverse and dispersed across and within countries with varying levels of required evidence.

PHP143

VALUE OF LIFE: AS PERCEIVED BY PHYSICIANS AND THE GENERAL PUBLIC

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OBJECTIVES: With the advancing process of HTA in the Czech Republic question emerged such as what is the willingness to pay (WTP) for health and life as well as what is the general awareness of the national health care policy and health economics. So far all estimations of WTP were largely based on academic deductions, thus we adopted a previously published approach to estimate the empirical WTP. **METHODS:** A total of 381 doctors of 15 specializations and 500 respondents from general population, both matching the CZ demography, were interviewed online. Doctors were asked directly to suggest reasonable WTP per equivalent of QALY. The general public was interview using the dichotomous double bounded choice method. The value of WTP, including 95% confidence interval, was determined using proc lifereg of the SAS system that allowed estimating averages for interval data. Optimal parametric extrapolation of the data was chosen based on the minimum value of Akaike's information criterion (AIC). **RESULTS:** Economics is the last criterion considered as important by doctors following the quality of life, clinical parameters and ethical/social aspects. Doctors not rejecting the concept of paying for health (28%) produced median of CZK 700,000 (EUR 27,129) to be an adequate payment for an extra year in full health, representing one QALY. General population suggested CZK 18.4 million (EUR 731,110) as an adequate WTP to be paid by the national health insurance fund, largely in contrast to only CZK 177,000 (EUR 6859) as suggested for the pay-of-pocket WTP. **CONCLUSIONS:** The awareness about health economics and its methodology is rather low among doctors and general public. While those medical doctors who expressed understanding for the concept of WTP and QALY suggested a value similar with the implicit WTP of CZK 1,000,000 (EUR 38,756) general public suggested extreme WTP from public budget, reflecting distant position of the public.

HEALTH CARE USE & POLICY STUDIES – Health Care Research & Education

PHP144

TOWARDS EVIDENCE-BASED EUROPEAN POLICY IN CLINICAL TRIALS THE SURVEY OF ATTITUDES TOWARDS TRIAL SITES IN EUROPE - THE SAT-EU STUDY™

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OBJECTIVES: Applications to run clinical trials in Europe have been falling since 2007. Costs, speed of approvals, and shortcomings of European Clinical Trial Directive (CTD) are commonly held responsible. However, there is no hard evidence on the actual weight of these factors, nor are policy recommendations typically founded on a research-based understanding of factors impacting trial site selection. Indeed, borrowing from the rigour of its own discipline, medical policy decisions ought to be "evidence-based". **METHODS:** The SAT-EU Study™ was an anonymous, cross-sectional Web-based survey designed to systematically assess factors impacting European clinical trial site selection. It explored 19 factors across investigator-, hospital-, and environment-driven criteria, and costs. It also surveyed perceptions of the European trial environment. Clinical Research Organizations (CROs), academic Clinical Trial Units (CTUs), and Industry were invited to respond. OUTCOME MEASURES: Primary: Weight assigned to each factor hypothesized to impact trial site selection and trial incidence; Secondary: Desirability of twelve European countries to run clinical trials **RESULTS:** Responses were obtained from 485 professionals in 34 countries: 49% from BioPharma, 40% from CTUs or CROs. Investigator-, environment-, and hospital-dependent factors were rated highly important, costs being less important ($P<0.0001$). Within environment-driven criteria, pool of eligible patients, speed of approvals, and presence of disease-management networks were significantly more important than costs or government financial incentives ($P<0.0001$). Germany, UK, and The Netherlands were rated the best trial markets ($P<0.0001$). **CONCLUSIONS:** Fostering European clinical research does not require additional government spending or a revamping of the clinical trial cost structure. Rather, it requires greater visibility of centres of excellence and the harmonised national adoption of recently approved revisions to the CTD. Carefully crafted harmonization of approvals, including aligned hospital contracting, speedier trial authorization and greater visibility of disease networks may bring significantly more clinical research to Europe and stimulate growth.

PHP145

JAPANESE REPRESENTATION IN LEADING GENERAL MEDICINE AND BASIC SCIENCE JOURNALS: A COMPARISON OF TWO DECADES

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OBJECTIVES: During 1991-2000, Japan contribution to the top basic and clinical science journals was less than 1% and 3%, respectively. The objective of this study was to compare the Japanese representation in 7 major general medicine journals and 6 basic science journals between the years 1991-2000 and 2001-2010. **METHODS:** Retrospective observational study. We measured the frequency of journal article publications in PubMed from Japan in both seven high-impact general medical and internal medicine journals and six high-impact basic science journals using Boolean operators to connect name of the journal, year of publication and corresponding authors' affiliation with different universities, cities and places in Japan. **RESULTS:** Japan represented 0.66% (260/39,255) and 0.74% (265/36,038) of journal articles in 7 of the top general medicine journals during 1991-2000 and 2001-2010, respectively. In contrast, the respective representation in 6 of the top basic science journals was 2.51% (849/33,779) and 3.60% (1364/37,908), respectively. Overall, we observed that the proportion of Japan-originated articles published in the top general medicine journals during 2001-2010 remained unchanged compared to 1991-2000 ($P=0.255$). However, the Japanese representation in basic science journals during 2001-2010 increased significantly compared to 1991-2000 ($P<0.001$). Japanese representation in basic science journals had an upward trend during the 1991-2000 period ($P<0.001$) but remained flat during 2001-2010 ($P=0.177$). In contrast, the trend of Japanese representation in general medicine journals remained flat during the period of 1991-2000 ($P=0.273$) but exhibited a marginally downward trend during 2001-2010 ($P=0.073$). **CONCLUSIONS:** Overall, the Japanese representation in top general medicine journals has remained negligible and unchanged over the last two decades. Representation in basic science journals remained unchanged during the time period of 2001-2010, although it had shown an upward trend during the years 1991-2000. Interventional measures are needed to address these trends.

PHP146

DETERMINANTS OF PROMPT ACCESS TO HEALTH CARE IN CHPS PROGRAMME IN RURAL COMMUNITIES OF BAWJIASE, GHANA

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OBJECTIVES: Prompt access to effective health care is a priority in the developmental agenda of Ghana yet only 20% of people who actually need health care have it. Evidence on the determinants of prompt access to health care in these CHPS programme is woefully inadequate. The study sought to assess the factors that influence prompt access to health care in CHPS settings. **METHODS:** A descriptive cross sectional study was conducted in 2011 with 230 respondents within the CHPS zones of Bawjiase Sub-district, Central region of Ghana. Data was collected on using structured questionnaire and analyzed using SPSS version 19 software. Logistic regression was run to access the correlation of the determinants on prompt access to health care in CHPS settings at 95% confidence interval. **RESULTS:** We identified that, factors which play a major role in prompt access of CHPS programme within the CHPS zones of Bawjiase sub - district include geographical accessibility (chi square = 33.57; p = 0.000) and service characteristics (chi square = 19.17; p = 0.001). Economic accessibility however, had no influence (chi square = 123; p = 0.975) on prompt access to CHPS programme. Factors which had strong influence on prompt access of CHPS programmes were age (chi square =12.39; p = 0.015), sex (chi square =15.25; p = 0.000), marital status (chi square =31.56; p = 0.000), education level (chi square =28.49; p = 0.000) and occupation (chi square =33.56; p = 0.000). **CONCLUSIONS:** The study concludes that geographical proximity, service characteristics and individuals' background factors influence prompt access to quality health care in rural CHPS setting.

PHP147

ASTROLOGICAL SIGNS AND HEALTH PROBLEMS; DEMONSTRATING THE MULTIPLE COMPARISONS PROBLEM

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OBJECTIVES: Astrological signs have been linked to numerous health problems, not only in pseudoscientific but also in high impact, peer-reviewed scientific literature. The aim of this study was to use a large prescription database to assess associations between astrological star signs and health problems. This study may demonstrate important statistical issues that arise when doing multiple comparisons. **METHODS:** For this cross-sectional study, patient and drug data were collected from a large prescription database in The Netherlands. Patients were followed for one year, starting from their birthday in 2010. Outcomes were drug prescriptions for one of four health problems: cardiovascular disease, depression, erectile dysfunction in men and fertility problems in women. The "determinant" was patients' astrological sign (based on Western-culture horoscope). Differences in prevalence rates between star signs were tested using logistic regression, adjusted for age and gender. Significance was set at P=0.05. **RESULTS:** Almost 300,000 persons were included for analysis. In our analysis, persons born under the star sign Aquarius were less likely to suffer from cardiovascular disease (P=0.001), whereas patients born under Scorpio or Sagittarius were more likely (P=0.011 and P=0.017). There were no effects on depression or erection dysfunctions. Women born under Gemini were 37% less likely to use fertility drugs (P=0.016). **CONCLUSIONS:** This study found several associations between star signs and health problems, none of which had any biologic plausibility. Interestingly, datasets filled with randomly generated star sign data also resulted in significant findings. Multiple comparisons without prespecified hypotheses, biological plausibility and adjustments for familywise error rates, can lead to false-positive findings. Multiple comparisons are common in outcomes research, appropriate use of statistics therefore is important.

PHP148
SELF- ASSESMENT OF HEALTH PROFESSIONALS' COMMUNICATION SKILLS WITH PATIENTS
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OBJECTIVES: Effective communication helps us to clearly understand patients or situation and enable us to make differences, build trust and respect. If a health professional does not have communication skills, it may reduce compliance and decrease the quality of health care. The aim of this study was to self-assess the communication skills during daily work in delivering care to patients by pharmacists and physicians at community settings. **METHODS:** This study is a pilot project of an ongoing Research Project aiming to investigate social and behavioral insights of pharmaciesy and physicians working in community settings in Serbia, started in November 2011. The rating scale is used to test pharmacists' skills and in-patient communication designed for the needs of the research consisted of 31 claims. **RESULTS:** The questionnaire completed 157 health professionals (physician, pharmacists) from the southeastern and central part of Serbia (75.3 % of which were females). The average age of participants were 40.42±9.38 and the average years of work experience were 12.92 ± 9.10 years.There is a correlation between the age of pharmacists and the following variables: assertiveness ($r = 0.456$, $p < 0.01$), active listening skills of patient ($r = 0.443$, $p < 0.01$), questioning patient ($r = 0.455$, $p < 0.01$), rhetoric skills ($r = 0.540$, $p<0.01$). ANOVA examined the effects of age on empathy ($F(4.64) = 1.52$, $p = 0.01$), assertiveness ($F(4.64) = 3.54$, $p = 0.01$), rhetoric skills ($F(4.64) = 2.48$, $p = 0.01$) and adherence to ethical principles ($F(4.64) = 1.53$, $p = 0.01$). **CONCLUSIONS:** Elder health professionals with greater empathy are more assertive having better rhetoric skills and adherence to ethical principles in communication. There is a need to improve the communication skills of young health professionals.

PHP149
REGULATORY AND GENERAL EPIDEMIOLOGICAL KNOWLEDGE ABOUT RARE DISEASES AND ACCESS TO TREATMENT FOR RARE DISEASES: HEALTH PROFESSIONALS' VIEW IN SERBIA
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OBJECTIVES: To assess the knowledge of health professionals about epidemiological and national regulatory issues concerning rare diseases (RD) and access to orphan drugs. **METHODS:** This paper reports some of the results from an ongoing KAP study on rare diseases and orphan drugs in the Republic of Serbia (RS). A prospective cross-sectional study was conducted from May to June 2013, on a convenient sample of licensed pharmacists and physicians from two, large cities' and its suburbies in the central parts of RS. A specially designed KAP instrument in a form of three-part questionnaire was applied and these results were related to the assessment of concerning knowledge (8 multiple-choice questions) and self-assessment of the participants (one question). **RESULTS:** The study population included 214 health workers (151 pharmacists and 63 physicians); the average age of participants was 40.80±9.45 and the average years of professional practice was 13.14 ± 9.68. Majority of the participants (57%) knew the true prevalence of RD and slightly less than third of the samples (26.2%) responded correctly to the question of the extent of European population suffering from RD. There are major differences in regulatory knowledge about access to treatment for rare diseases, as participants answered correctly in a wide range of 21% to 67.4%. Most of the health professionals self-estimated that possessed little (31.3%) or enough (43.5%) knowledge related to general epidemiological and legislative issues concerning RD and orphan drugs. The average level of overall knowledge assessment for all questions and self-assessmentin general was 3.53 ± 1.58 and 2.04± 0.87 respectively. **CONCLUSIONS:** The majority of respondents estimated that possess less knowledge on RD (general information) and drugs to treat RD, or insufficiently. The average level of respondents' knowledge on RD and drugs to treat RD was below the average.

PHP150
TIMING OF DISCHARGE MAKES A DIFFERENCE: THE EFFECTS OF LENGTH OF STAY AND DAY OF DISCHARGE ON 30-DAY READMISSIONS
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OBJECTIVES: The evidence on the influence of timing of discharge on readmission risk is inconsistent, showing that both increased length of stay (LOS) and early discharge are associated with an increased risk of readmission. We aimed to test whether LOS and day of discharge (i.e., weekend vs. work days) are associated with the risk of 30-day emergency readmission. **METHODS:** Data on first admission to internal medicine departments during January – March 2010 was retrieved from Clalit Health Services' data warehouse. Inclusion criteria: LOS of >= 2 nights, age 18+, readmitted to an internal medicine demartment or ICU. Predictors: LOS, ACG morbidity categories, age, socioeconomic status, and prior health care use. Logistic regression was used to model the effect of discharge day and LOS on 30-day emergency readmission, controlling for known risk factors. **RESULTS:** After adjustment for morbidity, clinical and demographic factors, there is an increased risk for 30-day readmissions associated with increased length of stay (OR=1.56 when LOS is 8+ days vs. 2-3 days, p<0.001). Focusing on 2-7 day hospitalizations, the same association is found (OR=1.47 for LOS > 5 days, p<0.001). Being discharged over the weekend increases the odds of readmission by 11% (p=0.04), controlling for all known risk factors. Modeling for an outcome of readmission or death, or for a 7-day readmission outcome, resulted in similar findings. **CONCLUSIONS:** Our study showed that contrary to some of the evidence, longer hospital stays were associated with increased risk of unplanned readmission. Being discharged over the weekend incurs mild additional risk for readmission, especially at shorter LOS. These findings suggest that despite short LOS in Israel, increasing LOS as a readmissions reduction strategy may be ineffective, unless the specific need and care content of these additional days is assured.

PHP151
MEDICATION ERRORS-INCIDENCE, CAUSES AND POSSIBLE PREVENTION STRATEGIES IN INDIAN HEALTH CARE SETTING
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OBJECTIVES: Medication errors (MEs) frequently contribute for patient's morbidity and mortality in health care settings. The present study was aimed to identify and assess the pattern of occurrence of MEs and to develop strategies to prevent these MEs. **METHODS:** It was a prospective study conducted in a teaching hospital over a period of 6 months. Trainee clinical pharmacists followed the patients admitted to general surgery (GS) wards. MEs occurred and the cause for ME was identified by reviewing medical records, interviewing patients and concerned health care professionals (HCPs). All identified MEs were documented electronically and were evaluated for its nature, extent, cause and outcome. Prevention strategies were developed accordingly. **RESULTS:** A total of 417 MEs were identified in 313 patients from 1125 patients followed. Calculated incidence of MEs in GS wards was 27.8%. The majority of them were prescribing errors (60.4%), followed by administration errors (38.6%) and dispensing errors (9.8%). The common reasons observed for MEs were omission error (25%), incorrect drug selection (14%), wrong frequency (10%), poor patient adherence to medicines (7%), drug use without indication (7%), improper dose (6%), wrong administration (4%) and wrong time (3%). Pantoprazole (27.5%), Ceftriaxone (9.8%), Piperacillin-Tazobactum (6.7%), Diclofenac (6.4%) and Tramadol (6.2%) were drugs commonly involved in MEs. Majority of MEs (96%) that reached to patients were not harmful but 32% of them needed monitoring/intervention to ensure patient safety. Around 60% of MEs were due to inappropriate prescribing by clinicians followed by patient non-adherence to therapy (14%), improper follow up by ward clinical pharmacists (15%) and nursing workload (11%). Strategies were designed to prevent commonly identified MEs. **CONCLUSIONS:** MEs can be minimized if patients are monitored correctly on time. Appropriate team work from all HCPs can certainly reduce the occurrence of MEs.

PHP152
THE RELATIONSHIP BETWEEN SCIENTIFIC RESEARCH, CLINICAL TRIALS AND FDA DRUG APPROVAL
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OBJECTIVES: An important aim of medical research is often to identify potential novel therapeutic targets for disease treatment. Here we investigated whether the amount of scientific research (measured as papers published) in a given disease area correlated with the number of clinical trials, and whether an increased amount of research in a disease area resulted in a higher number of FDA approved drugs. **METHODS:** FDA drugs approved between 2000-2013 were identified using the online database 'CenterWatch', and the number of papers and clinical trials for each disease area was established by running comprehensive searches on PubMed from 1975-2013, and ClinicalTrials.gov from 1999-2013, respectively. The total numbers of approved drugs, published papers and clinical trials were compared for each of 17 disease areas and, to analyse the correlations between these factors, simple regression analyses were performed. **RESULTS:** Analysis for correlation between the number of papers published and the number of clinical trials per disease area revealed a strong correlation between these two variables (R square: 0.69, p<0.001); thus, increasing numbers of published papers were associated with increasing numbers of clinical trials. Further analyses were carried out to investigate the relationship between the number of papers published, or clinical trials, and the number of drugs approved by the FDA. Interestingly, these analyses revealed that both clinical trials (R square: 0.05, p=0.41) and published papers (R square: 0.09, p=0.25) correlated poorly with the number of FDA approved drugs per disease area. **CONCLUSIONS:** These data suggest that the amount of research significantly correlates with the number of clinical trials in a given disease area. However, neither research nor clinical trials correlated with the number of drugs approved by the FDA. This may suggest that some disease areas could face a bottle neck at the drug approval stage, perhaps through difficulties in demonstrating efficacy.

PHP153
EFFECTS OF CHANGING HEALTH POLICY ON PHARMACOECONOMICS AND HEALTH OUTCOME STUDIES FROM 2000 TO 2012 IN TURKEY
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OBJECTIVES: Health policy chances may effect the conducted studies in all fields. Pharmacoeconomics dossiers for the reimbursement applications for new medicines were not mandatory before year 2008. New molecules need to show cost-effectiveness and possible budget effect with their applications for reimbursement to Social Security Institution from 2008. This policy changing may effect pharmacoeconomics and health outcome studies in Turkey. The aim of the study is to evaluate the improvement of pharmacoeconomics and health outcome studies which are specific for Turkey in years. **METHODS:** Database of ISPOR Outcome Research Digest were searched online from the begining of database (1998) to 2011 with the key words "Turkey" and "Turkish". The inclusion criteria were taken as study must be specific for Turkey and first author must be from Turkey. Included abstract evaluated for increasing in years, distribution in study topics and diseases areas. **RESULTS:** 121 abstracts were matched with inclusion criteria. First abstracts were published in 2000. There were only 16 abstracts in total until 2008. After year 2008, published abstracts numbers were increased year by year and reached up to 40 per year in 2012. 58.7% of all abstracts were Cost Studies(CS). It was followed by Health Care Use & Policy Studies(HP) (15.7%) and Patient Reported Outcomes & Preference-Based Studies (PRO) (12,7%). 49.3% of all Cost Studies were Cost-Effectiveness studies.

17.4% of all abstracts were in the Alergy diseases area. It was followed by Multiple Diseases (14%). **CONCLUSIONS:** It was shown that the policy changing in 2008 as to require pharmacoeconomics dossiers in the reimbursement application effected Turkey specific pharmacoeconomic and health outcome studies positively. In other words, pharmaceutical ýndustry and the government started to invest in pharmacoeconomics and health outcome studies after 2008.

PHP154

LONG TERM ANALISYS OF THE HUNGARIAN HOSPITAL BED CAPACITIES

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OBJECTIVES: To provide a long term analysis of the Hungarian hospital bed capacities. **METHODS:** During the preparation we performed bibliographic review including research of related statistical data collections, historical hospital works. Data were derived from the database of the Hungarian Central Statistical Office and from historical documents. The study covered the period between 1800-2010. The following indicators were used: number of hospitals and hospital beds. **RESULTS:** The first data available for hospital statistics dates back to 1800 and showed that there were 34 hospitals and 1590 hospital beds in Hungary. For 1867 the number of hospitals and hospital beds increased up to 46 and 4684 respectively. Shortly after the introduction of compulsory health insurance in 1891, the number of hospitals was 344 and the number of hospital beds was 16497 in 1895. After the First World War hospital number decreased to 183, and bed number increased to 26451. Since 1945 to 1990 the number of hospitals varied between 147-287, while the number of hospital beds continuously increased from 33162 to 105097. After the social and political changes in 1990, hospital bed number showed strong decrease to 71216 in 2010 with varying number of hospitals between 148-174. As a consequence in the changes of numbers of hospitals and hospital beds, the average bed number per one hospital continuously increased from 47 in 1800, 107 in 1915, 182 in 1950 and 710 in 1990. **CONCLUSIONS:** The definition and function of hospitals significantly changed during the past 200 years in Hungary. The former old fashioned small poor houses of the early 19th century have been replaced by hospitals with large number of hospital beds by 1990. After social and political changes in 1990, the number of hospitals beds in Hungary decreased and got closer to EU average.

PHP155

'BIG DATA' IN HEALTH CARE. WHAT DOES IT MEAN AND WILL IT MAKE A DIFFERENCE?

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BACKGROUND: With the evolution from data on paper into electronically available data, the term Big Data has made its entrance. This term is widely used and refers to the four V's: Volume, Velocity, Variety and Veracity. Big Data is being used in many sectors such as retail and banking, and also in the health care sector. However, within the health care sector, this term is ill defined. **OBJECTIVES:** The main purpose of this study is to get an understanding of the definition of Big Data in health care. Further, it's value and challenges will be explored. **METHODS:** : First, an attempt has been made to clarify the term Big Data in health care using the term "Big Data" in combination with 'health' in PubMed searches. Also, the internet and social media have been searched for definitions of Big Data in health care. Further, the potential use of Big Data in health care has been reviewed using these sources. **RESULTS:** In the medical literature, the term Big Data is rarely used in health care research and no standard definitions of Big Data big data are available. The term is used in combination with electronic health care records (EHR), claims data, registries, pharmacy utilization records, and linkages between these databases. On the internet and social media, various definitions for Big Data in the health care sector can be found." Values are: increased medical knowledge, improved quality of care, improved personalized medicine, better health outcome prediction, and lower costs. Challenges with Big Data in Healthcare are of technical (different data structures), ethical (patient privacy) and scientific (quality issues, biases, causality assessment) magnitude. **CONCLUSIONS:** Healthcare Big Data has poorly been defined. Use of Big Data can be beneficial in terms of better care and lower costs despite the challenges to be faced.

PHP156

DISEASE BECOMES SOCIAL. HEALTH RESEARCH CONDUCTED ON, OR USING, WEB 2.0 MEDIA: A SYSTEMATIC REVIEW

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OBJECTIVES: To assess the range and focus of health research that has involved interactive internet and mobile technology ("social media"; SM). **METHODS:** We conducted a systematic review of studies that investigated the use of SM, or used SM as a research tool, published in English since 2003 and indexed in MEDLINE and EMBASE. **RESULTS:** We identified 3,773 unique studies, of which 304 reported primary research or were systematic reviews of such studies. Of these, 192 (63%) were surveys of actual or potential users of SM, including health care professionals (20%), patients with a specific disease or problem (46%), or the general public (34%); 40 (13%) were articles describing SM tools or sites; 71 (23%) assessed the potential of SM to increase knowledge or improve clinical outcomes, of which 22 compared SM with more traditional support or information; 71 (23%) described SM users; 53 (17%) sought their views on the benefits of SM; 24 (8%) discussed the potential harm its use could do to professional-patient relationships; and 25 (8%) analysed SM content. SM were also used as a tool to recruit participants into research (85 articles, 28%), especially on topics such as sexual practices, intimate partner violence, or substance abuse, or involving groups typically underrepresented in clinical research. Of the various types of SM studied or used to recruit participants into research, Facebook was cited in 73 articles (24%); mobile apps in 40 papers (13%); PatientsLikeMe and Twitter in 13 articles (4%) each; MySpace in 3 articles (1%); and other online forums in 70 articles (23%). **CONCLUSIONS:** SM is a rich source of data on patients and health care professionals. It may be particularly useful in targeting patients with rare diseases, and studying attitudes and behaviours relating to taboo subjects. SM may also increase recruitment into research studies, especially from hard-to-reach groups.

PHP157

PHARMACO-ECONOMIC EDUCATION NEEDS INVESTIGATED BY ISPOR CHAPTER – EXAMPLE FROM BULGARIA

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OBJECTIVES: Education in pharmacoeconomics is one of the primary goals of ISPOR. This study is aiming to explore the needs for pharmacoeconomic educations by national chapter among different pharmaceutical stakeholders. **METHODS:** Inquiry research was performed among the participants in 2 educational initiatives of the Bulgarian ISPOR chapter. In both seminars attended representatives of payers - Bulgarian government (MoH, NHIF), as well as from pharmaceutical business, non-governmental organizations and academia. On total 48 individuals left feedback from over 60 participants in both seminars. The questionnaires focused on the topics covered in the seminars, organizational matters and needs of new educational themes. Preferred themes were assessed and results are consolidated **RESULTS:** Both seminars target the same groups of individuals – institutions, academia, pharmaceutical business, and non-governmental organizations. The first seminar was focused mainly on the pricing and reimbursement of the pharmaceuticals with international lecturers, while the second one covered basic pharmacoeconomic methods with national lectures. The overall satisfaction score from both seminars was very high (25%) and excellent (55%). The most preferred topic was the pricing and reimbursement of pharmaceuticals by 53%, followed by different modeling techniques (47%). Participants wanted to know more about the way of regulatory usage of pharmacoeconomics in pricing and reimbursement (70%). Focus groups discussion (98%) and practical of pharmacoeconomic were also a matter of high preference (30%). **CONCLUSIONS:** This study proves the necessity for education in the field of pharmacoeconomic, modeling, core models explanations and pharmaceuticals assessment. They also pointed out the place of national chapters as providers of education and independent organizers able to gather different stakeholders' point of view in non-formal discussions. Having in mind that BG is in the beginning of the HTA process obviously willingness to be educated among the whole Pharma environment is definitely high.

PHP158

PHARMACOECONOMIC EDUCATION FOR HEALTH CARE STUDENTS IN BOSNIA AND HERZEGOVINA

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OBJECTIVES: In order to examine the current situation related to education in the field of pharmacoeconomics and Health-economics, we investigate which universities and colleges provide such training. The study included pharmaceutical, medical and dentistry faculties and departments as well as the health care colleges. Information on health care colleges and faculties in B&H are taken from State register of accredited higher education institutions. **METHODS:** We have analyzed the on-line availability of the curricula at official websites of health care faculties, its content for each program of study at the undergraduate and postgraduate level. All programs are qualitatively analyzed in terms if they include pharmacoeconomics/health economics as a separate subject (mandatory or elective) **RESULTS:** Twenty-two high health care institutions are identified; 5 medical, 4 dentistry, 9 pharmaceutical faculties, 13 nursing and 6 othe. Seventeen of them have on-line available curricula, 3 are not available and 2 faculties do not have available websites, so we included 77,7% of all health care faculties program. In undergraduate courses pharmacoeconomics/health-economics is included in curricula at 5 faculties. Pharmacoeconomics as separate mandatory subject is included in curricula at 1 medical and 1 pharmacy faculty while at 3 health care colleges this area is covered through health-economics or health-management courses. In postgraduate programs (master and doctoral studies) just 3 faculties included health economics in its curricula; 1 medical faculty as mandatory subject, and 2 medical colleges as elective subject. **CONCLUSIONS:** Pharmacoeconomic education for health care students in Bosnia and Herzegovina is poorly organized and not satisfactory. There is growing need to educate health care professional and stakeholders in this field to ensure proper understanding and implementation in practice and decision-making process. Limitation of this study is that detail programs and structure of courses could not be examined since it is not on-line available. Further research is recommended to get deep insight into curricula.

HEALTH CARE USE & POLICY STUDIES – Health Technology Assessment Programs

PHP159

WORKSHOP IN PHARMACOECONOMICS: AN ITALIAN EXPERIENCE OF MULTI-STAKEHOLDER HTA CONSENSUS

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OBJECTIVES: To validate an innovative experience that aims at being recognized by Institutions as a national and independent HTA assessor, thus supporting both national and regional health care decison makers. This experience consists of a multi-stakeholder working group that, in the field of new technologies proposed for critical clinical areas, discusses and develops guide-lines and decision rules and comparatively examines local data. **METHODS:** The working method consists of a series of meetings (4 per year) of a scientific board (composed by high-profile experts covering all HTA domains) that carries out a nationwide analysis of the topic under examination and focuses on the main clinical, economic, organizational, social, and ethical aspects. Questionnaire-based surveys and Delphi panel are the main operational tools. WEF adopts standard HTA pro-

cedures according to the EUnetHTA Core Model. To avoid any conflict of interests, no fee is paid to any member. **RESULTS:** Since 2011, three HTA reports have been completed focusing in 2011-2012 on hepatology (HCV/HBV screening and treatments) and extending in 2013 to other topics including hepatocellular carcinoma and inflammatory bowel diseases; HIV is coming up next year. Along with 4 publications in international journals (mean impact factor 5.73), there have been auditions at the Italian Drug Agency (AIFA) and at the Healthcare Commission in Parliament that have facilitated the approval of new HCV drugs. Furthermore, delays in approvals by regional formularies have been reduced by about 65% (from 212 days after national marketing authorization to 74 days; Farmindustria data). **CONCLUSIONS:** This new multidisciplinary and multistakeholder approach proved to be well-accepted, and the "WEF method" is already recognized as a milestone in the Italian HTA landscape, by both Institutions (e.g. AIFA and Italian MoH) and Scientific Societies, thus helping payers in making rational decisions based on HTA methods.

PHP160

EXPLORING THE KEY DECISION DRIVERS PROVIDED BY HTA AGENCIES ACCEPTING SUBMISSIONS WITH ICERS HIGHER THAN THE THRESHOLD

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OBJECTIVES: Health technology assessment (HTA) agencies use an incremental cost-effectiveness ratio (ICER) threshold, generally understood to be £30,000 for NICE (England), £20,000 for the SMC (Scotland), CAN$50,000 for CADTH (Canada), and AUS$42,000 for PBAC (Australia). To help inform future submissions, we assessed the rationale provided by the four HTA agencies when submissions were accepted despite the reported ICERs being higher than these thresholds. **METHODS:** All HTA appraisals from January 2000 to May 2013 from NICE, SMC, CADTH, and PBAC were included in the analysis. Multiple technology appraisals, resubmissions, vaccination programmes, requests for advice, and submissions for which an ICER could not be determined were excluded from the analysis. The full responses of the remaining appraisals were reviewed, with the submitted ICER (with and without proposed PAS), recommendation, and reasoning behind the recommendation extracted. **RESULTS:** A total of 594 submissions met the inclusion criteria and 240 included a higher-than-threshold ICER, with 75 (31.6%) accepted. The key rationale for acceptance was a lack of alternative treatments (25/75). Submissions were also accepted based on the inclusion of a PAS (21/75), a demonstrated cost-effectiveness in a restricted patient population (16/75), and a robust economic evaluation resulting in a certain ICER (13/75). The agencies consistently based their rationale on clinical need and cost-effectiveness, although the proportions varied between the agencies: NICE (53.3%), SMC (59.4%), CADTH (70.0%), PBAC (81.8%). **CONCLUSIONS:** The majority of submissions reporting ICERs greater than the threshold ICER were rejected. ICERs over the threshold ICER were either brought in line with the threshold ICER through PASs or restricting the patient population; or accepted in spite of the high ICER based a clear clinical need or a robust and certain economic analysis. This highlights the importance for manufacturers to provide robust and appropriately justified economic evaluations, even at the expense of an ICER lower than threshold.

PHP161

ARE CONDITIONALLY APPROVED THERAPIES SUCCESSFUL IN GAINING MARKET ACCESS?

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OBJECTIVES: To evaluate all medicines that received a conditional regulatory approval in Europe and to compare these decisions with the products current market access status through the evaluation of Health Technology Assessments (HTAs). **METHODS:** A manual search of the European Medicines Agencies (EMA) website was carried out to identify all pharmaceuticals that received a conditional approval (January 2007 to May 2013). Of the medicines identified, the statutory funding status was checked by reviewing the websites of the key HTA agencies in the EU 5 countries-: HAS (France), G-BA (Germany), AIFA (Italy), DGFPS (Spain) and AWMSG, NICE, SMC (UK). **RESULTS:** A total of 15 pharmaceuticals were found that had received an EMA conditional approval. Of these, 10 met the inclusion criteria and were analysed further: etravirine, everolimus, fampridine, lapatinib, ofatumumab, panitumumab, pixantrone, pazopanib, stiripentol and vandetanib. Of the 10 pharmaceuticals, a total of 50 HTA assessments were conducted by the 7 agencies, with 31 (62%) of the HTAs reaching a positive funding decision. Both NICE and AWMSG recommended only 1 of the conditionally approved drugs for funding, G-BA recommended 2, SMC 3, DGFPS 6, AIFA 6 and HAS 8. Of the 10 drugs, everolimus was the most successful and is funded by 6 (of the 7) HTA agencies. The key reasons for the success of everolimus were due to convincing efficacy (prolonging progression-free survival), combined with an economic case that was considered demonstrated despite some uncertainties. **CONCLUSIONS:** Whilst regulatory bodies recognise the need to grant marketing authorisation on the basis of less complete data, this does not necessarily mean a straight forward path through market access. Although the majority of HTA agencies did provide a positive funding decision; sound health economic evidence remains essential for new medicines to increase the chances of market access approval.

PHP162

ARE HEAD-TO-HEAD DATA NECESSARY TO GAIN REIMBURSEMENT IN THE FRENCH NATIONAL HEALTH CARE SYSTEM?

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BACKGROUND: Since December 2011, pharmaceutical companies are required by law to provide the Haute Autorité de Santé with head-to-head (H2H) data against standard of care when available to be entitled for reimbursement. However, France is a market where health authorities rarely deny reimbursement to innovative drugs but rather where list prices are lower than in comparable countries. **OBJECTIVES:** The aim of this research is to understand the impact of H2H data on the Service Médical Rendu (SMR) and Amélioration du Service Médical Rendu (ASMR) ratings following passage of the law. **METHODS:** Transparency Commission (TC) reports for new drugs or indication expansions of existing drugs published between January 1, 2012 and March 31, 2013 were reviewed. The following data were gathered: 1) study type (placebo-controlled vs active H2H comparator); 2) comparator (if H2H); 3) availability of appropriate comparators in the marketplace; and 4) SMR/ASMR ratings. **RESULTS:** A total of 110 TC assessments of 88 drugs were identified and examined. Ninety-four of the 110 assessments were of drugs where an appropriate comparator existed in the marketplace. Of these 94 assessments, H2H trials were conducted in 54 assessments. The percentage of assessments in the H2H group obtaining an SMR of important (78%) was similar to those that did not conduct H2H trials (75%). In contrast, the percentage of assessments in the H2H group obtaining an ASMR of III or IV was greater than the non-H2H group (15% vs. 26%). **CONCLUSIONS:** The conduct of H2H trials does not guarantee an SMR of important for new drugs or indication extensions, but may improve ASMR rating. Although the TC mentions the lack of comparative data as a major contributing factor for an SMR of insufficient in their assessments of some products (Daxas, Xiapex), other factors, such as adverse events or efficacy data vs placebo are equally important.

PHP163

INFLUENCE OF PATIENT-REPORTED OUTCOMES ON HTA REIMBURSEMENT DECISIONS

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OBJECTIVES: To understand how patient-reported outcomes (PROs) influence decisions made by Health Technology Assessment (HTA) agencies. **METHODS:** Reports from five HTA agencies that make reimbursement decisions (NICE, HAS, SMC, PBAC and CADTH's CDR) were selected. The reports, taken from January 2005-April 2013, cover disease conditions in neurological and respiratory therapeutic areas. PROs within the HTA reports were identified and four analysts independently examined the stated rationales for the agencies' decisions to determine whether PROs had a positive, negative, or neutral influence on the decision. Discrepancies between the analysts were discussed in-depth until consensus was reached. **RESULTS:** A total of 262 HTA reports were analyzed from the five agencies selected. PROs were mentioned in 34% of the HTA reports, and were the primary endpoint in 6%. Twenty-five (10%) reports mentioned PRO in the clinical rationale for their decisions. Twelve of the 25 HTA reports (48%) contained PRO as a primary outcome, indicating that a PRO is more likely to influence the decision-making process if it is a primary outcome ($p < 0.001$). In 12 out of the 25 HTA reports, the clinical rationale for the decision stated that, for the PRO, the drug performed better than placebo or comparator. Ten (83%) of these reports resulted in a positive decision. In eight reports, the drug compared equivalently or unfavorably to placebo or comparator for the PRO and resulted in four (50%) positive decisions. There was no significant difference in agency decisions between the reports that positively reported PROs and the reports with negative or similar PRO results ($p=0.16$). **CONCLUSIONS:** In respiratory and neurological diseases, the use of PROs is more likely to influence decision-making by HTA agency when PROs are specified as primary outcomes. Future research directions include comparing these findings to the effect other clinical outcomes have on reimbursement decisions.

PHP164

HEALTH ECONOMIC (HE) DATA REQUIREMENTS AND AVAILABILITY IN THE EUROPEAN UNION. RESULTS OF A SURVEY

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OBJECTIVES: To compare data requirements and their availability for HE evaluations in 5 countries in Central/Eastern Europe - Poland, Czech Republic, Slovakia, Hungary, Romania (CEE) and 5 in Western Europe – UK, France, Germany, The Netherlands, Sweden (WE). **METHODS:** A questionnaire was developed and distributed to market access representatives from Pfizer who were asked to complete the questionnaire with opinion leader's support. The questionnaire focused on the obligation to conduct HE assessment for reimbursement submissions, local HE guidelines, applied discount rates for future costs and effects, willingness to pay (WTP) thresholds and available data sources. **RESULTS:** HE is mandatory in all CEE and 3 WE participating countries for reimbursement applications of innovative drugs. Usually cost-effectiveness (CEA) and budget-impact (BIA) analyses are required. The preferred outcome of CEA is quality-adjusted-life years. In Romania, France and Czech Republic guidelines could not be identified at the time of the survey. HE evaluations are usually prepared by the applicant; in Sweden, UK, The Netherlands and Poland unlocked models have to be presented for scrutiny. Discount rates vary from 1.5% to 5%; usually the same for costs and outcomes (except in The Netherlands and Poland). Only UK, Poland and Slovakia have an explicit WTP threshold. In Poland it is based on GDP per capita, in Slovakia on multiples of average monthly wages. Differences were found on data availability. In WE data can be acquired easier compared to CEE. Health insurance funds do not provide their data, unless they were published. Patient registries are either not available in CEE or difficult to access, so applicants mostly rely on retrospective medical chart data, hospital information systems or expert panels. **CONCLUSIONS:** We found similar requirements for HE analyses in CEE and WE but differences in data availability. This results in less accurate inputs across the CEE influencing analyses' outcomes.

PHP165

KEY DRIVERS OF PBAC DECISIONS FOR THE REIMBURSEMENT OF ORPHAN DRUGS ON THE LIFE SAVING DRUGS PROGRAM

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OBJECTIVES: In Australia, the decision process for the reimbursement of orphan drugs on the Life-Saving Drugs Program (LSDP) is centred on a drug's ability to meet strict criteria as specified and assessed by both the Pharmaceutical Benefits Advisory Committee (PBAC) and the LSDP Advisory Committees. The objective of this research was to investigate the key determinants of PBAC decisions with respect to the LSDP criteria in order to understand the key challenges facing new treatments seeking LSDP funding. **METHODS:** A systematic search was conducted of all available Public Summary Documents (PSDs) from July 2005 to April 2013, to identify products that have sought listing on the LSDP. The selected PSDs were reviewed and data extracted according to categories defined by the LSDP criteria. Data were then qualitatively analysed within and across categories to identify key themes and concepts influencing decisions. Quantitative analyses were also conducted on the number of submissions, rejections, deferrals and the time from when a product first sought reimbursement to when funding was initiated. **RESULTS:** Since the LSDP was created in 1995 only 12 products have sought LSDP funding, 10 are currently reimbursed covering 7 disease areas. Of the applications reviewed, 58% of submissions were immediately referred from the PBAC to LSDP for funding, 17% were initially rejected and after subsequent submissions have been funded, and 25% of applications are yet to receive funding. The average time from the first PBAC consideration of a product until funding on the LSDP is 19.7months. The most common reason for rejection was around uncertainty in a drug's ability to significantly prolong life and the appropriateness of surrogate outcomes to accurately predict long-term survival. **CONCLUSIONS:** This analysis shows there is a pathway to reimbursement of high cost orphan drugs when there is a reasonable level of evidence supporting survival gains.

PHP166

HOW DOES THE UNCERTAINTY AROUND THE EXPECTED ICER AFFECT NICE DECISIONS?

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OBJECTIVES: In the UK, NICE assesses health technologies based on clinical and cost-effectiveness evidence. Recommendations ensure NHS patients have access to the most clinically effective treatments, whilst using NHS resources cost-effectively. Nevertheless, cost-effectiveness analyses are susceptible to limitations which make the true value of a technology uncertain. This study investigates what other factors NICE considers when making recommendations under uncertainty. **METHODS:** All Single Technology Appraisals (STAs) published by NICE between 2011-2013 inclusive were reviewed. Recommendations were identified as being made under uncertainty if there was a less than 50% probability that the intervention was cost-effective at a willingness-to-pay threshold of £20,000 per QALY gained. NICE committee reports for these appraisals were reviewed to determine the factors taken into account when making a recommendation. **RESULTS:** Of 64 STAs published in the studied period, 31 interventions were identified with uncertainty at the willingness-to-pay threshold of £20,000, of which 18 (58%) were recommended by NICE. Moreover, only 4 (22%) recommended STAs with uncertainty at £20,000 had a greater than 50% probability of being cost-effective at a threshold of £30,000. Of the STAs recommended under uncertainty, 13 (72%) had a patient access scheme (PAS) in place, while 3 (17%) fulfilled end-of-life treatment criteria. Health-related benefits not captured in the manufacturer's economic model that were likely to lower the ICER, innovative technologies, or interventions satisfying an unmet clinical need were also taken into account. For example, fingolimod was recommended by NICE for treatment of multiple sclerosis based on its oral rather than intravenous formulation and because benefits from a reduced caregiving need were not accounted for in the manufacturer's economic model. **CONCLUSIONS:** Even under uncertainty, NICE often recommends new technologies, particularly if a PAS is in place or if additional costs are deemed to be justified by the benefit provided to patients or their families.

PHP167

ANALYSIS OF THE IQWIG COMMENTS ON THE EVIDENCE SEARCHES OF DOSSIERS IN THE GERMAN AMNOG PROCESS

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OBJECTIVES: The benefit assessment of new drugs in Germany requires the submission of a value dossier including systematic searches. The majority of dossiers are methodically inspected and assessed by the German Institute for Quality and Efficiency in Healthcare (IQWiG). The study's objective was the analysis of common deficiencies in systematic searches and their consequences for the IQWiG assessment. **METHODS:** A total of 37 IQWiG assessment reports were analysed with regard to all comments made on the presented systematic searches in the dossier of the pharmaceutical company. A distinction was made between literature and study searches. The respective IQWiG comments were categorized and listed. Inadequate searches were examined in terms of consequences for the assessment by the IQWiG. Consequences were divided into those affecting the search required for the substance itself and those carried out for indirect comparisons/ further investigations. **RESULTS:** A total of 4 of the 37 dossiers passed the IQWiG assessment without deficiencies. Out of all analysed searches a total of 104 deficiencies were found, of which the most frequent ones referred to the search strings (32%) and the documentation of the search (25%). In the consistency check on the number of hits deviations were found by the IQWiG in 13%; 92% of the inconsistencies occurred in study-registry versus 8% in literature searches. There were no consequences in 62% (23/37) for the substance-search and in 22% (8/37) for indirect comparisons/ further investigations. Non-consideration of study results, which was the most frequent consequence of an inadequate search, occurred in 24% for the substance-search and in 32% for indirect comparisons/further analyses. **CONCLUSIONS:** The methodological requirements for systematic searches to be accepted by the IQWiG are not achieved in the majority of dossiers. An adequate design and a careful documentation of the searches is crucial to ensure the best possible acceptance of evidence in the AMNOG process.

PHP168

ANALYSIS OF PUBLISHED HEALTH TECHNOLOGY ASSESSMENTS (HTA) IN RUSSIA AND ITS PLACE IN RUSSIAN REIMBURSEMENT SYSTEM

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OBJECTIVES: Currently there is no formal HTA agency in Russia, although the need for HTA as an evidence tool for policy makers is increasing due to budget constraints. However, there are HTA bodies which to some extent influence decison makers through publications of pharmacoeconomic studies. The objective of the present study was to gain insights into the current activities of existing HTA organizations and research trends in developing HTA in Russia. **METHODS:** A manual search of four Russian HTA organizations' websites was conducted to find pharmacoeconomic assessments published from 1998 onwards. Per agency, all relevant reports were categorized by therapeutic area and publication date. Any revealed patterns in the HTA topics were in-depth analyzed and compared with the World Health Organization (WHO) country profile of Russia. **RESULTS:** In total, 180 pharmacoeconomic assessments published by four Russian HTA organizations were identified. Overall, the majority of studies were performed in cardiovascular (n=45; 25%) and oncology (n=32; 18%) disease areas, which are according to the WHO, the two leading causes of death, both in Russia and globally. The total number of pharmacoeconomic publications per year has been constantly increasing from one study in 1998 to 26 in 2009, however with fewer reports published in 2010-2013 (32 HTAs in three years). When reported, the potential willingness-to-pay (WTP) threshold for cost-effectiveness was suggested to be 3*Gross Domestic Product (GDP) per capita as recommended by WHO, which equals to approximately 30,000 euro per Quality Adjusted Life Year (QALY) gained. **CONCLUSIONS:** Although formally Russia does not have a transparent HTA based reimbursement process, existing HTA organizations are constantly developing and gaining HTA experience by conducting assessments in the therapeutic areas with the highest burden on Russian population. These areas of interest, as well as an approach to define WTP threshold, match with WHO data and recommendations.

PHP169

SYSTEMATIC LITERATURE REVIEWS AT THE HEART OF HEALTH TECHNOLOGY ASSESSMENT: A COMPARISON ACROSS MARKETS

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OBJECTIVES: Requirements for systematic literature reviews (SLRs) within a Health Technology Assessment (HTA) submission vary across the world. The objective of this study is to compare clinical and economic SLR requirements issued by eight HTA agencies in the UK (England and Wales, Wales, Scotland), Ireland, Germany, Sweden, Canada, and Australia. **METHODS:** SLR requirements issued by the National Institute for Health and Care Excellence (NICE), All Wales Medicines Strategy Group (AWMSG), Scottish Medicines Consortium (SMC), National Centre for Pharmacoeconomics (NCPE), Gemeinsamer Bundesausschuss (G-BA) (Federal Joint Committee), The Dental and Pharmaceutical Benefits Agency (TLV), Canadian Agency for Drugs and Technologies in Health (CADTH), and Pharmaceutical Benefits Advisory Committee (PBAC) were compared, and a checklist of requirements was compiled. **RESULTS:** SLRs of the clinical and economic evidence underpin the HTA process. However, HTA agencies vary on the specific requirements for each and the need for critical appraisal of identified clinical studies and economic analyses. NICE requirements are the most prescriptive, whereas AWMSG and TLV have few stated SLR requirements. All agencies require a clinical SLR, although AWMSG does not specify outright but requires a clinical SLR to determine economic model inputs. Four agencies require both a clinical SLR and critical appraisal of the included studies (NICE, NCPE, G-BA, and PBAC), although recommended appraisal tools vary. NICE and CADTH require both an SLR and a critical appraisal of existing economic evaluations for the intervention of interest; PBAC requires an SLR of only economic evaluations. NICE, SMC, AWMSG, and NCPE require an SLR of utility data, and only NICE and SMC specify the need for an SLR of cost and resource use data. A more detailed analysis of specific methodology requirements will be presented. **CONCLUSIONS:** Although SLR requirements vary between HTA agencies, a clinical SLR is a key requirement for all eight agencies investigated.

PHP170

ANALYSIS OF TRANSPARENCY AMONGST INTERNATIONAL HEALTH TECHNOLOGY ASSESSMENT ORGANIZATIONS

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OBJECTIVES: To assess the level of transparency of health technology assessment (HTA) organizations in eight countries (Australia, Canada, Brazil, France, Germany, Italy, Spain, and the UK). **METHODS:** Nine national review bodies carrying out HTAs for the purposes of reimbursement and funding decisions within their respective countries were assessed according to 33 transparency parameters. The parameters were designed to assess the level of transparency in the HTA processes, clinical and economic reviews, and stakeholder involvement. Using a modified Delphi process, each parameter was weighted based on its importance to transparency and given a score from one to ten. A review of each national body was conducted to determine whether or not they included each of the 33 parameters. Data from public sources (i.e., organization websites) were utilized and interviews with international experts were conducted to verify the information. Total scores were calculated and converted to a transparency index, with 100% being the most transparent. The score was adjusted for review bodies that did not require economic evaluations for their HTA process. **RESULTS:** The level of transparency varies greatly amongst the HTA organi-

zations studied. The transparency index scores were as follows: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen/Gemeinsamen Bundesausschusses (Germany), National Institute for Health and Care Excellence (UK), pan-Canadian Oncology Drug Review (Canada), Common Drug Review (Canada), Pharmaceutical Benefits Advisory Committee (Australia), Comissão Nacional de Incorporação de Tecnologias (Brazil), Haute Autorité de Santé (France), Agencia de Evaluación de Tecnologias Sanitarias (Spain), and Agenzia Italiana del Farmaco (Italy) were 97%, 96%, 91%, 83%, 78%, 70%, 67%, 53%, and 25%, respectively. **CONCLUSIONS:** Transparency amongst HTA organizations is progressively becoming the international standard. However, the extent of transparent processes and procedures proves to be heterogeneous amongst international review organizations.

PHP171

EXPLORING THE KEY DECISION DRIVERS PROVIDED BY HTA AGENCIES REJECTING SUBMISSIONS WITH ICERS LOWER THAN THE THRESHOLD

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OBJECTIVES: Health technology assessment (HTA) agencies use an incremental cost-effectiveness ratio (ICER) threshold generally understood to be £30,000 for NICE (England), £20,000 for the SMC (Scotland), CAN$50,000 for CADTH (Canada), and AUS$42,000 for PBAC (Australia). To help inform future submissions, we assessed the rationale provided by the four HTA agencies when submissions were rejected despite the reported ICERs being lower than these thresholds. **METHODS:** All HTA appraisals from January 2000 to May 2013 from NICE, SMC, CADTH, and PBAC were included in the analysis. Multiple technology appraisals, resubmissions, vaccination programmes, requests for advice, and submissions for which an ICER could not be determined were excluded from the analysis. The full responses of the remaining appraisals were reviewed, with the submitted ICER, recommendation, and reasoning behind the recommendation extracted. **RESULTS:** A total of 594 submissions met the inclusion criteria. 354 submissions across the four HTA bodies included a lower-than-threshold ICER, with 107 (30.2%) of these submissions rejected. Across the agencies, the most common reasons for rejection were use of an inappropriate patient population or comparator (45/107), uncertainty regarding the clinical benefits (32/107), and use of economic evidence that was not sufficiently robust (40/107). The reasons for rejection were consistent across the four agencies, with a similar proportion basing their decision at least partly on one of the three reasons provided above: NICE (92.9%), SMC (92.0%), CADTH (93.3%), PBAC (93.8%). **CONCLUSIONS:** A large proportion of submissions were rejected despite ICERs below the threshold. In instances where decisions went against the ICER thresholds, there was a clear tendency for identifiable problems with the clinical and economic assumptions to diminish the reliability of the ICERs presented. This result highlights that a lower-than-threshold ICER is not enough for a positive recommendation and manufacturers must support their submission with accurate and reliable data to achieve a favourable outcome.

PHP172

CROSS-MARKETS VARIABILITY OF INNOVATION BENEFIT'S EVALUATIONS. HOW ITALY COMPARES TO FRANCE, GERMANY AND THE UNITED STATES

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OBJECTIVES: A new drugs' innovation benefit is commonly evaluated, both in Europe and the USA. Most of the new pharmaceutical launches have to be evaluated on the level of innovation that they offer as part of the market access process. The objective of this abstract is to give an example of the variability that emerges in the innovation scores given by the Italian agency, AIFA, as compared to those of France, Germany and the USA. **METHODS:** Drugs listed on the AIFA website as showing potential or important innovation, were used as a benchmark to measure how innovation benefit assessments performed in France, Germany and the USA deviate. The innovation benefit was measured through: the ASMR score (Amélioration du Service Médical Rendu) in France, as published on the HAS website (Haute Autorite' de Sante'); the level of additional benefit in Germany, as published on the G-BA website (Gemeinsame Bundesausschuss); the type of approval procedure as published on the FDA (Food and Drug administration) website. In the case of the USA, standard approval vs. priority review was used as a proxy measure of the level of innovation. **RESULTS:** The results of the innovation benefit's evaluations performed in France, Germany and the USA differ from those performed by AIFA in 74%, 33% and 58% of cases respectively. The lower percentage in Germany is due to limited available information compared to other markets. **CONCLUSIONS:** The level of variability that exists between the outcomes of the innovativeness evaluation performed in different countries suggests that although the definition of innovation may appear straightforward, it is open to different interpretations by different health care systems.

PHP173

NICE STA DECISIONS: AN ANALYSIS OF HOW ADVICE DIFFERS BETWEEN PRELIMINARY AND FINAL GUIDANCE

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OBJECTIVES: The National Institute for Health and Care Excellence (NICE) established the Single Technology Appraisal (STA) programme to evaluate the clinical and cost-effectiveness of medical technologies and provide mandatory guidance on how they should be used within the National Health Service (NHS) in the UK. The objective of this analysis is to explore how NICE advice differs between preliminary and final guidance in the STA process and identify actions manufacturers could take to increase their chances of a successful submission. **METHODS:** For STAs published between February 2010 and May 2013, the appraisal consultation document (ACD) and final appraisal determination (FAD) were identified. The guidance issued in these documents was compared and contrasted, and the key clinical and economic evidence that affected recommendations were extracted into an Excel workbook. **RESULTS:** Of the 71 STAs published, ACDs were produced for 60 technologies, while 11 (15%) proceeded straight to FAD. All submissions which proceeded directly to FAD were recommended (full or optimised) in the final guidance. Twelve STAs (20%) received a "minded no" at ACD; however, 11 of these (92%) were reversed within the FAD on the basis of additional data provided by the manufacturers in the form of economic analyses (n=5) or patient access schemes (PAS) (n=6). Of the 35 "not recommended" at ACD, 15 (43%) were ultimately recommended within the FAD through the introduction or revision of a PAS and/or submission of additional analyses. **CONCLUSIONS:** If manufacturers can demonstrate a robust clinical and economic argument in their initial submission the chances of a FAD being produced without the requirement of an ACD are greatly increased. Furthermore, ACD decisions can also be overturned; technologies which receive a "minded no" or "not recommended" at ACD stage can achieve a recommendation at FAD by presenting additional analyses or introducing/modifying a PAS.

PHP174

COMPARISON OF DRUG ASSESSMENTS IN FRANCE, GERMANY AND THE UNITED KINGDOM: IS EUROPEAN HTA A REALITY?

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OBJECTIVES: In 2006, the EUnetHTA project was launched. One of its main strategic objectives was to strengthen the link between HTA and health care policy making in the EU. Seven years after EUnetHTA establishment, the objective of this study was to compare HTA agencies' assessments in France, Germany and UK, focusing on method and outcomes. **METHODS:** Scope of the study was all the products getting a positive opinion from CHMP during two years, starting at January 1, 2011. Comparison between assessments was made for products assessed by the three HTA agencies: IQWiG, NICE, and HAS. **RESULTS:** A total of 87 drugs were included in this study. 11 (13%) have been assessed by the three agencies. Among these drugs, more than 50% (6) were cancer treatment. HAS was the first to assess drug in 6 cases (mean delay between CHMP positive opinion and assessment: 223 days), followed closely by IQWiG (242 days), then by NICE (354 days). IQWiG segmented the patient population defined by the manufacturer into different sub-populations in 6 assessments, HAS in 2, NICE never. NICE was the only agency who did not recommend a drug for cost-effectiveness reasons (2 assessments). In three assessments, IQWiG concluded that there was no benefit proven for the whole population; regarding the same drugs, HAS concluded there was minor improvement in actual benefit twice. **CONCLUSIONS:** Some major trends emerge in the assessments studied: use of indirect comparisons, added therapeutic value weighted by severity and frequency of side effects and uncertainty. Nevertheless, comparator choices, perception of clinical benefits and risks, budget impact and overall method still differ between the three HTA agencies studied, leading to different outcomes for drugs assessed.

PHP175

USING THE DELPHI METHOD FOR SELECTING MEDICAL TECHNOLOGIES UNDER BUDGET CONSTRAINTS: A FEASIBILITY STUDY

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OBJECTIVES: To examine whether the Delphi method can provide a convenient tool for selecting medical technologies for inclusion in the National List of Health Services (NLHS) in Israel under a pre-defined budget constraint. **METHODS:** The Delphi method was applied in two groups: medical specialists (oncologists and cardiologists) and observers in the NLHS committee. Participants in each group were anonymously asked to choose five of ten suggested technologies from the list of technologies submitted for inclusion in the 2012 NLHS and rank them according to importance. Subsequently, the participants repeated the experiment after receiving aggregated feedback on the relative ranking of each technology within the same group after the first round. Comparison of the results was performed using descriptive statistics and non-parametric tests. **RESULTS:** After two rounds of the experiment, observers and medical specialists reached agreement on four of the five highest ranked technologies in each field (oncology and cardiology) regarding their importance to be included in the NLHS. Three of these four technologies were indeed included in the NLHS for 2012. **CONCLUSIONS:** The Delphi method is one of the best-known techniques to control group interaction and reach a consensus by utilizing the expertise of committee members. The study demonstrated the feasibility using the Delphi method for ranking health care technologies.

PHP176

WHICH SHOULD BE THE CORRECT NMA TO BE USED? A REVIEW OF HTA RECOMMENDATIONS

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OBJECTIVES: In the lack of head-to-head comparative trials to demonstrate the efficacy of new treatments, it is common to use network meta-analysis (NMA), including indirect treatment comparison (ITC) or combine direct and indirect evidence through mixed treatment comparison (MTC). Due to the increasing number of drugs approved for the same indication and the increasing complexity of networks for treatments comparisons, new methods of MTC taking into account all the comparisons have aroused. Health Technology Assessment (HTA) bodies increasingly demand NMA although different recommendations about the methodologies to be applied exist. This study aims to review recommendations regarding ITCs and MTCs among the main HTA bodies. **METHODS:** A review of methodologies for drug comparison recommended by the main HTA bodies was performed. Recommendations related to evidence identification methods, assessment of homogeneity of studies and populations to be combined and statistical approach for the analysis were also reviewed. **RESULTS:** A systematic literature search is a prerequisite for most HTA bod-

ies, as well as demonstrating homogeneity and consistency among studies. Regarding to the statistical analysis, Bucher's method is the most commonly used and is recommended by most HTA bodies for indirect comparisons. Nevertheless, some HTA bodies (e.g. HAS, SMC), EUnetHTA and ISPOR Task Force on Indirect Treatment Comparisons consider that even if some direct evidence is available it is appropriate to validate the results using MTCs. According to these institutions, Bucher's method is not appropriate for the analysis of complex networks, while Bayesian approach is a more comprehensive method that can include meta-regression and study-level covariates. The use of the non-appropriate methods can derive to biased results. **CONCLUSIONS:** Methodology used for NMA should include all available evidence. Due to the increasing complexity of network patterns, Bayesian analysis better meets HTA needs than the Bucher's method, and is also a stronger evidence-deriving tool.

PHP177

SCANDINAVIAN DRUG REIMBURSEMENT AND COVERAGE DECISIONS: THE ROLE OF HTA

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OBJECTIVES: To examine and explain differences and similarities in coverage decisions for outpatient pharmaceuticals in Denmark, Norway and Sweden, and to provide a better understanding of the current and future role of HTA in these countries. **METHODS:** A comparative analysis of all outpatient drug appraisals carried out between 2009 and 2012, including an analysis of divergent coverage decisions for outpatient drug-indication pairs appraised by all three countries was performed. Agreement levels between HTA agencies were measured using kappa scores. Primary data collection through consultation with decision makers and academics in the three countries was carried out to obtain insight on how coverage decisions are made and why reimbursement outcomes differ in the three countries. **RESULTS:** A total of 19 outpatient drug-indication pairs appraised in each of the three countries were identified, of which six pairs (32%) had divergent coverage decisions. An uneven distribution of coverage decisions was observed, with the highest number of overlap in appraisals in Norway and Sweden (freemarginal kappa 0.89). Similarities were found in the criteria for reimbursement and the reasoning for coverage decisions. Differences in the appraisal methods applied and the interpretation of the evidence considered may explain divergent decisions. **CONCLUSIONS:** The study suggests that Norway and Sweden employ similar methods for outpatient drug appraisals and have less divergent reimbursement outcomes, while health economic evaluation is less prominent in Danish outpatient drug appraisal, leading to a lower percentage of reimbursements with restrictions or criteria.

PHP178

THE IMPORTANCE OF SAFETY ASPECTS IN THE AMNOG PROCESS IN GERMANY: IS THE G-BA ASSESSMENT CONSISTENT WITH THAT OF THE CHMP?

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OBJECTIVES: To assess the role of safety aspects in the overall AMNOG benefit assessment in Germany. Special attention was given to two aspects: (1) Are adverse events (AE) used systematically to change the benefit assessment in any direction? (2) Are safety aspects considered in the assessment in accordance with the scientific CHMP opinion? **METHODS:** Twenty-six benefit assessments decided and published by the Federal Joint Committee (G-BA) between Jan 1st 2011 and Jun 6th2013 were analyzed regarding the extent of harm. For each drug the extent of harm included with the consecutive influence on the overall benefit rating including potential changes in the overall rating scores was determined. Additionally, the safety aspects considered in the G-BA decision were compared to the CHMP assessments. **RESULTS:** For 19 of 26 drugs (73.1%), a greater or less harm vs. the comparator determined by the G-BA was considered. In 12 of these 19 substances (63.2%) the rating of the additional benefit drawn from efficacy results remained unaltered due to safety aspects. In 5 procedures (26.3%) the G-BA rated the additional benefit solely on the basis of less harm vs. the comparator. In 2 procedures (10.5%) the G-BA found a greater harm vs. the comparator which negatively impacted the overall rating. Statistically significant results of 'overall incidence of AE', 'AE grade 3-4', 'serious AE' and 'AE leading to study withdrawal' were always considered by the G-BA. In 8 cases (42.0%), the G-BA weighted safety aspects differently from the EMA in its overall rating process. **CONCLUSIONS:** The AE profile is of major importance in the AMNOG process. It changed in more than one third of the drug assessments (7 cases; 36.8%) the efficacy based benefit ratings. In 8 cases (42.0%) the G-BA assessment deviated from the conclusions considered by the EMA.

PHP179

ARE MONOCLONAL ANTIBODIES STILL CONSIDERED AS INNOVATIVE BY THE FRENCH HEALTH CARE SYSTEM? A RETROSPECTIVE ANALYSIS 2000-2012

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OBJECTIVES: To understand the dynamics of the Transparency Committee (TC) assessments of monoclonal Antibodies (mAbs) through the improvement in therapeutic benefit (known as "ASMR") ratings from 2000 to 2012. ASMR ratings are divided into two main groups by the French health care system. ASMR I to III allow manufacturers to notify price to the pricing committee based on the innovative character of the product and on the improvement provided over standard of care. This allows pricing at the "European" level. ASMR IV and V are given to non-innovative products adding at best minor improvement to standard of care. **METHODS:** mAbs (excluding radiotherapeutics) online published reports from the TC from 2000 to 2012, including new indications and reassessments, were analysed. The TC has evaluated a total of 26 mAbs, leading to 105 ASMR ratings during the period studied. **RESULTS:** From 2000 to 2006, 83% (n = 29) of the TC evaluations of mAbs led to ASMR I, II or III and only 17% of the TC evaluation lead to ASMR IV or V (n = 6). During the following period, from 2006 to 2012, the TC granted only 30% (n = 21) of the assessments with an ASMR I, II or III. 70% (n = 49) of the remaining evaluations where ASMR IV or V. **CONCLUSIONS:** In the first six years mAbs were perceived as a disruptive innovation to a significant proportion of ASMRs between I and III as a reward for research and development efforts of the manufacturer. This research suggest that mAbs manufacturers no longer benefit from a 'first mover' advantage and may face higher scrutiny from the TC and greater price pressure from the French pricing committee.

PHP180

HEALTH TECHNOLOGY ASSESSMENTS OF MEDICAL DEVICES: IS HELP OUT THERE?

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OBJECTIVES: Small-Medium Enterprises (SMEs) should assess the potential profitability of new medical devices early in their development. This can be achieved via early-stage health technology assessments (HTAs). However, many SMEs will not have the skills necessary to undertake these HTAs, so tools and frameworks that aid this process are likely to be beneficial. A systematic review of the literature was undertaken to identify resources that can facilitate early-stage HTAs. **METHODS:** Electronic databases, such as MEDLINE and ECONLIT, were searched in February 2013. Papers were included if they met all of the five selection criteria used. **RESULTS:** Of the 4729 papers identified, ten were included in the final analysis. Only one interactive tool, a decision analytic model which is operational via Microsoft Excel, was identified. Of the remaining nine articles, five were classified as frameworks. Of these five articles, the most comprehensive outlines a multi-criteria decision analysis (MCDA) value matrix. The final three articles included in the final analysis contained descriptive methods with information that was considered useful. **CONCLUSIONS:** The resources available to aid the undertaking of early-stage HTAs is very limited. Ideally, an interactive spreadsheet tool that generates intuitive results would be available. However, the one identified tool is too inflexible and most users would struggle to find accurate data to populate it. Unfortunately, these issues are likely to be endemic to any interactive tool for early modelling. As such other guidance, including frameworks, may be more useful if they are comprehensive. Only the MCDA framework article contained methods that the authors of this article considered comprehensive, and the use of MCDA for early-stage HTAs has its own issues. Therefore, there may be a place in the literature for more complete pieces of guidance to undertaking early-stage HTAs.

PHP181

THE NICE MEDICAL TECHNOLOGY EVALUATION PROGRAMME (MTEP) – INSIGHTS FOR MANUFACTURERS CONSIDERING NOTIFICATION

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OBJECTIVES: The Medical Technologies Evaluation Programme (MTEP) was established to promote the uptake of innovative medical technologies through the publication of Medical Technology Guidance (MTG) by the National Institute for Health and Care Excellence (NICE) to the National Health Service (NHS) in the UK. The objective of this analysis is to report data on the MTEP, which are not currently collated on the NICE website, in order to provide insights to manufacturers on the process, outcomes and implementation of guidance. **METHODS:** Information published on the NICE website was used to identify notified technologies, the proportion routed to the MTEP, and the subsequent NICE recommendations. **RESULTS:** Between January 2010 and December 2012, 102 technologies were notified to the MTEP. Of these notifications, 21 technologies were routed to MTEP and 15 were routed to the diagnostics assessment programme (DAP), giving a routing rate of 20% and 15%, respectively. Of the 21 technologies routed to MTEP, 13 technologies have had guidance issued: 10 (77%) had a positive recommendation and 3 (23%) were not recommended for use in the NHS. Whilst a positive recommendation for use is likely to encourage uptake, it is not guaranteed. Following a positive MTEP recommendation for CardioQ-oesophageal doppler monitor (ODM), the implementation levels were relatively low (31% increase in use). **CONCLUSIONS:** Many of the notified technologies are not selected at notification stage. However, once selected and routed to MTEP, most technologies receive some form of positive recommendation. Evidence on implementation levels following a positive recommendation by the NICE MTEP indicates that the implementation of guidance by the NHS may not always be optimal. The new NICE Health Technology Adoption Programme should help to improve implementation levels in the future. To ensure optimal implementation, manufacturers should consider developing tools to support the uptake of technologies alongside a NICE positive recommendation.

PHP182

NUMBER OF SUBMISSIONS NEEDED TO REACH A POSITIVE REIMBURSEMENT DECISION FROM SMC, CADTH, AND PBAC

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OBJECTIVES: Often positive reimbursement decisions are only achieved after multiple submissions. Multiple submissions can delay patient access to necessary therapies and be costly for the manufacturer. This study analyzes the number of submissions needed to gain a positive decision and determines the lag time between the first submission and the positive decision. **METHODS:** The data covered three agencies: SMC, PBAC, and CADTH's Common Drug Review. The reviews spanned 23 disease conditions and included 396 Health Technology Assessments (HTAs). **RESULTS:** A positive decision was achieved after the first submission in 50% of the HTAs analyzed. At 1.57 submissions, PBAC had the highest average number of submissions needed to achieve a positive decision. PBAC's average was statistically higher than that of both CADTH and SMC ($p<0.001$). On average, CADTH and SMC needed 1.17 and 1.16 submissions, respectively, to obtain a positive decision. Also, for drugs that were resubmitted, it took on average 430, 924 and 1,189 days to gain a positive decision from SMC, CADTH, and PBAC. For CADTH and SMC, there appears to be a modest linear relationship between the number of resubmissions needed

to obtain a positive decision and the number of unique drugs reviewed within the disease condition (r= .46 and .41, respectively). This relationship was not observed for PBAC (r=0.01). **CONCLUSIONS:** PBAC required a greater number of submissions to gain a positive decision and the lag time to a positive decision is longer compared to SMC and CADTH. The number of submissions needed to gain a positive decision by CADTH and SMC were similar, but CADTH's lag time was double that of SMC. For both SMC and CADTH, the number of drugs reviewed in a disease condition was positively correlated with the number of times a drug had to be submitted in order to gain a positive decision.

PHP183

DRAFT VERSUS FINAL GUIDANCE IN NICE'S DRUG TECHNOLOGY APPRAISAL PROCESS

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OBJECTIVES: The study sought to establish the pattern by which draft versus final technology appraisal's (TA) for drugs have been issued by UK's NICE. In particular, the study focused on variations between the draft versus final guidance, and the rationale for any changed recommendations during the appraisal process. **METHODS:** The current study is based on a review of NICE's 13 draft guidance and subsequent final guidance issued over the time period from November 2010 to mid June 2013. **RESULTS:** NICE issued five recommendations, four rejections and four recommendations subject to restriction, on drugs for use within the NHS in England and Wales. Four out of the five final recommendations had been overturned from an initial non- recommendation, to gaining a positive decision in final guidance. Meanwhile, all four final rejections corresponded to the recommendations made in its respective draft guidance. With one exception, all recommended drugs had an ICER below GBP30,000. None of the drugs rejected in the final guidance had a Patient Access Scheme offered. **CONCLUSIONS:** One-third of the 13 decisions were positive recommendations, a trend that is significantly lower than the average between 1 March 2000 to 31 May 2013, when 62% of TA's gained a positive final recommendation. Aside from clinical issues, the overriding rationale for the rejections were attributed to the high ICERs, coupled with the lack of PAS. This is compared to the case of, for example, ipilimumab, where a PAS offered in the final guidance lowered the ICER from GBP54,000 - GBP70,000 per QALY gained to GBP42,200 and essentially overturned NICEs initial non-recommendation. As seen in half of the initial rejections, NICE has overturned several decisions in favour of the manufacturer prior to final guidance.

PHP184

ACCEPTANCE OF SURROGATE ENDPOINTS BY HTA AGENCIES IN EUROPE

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OBJECTIVES: To compare how different European HTA agencies assess surrogate endpoints to demonstrate efficacy. **METHODS:** We identified 8 therapies with surrogate endpoints that were evaluated in the last 6 years by NICE and/or SMC (UK), HAS (France) and G-BA (Germany). The acceptability of the use of surrogate endpoints and any specific comments made by these agencies were analysed. **RESULTS:** Commonly used surrogate endpoints such as glycated haemoglobin (HbA1c) in diabetes, progression free survival (PFS) in oncology and forced expiratory volume (FEV1) for respiratory diseases have been generally accepted as sufficient evidence to gain reimbursement by HTA agencies. Especially when a surrogate endpoint has been accepted by EMA, it is usually considered a valid outcome measure. Less well-accepted were several surrogate cardiovascular endpoints such as 6 minute walk test, blood pressure and LDL cholesterol. For G-BA it is important that surrogate endpoints have been properly validated and are patient relevant but they did accept endpoints such as sustained virological response (SVR) for hepatitis treatments, FEV1 and body mass index (BMI) based on minor evidence. NICE and SMC also strongly value evidence to demonstrate the correlation between surrogate endpoints and clinical outcomes. Interestingly SMC has recently become more cautious in accepting widely established endpoints such as HbA1c. With regards to the HAS, they often did not comment on the use of surrogate endpoints at all in their published reports. **CONCLUSIONS:** The use of surrogate endpoints in the assessment of clinical benefit is still controversial; however, attempts are made to establish clearer regulations such as the recently published EUnetHTA guidelines regarding surrogate endpoints. In the absence of evidence on final patient-relevant clinical endpoints, several commonly used biomarkers and intermediate endpoints will be considered as valid surrogate endpoints by HTA agencies. Newer, less established surrogate endpoints will be more subject to strict validation requirements.

PHP185

A COMPARISON OF GERMAN BENEFIT ASSESSMENTS BY G-BA, IQWIG AND MANUFACTURERS

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OBJECTIVES: In the German HTA process (AMNOG) the choice of the patient-relevant endpoint, the appropriate comparator and the method of analysis are known to be decisive for the G-BA's resolution of an additional benefit. Therefore, we aimed to analyze differences between manufacturer's dossiers and G-BA / IQWiG assessments. **METHODS:** The analysis will take into account all completed AMNOG assessment procedures. We analyzed all G-BA resolutions in comparison to IQWiG assessments and the manufacturer. **RESULTS:** One major point of discrepancies occurred in the declaration of patient-relevant endpoints. By June 2013, 58 surrogate endpoints were declared by IQWiG and manufacturers mainly in the indications oncology, infectious diseases and diabetes. The G-BA clearly states that only valid patient relevant endpoints are to be considered. However, there remains uncertainty around the term "patient-relevant" and which criteria have to be met for the IQWiG to accept an endpoint as patient-relevant. To date, 54 comparisons were made in the dossiers to show an additional benefit of a new agent. The pharmaceutical manufacturer and the IQWiG often disagree when it comes to the choice of the method of analysis. Cases of disagreement between G-BA and IQWiG are rarer in this area. In the case of Belimumab, the manufacturer chose to demonstrate the additional benefit by showing the add-on effect of the agent on-top of the appropriate comparator and not against it. This resulted in diverging benefit assessment by IQWiG and G-BA. **CONCLUSIONS:** The analysis of the assessment for all new active agents shows disparities between the assessments of all parties involved. The AMNOG legislation has been in place for about two years and still, there are uncertainties in the choice of patient-relevant endpoints, comparators and method of analysis in the German benefit assessment process. Discussion is necessary to resolve diverging expectations about required methods and following assessments.

PHP186

THE IMPACT OF COST EFFECTIVENESS ON REIMBURSEMENT APPROVALS IN FRANCE: A COMPARISON OF FRANCE AND THE UNITED KINGDOM

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OBJECTIVES: To estimate the potential impact of the new health economic assessment requirement on innovative products that came into law in October 2012 in France, by comparing the outcomes of recent Health Technology Assessments (HTA) in France (HAS) and the UK (NICE, SMC, AWMSG, JCVI). The hypothesis is that reimbursed products that achieved a high benefit score in France may have been rejected if the health economic case had to be demonstrated, as is required in the UK. **METHODS:** A search was conducted to identify all therapies evaluated by HAS which were given a significant, important or moderate therapeutic improvement score (ASMR I, II or III) between January 2010-June 2013. We then identified the assessments of the same product in the UK and compared the outcome of the assessment and the role of the economic evidence that was submitted. **RESULTS:** Thirty-six therapies rated an ASMR I-III by HAS were found. Out of these 36, 19 products had not (yet) been evaluated in the UK. For the remaining 17 that had been assessed by both countries, only one was not recommended by at least one of the UK agencies. NICE's primary reason for rejecting the said intervention was due to the 'clinical and cost effectiveness'. Similarly the SMC stated the economic case of the drug had 'not been demonstrated', and the long term clinical effect remains unknown. **CONCLUSIONS:** Initially, it doesn't appear that economic evaluations based on QALYs considerably influence the outcomes of HTAs. Only one assessment was rejected by both UK agencies based on economic grounds but was awarded an ASMR III. Since most products have been endorsed by the UK agencies, the French system's incorporation of health economics will not necessarily be an additional hurdle that cannot be overcome.

PHP187

WEB-BASED OF TOPIC SELECTION FOR COMPARATIVE EFFECTIVENESS RESEARCH IN KOREA

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OBJECTIVES: As the only health technology evaluation institution in Korea, National Evidence-based Healthcare Collaborating Agency has made efforts to establish the topic selection model of comparative effectiveness research which corresponds to Korean situations in order to revitalize it since 2012. **METHODS:** As a result of preparing thetopic selection process of the comparative effectiveness research according to these efforts and of conducting model operations in 2012, solution to access to the proposal process of research topics and a close examination of research methodologies was proposed as improvement point. **RESULTS:** Accordingly, web-based research topic proposal systems(www.necacer.re.kr) were designed in order to solve access to the proposal process of research topics and to increase transparency of the early stage of research in 2013. To make a close examination of the possibility of research performance in multidisciplinary fashion, evaluation systems of three stages were divided to operate but web-based design which is the same as topic proposal systems was done reflecting the evaluator's geographical access etc. Concretely, web-systems for topic proposal are composed of writing proposed research topic, writing proposed content of a topic, and confirming and submitting stages after writing basic information after login, and evaluative web systems were composed as follows: Step 1 is composed of quantitative evaluation based on 6 standards, step 2 qualitative evaluation based on 6 standards, and step 3 investigation process based on 4 standards in relation to research topics refined. **CONCLUSIONS:** It is conceived that Korean web-based topic selection systems of comparative effectiveness research prepared systematically taking Korean situation into consideration will be able to contribute to improving qualitative aspects of research and enhancing researchers' credibility by transparent opening the whole process of proposing, selecting and confirming topics.

PHP188

RELEVANCE OF INDIRECT COMPARISONS IN THE GERMAN EARLY BENEFIT ASSESSMENT (AMNOG)

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OBJECTIVES: Early benefit assessment in Germany under the AMNOG legislation requires a direct comparison with the appropriate comparator determined by the Federal Joint Committee (G-BA). In case no head-to-head studies are available, submission of indirect comparisons is permitted to assess the additional benefit of the new drug. The aim of this study was to comprehensively analyze the submissions of indirect comparisons reviewed so far by the Institute for Quality and Efficiency in Health Care (IQWiG) from January 2011 until May 2013. **METHODS:** A systematic review of all 48 published assessment reports was performed. **RESULTS:** There is a mismatch between the original intention of the early benefit assessment and its actual outcome. Until May 2013, 14 indirect comparisons have been conducted and submitted by manufacturers regarding the early benefit assessment. Only one indirect comparison has been accepted in a subindication by the IQWiG. However

the results did not cause an added value of the drug in this respective application. In seven cases the indirect comparison was declined due to a different comparator as determined by the G-BA. Three indirect comparisons were declined because of methodological deficiencies and another three indirect comparisons were declined because non-adjusted indirect comparisons were performed. **CONCLUSIONS:** The IQWiG only accepts adjusted indirect comparisons. The application of the correct methodology is necessary to gain valid results and shall not be questioned. The IQWiG approach is accurate with regard to contents and correct in a legal sense. However the procedure shows, that the external preconditions and methodological requirements are demanding and almost impossible to fulfill. Main reason for denial is the divergence from the prespecified appropriate comparator set by the G-BA. To get back to the original aim of the early benefit assessment, a more realistic and reasonable determination of the appropriate comparator would be desirable.

PHP189

THE ADOPTION OF HEALTH TECHNOLOGIES: A SURVEY OF BRAZILIAN POLICY MAKERS

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OBJECTIVES: Policy makers of municipalities decided to adopt health technology into the Brazilian Public Health System (SUS). This group met during national conferences. The last conference, "The XXVIII National Congress of Municipal Health Secretariats (CONASEMS)", took place during June 11 to 14, 2012. The aim was describe the views of participants at the CONASEMS event regarding technology assessment criteria for the Brazilian Public Health System (SUS). **METHODS:** A survey applied at the Ministry of Health's exhibition booth, June 11 to 14, 2012. Three variables were studied for the survey: "Participant Profile", "Knowledge of Health Technology Assessment for Adoption by the SUS" and pre-selected criteria for assessing health technologies (where 1=most important and up to 9=least important) **RESULTS:** The survey encompassed 5.6% (244/4.328) of all conference participants. Of these, 43% represented policy makers; 35% health professionals and 22% others. Of the total amount of participants, 67% have little or average knowledge of HTA and 14% declared having no knowledge of the area. The values in the adoption of health technologies were ranked by delegates. The score of one was: evidence on patient safety, improved quality of life and patient survival, impact on the population's health. The score nine was: relationship between benefits and costs, health system costs and patient costs. **CONCLUSIONS:** Considering the results, the value related to criteria regarding quality of life and survival were the most important in detriment to cost criteria. It is important to involve the Brazilian Network for Health Technology Assessment (REBRATS) as an additional contribution to the application of the new Brazilian law regarding the incorporation of health technologies.

PHP190

ORPHAN DRUGS IN THE GERMAN EARLY BENEFIT ASSESSMENT– REAL WORLD VERSUS G-BA BUREAUCRACY

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OBJECTIVES: Early benefit assessment pursuant to AMNOG was introduced to cut costs and illustrate the additional benefit of new pharmaceuticals including orphan drugs at launch in Germany. In this process orphan drugs have a special status. The EMA orphan drug designation implies the assumption that at least a not-quantifiable additional benefit is set by law. However the extent of the additional benefit still has to be demonstrated by the manufacturer. **METHODS:** By June 2013 seven orphan drug dossiers have been submitted and assessed. Only one product has been admitted an important additional benefit. Four substances had a minor additional benefit and two substances had a not-quantifiable additional benefit. **RESULTS:** An additional benefit needs to be proven against a comparator. But the G-BA will not define an appropriate comparator as for non-orphan drugs. Instead, the assessment of orphan drugs is based on the pivotal trial; the comparator will be derived from this trial. Due to the early phase of pivotal trials in rare diseases, using a comparator is not common. Furthermore, phase II trials often do not meet requirements in terms of evidence level requested: randomized controlled trials with large patient populations are unusual in orphan diseases as well as investigation of valid patient relevant endpoints or validated surrogate endpoints. **CONCLUSIONS:** The G-BA requirements for HTA assessments are drawn from phase III trials and demonstration of an additional benefit over an appropriate comparator, which also serves as price benchmark. The requirements derived for all newly launched products do not reflect orphan drug reality, which is indication and not agent based. In summary the EMA declaration of early admission of orphan drugs in phase II conflicts with the G-BA's methodological requirements for the quantification of an additional benefit. In fact, manufacturers of orphan drugs face an additional barrier before launch in Germany.

HEALTH CARE USE & POLICY STUDIES – Population Health

PHP191

VARIATIONS IN THE HEALTH STATUS OF IRISH REGIONS

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OBJECTIVES: This paper constructs a composite index that is sufficiently comprehensive to rank the overall health status of Irish regions and sufficiently detailed to identify the principal sources of varying regional health status. **METHODS:** We draw on the CSO (Central Statistics Office), PCRS (Primary Care Reimbursement Service) and IPH (Institute of Public Health) health and medicines databases to construct a composite index of the health status of the 8 HSE regions in Ireland in 2010. Our composite health index (CHI) has 6 component indices. Each maps the regional prevalence of major health conditions for which an ATC (Anatomical Therapeutic Classification) group of drugs was prescribed. Our composite health index, CHI, is a coverage-weighted average of the separate indices we construct for persons covered by each community drug scheme in each region. **RESULTS:** Respiratory health status varies most across Irish regions but Cardiovascular, Central Nervous System and 'Other' health conditions have higher CHI weights and contribute more to overall regional health disparities. The Midlands region had the poorest health status in 2010 (8% below the national average); the Eastern region had the best (6% above average), followed closely by the Mid-West. The Mid-West has a better health status than the Midlands despite having lower income and a larger elderly population share. The health status of the Eastern region is just 2% higher than the Mid-West even though its income is 6% higher and the percentage of its population aged over 65 is 1.8 percentage points lower. Simple economic and demographic variables - mean income and the elderly population share – correlate well with health status. **CONCLUSIONS:** Our index maps significant regional disparities and paves the way for complementary epidemiological studies to trace their underlying lifestyle and medical causes and inform regional health policy.

HEALTH CARE USE & POLICY STUDIES – Prescribing Behavior & Treatment Guidelines

PHP192

FEASIBILITY OF MEDICINES REVIEW TO REDUCE POTENTIALLY INAPPROPRIATE MEDICINES IN THE ELDERLY: THE OPTI-SCRIPT CLUSTER RANDOMIZED CONTROLLED TRIAL

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OBJECTIVES: Potentially inappropriate medicines (PIMs) can result in increased morbidity, adverse drug events and hospitalizations. Polypharmacy is the strongest predictor of PIMs,the prevalence of which was 36% in 2007 in those aged ≥ 70 years , with an associated expenditure of over €45 million. Medicines review may have the potential to improve patient outcomes and reduce prescribing costs. This study aims to assess the feasibility of introducing medicines review to reduce PIMs in older patients. **METHODS:** OPTI-SCRIPT is a cluster randomized controlled trial (RCT), that aims to assess the effectiveness of a complex intervention incorporating academic detailing, a medicines review with web-based pharmaceutical treatment algorithms that provide recommended alternative treatments, and tailored patient information leaflets in reducing PIMs. A qualitative evaluation is being conducted to determine the feasibility and acceptability of the intervention. **RESULTS:** Twenty-one GP practices (response rate 32.3%) participated. Identifying patients with a PIM required considerable time and expertise. Practices screened all patients aged ≥ 70 years to identify those suitable to participate. A pharmacist reviewed their repeat medications, identifying patients with a PIM who were then invited to participate. Despite being offered a once off review of their current prescriptions with their GP, only 37.4% (196) agreed to participate. Preliminary qualitative findings indicate that intervention group GPs valued the review process as an opportunity to reflect on their prescribing practice. Some GPs highlighted that conducting routine structured reviews with older patients wouldn't be feasible due to the time, resources and funding available to them currently in primary care. Participating patients placed a high value on their medicines review. **CONCLUSIONS:** Preliminary findings illustrate that implementing a system of structured reivews for older patients with a PIM is challenging. However, participating GPs and older patients saw the value of conducting medicines reviews, but formal resourcing of such services would need to be considered.

PHP193

USE OF CLINICAL PRACTICE GUIDELINES BY PHYSICIANS IN JAPAN

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OBJECTIVES: The present study aimed to determine the proportion of physicians in Japan who use clinical practice guidelines, as well as factors influencing this choice. **METHODS:** We conducted an on-line cross-sectional survey throughout Japan on general internists, gastroenterologists, cardiologists, endocrinologists and general surgeons, including gastrointestinal or breast surgeons, who registered for marketing research. Questions addressed their usage of CPGs in practice, education, and research, as well as their attitudes toward CPGs. We then investigated associations between usage and characteristics of the respondents. **RESULTS:** We received responses from 1342 physicians, 1222 (91.1%) of whom were male (mean age (SD), 46.5 (9.6) years). The proportion of respondents who always or often use CPGs in several practice settings, such as when providing explanations to patients based on CPGs, ranged from 27.7% to 54.6%. Among them, 822 respondents (61.3%) applied 1 to 4 CPGs, and 381 (28.4%) applied 5 to 9. Usage differed according to age group, subspecialty, and workplace. After multivariate adjustment, the mean probability (95% confidence interval) of a high usage of CPGs when providing explanations to patients was 65% (60% - 71%) and 40% (30% - 50%) for those aged < 40 y and ≥ 60 y, respectively, 44% (38% - 50%) for general internists, 65% (59% - 71%) for surgeons, and 51% (46% - 57%) and 65% (58% - 72%) for those working in clinics and university hospitals, respectively. Attitudes towards the trustworthiness and convenience of CPGs were associated with usage, although this was unable to explain all differences in usage among subgroups. **CONCLUSIONS:** A substantial proportion of Japanese physicians use CPGs in clinical practice. Age, subspecialty, and workplace were independently associated with CPG usage. This should be considered during the process of CPG implementation.

PHP194

SYSTEMATIC REVIEW ON USE OF ECONOMIC EVIDENCE BY CLINICAL GUIDELINES

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OBJECTIVES: The recent reforms and policy changes have increased the cost pressures on all health care stakeholders, including clinical experts. In the past, clini-

cal guidelines were developed independent of cost or economic considerations. However, increasingly, more clinical guidelines are mentioning cost concerns and referring to economic data in new recommendations. The objective of this study was to analyze trends in the use of health economic information for developing clinical guidelines. **METHODS:** To understand trends in use of health economic information we conducted targeted search for clinical guidelines, expert recommendations, and consensus statements with specific mention of "cost" or "economic" or related terms. A systematic literature search was undertaken for the databases Pubmed, Google Scholar and Cochrane. The guidelines published between 2003-2012 were included. For guidelines which met the search criteria, data was collected for the name of the authors, indication, year of publication, country/region, and context of use of cost/economic evidence. **RESULTS:** Sixteen clinical guidelines published between 2003-2012 met the inclusion criteria for specific mention of cost/economic evidence. More than 50% of these guidelines were published between 2006-2012. For indication, 3 out of 16 guidelines were for diabetes, while the rest were for different indications. In these 16 guidelines "cost effectiveness" was mentioned 14 times, either referencing cost-effectiveness data or to mention the importance of such data for selecting treatment options. The guidelines commonly cite high cost of disease or high economic burden as one of the considerations for developing new recommendations (11 out of 16). Another term that was commonly used by these guidelines was "cost-benefit," which was mentioned 5 times in these guidelines. Notably, QALY was rarely mentioned (1 out of 16 times) in these guidelines. **CONCLUSIONS:** This analysis suggests that some clinical experts groups are increasingly showing willingness to use and incorporate health economic information for developing new recommendations.

PHP195

REASONS GIVEN BY THE EUROPEAN MEDICINES AGENCY FOR REVISING DISEASE-SPECIFIC SCIENTIFIC GUIDELINES

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OBJECTIVES: To review all the reasons provided by the European Medicines Agency (EMA) to substantiate the need for revisions to or updates of disease-specific scientific guidelines developed by the Committee for Medicinal Products for Human Use (CHMP). **METHODS:** All the scientific guidelines issued by the CHMP were reviewed on the EMA's website. The guidelines not focusing on disease-specific issues were not selected, i.e., guidelines listed in the following sections: Clinical Pharmacology and pharmacokinetics, General, Herbal Medicinal products, Information on medicinal products, and Radiopharmaceutical and diagnostic agents. **RESULTS:** A total of 182 disease-specific scientific guidelines were reviewed. The review identified 21 concept papers developed with the intent of revision (11.5% of specific guidelines). The analysis of the concept papers revealed that four main reasons were claimed: 1) Clarifications needed for pediatric development [10 concept papers: acute heart failure, asthma, Crohn's disease, hepatitis C, hypertension, glucocorticoid-induced osteoporosis, irritable bowel syndrome (IBS), multiple sclerosis, pain, and ulcerative colitis); 2) Evolution in the field and treatments (n=9); 3) Clarifications on endpoints identification and measurement (n=7); and 4) Safety aspects (n=6). For instance, in asthma, one of the critical aspects to be discussed regarding endpoints was "*the need to reinforce the use of clinical measurements (symptoms) and patient-reported outcome measures to complement lung-function parameters*." In IBS, regulators asked that "An evaluation whether more clear recommendations as regards the use of certain scales or newly developed PROs can be made is also desirable." **CONCLUSIONS:** The main reason for the EMA to revise disease-specific guidelines is the need for providing guidance in pediatric issues. This is in line with the introduction of Pediatric Investigation Plans (PIPs) by the European Commission in January 2007 to help ensure that medicines for children are included in the mainstream drug development process in Europe.

HEALTH CARE USE & POLICY STUDIES – Quality of Care

PHP197

REDUCTION IN FIXATION TIME AND RELATED SURGICAL STRESS WITH THE USE OF ETHICON SECURESTRAP™ OPEN ABSORBABLE STRAP FIXATION DEVICE IN THE DEPLOYMENT OF INTRA-PERITONEAL ONLAY MESH (IPOM) FOR OPEN VENTRAL HERNIA REPAIR

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OBJECTIVES: This study compared fixation time using ETHICON SECURESTRAP™ Open device to suture fixation of IPOM mesh in ventral/ incisional hernia repair. It also assesses surgeon-reported levels of task load experienced during the two fixation approaches. **METHODS:** Nine surgeons inserted skirted mesh using IPOM technique on created incisional defects in live swine models. Each surgeon performed two suture (using their standard technique) and two ETHICON SECURESTRAP™ Open fixation procedures. The duration of fixation procedure starting from mesh preparation through the last firing or suture knot was recorded. Surgical workload was measured using the validated Surgery Task Load Index (SURG-TLX) questionnaire. Time savings and task load reduction were determined by the lower limit of the two-sided 95% confidence interval for the difference between suture fixation and ETHICON SECURESTRAP™ Open groups. **RESULTS:** A total of 38 IPOM fixation procedures were performed with equal numbers using suture and ETHICON SECURESTRAP™ Open. 89% reduction in mean fixation time was observed from suture to mechanical fixation with ETHICON SECURESTRAP™ Open [mean reduction: 34.9 minutes (SD: 17.9 minutes); p<0.0001]. Similarly, 55% reduction in perceived overall workload was observed with SECURESTRAP™ Open compared to suture fixation [mean reduction: 22.17 (SD: 15.12); p=0.0003]. ETHICON SECURESTRAP™ Open demonstrated significantly lower ratings in five of the six elements of surgical task load, namely – Mental Demand, Physical Demand, Situational Stress, Task Complexity, and Temporal Demand [p<0.05 for all] compared to suture fixation. **CONCLUSIONS:** Time for fixation and related surgical task load can be significantly reduced by using the ETHICON SECURESTRAP™ Open fixation device compared with suture fixation of IPOM mesh. This shows promise of reducing open IPOM procedure time which may realize related patient benefits of reduced anesthesia time, infection risks, costs etc. Also, reduction in surgical stress could potentially offer improvement in surgical performance – benefiting the surgeon, the patient and the health care system.

HEALTH CARE USE & POLICY STUDIES – Regulation of Health Care Sector

PHP198

COST SAVINGS IN THE HUNGARIAN CARE MANAGING PROGRAMME

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OBJECTIVES: A pilot care managing programme was introduced in Hungary in 1999. The conceptual foundations of the Hungarian implementation of managed care is closer to what was called the GP fundholding in the UK than HMOs in the USA. The purpose of the study is to analyse the cost savings realized within the Hungarian care managing programme. **METHODS:** The data derive from the financial database of the Hungarian National Health Insurance Fund Administration (NHIFA) covering the period 1999-2007. We identified the annual cost savings realized by the Care Managing Organizations. The Hungarian CMOs was financed through a risk adjusted capitation fee and the health services covered by CMOs were defined in legal regulations. Cost saving was defined as the difference between the annual revenues (capitation fee) and expenditures (real utilization) of care managing organizations. **RESULTS:** During the study period the total number of persons covered by the care managing programme increased from 1.5 % of the Hungarian population to its peak of 19.4 % in 2005. The cost saving of the care managing programme was 63138000 Hungarian Forint (HUF) or 249756 Euro (EUR) in 1999; 457662600 HUF (1759945 EUR) in 2000, 1109442300 HUF (4322246 EUR) in 2001; 2710926900 HUF (11157503 EUR) in 2002; 1452041100 HUF (5727683 EUR) in 2003, 3799000306 HUF (15094804 EUR) in 2004; 3709400000 HUF (14954510 EUR) in 2005; 4964600000 HUF (18786048 EUR) in 2006 and 3669000000 HUF (14599437 EUR) in 2007. These amounts resulted in the following annual savings rate: 1999: 3.6%; 2000: 10.4%; 2001: 6.5%; 2002: 8.7%; 2003: 3.4%; 2004: 4.0%; 2005: 2.1%; 2006: 2.9% and 2007: 2.9%. **CONCLUSIONS:** With the development of the Hungarian care managing system, the average number of enrolees increased. Cost savings of Care Managing Organizations varied between 2.1-4.0 % during the mature period of this programme.

PHP199

SYSTEMATIC REVIEW ON THE IMPACTS OF STRICT PHARMACEUTICAL PRICE CONTROLS

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OBJECTIVES: To systematically review and synthesize published evidence on the impact of pharmaceutical price controls, such as price cuts, price caps, price freezes or international price referencing. **METHODS:** A literature search was conducted in Medline, Scopus, Econlit, Web of Science and ABI/INFORM to identify relevant studies published in English to March 2013. **RESULTS:** Forty-seven out of 3787 initial studies were included. Price caps and price reductions were most commonly studied in the literature, followed by reference pricing and price freezes. The evidence indicates that price controls reduce company profits and have a detrimental effect on pharmaceutical research and development, pipeline productivity and investment. They may also inhibit, reduce or delay new product launches, increase parallel exports and diminish availability of generics due to disincentives and, hence, may reduce product availability, increase withdrawals and shortages. In terms of public expenditure about half of the studies indicate realized savings, but the other half indicate no effect or even increases in expenditure. In terms of effects on patients, studies indicate in the short term welfare gains due to lower cost and better access, but also losses due to drug shortages and availability issues. Long-term effects appear to be welfare losses due to reductions of discoveries, resulting from the disinvestment associated with the lower revenues. **CONCLUSIONS:** Effects of price controls are ambiguous in the case of pharmaceuticals. Price controls reduce drug acquisition cost and increase access in the short run. On the other hand, they may decrease patient welfare and access as they can cause product shortages, withdrawals and launch delays. Moreover, they may reduce the likelihood for new product discoveries. Contrary to common beliefs, price controls not always reduce expenditure. Thus careful consideration is needed in designing drug price policies. Value based pricing approaches may be more effective alternatives compared to price cutting.

PHP200

GUIDANCE FOR PARTNERSHIP WORKING BETWEEN CATSALUT AND THE PHARMACEUTICAL INDUSTRY

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OBJECTIVES: Relationships between National/Regional Health care Systems (NHS) and pharmaceutical companies can and should be based on a cooperative venture, built on the expertise of each side, that best meets clearly defined public needs through the appropiate allocation of resources, risks and rewards, while preserving transparency and its independence. However, joint working can be difficult to initiate due to the number of parties involved and the lack of clear shared objectives. Guidelines can be very useful to support the NHS/Pharmaceutical Partner's commitment. To our knowledge, there are no such published guidelines in Spain. This first guidance in Spain was designed with the main aim of identifying and simplifying the initiation, the start-up phase and the remainder of joint working projects between the Catalan Heath System (CatSalut) and pharmaceutical companies. **METHODS:** A flowchart was designed to describe the standard steps and timelines suggested to start, implement, monitor and evaluate a Joint Working pro-

ject, applicable to both single and multi-company projects. Any obligatory internal processes should be completed in tandem. **RESULTS:** Health outcomes studies, pharmacoeconomic evaluations, and risk sharing agreements for the access of new pharmaceuticals were identified as projects of high priority to implement in the following years. **CONCLUSIONS:** The steps outlined in this guidance, although not compulsory, will provide useful practical tips for how to go about setting up a Joint Working project in Catalonia (Spain), and to assist through the remainder of it. This guide is not a substitute for suitable regulatory or legal advice.

PHP201

MAPPING AND ANALYSING PHARMACEUTICAL POLICY SETTINGS WORLDWIDE

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OBJECTIVES: In the context of increasing demand and expenditure for health services it is important to elaborate policies which maximise efficiency. Pharmaceuticals account for about a fifth of total health care expenditure and are often target of health care efficiency policies. The aim of this study is to classify and grade pharmaceutical supply and demand control policies across the globe and cluster systems by regulatory rigidity. **METHODS:** Pharmaceutical policies and market data across 65 countries were researched in the literature with emphasis on pricing, reimbursement, dispensing, expenditure and demand control domains. Policies were classified by domains and graded through a multi-country expert survey for the degree of regulation. Cluster analysis helped to group countries by policy types. **RESULTS:** Pricing policies for on-patent products (with increasing degree of regulation) include: free pricing, direct negotiations, value-based-pricing, cost-plus-pricing, conditional-pricing, reference-pricing, state dictates and tenders. Cost control policies include: discounts, rebates, risk-sharing agreements, price-volume agreements, profit controls, pay-backs, claw-backs, margin cuts, price cuts, freezes, and tenders. Reimbursement policies include: variants of ATC5-based internal referencing, variants of statutory copayments, and variants of ATC4-based internal referencing. Dispensing policies were: no restrictions, indicative substitution, mandated or compulsory substitution. Demand controls include: educational campaigns, prescription aids, indicative prescription guidelines, indicative INN prescription, prescription monitoring, quotas, targets, predefined budgets, compulsory INN prescription, mandatory electronic prescription, compulsory prescription guidelines, prior/posterior approvals, sanctions and incentives for target/guidelines adherence. Cluster analysis identified a set of countries using an intermediate regulation policy approach and another with a more rigid approach. These did not differ significantly (p: 0.20) concerning pharmaceutical expenditure as % of GDP. **CONCLUSIONS:** A variety of policies were used in recent years for controlling pharmaceutical expenditures. Countries fall into two subsets based on the intensity of the regulation. More regulated systems do not appear to be associated with lower pharmaceutical expenditure.

PHP202

THE COST-EFFECTIVENESS OF PERIODIC SAFETY UPDATE REPORTS (PSURS) FOR BIOLOGICALS IN EUROPE

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OBJECTIVES: The safety profile of new drugs is usually not fully established upon market entry, giving cause for Europe's comprehensive pharmacovigilance system. A key regulatory vehicle to communicate the outcomes of pharmacovigilance activities is the Periodic Safety Update Report (PSUR), which summarizes a product's worldwide safety data and facilitates periodic assessment of its benefit-risk profile. We assessed the cost-effectiveness of all PSURs submitted in Europe during 1995-2009 for biologicals, using a societal perspective. **METHODS:** We evaluated two regulatory scenarios: Full Regulation (pharmacovigilance including PSURs) and Limited Regulation (pharmacovigilance without PSURs). We assessed the source of regulatory action for all urgent safety issues that were identified for biologicals during 1995-2009. In two out of 24 urgent safety issues (systemic spread of botulinum toxin and edema after use of dibotermin-alfa), PSURs were the regulatory instrument that identified the safety issue and we assumed these issues would have been discovered five years later under limited regulation. Estimates from the literature and Markov-chain life tables were used to calculate costs and effects of PSURs for biologicals. **RESULTS:** The incremental cost-effectiveness ratio (ICER) of Full Regulation versus Limited Regulation was €342,110 per quality-adjusted life year gained. Extensive sensitivity analyses indicated a low probability of the Full Regulation scenario being cost-effective. Only two parameters resulted in a more favorable ICER: a 100% risk reduction after identification of the urgent safety issues (base-case assumption was 25%) and a high risk (1 in 1,000 patients) of severe systemic spread after therapeutic use of botulinum toxin (base-case assumption 1 in 10,000 patients). **CONCLUSIONS:** Regulatory cost-effectiveness analysis is a feasible instrument for assessing the (added) value of parts of the drug regulatory framework. In light of high costs of regulatory compliance, cost-effectiveness should be a consideration in deciding whether or not safety-related regulatory actions are required.

PHP203

UTILIZATION OF THE HUNGARIAN PUBLICLY FINANCED HEALTH CARE SYSTEM BY THIRD (NON EU) COUNTRY CITIZENS

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OBJECTIVES: The number of citizens from third countries (outside of European Union or stateless) permanently living in Hungary is 205 000, and annually ca. 23000 people get permit to settle. Current study aims at exploring what group of foreigners, when and for what type of service use publicly financed health care. **METHODS:** Data was retrieved from National Health Insurance Fund Administration of Hungary (*NHIFA*) and Central Statistical Office. Current study's base was processing the last five years' statistical data (2007-2012), concerning health care of third country citizens permanently living in Hungary. We analyzed the volume, place and medical specialty of these services. **RESULTS:** In the last 5 years third country citizens required inpatient care 9414 times (61% in Budapest), emergency care 11776 times (63% in Budapest), out-patient care 72306 times (57% in Budapest). Patient accessed health care providers due to medical problems in the following medical fields: obstetrics (19%), surgery (18%), laboratory (18%), pediatrics (7%), and ophthalmology (6%). Most of the patients are from Ukraine (42 %), China (22 %), Vietnam (11 %), ex-Yugoslavia (6 %) and Russia (6 %). Analysis by nationalities shows that Chinese population requires health care relatively few times (for instance, 2011: 5%, in 2012: 6%) and even these are almost exclusively done in Budapest. In contrast USA citizens see doctors relatively often (2011: 8%, 2012: 8%), mainly in relation to diagnostics and curative surgery. From the neighboring non-EU states (23095 people, 31%) Ukrainian and (5709 people, 7%) ex-Yugoslavian citizens needed health care in the investigated period. Despite previous expectations, need for health care is not the characteristics of border regions but the capital city. **CONCLUSIONS:** Utilization of the Hungarian publicly financed health care system is significant by third country citizens. When planning health care capacity, this crucial fact must be taken into consideration.

PHP204

PHARMACEUTICAL REGULATION IN EUROPE AND ITS IMPACT ON CORPORATE R&D

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OBJECTIVES: Many European countries regulate drug prices in order to cope with rising health expenditures. On the other hand, price regulation distorts incentives to invest in pharmaceutical R&D. This study aims at empirically assessing the impact of price regulation on pharmaceutical R&D expenditures. **METHODS:** We analyze a sample of 20 leading pharmaceutical companies between 2000 and 2008. The share of sales in Europe serves as a proxy for the degree of price regulation. We control for other determinants of R&D such as cash flow, company size, leverage ratio, growth rate, and Tobin's q. **RESULTS:** Our results suggest a nonlinear relationship between European sales ratio and R&D intensity. Beyond a threshold of 33% of sales generated in Europe, a higher presence in Europe is associated with lower R&D investments. **CONCLUSIONS:** Price regulation has a negative impact on pharmaceutical R&D investments. Policy makers must take long term effects of regulation into account.

PHP205

ELICITING THE RELATIVE IMPORTANCE OF KEY ELEMENTS FOR BENEFIT-RISK ASSESSMENT: A COMPARISON AMONG GENERAL POPULATION, HEALTH AUTHORITY AND MEDICAL DOCTORS

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OBJECTIVES: This research was designed to find out the key attribute for benefit-risk assessment using swing weight method in general population, health authority and hospital doctors. **METHODS:** We selected six important elements for each benefit and risk assessment based on previous study. The elements of benefit assessment consisted of disease severity, size of population affected by disease, clinical guidelines recommendation, comparative interventions limitation, improvement of efficacy/effectiveness, improvement of quality of life. The attributes of risk assessment contained overall incidence of adverse events, overall incidence of serious adverse events, discontinuation rate due to adverse events, drug or food interactions, drugs of potential misuse, risk management. 583 subjects constituted 3 groups (general population, health authority and hospital doctors) were selected across the country by quota sampling method and performed survey to evaluate preference of each elements with the swing methods repeatedly. The trained interviewers assisted participant successfully completed survey. **RESULTS:** Improvement of efficacy/effectiveness and overall incidence of serious adverse events were revealed as the most important attributes than others for benefit- risk assessment in all three groups. Health authority group outweighed the improvement of efficacy/effectiveness [Mean (±SD): 0.208(±0.04)] and overall incidence of serious adverse events [Mean (±SD): 0.220(±0.05)], while 0.204(±0.03), 0.216(±0.04) in doctor group and 0.197(±0.04), 0.185(±0.04) in general population respectively. In six benefit attributes, the lowest preference score was clinical guidelines recommendation [0.114(±0.04)] in health authority group and [0.144(±0.04)] in general population while size of population affected by disease [0.126(±0.04)] in hospital doctor group. Among six risk elements, the lowest preference was drugs of potential misuse showed in health authority [0.117(±0.04)] and in hospital doctors [0.121(±0.04)] while risk management [0.121(±0.04)] in general population. **CONCLUSIONS:** This shows that improvement of efficacy/effectiveness among benefit attributes and overall incidence of serious adverse events among risk attributes are key elements for benefit-risk assessment.

HEALTH CARE USE & POLICY STUDIES – Risk Sharing/Performance-Based Agreements

PHP206

COVERAGE WITH EVIDENCE DEVELOPMENT IN SWEDEN – FORMALITY OR EFFECTIVE WAY TO REDUCE UNCERTAINTY?

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OBJECTIVES: TLV (formerly LFN) is responsible for reimbursement decisions in Sweden. They regularly give temporary reimbursement with request for additional

data: Coverage with Evidence Development (CED). The objective of this study was to review the outcomes of the CEDs granted by TLV during the years 2005 to 2012, and to appreciate if it is an effective way to manage uncertainty. **METHODS:** All decisions published from January 2005 to December 2012 on the TLV website were screened. All decisions that included a CED were reviewed and the information on the initial decision for a CED and the final decision based on the evidence developed were extracted in a standardized way. The information was then analyzed. **RESULTS:** During the period TLV issued 38 decisions with a CED, 4 in 2012, 5 in 2011, 11 in 2010, 3 in 2009, 2in 2008, 8 in 2007, 5 in 2006 and none in 2005. For 10 CEDs issued 2010 to 2012 the time for evaluation had to yet been reached. For 12 CED decision taken from 2006 to 2010 the time for evaluation was reached but no decision had been taken and the products continue to be reimbursed according to the conditions in the temporary reimbursement decision. 7 products were granted general reimbursement and 9 limited reimbursement based on the evaluation of the evidence. No product was rejected reimbursement. **CONCLUSIONS:** Although it is early to draw any final conclusions, a significant number of CED decisions were not followed up with a final decision, which leads to continued reimbursement. The risk of de-reimbursement based on a CED seems minimal in Sweden. Therefore it is unclear if CED will actually contribute to manage uncertainty in Sweden.

PHP207

VARIANCES IN INDIVIDUALS' PRESCRIPTION DRUG COSTS IN IRELAND

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OBJECTIVES: To assess the average individual's drug costs prescribed under the main community drug scheme in Ireland over time, by age cohort and by geographical region. It also examined regional costs having standardized for age and sex. **METHODS:** The 2002 to 2012 average pharmacy payment per eligible person, number of items prescribed per person and the average cost per item prescribed were calculated. The most recent average individual cost of medicines was examined for each of the 4 health regions and 32 sub-regions by 22 age and sex cohorts. Regional age and sex adjustments were made by applying the scheme's national age and sex weights to each region's costs. This produced regional cost estimates independent of age and sex variations. **RESULTS:** Community drug expenditure has undergone substantial growth in the past 10 years with costs more than doubling and the number of persons covered by the main scheme increasing by nearly 60%. Nationally an individual's average cost of medicines was €713 in 2011, varying from €670 (-6%) in HSE-West to €762 (+7%) in HSE-South. Sub-regional LHO (local health office) cost variances were significantly greater ranging from €200 to €1,200. Average cost increases with age and for persons over 75 was nearly 4 times those aged 35 to 44 (€1,689 versus €446). Removing the impact of age and sex increases cost variances marginally overall, restraining some regions costs and promoting others. **CONCLUSIONS:** Individuals' prescription drug costs vary significantly by age and sex however regional cost differences are not explained by variances in age and sex and may be a result of other factors such as prevalence of chronic health conditions and GP prescribing patterns.

PHP208

ANALYSIS AND CLASSIFICATION OF RISK-SHARING SCHEMES PROPOSED IN REIMBURSEMENT APPLICATION RECEIVED BY AHTAPOL IN 2012

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OBJECTIVES: To analyze and classify the Risk-Sharing Schemes (RSSs) proposed in reimbursement applications received by Agency for Health Technology Assessment in Poland (AHTAPol) in 2012. **METHODS:** Risk-Sharing Schemes proposed in reimbursement applications received by AHTAPol in 2012 were quantitatively and qualitatively analyzed. The classification of the RSSs was also conducted based on both Carlson's approach and the Polish Act on Reimbursement of medicinal products. **RESULTS:** In the studied period, 52 reimbursement applications with 26 proposed RSSs were received by AHTAPol. They were classified into 5 categories according to the Act on Reimbursement. The most common category was making the official sales price dependent on the applicant providing supplies at a reduced price, as specified in the negotiations on the price of the medicine (34.61%). Further categories were: making the official sales price dependent ona pay-back of a part of the reimbursement obtained to the entity which is obliged to finance benefits with public funds (23.08%), making the official sales price dependent on the level of turnover of the medicine (11.54%) and making the level of the applicant's revenues dependent on the health effects achieved (3.85%). RSSs classified as others constituted 26.92% of all. Among 26 proposed RSSs only 8 of them could be classified according to the Carlson's approach (1 proposition included more than one category). As a results, 4 Price Volume Agreements, 4 Manufacturer Funded Treatment Initiation and 1 Conditional Treatment Continuationwere identified. **CONCLUSIONS:** Most of the propositions should not be considered as RSS according to the Carlson's approach. The most common propositions were related to medicinal product's price reduction and did not include any risk sharing. There is a strong need for further research.

PHP209

RISK SHARING FOR INNOVATIVE PHARMACEUTICALS WITHIN SOCIAL HEALTH INSURANCE: EXPERIENCES FROM CHINA

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OBJECTIVES: To understand current risk sharing scheme landscape for innovative pharmaceuticals in some typical provinces and cities of China. **METHODS:** Risk sharing schemes for pharmaceuticals in four provinces (Guangdong, Zhejiang, Jiangsu and Sichuan) and three cities (Guangzhou, Hangzhou and Chengdu) were systematically collected through visiting social health insurance bureau websites, literature review and key informant interview. Case study and comparison analysis were conducted among these schemes. **RESULTS:** Two kinds of risk sharing schemes, performance based scheme and financial based scheme, were employed in sampling provinces and cities, with the latter model more often implemented. Performance based scheme has only been developed in one city (Guangzhou) for a non-small-cell lung cancer drug. Patients eligible for inclusion criteria and treated in one of three designated hospitals could be qualified to reimburse for more than one year treatment if they were responsive to the drug. Other provinces and cities has adopted the financial based scheme, mainly focusing on increasing patients access to expensive drugs, usually for breast cancer, leukemia and non-small-cell lung cancer and not covered by health insurance schemes. For instance, local health insurance fund of Zhejiang and Jiangsu province would only reimburse patients' five to six months treatment and pharmaceutical company should sponsor patients' treatment for the next six months. Besides, cities like Qingdao and Chengdu implemented the price volume scheme for special drugs and medical materials in order to control fund expenditure. **CONCLUSIONS:** By risk sharing scheme, some innovative drugs, previously not covered by social health insurance, can be reimbursed, which will increase patients' access, reduce patients economic burden, and help expending pharmaceutical companies' market share. However, as risk sharing scheme in China has only been adopted for only one or two years, long-term impact still needs to be observed and evaluated.

PHP210

SQUARING THE CIRCLE: INNOVATIVE CONTRACTING TO ACHIEVE MARKET ACCESS FOR INNOVATIVE PRODUCTS

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In an increasingly resource-constrained environment, a variety of innovative contracting arrangements exist, representing an alternative to conventional pricing and reimbursement agreements between payer and manufacturer. There are various tools and resources that may influence funding with which payers and prescribers would welcome support from manufacturers. **OBJECTIVES:** To gain an overview of contractual agreements currently used within the pharmaceutical sector and to uncover how innovative contracting has, and continues to, evolve. **METHODS:** Secondary research was conducted to identify examples of innovative contracting, highlighting elements that work and associated hurdles, in order to understand issues relating to transparency and implementation. **RESULTS:** Sixteen markets worldwide embrace innovative schemes with a further 5 markets beginning to show uptake. In the past, agreements were predominantly performance-based. However, companies are increasingly moving towards financial schemes such as product bundling, confidential discounts and fixed price treatments. The most common elements of risk-sharing agreements are price volume agreements (39%), requirement for data collection (29.5%), and access limited only to eligible patients (13.1%). Innovative contracts are predominantly used for drugs that relate to high cost or high performance with oncology being the therapeutic area that dominates these agreements. **CONCLUSIONS:** Innovative contracting schemes can aid manufacturers with market access, help to maintain price and increase usage. However, the current design of many agreements is suboptimal, and there are hurdles which need to be overcome. It is important that there is a balance between risk and incentive for all stakeholders, and this balance between the benefits and cost implications must be carefully considered.

HEALTH CARE USE & POLICY STUDIES – Conceptual Papers

PHP211

THE HEALTH OF HEALTH TECHNOLOGY ASSESSMENT IN IRELAND: FIVE POINTS FOR IMPROVEMENT

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This study critically appraises the contribution of cost-effectiveness analysis (CEA) in improving the rational allocation of health care resources in Ireland. While Ireland has successfully established some of the institutional infrastructure for CEA, there remain key areas for improvement: 1) Ireland has an explicit cost-effectiveness threshold of €45,000/QALY. It resulted from negotiations between the pharmaceutical industry and the public health service and only applies to pharmaceutical interventions. If Ireland is to use a threshold, it would be better served by an empirically determined threshold that applies to all interventions. 2) The threshold has recently been exceeded by a number of expensive drugs, in some cases by a very large margin. Conversely, despite being highly cost-effective, colorectal screening remains unimplemented due to a failure to allocate resources. In the absence of clarity around these decisions, the allocations appear to indicate that considerations of budget impact are dominating rather than complementing those of cost-effectiveness. 3) Recent CEAs by Ireland's statutory health technology assessment authority, the Health Information and Quality Authority (HIQA), appear to confuse average cost-effectiveness ratios with incremental cost-effectiveness ratios (ICERs). Clarity around the interpretation of cost-effectiveness evidence is required to instil confidence in the process. 4) Ireland has an established CEA process to appraise new drugs. However, this process has been bypassed in recent cases, as some costly cancer drugs have been approved before being subject to CEA, despite recommendations that these drugs be assessed. Consistency in approach is required to instil confidence in the process. (5) Greater transparency around reimbursement decisions would be desirable, whereby the relevant bodies issue documentation explaining their decisions and deliberations. In conclusion, CEA could make a greater contribution to rational resource allocation in Ireland if more rigorous and consistent decision rules were applied. Greater accountability of the decision making process should further that goal.

PHP212

OBTAINING OPTIMAL PERSONALIZED SURVEILLANCE STRATEGIES FOR PATIENTS WITH SCREEN-DETECTED COLORECTAL ADENOMAS USING DISCRETE EVENT SIMULATION

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BACKGROUND: Colorectal cancer (CRC) screening in Spain uses a fecal-occult blood test (FOBT) for screening and colonoscopy as diagnostic tool. Adenomas constitute the most frequent findings of this colonoscopy, and the removal of these premalignant lesions is considered the main contributor to the reduction of mortality and incidence of CRC. There is no clear agreement regarding the risk classification of adenomas as well as the optimal surveillance strategy for each degree of risk. Genomics may contribute to further delineate individual risk, and its characterization is crucial for improving the effectiveness of surveillance strategies by targeting individuals who would benefit the most. **OBJECTIVE:** To optimize, within a CRC screening program, surveillance of premalignant lesions using individual risk-based strategies, based on genetic analysis, that take into account benefits, harms and costs. **METHODS:** A discrete-event simulation model that reproduces the process of screening and takes into account the costs at every stage, from invitation to screening to surveillance of findings will be upgraded. The natural history of the disease will be included, with special emphasis on the events after adenoma detection at screening colonoscopy. Based on the results of a study aimed at identifying common genetic variants associated with an increased susceptibility to develop colorectal adenomas, the risk of developing cancer or recurrent adenomas according to the clinical characteristics of the patients will be included in the model. The interval between surveillance colonoscopies will be optimized with the objective of minimizing the number of colonoscopies while keeping the same level of effectiveness, defined as the impact on incidence of advanced adenomas and cancer over time. IMPLICATIONS: Simulation models can help in the design of personalized screening strategies. Personalizing CRC screening through surveillance strategies may improve allocation of resources under cost constraints, minimize harms and maximize benefits of population-based programs, affecting millions of people.

PHP213

FIXED REFERENCE PRICING OR BENEFIT ASSESSMENT OF ESTABLISHED PRODUCTS – FROM THE FRYING PAN INTO THE FIRE?

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For nearly 25 years, the most effective tool for containing public spending on pharmaceutical drugs in Germany is the formation of fixed reference price groups (FRPG) - the annual savings have continuously risen from 0.31 billion Euros in 1990 to 4.32 billion Euros in 2009. Hereunder, the so-called "jumbo groups" (patent-free and patented substances) that were introduced with the SHI Modernization Act of 2004 have been of high importance. With the recently published, first-time call for benefit assessments of substances in the established market (April 2013), the Federal Joint Committee (FJC) has yet launched another potent mean of reducing costs. Unlike the early benefit assessment of new active ingredients where several substances have undergone scrutiny since January 2011, it is unclear what the outlook is for the substances in the established market. Therefore, the objective of the presentation is to assess whether a FRPG or a benefit assessment is to be preferred by pharmaceutical companies for established substances. Fixed reference price scenarios are calculated for therapeutically comparable substance classes within the call for benefit assessment of substances in the established German drug market. For the established substances, a risk assessment and benchmark is performed based on the criteria in the code of procedure of the FJC and the assessment of new active ingredients, respectively. The results of the ongoing FRPG scenario evaluation will be displayed as bar charts by savings in €. The risk assessment is displayed in a tabular format. Apart from discussing the results of the FRPG calculations compared to the benefit assessment of established substances, the presentation discusses implications for international reference pricing, since the German market has been regarded as the last bastion of free pharmaceutical pricing for a long time.

PHP214

HTA NATIONAL PUBLIC POLICY AND THEIR SOCIO-ECONOMIC ENVIRONMENT: A EUROPEAN PERSPECTIVE

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OBJECTIVES: Socioeconomic factors are important components of Health Technology Assessment's (HTA) institutionalization. If most of the countries have established HTA agencies, they required scientific expertise to emerge and become institutionalized. In a previous scientometric work, we did an analysis of scientific conditions of HTA emergence in the scientific literature. Our observation allowed us to link HTA research capacity and HTA institutionalization in a given country. **METHODS:** In order to explore endogenous as well exogenous factors sustaining HTA expertise, we undertake a principal component analysis as multivariate analysis technique in order to establish which variable are more appropriate for the assessment of scientific expertise in the context of HTA public policy. **RESULTS:** HTA national public policy could be ranked according to their academic expertise. Country HTA publications productivity matched in comparison with health expenses & gross product in several countries. Nevertheless this ranking doesn't tell us why some country like UK perform well while others like France don't. **CONCLUSIONS:** Our results underline the country difference of arbitration between public policies such as public health, and industrial or innovation policy. Among tested variables, it appears that the regulation of drug pricing and market access, or the macroeconomic impact of pharmaceutical industry in a country contribute to determine the scope of HTA policies.

PHP215

CLINICAL, EPIDEMIOLOGICAL AND ECONOMIC METRICS DIFFERENCE BETWEEN HPV-RELATED AND TRADITIONAL HEAD AND NECK CANCERS

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Excessive smoking and alcohol consumption were the traditional causal factors in many head and neck cancers in the United States and Western Europe. However, the Human papilloma Virsus (HPV) is now responsible for up to 80% of cancers of the oropharynx. HPV-related oropharyngeal cancers are a distinct clinical, epidemiological and molecular entity. This poster will show that the metrics used to describe the burden of a cancer to policy makers are very nuanced. As the patients with HPV-associated oropharyngeal cancers are younger and healthier individuals, they have been shown to have a better prognosis than traditional head and neck cancers. The goal of treatment has shifted from mortality to morbidity in these cancers. Measures of morbidity (functional status) are now important considerations in treatment options. This poster will compare and contrast various epidemiological measures - Incidence /100,000, Prevalence, Years of Life Lost, Mortality to Incidence Ratio with respect to HPV-related and unrelated head and neck cancers. Finally, we will discuss the economic metrics (e.g. Disability adjusted life years, Years of working age lost) used to portray a cancer and make a link with research funding in various countries. The question posed is whether mortality or morbidity should predominate in resource/research allocation decisions?

PHP216

COMPARING THE VALUE OF DIFFERENT HTA DECISION MAKING PROCESS: EVALUATING THE EVALUATORS

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OBJECTIVES: How health care decision makers arrange their appraisal process of new health care technologies have direct impact on population health. However, no consensus exists on how the appraisal process should be designed to maximise population health or societal welfare. The purpose of this work is to develop a simple analytic framework that enables analysis of the different stakeholders' (decision makers and manufacturers) payoffs from alternative appraisal processes. **METHODS:** The analytic framework outlined in the paper is based on viewing the appraisal processes as a diagnostic test aimed at identifying cost-effective (true positives) and cost-ineffective (true negative) technologies. Based on this characterisation pay-off functions are formalised to analyse how design and operation of the appraisal process impacts population health and manufacturers' earnings. **RESULTS:** The framework identifies those factors that have the greatest influence on population health and manufactures payoffs and illustrates how this leads to conflicting interests towards how the appraisal process should be set up and operated. It is demonstrated that there is no uniquely optimal way to design and operate the appraisal of new health care technologies, since optimal design and operation depends on the price of technologies that undergo appraisal. The analysis also shows that operating a given reimbursement system implies a trade-off between incentivising cost-effective pricing (pricing below the threshold/willingness to pay) and rejecting more cost-effective technologies (increasing the proportion of false negatives). It is further demonstrated how the framework can be used to gain insight into current policy questions including who should bear the burden of proof and how rigorous the process should be. **CONCLUSIONS:** There is no unique way to design and operate the appraisal of health care technologies in order to maximise population health or societal welfare. Improving health or societal welfare through the appraisal process requires careful consideration of payoffs and incentives of all stakeholders.

PHP217

THE FRAMEWORK FOR HEALTH ECONOMIC MODELING AND MULTI-CRITERIA DECISION ANALYSIS (MCDA) ON THE EXAMPLE OF THE MOBILE STROKE UNIT (MSU)

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OBJECTIVES: The generation of evidence in the early development of a technology is a bottle neck for uncertainty in decision making. Health economic modeling can support the assessment of early innovation, but complex modeling approaches are criticized for being "black boxes" which in turn reduce their acceptance in health policy. **METHODS:** MCDA can address the gap about what matters to health care decision makers and data collection by explicitly structuring decision criteria. The combination of MCDA modeling and health economic modeling implies a potential for gaining efficiency. The simulation model of the intervention for stroke, the MSU, is analyzed regarding application of MCDA. **RESULTS:** Experts and stakeholders can support the: 1) Definition of model factors e.g. outcome parameter, which is generally accepted (Barthel-Index for Stroke outcome); 2) Evidence collection e.g. is the data valid? (outcome of thrombolysis); 3) Model structure e.g. interrelation between input parameters (stroke incidence, risk factors and population); 4) Validation of a model e.g. reassessment of step 1-3; and 5) Final analysis by using MCDA e.g. importance of economic vs. medical benefit. **CONCLUSIONS:** The methodological combination is advantageous because simulation modeling as well as MCDA have a similar sequence of events. The simulation output, which is commonly validated by technical and medical experts, can gain validity by the heterogeneous perspectives of participating stakeholders in the validation process. For example, this raises

questions about priority and importance of certain outcome parameters like the thrombolysis rates vs. the independence of patients after 3 months. Finally, the combination of MCDA and simulation modeling contributes to a transparent analytic process and results in a more complex understanding of the technology.

PHP218

MECHANISM OF COORDINATED ACCESS TO ORPHAN DRUGS

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Although the EU Council stated that *"All health systems in the EU aim to make provision, which is patient-centered and responsive to individual need"*, unacceptable differences in access to orphan medicinal products (OMP) in the Member States of the European Union are identified. In the context of the 2010 Belgian EU presidency initiative on 'Innovation and Solidarity' and within the framework of the process on corporate responsibility in the field of pharmaceuticals, EU Commissioner Tajani therefore launched the project Mechanism of Coordinated Access to OMP.**OBJECTIVES:** Designing a operational mechanism of coordinated access to OMP for patients, stakeholders and Member States to provide, irrespective of the local conditions, access for patients with unmet medical needs and for whom these solutions would otherwise be out of reach – in an affordable and sustainable way ("real life access"). **METHODS:** The project is managed by Belgium (NIHDI), supported by the European Commission and Eminet. Thirteen Member States participated, with the stakeholders (AIM, EPF, ESIP, Eurordis, CPME, EFPIA, EGA, EuropaBio, GIRP). Three Workpackages cover the different aspects of granting effective access to medicines: Identifying and assessing a relevant orphan drug (assessment/evaluation) - Selection of target population and mechanisms of funding (structural access) - Treatment (individual access). Feasibility at present and opportunities for near future development of desirable activities were studied, and no-go solutions were documented and rejected in order to develop implementable scenarios for pilot projects and policy recommendations. Discussion: Although coordinated access at an European level will be organized on a voluntary basis, some sort of commitment from the participating partners is required. Moreover, it is crucial that the subsidiarity principle is not jeopardized or compromised. Duplication of efforts will be avoided and previously made investments – in terms of financial and human resources, expertise and experience - (ex. by EUnet HTA, EMA COMP, EUCERD, CAVOD,…) will be valorized.

PHP219

THE FUNDING OF ORPHAN MEDICINES IN EUROPE: PAYERS ACHILLES' HEEL?

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OBJECTIVES: To look at the affordability of orphan medications across Europe and whether payer attitudes to high-price medications are changing in the face of rising health care expenditure and tighter budgets. **METHODS:** A detailed review of 7 EU markets (France, Germany, Italy, The Netherlands, Poland, Spain, UK) looking at payer attitudes and funding decisions for key orphan drugs and the political, economic and societal impact of these. A key focus of the research was insight into payer attitudes towards the evidence base for the purpose of pricing negotiations and how anecdotal evidence, such as Patient Reported Outcomes (PROs) and patient case studies, have an impact on decision-making. Detailed research was also undertaken to ascertain the pricing levels achieved for a number of orphan drugs across Europe looking at payer thresholds and the implications of these for the purpose of reimbursement. **RESULTS:** The research demonstrates that there is considerable variation in pricing levels across the European markets and difference in payer attitudes towards the way orphan drugs are funded. Overcoming evidence challenges in orphan diseases remains a headache for payers and scepticism remains around dosing, innovation and whether approaches such as "coverage with evidence development" are adequate and/or sustainable in the long-term following initial approval. **CONCLUSIONS:** The environment for orphan medicines in Europe is changing; and as the financial performance of European countries begins to diverge, so do attitudes towards the funding of orphan medicines. Orphan medicine prices are rarely justified on the basis of traditional cost-effectiveness thresholds and most markets still differentiate them from other pharmaceuticals. However, payers are afraid of uncertainty and, given the increasing number of orphan drugs and the often tentative evidence base at launch, may be forced by overwhelming financial necessity to make tougher decisions on funding.

PHP220

BUDGET IMPACT AND THRESHOLDS: HOW ARE REAL DECISIONS MADE? - EXPECTED UTILITY OR PROSPECT THEORY?

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Decision making rules in health technology assessments are often based on a fixed willingness to pay threshold for the incremental cost effectiveness. This may be thought of as consistent with expected utility – with utility here defined in terms of Incremental Net Benefit (INB) – a combination of QALY gain and the threshold value. Alternative methods such as multi criteria decision analysis allow incorporation of other dimensions into the decision space. These seek to explore whether utility may be driven by factors other than simple QALY gain. Prospect theory suggests that decision makers are concerned in practice with the 'size' of a given decision. Also, they handle investment and disinvestment differently. In the Irish State, every new drug is examined. In order to look at actual decisions, lifetime QALY gains were extracted from completed economic evaluations submitted to the Irish health care payer. Total spend on these was calculated using a combination of the payer reimbursement database and predicted budget impact. Real choices indicate that where the budget impact is relatively small the drug is more likely to be reimbursed even with a comparatively small QALY gain. Technologies in areas of cancer and orphan diseases often lie outside of the threshold where a technology would be accepted. Decision makers are faced with choices with varying degrees of risk. Choices associated with a low budget impact are deemed to be less risky. This is pragmatic; it reflects a preference on behalf of the decision maker. Reality does not always match the ideal of a fixed threshold.

PHP221

DOES HTA PROCESS HELP TO ACHIEVE THE HEALTH OBJECTIVES OF THE MILLENNIUM? A SOUTH AMERICAN ANALYSIS

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OBJECTIVES: South America (SA) is a continent with 400 million people and occupies 12% of the world's territory. It is composed by 12 countries and 6.75% of its population is below the poverty line, as defined by UN. The proper distribution of financial health resources, through an HTA process in public systems is potentially essential to improve the quality of health care expenditure. The objective of this study is to understand the incorporation process of new health technologies and compare the general health status in each country, regarding the Objectives of the Millennium (OM). **METHODS:** A public data collection was performed in official sources linked to UN, to governments of SA and the Unión de las Naciones Suramericana (UNASUR). **RESULTS:** The public health financing in SA countries was between 2.43% and 6.20% of the GDP. An HTA process in an institutionalized and specialized form is in place in only 3 countries (Argentina, Brazil and Peru). Bolivia, Chile, Colombia, Paraguay and Venezuela do not have a specialized HTA process and the other four countries have no HTA process at all. Regarding the OM the decrease in child mortality, increase in vaccination, increase in malaria and tuberculosis treatments are among the closest to be achieved in all countries. There is a linear positive correlation of OM with the Human Development Index and with the percentage of GDP invested in public health but not with having a HTA process in place. **CONCLUSION:** At this moment, there is no evidence that an HTA process in place helps SA countries to achieve the OM.

PHP222

THE NEW ITALIAN HEALTH CARE REFORM: INTRODUCING NEW MEASURES TO SPEED UP MARKET ACCESS

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OBJECTIVE: The Balduzzi law (189/2012) introduced several changes aimed at promoting the country's development through a higher level of health protection and at bridging the gap left by the rationing of health care resource from the Spending Review (135/2012). Reducing the time to drug market access is one of the main purposes. The aim of the research is a critical analysis of this law to understand its actual and future impact on the health care scenario. **METHODS:** An evaluation of the laws issued in the last three years that aimed at regulating the drug market was carried out. To build a future scenario analysis, we focused our attention on the Balduzzi law and two of its articles (11 and 12) and on the new drugs approved by AIFA and commercialized under the new regulation. **RESULTS:** The changes that will have a major impact on the drug market are: the allocation of the medicines approved under centralized procedure in the non-negotiated C Class within 60 days from the publication in the Official Gazzette of the European Union and the direct placement of generics and biosimilars in the reimbursement class of the originator without any price negotiation. As of now, a total number of 49 drugs have been included in the non-negotiated C Class, within this new group there are 15 first drug authorizations. **CONCLUSION:** The new reform can be potentially an interesting innovation to speed up market access, though the impact of including new drugs in the C class (at patient charge) before the price negotiation is still under debate. The increased competitiveness coming from having a faster introduction in the market of generics/biosimilars could lead to important savings for the National Healthcare System over the next years.

PHP223

INVESTING IN EUROPEAN HEALTH R&D – A PATHWAY TO SUSTAINED INNOVATION AND STRONGER ECONOMIES

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A large number of factors point to an unavoidable rise in health care expenditure to 13%-18% of Europe's GDP by 2030, even with policy interventions or budget caps that aim to counterbalance these pressures. This growth in health care costs need not be undesirable especially so when higher spending on health care leads to improved health care quality and life expectancy. Therefore, the challenge is not "how do we reverse the growth of health care costs?" but "how can we best deploy the increasing resources spent on health care to create optimal benefits for the European population?" Health R&D is the key to being able to respond to this dilemma. Increased investment in R&D leads to improved health outcomes, long term efficiency gains, better productivity and high economic yields. However, the outlook for Europe is not as positive as it could be. Recently, there has been a stagnation or even decline in European private and public investment in R&D, which is in sharp contrast with the much higher investments in the US. Private biopharmaceutical investments in health R&D, which are double the size of public health R&D, in 2011 actually decreased in absolute terms. Public R&D investments declined or stagnated in most European countries and will be further under pressure in the near future due to public budget deficits. Janssen commissioned the Deloitte European Center on Health Economics and Outcomes Research to set out the arguments in support of increased investment in health R&D in Europe. The paper demonstrates that, even in times of austerity, policymakers need to prioritise approaches that will enhance public R&D investments and adopt strategies that produce incentives for private enterprises so that the current decline in private sector investment is halted.

PHP224

HOW DO ONCOLOGY DRUG PRICES VARY ACROSS EU5, THE UNITED STATES, AND BRIC MARKETS?

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OBJECTIVE: Pharmaceutical pricing is characterized by a consistent variability across markets. Social and economic differences represent only the easiest-to-predict reason for such variability. Stricter regulatory hurdles, market landscape, challenging negotiation processes, varying business strategies, and sometimes unplanned outcomes of pharma launch decisions concur in the final price for a specific drug. A better understanding of price trends and out-patterns is a useful insight to help improving pricing strategies by targeting realistic pricing expectations, and studying competitors' pricing mistakes and successes. This paper shows the price variability of ten different pharmaceuticals in ten key markets (France, Germany, UK, Italy, Spain, US, Brazil, Russia, India, and China). Common trends, similarities and particularities are discussed. **METHODS:** Using PRICENTRIC™ data, we collected ex-factory prices for various oncology products, and we defined whether a country fell into a HTA system or free pricing group. We also compared the product prices to GDP per capita (International Monetary Fund 2012) to investigate trends between the two parameters. The analysis investigates two key areas: 1. Difference in price depends on social, economic considerations but also by the nature and complexity of market access process 2. The relationship between prices and GDP per capita across countries. **RESULTS:** The US and Germany have the highest prices of all studied countries. They are also the only two countries where prices are freely set by manufacturers. Prices are slightly higher in countries having a high GDP per capita. However, countries like France and UK having strong HTA authorities and pricing regulations do have a small correlation to this trend line. **CONCLUSION:** Our analysis shows that pricing and pharma strategies can be based on countries' economic situation. Nevertheless, formal established HTA bodies with clear pricing rules help controlling pricing.

PHP225

A SYSTEMS-THINKING APPROACH FOR THE HEALTH CARE INDUSTRY: STRATEGIES AND INSIGHTS FOR BIOPHARMA, PAYERS AND PROVIDERS

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Collaboration with health care stakeholders is a fundamental component of a systems-based health care economy, and it will become the dominate business model going forward. Yet most health care industry stakeholders are failing to accept this inevitable transition. While many acknowledge the need to move toward a more integrated "systems thinking" approach – one that maps influence patterns, amplifies interdependencies, and drives collective outcomes, they struggle with actual implementation. A viable and sustainable information network provides the structure, aligned incentives and competitive collaboration the bricks and mortar, and trust the cornerstone. Until they can build that and foster a culture of transparency, they won't achieve the cost and innovation benefits inherent in these cross-industry partnerships. Although health care stakeholders know they need to partner with others to be successful in this new systems-thinking economy, they need actionable strategies to demonstrate how the benefits of ongoing collaborations far outweigh the risks. This podium presentation will present original research aimed to qualify stakeholder perceptions on alignment and collaboration around the delivery of health care, in addition to critical hurdles they must overcome. A recent survey of close to 300 Biopharma executives, EU and US Payers, and US providers provides insight into their needs, their disparate perceptions, and their levels of confidence in the ability to shift to a systems-thinking collaborative culture. Approximately 25% of respondents stated they were not aligned with other stakeholders, though agree they need better alignment and foresee closer collaboration in the future. Over 70% of stakeholders believe data transparency and information-sharing is critically important to a successful and interoperable health care system, yet very few from each group were willing to demonstrate such transparency. Further detail will be given on insights and challenges gleaned from interviewing large and small stakeholders as well as practical strategies to guide the transformation to a systems-thinking industry.

PHP226

INTRODUCING THE ENCEPP WORKING GROUP (WG) ON HEALTH TECHNOLOGY ASSESSMENT (HTA): ENHANCING THE GENERATION OF ADDITIONAL EVIDENCE FOR HTA PROCESSES

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The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) is a project led by the European Medicines Agency aimed at further strengthening the post-authorisation monitoring of medicinal products in Europe by facilitating the conduct of multi-centre, independent post-authorisation studies focusing on safety and benefit/risk assessment. ENCePP has recently established a WG on HTA to develop methodological guidance to supplement the efficacy and safety aspects of medicines known at the time of marketing authorisation (MA) and to bridge the needs of HTA and post-marketing benefit-risk assessments. Decision makers are often faced with the challenge that long-term, real-world data on safety and effectiveness is lacking at the time of MA. This creates uncertainty around the medicines' risk-benefit profile while manufacturers, health care providers, and patient groups exert pressure by demanding early decisions and rapid access. Decision makers may unduly delay potential benefits to patients by waiting for stronger evidence, or may endorse medicines that later turn out to have a less robust benefit-risk ratio, to be ineffective, cost-ineffective, or even harmful. Hence, many countries have developed mechanisms that allow temporary access to promising medicines while concurrently requesting the generation of additional evidence to reduce uncertainty. Their objective is an optimal trade-off between different stakeholder needs, flexibility, responsiveness, and rigor as well as the flexibility to revise decisions on access when new evidence becomes available. The ENCePP WG on HTA has the potential to become a capacity building tool for regulatory and HTA agencies to develop research structures aimed at complementing the evidence generation for MA and market access. Post-authorisation studies developed under the auspices of ENCePP could provide new safety and clinical effectiveness information of marketed medicines. ENCePP expertise, research experience and health care databases may also contribute to the coordination, methodological guidance and data sourcing for the enhancement of HTA processes.

PHP227

HEALTH TECHNOLOGY ASSESSMENT OF HIGH-VALUE THERAPIES

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OBJECTIVES: Main function of a health system is to prevent diseases, restore health status and reduce health impairment. Health systems are mainly organized on efficacy based decisions, but sometimes their social functions modulate this principle. In case of small patient groups, end-stage status and unmet health needs, usually decision are made on the basis of equity, instead of efficacy. These demands create special development conditions; eventuate in high prices on the supply side, therefore cost-effectiveness cannot be guaranteed, not even with substantial health benefits. Numerous expensive drug therapies are available in Hungary with reimbursement, but due to fiscal restrictions, new therapies are not able to access reimbursement. These tendencies create a paradox situation, since equity is implemented occasionally in absence of objective criteria. Due to the huge differences among these therapies, a standardized decision-making principle does not exist, but a general framework can be developed. In our study, methods and techniques are introduced, which can help to assess these therapies and organize a transparent system. **METHODS:** For the general assessment of therapies, many methods are available. In our research, we reviewed these tools and investigated their combinability in the special situation of "high-value" therapies. **RESULTS:** A wide range of evidences (clinical trials, meta-analysis, health-economy analysis, HTAs) provide a robust background to compare high-value therapies between different therapeutic areas. Outputs (LYG, OS, QALY, costs etc.) show a significant variation following different clarification process. A standardized process needed to earn comparable outputs from evidences. **CONCLUSIONS:** As we found, these tools could help decision making on prioritizing therapies, allocate resources with a higher control and reduce the risk of reimbursement.

PHP228

ORPHAN DRUG LEGISLATIONS: HEYDAY OR HAD THEIR DAY?

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Orphan Drug Legislation incentivises the development of treatments for rare diseases that would otherwise not be profitable investment opportunities. However, with budgets squeezed and diseases increasingly stratified, we question whether this legislation is fit for purpose. Segmenting diseases into genetically-defined subgroups, most notably among some cancers, has enabled increased pharmacological targeting. Common diseases are thus being reconsidered as multiple rare conditions, each eligible for orphan designation, entitling the treatments to the economic benefits afforded by legislation. Stratification also occurs in diseases which are already rare (e.g. cystic fibrosis), and new treatments, such as ivacaftor, are being developed to target specific mutations. Orphan status for a drug is maintained regardless of whether the overall population size, for which the drug is licensed, exceeds prevalence thresholds enabling companies to take a strategic approach to development. The high prices of orphan drugs impact on access. However, typical cost-effectiveness thresholds are often waived suggesting that greater value is placed on treatments for rare conditions, compared with prevalent diseases that are equally severe and debilitating. Population surveys indicate that funding policies that take resources from elsewhere in health economy budgets to fund these treatments are not in the public interest. At the same time, research and development into certain common diseases such as stroke, where the burden is much higher, has been somewhat neglected. We believe it is time to revisit orphan drug legislation. Regulators should be able to limit the benefits of orphan designation should the cumulative eligible population exceed a certain threshold. More robust criteria need to be applied for defining a "medically plausible subset" and pricing should to be brought closer in line with drugs for non-rare diseases. Furthermore, the focus of incentives should move more towards areas of unmet need where disease burden is greatest.

PHP229

REVIEW OF ECONOMIC PRINCIPLES OF BRANDED "ME-TOO" DRUGS MARKET

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In this paper, we review a well-known phenomenon of »me-too« drugs in the pharmaceutical branded markets, which has gained wide attention during the recent years. A branded "me-too" drug is deemed having somewhat similar therapeutic effect as the "breakthrough" drug, although from an intellectual property right perspective, there is no difference between the two. Definition of "me-too" drugs has yet to reach consensus and it would likely be ferociously disputed by the branded firms. When the first branded »me-too« drug enters the market, we are dealing with oligopoly, or more precisely, duopoly, described by Cournot model. From an oligopoly model, we would expect at Nash equilibrium both price to decrease and total volume to increase compared to shared monopoly conditions. An oligopolistic structure of a »me-too« pharmaceutical market puts substantial emphasis on branding and promotion (to achieve

horizontal differentiation), which is often cited (beside R&D costs) as the second barrier to entry to the branded market. Here, we have discussed several examples of Cournot model within various ATC4 groups and jurisdictions. We have also critically examined preponderance of »me-too« entries, particularly in the light of an R&D investment of the branded firms. Historically, »me-too« drugs are more ubiquitous than often realized by regulatory agencies, payers, and also the pharmaceutical industry itself. This unfortunately presents an inefficient use of resources as the breakthough innovation is nowadays, in the time of austerity measures, a real necessity. The models that would give incentives to the industry to invest in R&D for breaktrough therapies are possible and would not only contribute to optimization of societal welfare but would also in the long run increase an R&D productivity of branded firms.

PHP230

CELL THERAPIES: ASSESSING THE PATIENT ACCESS OPPORTUNITIES AND CHALLENGES THAT LIE AHEAD

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This poster seeks to highlight the key challenges and opportunities surrounding patient access to innovative cell therapies in the EU5 and US. The findings are based on secondary research of commercialised cell therapies as well as primary research with payers in EU5 and US. Cell therapies have a unique opportunity to improve patient outcomes but face their own set of challenges due to being cell based. As many of these therapies involve manipulation of the patients' own cells before being reintroduced (e.g., ChondroCelect), the associated side effects are likely to be minimal. Other therapies (e.g., gene therapy, Glybera) involve the introduction of foreign genetic material but provide a potential long-term cure. However, there are some important challenges that must be assessed when considering how to commercialise such therapies. In the case of therapies where a patient's cells are manipulated *ex vivo*, who bears the risk if the patient does not receive their individualised treatment? For those therapies that purport to cure disease, how much are health care systems willing to pay for them and what evidence would be required in order to justify a high price? Moreover, for all therapies, there is the uncertainty regarding access pathways: will cell therapies necessarily undergo an HTA evaluation to gain access in the EU? What are the criteria that will be used to determine whether such a therapy is deemed a product (and, hence, undergo an assessment like a regular biopharmaceutical) or a procedure (and likely bypass a national evaluation)? In conclusion, cell therapies face uncertainties in market access and funding due to unestablished pathways for the spectrum of interventions that fit under the cell therapy umbrella. Until frameworks have been put in place, each cell therapy should be assessed individually in order to determine likely pathway to patient access.

PHP231

THE IMPACT OF RECENT GENERIC DRUG PRICE POLICIES ON PHARMACEUTICAL INNOVATION: A THEORETICAL RATIONALE AND PROPOSAL OF A METHOD SUPPORTING INNOVATION IN AREAS OF UNMET MEDICAL NEED

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New discoveries are a critical priority for the pharmaceutical industry, for which the primary aim should be to address unmet medical needs. However, the use of fixed cost-effectiveness (ICER) thresholds for health technology assessment (HTA) may tend to decrease incentives to innovate and affect future treatment options. This presentation highlights, using a case study, the impact of recent generic drug price policies on pharmaceutical innovation in the context of fixed ICER thresholds and proposes a new consideration for the cost-effectiveness analysis (CEA). There is a direct causal relationship between HTA and the market price of a drug; in jurisdictions where HTA agencies apply fixed ICER thresholds as an important reimbursement listing criterion, the incremental cost of a new drug is expected to be proportional to its incremental benefit over the comparator. However, the comparator price is subject to market forces or sudden policies and may change markedly affecting the cost-effectiveness assessment (e.g. where the comparator patent has expired). Since recent generic price regulations (e.g. 18% or 25% of the innovative price in Canada) increased the price gap between drugs' generic and patented versions, it is harder to achieve a sufficient level of incremental benefits in order to offset incremental prices of new treatments. This analysis thus demonstrates that with recent changes in generic drug prices in Canada and other jurisdictions, even promising drugs will have challenges to show attractive ICERs. Traditional decision-making process should be adapted to reflect these changes and to promote innovation in therapeutic fields with unmet medical needs. A compromise would be to include the comparator's patented price in the CEA instead of the generic drug in certain areas of unmet needs. By identifying the relevant disease areas, decison makers and HTA authorities could convey the importance of investing in these therapeutic areas to manufacturers.

PHP232

THE EXPANDING SCOPE OF COMPARATIVE EFFECTIVENESS REVIEWS REQUIRES COLLABORATIVE INFORMATION SYSTEMS SOLUTIONS

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BACKGROUND: The scope of systematic reviews and health technology assessments is rapidly expanding due to increasing demand for more complex models that account for patient, treatment, and trial characteristics, network meta-analyses that include more interventions, and the growing number of clinical trials. By the year 2000, the effort required to publish a typical systematic review had already reached the thousands of person-hours, which were predominantly spent on data acquisition tasks. Innovative solutions are required to prevent the costs of comparative effectiveness research from ballooning out of proportion. **PROBLEM:** Typically only the end product of systematic reviewing, a report summarizing the evidence, is made widely available. However, capturing the intermediate results of literature searching, publication screening, and data extraction has the potential to greatly enhance the efficiency of future reviews. In the face of the increasing scope of systematic reviews, this unnecessary duplication of effort must be eliminated. However, doing so is difficult due to the current culture of data protectionism and a lack of suitable software that enables convenient and useful sharing of the intermediate results. **APPROACH:** Building on our previously published reviews of software for systematic review and trial analytics, the talk identifies the technical and cultural challenges to be met. We propose that a web-based solution enabling the global research community to contribute their intermediate results in exchange for access to the data contributed by others could rapidly gain momentum. Such a system would challenge data protectionism by greatly reducing the level of investment required for data acquisition. **CONCLUSION:** A disruptive web-based system enabling a massively collaborative approach to systematic reviewing can make data protectionism obsolete and eliminate much of the effort required for future systematic reviews.

PHP233

VALUE-BASED PRICING IN THE UK AND POTENTIAL PATIENT ACCESS HURDLES TO INNOVATIVE DRUGS

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The UK government plans to introduce value-based pricing (VBP) for medicines in England and Wales from January 2014, and one of the key tenets of the scheme is to improve patient access to new innovative drugs. This poster aims to explore the extent to which VBP is likely to achieve this goal. To meet this objective, an in-depth review of available literature (including white papers from key stakeholders and scientific publications) was conducted. Targeted interviews with five leading thought-leaders in the implementation of VBP were also conducted to support analysis. Research identified a number of areas of uncertainty in VBP implementation that could detrimentally impact patient access to new drugs. First, the timeline for the VBP negotiation process remains unclear. Currently, it takes NICE on average 48 weeks to issue guidance on a single technology appraisal, which could be extended if a technology is not considered cost-effective. Under VBP, manufacturers will still be required to negotiate their price with the Department of Health if the calculated VBP price by NICE is unfavorable, and the VBP HTA methodology itself could be more complex than the current cost-per-QALY approach. Protracted negotiations could also delay access in Scotland and Northern Ireland. Equally, manufacturers may postpone launch in the UK if they consider VBP a threat in their price corridor in other markets. Finally, it is not clear if additional regional or local level negotiations will take place, which could further delay access. In conclusion, although there is potential for the new adjustable QALY threshold (which remains to be confirmed) to foster innovation, the ability of the new VBP process to expedite patient access remains uncertain.

PHP235

A CHOICE OF BUSINESS FOR THE PHARMACEUTICAL INDUSTRY "SEGURO POPULAR" IN MEXICO

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A choice of business for the pharmaceutical industry "Seguro Popular" in Mexico. Abstract Mexico has various providers of health services each one determined to a sector of the population where we can find the Mexican Social Security Institute (IMSS) that is specifically for workers in the private sector employees and their families, the Institute for security and services social of the State workers (ISSSTE) for workers in the service of the State or public sector and their families starting 2003 ushered to the Seguro Popular that extends to the population without social security or in State of helplessness in these three mentioned health are emerging as institutions providing health services larger Mexico insomuch that by 2013 the Seguro Popular has approximately 54 million affiliates number of successful membership in less than 10 years in a country where there is little more than 110 million of people Seguro Popular is placed, on par with the historic and hegemonic IMSS, as the largest buyer of drugs, aware of this are his consumption figures that since 2008 has been made public, in such data can find that from 2008 to 2012 they have bought 1,241,637,748.68 US Dlls only in drugs consumption regularly since the Seguro Popular has several portfolios of services where separate regular conditions of sufferings of low frequency and high cost and conditions of very low frequency and high cost for children under 5 years who in turn have specific budgets.

DISEASE-SPECIFIC STUDIES

GASTROINTESTINAL DISORDERS – Clinical Outcomes Studies

PGI1

UNDERSTANDING THE EFFECT OF CLOSTRIDIUM DIFFICILE INFECTION ON HOSPITAL MORTALITY IN ENGLAND, THE NETHERLANDS, AND SPAIN

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OBJECTIVES: Increasing rates of *Clostridium Difficile* Infection (CDI), a hospital-acquired infection, has stimulated a number of financial incentives and government sponsored initiatives to quell the spread of the disease. Previous research has shown the impact of CDI on hospital length of stay to attempt to quantify the resource implications. The purpose of this study is to evaluate the impact of CDI on in-hospital mortality. **METHODS:** Data were obtained from national hospital episode databases in England, The Netherlands, and Spain. Only patients over the age of 50 and those diagnosed with diabetes, chronic kidney disease, heart failure, and chronic obstructive pulmonary disease (COPD) were included in the analysis. Cases of CDI were stratified between hospital-onset and community-onset cases. Only those that were assumed to be hospital-onset were included in the analysis. A logistical regression was used to predict the relative effect hospital-onset CDI had on in-hospital mortality. A number of covariates were controlled for including: age, sex, comorbidities, and length of stay but varied between countries depending on the availability of data. **RESULTS:** Patients with hospital-onset CDI had an overall higher mortality rate compared to those who

did not have the disease, demonstrated by a crude relative risk of 6.06 in England (37.6% vs. 6.2%), 2.68 in The Netherlands (19.0% vs. 7.1%), and 1.97 in Spain (14.9% vs. 7.5%). When controlling for covariates, predictive models found a considerable impact of hospital-onset CDI on mortality with odds ratios of 2.57 for England (p<0.001), 1.88 for The Netherlands (p<0.001) and 1.33 for Spain (p<0.001). **CONCLUSIONS:** This research demonstrates the significant impact of CDI on hospital mortality and the need for more preventative measures within the hospital setting. Further research using death certificate data could improve the predictive results of models by ensuring that causal effects of CDI are accurately accounted for.

PGI2

RULING OUT IBD IN THE UNITED KINGDOM AND SPAIN: IS THE USAGE OF F-CALPROTECTIN IN PRIMARY CARE COST-EFFECTIVE?

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OBJECTIVES: The inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the gastrointestinal tract; the irritable bowel syndrome (IBS) is a functional disorder (prevalence 10%-20%). They present overlapping symptoms, making diagnosis difficult in primary care. Endoscopy is the gold standard for IBD, but it often turns negative due to IBD's low prevalence, it is expensive, uncomfortable and risky for the patient. F-Calprotectin is a marker of intestine inflammation: as IBD patients exhibit levels higher than the general population and IBS patients, F-Calprotectin can be used to rule out IBD. The only CE evaluation on F-Calprotectin has been published by NHS (CEP09041, 2010); based on new evidence, we propose a refined model to evaluate the CE of F-Calprotectin compared to the standard pre-endoscopic serologic test (CRP+ESR) to distinguish IBD from IBS in the UK and Spain. **METHODS:** F-Calprotectin sensitivity (0.96) and specificity (0.96) were evaluated from a meta-analysis performed in March 2013; CRP+ESR sensitivity (0.35) and specificity (0.73), and the costs come from CEP09041. Published HRQoL values for IBD and IBS were transformed in QALYs with transfer-to-utility techniques. The outcomes included cost savings, cost per QALY. Uncertainty was addressed with a probabilistic sensitivity analysis. **RESULTS:** Results for UK show that F-Calprotectin is CE with respect to CRP+ESR: a) it results in more corrected IBD diagnoses at a lower price (it costs 113£ and 85€ less per patient); b) it reduces the number of unnecessary endoscopies, increasing the number of correctly diagnosed IBD (N=59) and IBS (N=195) patients; c) it brings about a QALY gain per patient equal to 0.0034QALYs; in the UK, the ICER of the CRP+ESR diagnostic strategy is 47,783£ (25,941€ for Spain), falling well outside the cost-effectiveness bounds (20,000–30,000£ per additional QALY). **CONCLUSIONS:** F-Calprotectin is CE to rule out IBD in primary care in UK and Spain.

PGI3

DIAGNOSIS OF PANCREATIC EXOCRINE INSUFFICIENCY IN CHRONIC PANCREATITIS, PANCREATIC CANCER AND GASTROINTESTINAL OR PANCREATIC SURGERY PATIENTS: A SYSTEMATIC LITERATURE REVIEW AND EXPERT CONSENSUS ON THE ACCURACY OF DIAGNOSTIC TEST USED IN SPAIN

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OBJECTIVES: To systematically appraise the literature on the accuracy of four widely used tests to diagnose Pancreatic Exocrine Insufficiency (PEI) secondary to chronic pancreatitis (CP), gastrointestinal/pancreatic surgery or pancreatic cancer in Spain, namely: coefficient of fat absorption (CFA); mixed 13C-triglyceride breath test (MTG); fecal elastase-I (FE-I); and serum nutritional markers (SNM). **METHODS:** A systematic review of the literature (March, 2013) was performed (*MedLine/PubMed*, Cochrane Library, CRD, MEDION, ARIF, MEDES, IBECS, ISI WOK, SCOPUS), based on the Cochrane and NHS Centre for Reviews and Dissemination recommendations for reviewing diagnostic test accuracy studies. Expert validation of the review strategy and results were achieved by two consensus meetings. **RESULTS:** Out of 13.379 publications, 16 from the systematic search and 3 from hand-search were reviewed: 11 in CP and 8 in cancer/surgery patients. Fourteen of these used the secretin/cerulein test as the reference standard. According to experts, CFA is the gold standard for PEI diagnosis (assumed accuracy 100%). 4 publications using CFA as the reference standard were selected: FE-I sensitivity and specificity in 58 CP (cutoff <218μg/g) and 40 cancer/surgery patients (cutoff 200μg/g) were 68% and 98%, and 91% and 35%, respectively. MTG was ≥90% sensitive and specific in all populations (63 patients), experts considered this a good reference standard. Sensitivity and specificity for SNM vs. MTG were 80% and 81%, respectively and considered by experts as similarly accurate in the cancer/surgery population. **CONCLUSIONS:** This is the first systematic review to confirm the accuracy of four diagnostic tests for PEI in CP and cancer/surgery patients, with the final selection of results being based on expert consensus to ensure that the data are representative of Spanish clinical practice. These data, together with resource use and cost information from clinical practice will feed an economic tool to assess the cost of PEI diagnosis in Spain.

PGI4

NETWORK META-ANALYSIS OF APPROVED BIOLOGIC INTERVENTIONS FOR THE INDUCTION OF RESPONSE IN ULCERATIVE COLITIS

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OBJECTIVES: To evaluate the comparative efficacy of approved biologic treatments for ulcerative colitis (UC), with a focus on golimumab(GOL), adalimumab(ADA), and infliximab(IFX) in the induction periods of clinical trials. **METHODS:** A systematic literature review was performed to identify relevant randomized controlled trials (RCTs). Data were extracted on study design and patient characteristics. Endpoints concerning efficacy were evaluated using network meta-analyses. Clinical response was defined as a decrease in Mayo score of ≥30% and ≥3 points, accompanied by a decrease in rectal bleeding score of ≥1 point or rectal bleeding score of 0 or 1. Clinical remission was defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Mucosal healing was defined as absolute subscore for endoscopy of 0 or 1. Bayesian network meta-analyses (NMA) were conducted to evaluate each efficacy endpoint for TNF-naïve patients at the end of induction. All analyses were conducted using the OpenBUGS software package. **RESULTS:** Six RCTs were identified from the literature. Similar clinical response was observed between the IFX and GOL treatment regimens (IFX 5mg: OR=2.74, 95%CrI [1.48-5.1], IFX 10mg: 2.54 [1.37-4.73], GOL 200/100mg: OR=1.7 [0.93-3.14], GOL 400/200mg: 1.95 [1.05-3.58]) when compared to ADA 160/80mg. These similarities were also seen for mucosal healing (IFX 5mg: 2.66 [1.43-4.94], IFX 10mg: 2.57 [1.38-4.77], GOL 200/100mg: 1.54 [0.83-2.85], GOL 400/200mg: 1.68 [0.91-3.10]). IFX demonstrated slightly greater clinical remission than GOL (IFX 5mg: 1.96 [0.80-4.65], IFX 10mg: 1.51 [0.61-3.62], GOL 200/100mg: 1.55, 0.59-4.06], GOL 400/200mg: 1.47 [0.56-3.84]) when compared to ADA 160/80mg. **CONCLUSIONS:** The NMA allowed the estimation and comparisons of clinical response, remission, and mucosal healing of interventions for UC evaluated in different RCTs. The findings suggest that the greatest induction of response in moderate to severe UC patients is most likely achieved with IFX and GOL compared to ADA.

PGI5

NETWORK META-ANALYSIS OF APPROVED BIOLOGIC INTERVENTIONS FOR THE MAINTENANCE OF RESPONSE IN ULCERATIVE COLITIS

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OBJECTIVES: To evaluate the comparative long-term efficacy of approved biologic treatments for ulcerative colitis (UC), with a focus on golimumab(GOL), adalimumab(ADA), and infliximab(IFX). **METHODS:** A systematic literature review identified 4 randomized controlled trials (RCTs) assessing the efficacy of IFX (5mg, 10mg), ADA (160/80/40mg) and GOL (100mg, 50mg) as maintenance treatment for moderate to severe UC. Data were extracted on study design and patient characteristics. Endpoints concerning efficacy were evaluated using network meta-analyses (NMA) within a Bayesian framework. Analyses were conducted to evaluate sustained response to therapy at both the mid-point (week 30/36) and completion (week 52/54/60) of each trial. An additional sub-analysis was conducted because the PURSUIT trial design included a re-randomization of induction responders to placebo, GOL 50mg or GOL 100mg. This sub-analysis was limited to patients who received an induction regimen of GOL 200/100mg followed by 100mg during the maintenance period and induction non-responders who received 100mg as per protocol. All analyses were conducted using the OpenBUGS software package. **RESULTS:** 4 RCTs were identified from the literature. Overall, IFX and GOL showed greater sustained response, remission and mucosal healing when compared to ADA 160/80/40mg. Between IFX and GOL, IFX doses showed greater remission at trial's completion (IFX5mg OR=2.04, 95%CrI 0.6-7.03; IFX10mg 1.96, 0.6-6.8; GOL50mg 1.24, 0.4-3.9; GOL100mg 1.79, 0.6-5.4), response (IFX5mg 1.88,0.8-4.4; IFX10mg 1.73, 0.7-4.1; GOL50mg, 1.38, 0.6-3.1; GOL100mg 1.45, 0.6-3.3) and mucosal healing (IFX5mg 1.51,0.7-3.4; IFX10mg 1.53, 0.7-3.5; GOL50mg, 1.38, 0.6-3.3; GOL100mg 1.38, 0.6-3.2. During the sub-analyses, GOL100mg and both IFX doses demonstrated greater sustained response and sustained remission when compared to ADA 160/80/40mg. Sustained mucosal response increased for IFX 5mg and IFX10mg but decreased for GOL100mg. **CONCLUSIONS:** Based on indirect comparison of RCT evidence, IFX and GOL are more efficacious to induce and maintain long term response than ADA among moderate to severe UC patients.

PGI6

A SYSTEMATIC REVIEW OF ANTIDEPRESSANTS IN IRRITABLE BOWEL SYNDROME: A QUALITATIVE ANALYSIS

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OBJECTIVES: To systematically identify and review published evidence on the efficacy of antidepressants (tricyclic antidepressants (TCA) and selective serotonin inhibitors (SSRI)) for irritable bowel syndrome (IBS). **METHODS:** A systematic search of the medical literature was conducted using PubMed, Embase, and Cochrane databases. Search terms included 'irritable bowel syndrome', 'spastic colon', 'irritable colon', 'functional diseases, colon' and a mixture of agent terms – including antidepressants, tricyclic, and SSRIs. Randomised placebo-controlled trials evaluating the efficacy of antidepressants (SSRIs and TCAs) in adult patients with IBS were eligible for inclusion. Exclusion criteria included absence of placebo arm, patients<18 years of age, and dual publication. **RESULTS:** A total of 628 unique titles and abstracts were retrieved; 579 records were excluded upon title (or abstract) review and 31 upon full-text review. The final review included 17 studies, 10 reporting on TCAs, 6 on SSRIs, and 1 comparing both an SSRI and a TCA vs. placebo, and assessed the methodological compliance of each included study with that used in regulatory submissions. In these studies, the majority of patients had diarrhea, and only one study, (on SSRIs) reported specifically on IBS-C. Treatment duration ranged from 4-12 weeks. A range of outcomes were reported, most commonly global symptom relief, and improvements in abdominal pain/discomfort. Three studies reported on quality of life, while no studies reported specifically on treatment satisfaction. Most outcomes did not align well with those now required for FDA and EMA regulatory approval. Across all studies, patient dropouts were common, and reporting on per-protocol and intention-to-treat (ITT) populations varied and in many cases was not explicitly reported. **CONCLUSIONS:** The evidence base was of low quality, making estimates of effect very uncertain. Data for the efficacy of antidepressants in IBS subtypes is especially limited. Further studies are required to support the off-label use of antidepressants in IBS-C.

PGI7
CHARACTERISTICS OF CHILDREN AND ADOLESCENTS USING PROTON PUMP INHIBITORS OR HISTAMINE-2-RECEPTOR ANTAGONISTS: ANALYSIS OF THIN AND PHARMO DATABASES
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OBJECTIVES: To describe demographics and co-morbidities of children starting PPI or H2RA use. **METHODS:** Data were obtained from The Health Improvement Network (THIN, a UK primary care database) and the Dutch PHARMO Database Network (including outpatient pharmacy and hospital databases). Children (<19 years) starting a PPI or H2RA between 2009–2012 (THIN) and 2008–2010 (PHARMO) were selected. Demographics, medical history, co-morbidities and co-medication were assessed. **RESULTS:** The study included 15782 PPI starters (THIN, n=5957; PHARMO, n=9825) and 8980 H2RA starters (THIN, n=5696; PHARMO, n=3284). The proportion of males was similar between PPI and H2RA starters in each database (THIN, 41% vs 48%; PHARMO, 44% vs 48%). H2RA starters more often were <12 years of age (THIN, 73% vs 26%; PHARMO, 58% vs 36%) and PPI starters more often had received other prior acid-suppressing treatment (THIN, 9% vs 2%; PHARMO, 10% vs 7%). In THIN, a history of infectious or respiratory disease was more common in PPI starters: infectious disease, 89% vs 65% (odds ratio (OR) 1.20; 95% confidence interval (CI) 1.05–1.37); respiratory disease, 77% vs 49% (OR 1.20; 95%CI 1.08–1.34). In PHARMO, PPI starters were also more likely to suffer from asthma/chronic obstructive pulmonary disease (8% vs 6% (OR 1.35; 95%CI 1.14–1.60)) and more often used antibiotics (20% vs 13% (OR 1.53; 95%CI 1.37–1.72)) and non-steroidal anti-inflammatory drugs (25% vs 5% (OR 4.48; 95%CI 3.80–5.29)). PPI starters in PHARMO were also more likely to have a history of diabetes or epilepsy (diabetes, 1% vs <0.5% (OR 5.00; 95%CI 2.33–10.73); epilepsy, 2% vs 1% (OR 1.69; 95%CI 1.16–2.45)). **CONCLUSIONS:** Results from both databases indicated that H2RA starters were younger than PPI starters. PPI starters were more likely to have received other prior acid-suppressing treatment and had more co-morbidities than H2RA starters.

PGI8
HEPATOCELLULAR CARCINOMA: AN EPIDEMIOLOGICAL AND MANAGEMENT SURVEY-BASED ANALYSIS IN ITALY
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OBJECTIVES: To verify how Hepatocellular Carcinoma (HCC) management is carried out in Italy and to point out the organizational key variables useful for an economic assessment, considering that Italy is among the European States with the highest incidence of HCC according to recent published data and that HCC is the final and highest cost health state along the natural history of liver diseases. **METHODS:** A questionnaire was set up jointly by clinicians (hepatologists and infectivologists), pharmacoeconomists and HTA experts, and submitted to 9 centers in order to collect epidemiology and management data. The survey consisted of a series of questions regarding HCC patients: gender and age, HCC etiology, BCLC (Barcelona Clinic Liver Cancer) staging at diagnosis, current treatments, hospitalization regimens, number and description of diagnostic/outpatient procedures, other relevant concurrent pathologies. The survey was administered to patients in four Italian centers of excellence for liver diseases with well-established experience in treating HCC patients. **RESULTS:** A total of 596 questionnaires were collected, the majority of which regarding male patients (79%), with a mean age of 67. Etiology proved to be mainly HCV-related (56%) and most patients underwent full hospitalization (81%) with a mean duration of 16.5 days, with a wide variability among centers, concerning both diagnostic procedures (CT, MRI, ecography…) and treatments (surgery, liver transplantation, drugs…). **CONCLUSIONS:** The collected data show a major heterogeneity, linked to the different etiology and epidemiology of the disease along the peninsula, well characterized by a number of published studies, but prove to be very helpful in describing the current situation regarding HCC in Italy. This descriptive analysis will be useful to set up a prospective study with the aim to implement an economic model able to compare different treatments and diagnostic procedures, and including organizational aspects in accordance to a cluster-randomized logic.

PGI9
INCIDENCE OF ANASTOMOTIC LEAKS AFTER COLORECTAL SURGERIES USING HOSPITAL EPISODE STATISTICS IN THE UNITED KINGDOM
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OBJECTIVES: Reported incidence of gastrointestinal anastomotic leaks after colorectal surgeries varies across regions, mainly due to different definitions of anastomotic leaks. A recent study using Premier Perspective administrative database reported 6.18% incidence of post-operative anastomotic leaks in US. The objective of this study is to apply a similar definition of anastomotic leaks from the US study and estimate incidence of anastomotic leaks after colorectal surgeries in UK. **METHODS:** Hospital Episode Statistics database was used to identify patients receiving colorectal surgeries from January 2007 to December 2011. The index colorectal surgeries included colectomy, hemicolectomy, sigmoid colectomy, and low anterior resection identified by OPCS-4 codes. The anastomotic leak event was defined by re-intervention (OPCS-4 codes) or diagnosis (ICD-10 codes) within 30-day window following index colorectal surgeries. The re-intervention included re-operation, re-anastomosis, stent, colostomy, image guided drainage, abscess, and washout. The diagnosis was generalized acute peritonitis. Chi-square and t tests were used to compare demographic characteristics between patients who had leaks and those who did not. **RESULTS:** A total of 132,045 patients (mean age: 65 years, 50% male) received colorectal surgeries during 2007-2011. Of these, 8,434 (6.38%) had anastomotic leaks within 30 days of the colorectal surgeries. 2.63% leak cases were defined by reoperation, 1.82% by diagnosis of generalized acute peritonitis, 1.24% by colostomy, 0.9% by image guided drainage, 0.7% by washout, 0.62% by abscess, 0.42% by re-anastomsis, and 0.01% by stent. Patients with leaks tended to be slightly younger and male, had higher Charlson Co-morbidity Index, and more likely admitted through emergency vs. elective surgery (p<0.05). **CONCLUSIONS:** Our study indicated an incidence rate of 6.38% for post-operative anastomotic leaks among patients undergoing colorectal surgeries in UK, compared to 6.18% leak rate seen in the US study. The results highlight the importance of future study in evaluating the impact of anastomotic leaks on patient's clinical and economic outcomes in UK.

PGI10
RESOURCE USE AND DISEASE PROGRESSION AMONG HCV-POSITIVE PATIENTS
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OBJECTIVES: Hepatitis C is an infectious disease affecting the liver; chronic infection can lead to cirrhosis. The actual standard of care in Italy is Peginterferon+ribavirin. Our aim was to describe treatment patterns, disease progression and resource use in HCV. **METHODS:** An observational retrospective cohort analysis based on 4 Local Health Units administrative and laboratory databases was conducted. HCV-positive patients between January 1, 2009- December 31, 2010 were included and followed-up for one year. To explore which covariates were associated to disease progression (cirrhosis, hepatocellular carcinoma -HCC-, death for any cause), Cox proportional hazards models were performed. **RESULTS:** A total of 9514 patients were analyzed, 55.6% male, age 58.1±16.1; 5.8% had HIV, 3.0% HBV, 1.6% HCV+HBV+HIV, 26.1% cirrhosis, 4.3% HCC. Genotypes frequencies were 1a (17%), 1b (34%), 2 (24%), 3 (19%), 4 (5%). Antiviral treatment was not administered to the majority of patients (79%); the main factors affecting this decision were: age >65 years (44%), females (46% VS 40% of treated), cirrhosis (30%), normal liver enzymes (28%), ongoing substance/alcohol abuse (7%), HCC (5%). Disease progression in the observed timeframe was less frequent among treated patients (incidence rate per 100 patients/year: cirrhosis 2.1±0.7 VS 13.0±1.0, HCC 0.5±0.3 VS 3.6±0.5, death for any cause 0.5±0.3 VS 6.4±0.7); at multivariable Cox regression models, hazard ratios were, respectively, 0.30 (0.21-0.43), 0.41 (0.19-0.92) and 0.24 (0.12-0.48) (all p<0.05). For genotype1 subgroup, results were not statistically different between Peginterferon+ribavirin treated and untreated (cirrhosis: HR=0.82 (0.32-2.11), p=0.682). The annual expenditure for HCV management (drugs, hospitalizations, outpatient services) was €4,700 per patient. **CONCLUSIONS:** Actual standard of care was not widely used, especially for sensitive subgroups such as women and the elderly; in this context, there is an urgent need for treatment, but current therapies do not appear to be adequate for all patients, especially those with genotype1, which represents 60% of the Italian HCV population.

GASTROINTESTINAL DISORDERS – Cost Studies

PGI11
PERITONITIS FLUID TREATMENT IN RUSSIAN FEDERATION: EVALUATION OF ECONOMICAL BURDEN IN REAL CLINICAL PRACTICE
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OBJECTIVES: Peritonitis is an inflammation of the parietal and visceral peritoneum which is accompanied by severe general condition of the body. Peritonitis as a complication of acute inflammatory diseases of the abdominal cavity is found in 15-20% of clinical observation and about 6% of all surgical procedures on the abdominal cavity. The research is conducted in regard to 4 technologies of fluid treatment, including: Reamberin, Ringer's solution, Plasma-Lyte and Sterofundin. **METHODS:** Retrospective researches analysis is considered as a source of data on real effectiveness. The decree of the RF Ministry of Health No 669 of October 15, 2007 is considered as a source of data on commonly used drugs and medical services. The price-list of the Clinical Center of the First MSMU charges for medical services is incorporated as the source of data on the price of medical services. **RESULTS:** The calculation is made for the hypothetical group of 100 patients with the peritonitis disease. During the cost of illness analysis of peritonitis the direct costs are estimated. They include: medical services and pharmacotherapy in the period of the residence in the in-patient department(euro per patient: 9 241 for Reamberin, 10 554,8 for Ringer's solution, 9 755,7 for Plasma-Lyte and 9 756,4 for Sterofundin). The cost-effectiveness analysis(CEA) results are the following: 10 241 euro for Reamberin, 12 639 euro for Ringer's solution, 12 302 for Plasma-Lyte and 11 683 euro for Sterofundin. The budget impact analysis(BIA) show that the 100% switching patients from Ringer's solution, Plasma-Lyte and Sterofundin to Reamberin saves respectively: 131 377 euro, 51 465 euro and 51 538 euro. **CONCLUSIONS:** Cost of illness analysis, CEA and BIA of peritonitis indicate that the scheme of therapy including Reamberin is the dominant one. Total costs are 9 241 euro per patient, CER is 10 241 euro per saved live.

PGI12
ORGANIZATIONAL AND ECONOMIC ISSUES RELATED TO THE INTRODUCTION OF BOCEPREVIR IN THE TREATMENT OF PATIENTS WITH GENOTYPE 1 CHRONIC HEPATITIS C IN ITALY
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OBJECTIVES: To present the critical points concerning organizational and economic issues of the introduction of boceprevir in the treatment of patients with genotype 1 chronic hepatitis C in Italy. **METHODS:** A budget impact analysis was conducted adapting the NICE (UK) scheme for this drug, using the Italian epidemiological context and the perspective of the National Health Service. The cost-utility analysis (CUA) was carried out using a Markov model comparing the triple therapy (TT) with peginterferon alfa, ribavirin and boceprevir to the double therapy (DT) with peginterferon alfa and ribavirin. Available Italian published scientific literature provided data source. The main outcome of the CUA was the incremental cost-effectiveness ratio (ICER). The organizational aspects

considered were: clinical management of patient with HCV chronic infection, access modalities, outpatient visit, planned and unplanned visits, hospital admission, role of the general practitioner (GP). **RESULTS:** The budget impact analysis shows that, considering both naïve and previously treated patients, the treatment with boceprevir has an impact on the National Health Service of almost €66 million for the first year. Compared to treatment with DT, the cost-utility analysis shows for the boceprevir-based treatment strategy an ICER of €8.622,00. The management of TT for its intrinsic complexity requires monthly outpatients visits, at least at the beginning of treatment, for monitoring the compliance to treatment, efficacy and side effects. A critical organizational point is potentially the request for boceprevir for each single patient by the medical prescriptor, who needs to fill in detailed form from the Italian Agency of Drug (AIFA). **CONCLUSIONS:** The impact of the introduction of boceprevir on the budget is high, even if the ICER is favourable. Patients' management is particularly complex and there is the need for an alliance between the patients, their relatives, GPs and specialized centers.

PGI13

ENTERAL DIETS (ED): A COST-COMPARISON ANALYSIS FOR IN-HOSPITAL PREPARATIONS BASED ON REAL WORLD OBSERVATION

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OBJECTIVES: ED can be administered based on three different systems – powder based (Po), open, liquid (Op), and a completely closed (Cl). There are differences in the preparation, installation and delivery and in the diarrhea rates among them. Our aim was to measure the total costs for each system, considering the resources needed to prepare, delivery administer and discard of each system (hidden costs). **METHODS:** We measured the human (nurse, nutritionist, auxiliary personnel) resources involved in ED preparations in three hospitals of Brazil. Then, we calculated the costs of the process, based on the minimum official wage for each professional category. After, we added the costs of the diets and materials needed to the infusion. We used as base case a daily need of 1 000Kcal / patient. Additional analyses were performed to include the side effects of ED system. **RESULTS:** There were differences among the human resources needed for each system. Hidden costs were 63% of the total for Op, 58% for Po and 53% for Cl. Particularly, the nurse time varied from 18 minutes for Po and Op and 5 min for Cl for each infusion. Considering that and average patient would require daily 4 infusions of Po or Op, that represents a total of 72min of nurse time to these systems, against 5 min to Cl. Total daily costs, were Op US$ 62.05; Po US$ 50.75 and Cl US$48.03. If we consider the costs of side effects, such as diarrhea, the costs are: Op US$ 73.42; Po US$ 62.15 and Cl 56.35. This increase in the difference amog the costs is due to a lower incidence of diarrhea in Cl systems. **CONCLUSIONS:** There are many hidden costs on the ED systems. If we consider them Cl systems are less costly than Op and Po.

PGI14

COST ANALYSIS OF PROTON PUMP INHIBITORS IN THE TREATMENT OF ULCER DUODENUM IN UKRAINE

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OBJECTIVES: Proton pump inhibitors (PPIs) are essential components schemes of antyhelicobacter therapy (AT) of peptic ulcer disease. The aim of research - to determine the costs of the use of PPIs in the traditional triple schemes AT (first and second line) of the working age patients with a duodenal ulcer in Ukraine. The objects of research - preparations of omeprazole, pantoprazole, rabeprazole, lansoprozol, ezomeprazol, which are present in Ukraine. **METHODS:** Cost analysis on the use of PPIs in the schemes of AT was performed per one patient for 14 days with the daily doses of drugs: omeprazole - 40 mg, pantoprazole - 80 mg, rabeprazole - 40 mg, lansoprozol - 60 mg, ezomeprazol - 40 mg (according to the recommendations of the "Maastricht IV", 2010). For determining the costs only the costs of the PPIs were taken into account. The prices of drugs were taken from the information system "Drugs" of Company "Morion" (December, 2012). The currency ratio of UAH to dollar (USA) on 10.12.12 was 7.99:1. To determine the range of costs for use of PPIs determined their trade names with the minimum and maximum costs for the AT. **RESULTS:** The range of costs for use of PPIs in the traditional triple schemes AT in Ukraine is wide enough, respectively: omeprazole - 1.15 - 19.15 $, pantoprazole - 5.11 - 49.28 $, lansoprozol - 5.14 - 10.66 $, rabeprazole - 4.27 - 63.40$, ezomeprazol 1.81 - 36.42$. **CONCLUSIONS:** Costs only for the use of PPIs in the schemes of AT of duodenal ulcer can be quite high in Ukraine. In this regard, the choice of PPIs for inclusion in the schemes of AT is advisable to use the results of pharmacoeconomic studies that will optimize the costs of the payer.

PGI15

ECONOMIC ANALYSIS OF USE OF HARMONIC DEVICES IN INPATIENT LAPAROSCOPIC CHOLECYSTECTOMY IN THE UNITED STATES

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OBJECTIVES: Harmonic® ultrasonic energy devices have been developed as a safer and more efficient alternative to traditional electrosurgery (monopolar and bipolar) in laparoscopic cholecystectomy. However, the economic impact on hospital cost has not yet been assessed in the United States. The aim of the study is to evaluate the total cost of laparoscopic cholecystectomy performed with an ultrasonic device versus electrosurgery from a hospital perspective. **METHODS:** A literature review was performed to identify publications via EMBASE and MEDLINE database. Nine randomized controlled studies were included in this analysis based on inclusion criteria. The clinical results were weighted based on No. of patients to calculate averages for both energy devices. The total departmental cost data for electrosurgery group were obtained from a large US payor (PREMIER database) to apply the clinical findings to calculate the cost for the Harmonic group. The total cost in laparoscopic cholecystectomy with two energy devices was compared to determine which modality is more cost effective. **RESULTS:** The total case cost using an ultrasonic device in an inpatient laparoscopic cholecystectomy is $7701 v.s. electrosurgery is $8637. The use of an ultrasonic device provides a hospital savings of $936 per patient treated. The savings mainly resulted from shorter operating time (13 Minutes) and decreased hospital stay (0.7 days). **CONCLUSIONS:** Although the instrument cost is higher for the ultrasonic device, the total procedural cost is lower compared to electrosurgery. Utilization of the Harmonic® ultrasonic device in laparoscopic cholecystectomy can lead to substantial cost savings for US hospitals.

PGI16

MORTALITY AND MEDICAL COSTS ASSOCIATED WITH LIVER-RELATED DISEASES AMONG PATIENTS WITH HEPATITIS C VIRUS(HCV) INFECTION IN TAIWAN

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OBJECTIVES: To examine the mortality and medical costs during the first and the 2nd year following the onset of the five liver-related diseases, i.e. HCV infection, compensated cirrhosis (CC), decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), or liver transplantation. **METHODS:** Patients with HCV infection and patients who transitioned to the health state of liver-related disease were identified from the National Health Insurance Research Database (NHIRD) during 2008-2010 if any outpatient/inpatient service with primary diagnosis code of 070.54 for HCV infection or 571.5 for CC occurred, or if patients registered in the Registry of Catastrophic Illness with diagnosis code of 571.5 for DCC, 155 for HCC or V42.7 for post liver transplantation. Dual infection patients with diagnosis code of 070.30 for HBV or 042-044 for HIV were excluded. The date that the outpatient visit/admission with the diagnosis code associated with each health state of liver-related disease firstly occurred was defined as the index date. Regression-adjusted medical costs associated with each health state of liver-related disease within 1st year and 2ndyear after the index date were estimated by generalized linear regression model. Excess risks of death for patients with DCC, HCC, or liver transplantation were assessed by Cox proportional hazard model. **RESULTS:** First year total medical costs associated with HCV infection, CC, DCC, HCC and liver transplantation were NT$25,345, NT$49,793, NT$187,428, NT$197,835, NT$487,816, respectively. The 2nd year total medical costs associated with DCC, HCC and liver transplant were NT$194,016, NT$176,167 and NT$270,009, respectively. Patients in the health states of DCC, HCC and liver transplantation posed higher risk of death with hazard ratio of 14.5when compared with their matched control counterparts. **CONCLUSIONS:** Liver-related diseases followed by HCV infection impose substantial economic burdens to the National Health Insurance in Taiwan. Effective treatment for HCV infection may imply potential savings to the society.

PGI17

RESOURCE UTILIZATION AND COSTS FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASES IN ITALY: A POPULATION-BASED ASSESSMENT

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OBJECTIVES: To describe health care resource utilization in treating patients affected by inflammatory bowel diseases (IBD) and to assess the related direct costs to the Italian health care system (HS) in its most populated region. **METHODS:** A retrospective observational study was conducted using data from DENALI, a data warehouse that organizes and integrates the health care administrative databases of the national HS in Lombardy (northern Italy) with a probabilistic approach. The Italian HS provides universal coverage and records the accesses to health care services at regional level. We enrolled adult patients with Ulcerative Colitis (UC) or Crohn's Disease (CD) diagnosed during the period 2003-2009. Patients were classified in two cohorts in relation to the type of IBD and were followed until December 31st, 2009 to assess the mean annual consumption of resources (hospitalizations, pharmaceutical prescriptions, outpatient services) and the related costs incurred by HS. **RESULTS:** We identified 5,523 patients with UC and 3,321 with CD and the mean annual cost per-capita was €2,386 (95%CI: 2,241-2,516) and €2,699 (95%CI: 2,538-2,914) respectively. The breakdown of expense was similar in the cohorts: pharmacological treatments accounted for 37% , hospitalizations for 47% and outpatient services for 16%. Use of mesalamine was high in patients with UC and CD:94% and 88% of subjects was respectively prescribed at least one package during follow-up. High adherence (≥70%) to oral mesalamine was observed in 39% of patients with UC and in 24% of CD cohort. Less than 6% of patients used biologics, which were used only from 2008. **CONCLUSIONS:** This study confirms that patients with IBD represent a considerable economic burden for the Italian HS: prescribed drugs, especially mesalamine, account for a substantial proportion of health care costs. The results underline the importance of administrative databases and the need for further research, since the recent widespread use of biologics for treating IBD.

PGI18

UTILISATION AND COSTS OF INPATIENT AND OUTPATIENT SERVICES AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME- A STUDY USING THE CLINICAL PRACTICE RESEARCH DATALINK (CPRD)

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OBJECTIVES: Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder. We assessed utilisation of secondary care services and associated costs among patients with IBS. **METHODS:** IBS was identified by medical diagnosis and/or prescribing in the UK primary care setting. Patients had ≥12 months of medical history prior to diagnosis. Absolute resource use and expenditure were assessed post IBS and over four years (01/04/2008-31/03/2012) using Hospital Episode Statistic data. Inpatient admission, outpatient attendance and length of stay for any cause including IBS related conditions were assessed. Inpatient costs for the period were estimated using allocated Health Resource Group coded data. Outpatient costs

were estimated using national average reference costs based on treatment speciality. Costs of medications prescribed in secondary care were not included. Total, mean and annual visits and costs were estimated and stratified by gender, age and treatment speciality. Prices were adjusted to 2011/2012. **RESULTS:** We identified 79,303 patients with IBS with an average follow-up of 3.38 years. Of these patients, 46,814(59%) had ≥1 contact with secondary care for any cause; 22,685(48.5%) patients attended outpatient services only. Patients using secondary care had about 2 hospitalizations on average and 3-4 outpatient visits annually. Mean inpatient stay declined from 4 days in 2008/2009 to 3 days in 2011/2012. The total cost of hospitalisation during the period was over £114 million, including about £35(30%) million for emergency inpatient admissions and £33.8 million for outpatient attendance. Digestive disorders accounted for around 30% of inpatient admissions and 21% of expenditure incurred. Mean cost of inpatient admissions for digestive conditions was £1,993, average costs per patient was £4,871 and £2,779 for elective and emergency visits respectively. **CONCLUSIONS:** Utilisation and costs of secondary care among IBS patients is substantial, not only for the management of IBS and related conditions, but also for other co-morbid medical conditions.

PGI19

INTERIM RESULTS FROM THE BURDEN OF BOWEL DYSFUNCTION IN SPINAL CORD INJURY STUDY

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OBJECTIVES: There are approximately 40,000 Canadians living with spinal cord injury (SCI). Most individuals with SCI experience some type of bowel dysfunction (BD), which can contribute to a high burden in individuals and caregivers, and a decrease in quality of life. This study aims to identify and measure resources, costs, health preference and quality of life associated with BD and its management in a cohort of SCI individuals living in a community setting in Ontario over a 6-month period. **METHODS:** This study is a prospective, observational study with 80 adult participants being recruited at three SCI clinics in Ontario, Canada. Questionnaires are completed by participants over a 6-month period (baseline, three weekly and five monthly). Information related to demographics, BD (e.g., neurogenic bowel dysfunction score), health preference (e.g., Health Utility Index (HUI) Mark 3) and resource utilization (e.g., physician, medication, caregiver burden, etc.) attributed to BD is being collected. **RESULTS:** Results from three clinics are being evaluated. 45 participants have completed the questionnaires to-date. The majority of participants are male (60.00%). Mean time since SCI was 20.2±13.7 (2 – 42) years. Twenty (44.4%) participants were employed. At baseline, the mean neurogenic BD score was 14.37±6.05 (0 – 31). At 6 months, the score was 12.9±6.6 (2 – 28). The mean HUI-3 score at baseline was 0.17±0.31 (-0.37 – 0.95). At 6 months the score was 0.19±0.33 (-0.37 – 1). The mean number of visits to primary care physicians by participants was 8.3 ± 8.6 (0 – 33) times over 6 months. 52.21% of participants required caregiver assistance. 12.50% of participants required a mean 1.21±0.67 (0.3 – 2) hours daily assistance with their bowel routines. **CONCLUSIONS:** Results from the 45 SCI individuals with BD indicate a variety of health resources are being utilized over a 6-month period. Future results will have resources associated with BD quantified.

PGI20

A COST-OF-ILLNESS ANALYSIS OF HEPATITIS C IN GREECE

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OBJECTIVES: Hepatitis C virus infection is accompanied by significant disease and economic burden internationally. In absence of data, the objective of this study was to estimate the annual cost of hepatitis C treatment and follow-up, in Greece, according to disease severity. **METHODS:** Resource utilization for "typical patient" scenarios, according to disease stage, was elicited via an expert panel (gastroenterologists and hepatologists from major hospital units of the Greek NHS). Patients were stratified based on disease stages; (a) fibrosis stage F0 to F3, (METAVIR score) (b) compensated cirrhosis (c) decompensated cirrhosis – first year (d) decompensated cirrhosis – subsequent years (e) hepatocellular carcinoma (HCC) (f) liver transplant (LT) – first year (g) LT – subsequent years. Direct cost categories included yearly costs of consultations, laboratory and PCR tests, medications and hospitalization. Cost calculations were based on 2012 fixed fees and prices, from a Social Security perspective. **RESULTS:** The average direct annual cost per patient for F0-F3 patients was estimated at 642.7€, excluding the cost of medications or 12,685.1€, including the cost of standard of care with PegIFN/ribavirin regimen. Respective annual costs for states (b) to (g) were: 636.7€ (compensated cirrhosis), 2,250.1€ and 5,934.5€ (decompensated first and subsequent years), 21,890.1€ (HCC), 35,051.1€ and 4,001.5€ (LT first and subsequent years). Main cost variables were hospitalizations [48.9%, 53.3% and 88.2% of the total cost for states (c) (d) and (g)], medications [93.2% and 50.1% of the total cost for states (e) and (g)] and laboratory tests [89.1% and 83.0% of the total cost for states (a) and (b)]. **CONCLUSIONS:** This cost analysis of chronic hepatitis C in the Greek health care system has shown that there is a substantial economic burden, significantly increasing in advanced liver disease. Standard and new interventions that slow disease progression or achieve virus eradication are deemed necessary from a clinical and economic perspective.

PGI21

SYSTEMATIC REVIEW: THE ECONOMIC BURDEN OF CROHN'S DISEASE IN EUROPE IN ADULTS AND CHILDREN

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OBJECTIVES: Crohn's Disease (CD) is an immune-mediated disorder characterised by recurrent chronic uncontrolled inflammation on the intestinal mucosa affecting any part of the gastrointestinal tract. Although most people with CD lead active lives, five years after onset 15% to 20% of patients are disabled by their disease to some degree. The purpose of the current review was to evaluate recent data from the literature on the economic burden of CD in European countries in adults and in children, using US data as a benchmark. **METHODS:** A systematic review of the data on economic and humanistic burden for adults and children in Germany, France, UK, Italy, Spain and the US was performed covering the period 2000 to 2012. The methods followed recommendations and guidance published by the Centre for Reviews & Dissemination, York, UK. **RESULTS:** Of the 425 publications identified on the economic burden of CD, 92 were suitable for further evaluation, and 39 were selected. Among these studies, five presented total costs of CD management in adults, ranging from €1,425 to €15,521 per patient depending on the country. Most of the direct costs were due to hospitalisations, surgeries or use of biologic drugs. Patients with severe disease and those requiring hospitalisation had disproportionately higher costs (5.6 times higher) compared to those with milder disease. Direct costs were more important for relapsing disease than quiescent disease. Only one European study focused on children using biologic drugs as maintenance treatment. **CONCLUSIONS:** Research on the economic burden of CD management has been mainly published on adults in the US and UK, with limited data from Germany, Spain and Italy. Similar data for paediatric CD is almost non-existent. More research is needed to better understand the economic and humanistic burden faced by paediatric CD patients in Europe.

PGI22

ECONOMIC CONSEQUENCES OF NONALCOHOLIC STEATOHEPATITIS IN THE UNITED STATES

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OBJECTIVES: Non-alcoholic steatohepatitis (NASH) is a progressive form of non-alcoholic fatty liver disease that becomes increasingly prevalent with the growing epidemic of obesity and diabetes in the United States. An estimated 3% of adults in the US have NASH and are at high risk of severe liver complications, including cirrhosis, liver failure, and hepatocellular carcinoma (HCC). Despite the rising prevalence, data on its economic and clinical consequences are limited. The objective of this study was to predict the long-term clinical and economic consequences associated with the adult NASH patients in the US over the next 20 years, including NASH-related complications, morbidity, mortality and health care costs. **METHODS:** We developed a Markov cohort model to estimate the consequences of NASH, which included six Markov states: NASH, compensated cirrhosis, decompensated cirrhosis, HCC, liver transplantation, and death. We estimated the number of liver complications, their associated health care costs, and NASH-related mortality. **RESULTS:** By 2033, 53.1% and 32.8% of NASH patients would progress to compensated and decompensated cirrhosis, respectively. An estimated 13.7% of patients developed HCC, and 13.3% eventually underwent liver transplantation. Among NASH patients, 16% had Type II diabetes and 44.8% and 23.8% would develop decompensated cirrhosis and HCC. The model predicted hepatic-related mortality of 24.2% and 12.6% for patients with and without diabetes, while the cardiovascular-related mortality was estimated to be 12.1% and 8.8% for NASH patients with and without diabetes. The direct health care cost was estimated at $72,170 and $120,165 for patients with and without diabetes, resulting in a total of $574 billion health care cost over the next 20 years. **CONCLUSIONS:** NASH patients were expected to have substantial risks for chronic liver failure and result in an increasing financial burden on the US health care system.

PGI23

ECONOMIC EVALUATION OF TIPS COMPARED TO LARGE VOLUME PARACENTESIS IN PATIENTS WITH REFRACTORY ASCITES

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OBJECTIVES: Undertake an economic evaluation of transjugular intrahepatic portosystemic shunts (TIPS) compared to large volume paracentesis (LVP) in patients with refractory ascites. Paracentesis, although the standard treatment for refractory ascites, does not treat the underlying portal hypertension. According to a meta-analysis of individual patient data, using TIPS with bare metal stents (BMS) rather than LVP showed improved survival and lower recurrence of ascites although with a higher number of hepatic encephalopathy episodes (Salerno 2007). **METHODS:** A Markov economic model was developed to measure the incremental resources and costs associated with TIPS, using costs for ePTFE covered stent-grafts configured for TIPS (SG), compared to LVP over two years. Clinical data came mainly from the meta-analysis, whilst health care costs were from UK national databases. **RESULTS:** Use of TIPS rather than LVP to manage refractory ascites was estimated to save almost £1,600 per patient over 2 years. Total costs for the treatment pathway were £8,310 with TIPS and £9,907 with LVP treatments. The TIPS implantation, together with the associated costs of re-intervention & complications cost £6,760 but there were estimated savings of £8,360 from avoided LVP procedures. Using TIPS to manage refractory ascites, rather than LVP, was cost saving under all the sensitivity analyses undertaken. **CONCLUSIONS:** The economic model demonstrated a total cost reduction of £1,600 per patient from TIPS with SG compared to LVP. Actual cost reduction may be greater as clinical data used from the meta-analysis was for BMS. Compared to BMS, SG have improved patency resulting in fewer reinterventions (Bureau 2007) which may reduce overall costs.

PGI24

AN ECONOMIC EVALUATION COMPARING EPTFE COVERED STENT-GRAFTS CONFIGURED FOR TIPS WITH BARE METAL STENTS IN PROCEDURES FOR THE TREATMENT OF PORTAL HYPERTENSION COMPLICATIONS

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OBJECTIVES: Establish the potential resource and cost savings from using ePTFE covered stent-grafts configured for TIPS (SG) compared to bare metal stents (BMS). Most centres have adopted SGs to treat portal hypertension because of their reduced re-intervention rates, elimination of regular monitoring of patency and improved survival. However there is no published economic analysis identifying the related cost consequences. Understanding the improved efficiencies is essential in the current financial environment. **METHODS:** A Markov economic model was developed to measure the incremental costs of the initial procedure and re-interventions with SG compared to BMS. Re-intervention procedures included angioplasty (67%), introducing a balloon expandable stent (22%) or a second stent (10%). The adverse events were hepatic encephalopathy and clinical relapse. Clinical data came mainly from a published RCT (Bureau 2007), whilst health care costs were from UK national databases. **RESULTS:** Compared to BMS, using SG in TIPS resulted in a cost saving of over £1,150 per patient over 2 years. Modelling 100 patients, compared to BMS, the SG cohort had 25 fewer re-interventions including angioplasties, saving 41 hours staff time in theatre and 16 inpatient days; with fewer cases of encephalopathy (16), recurrent ascites (8), variceal bleeds (5) and a markedly reduced mortality (13). **CONCLUSIONS:** The model showed that ePTFE covered stent-grafts configured for TIPS reduced mortality and re-interventions, saved theatre time and bed-days, and reduced overall costs despite the higher initial device cost.

PGI25

AN ECONOMIC EVALUATION OF THE TRIPLE HCV TREATMENT REGIMEN FOR G1 NAÏVE PATIENTS IN THE GREEK HEALTH CARE SYSTEM

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OBJECTIVES: In 2011 EMA approved Boceprevir and Telaprevir with PegIFN and Ribavirin for the treatment of Genotype 1 Chronic Hepatitis C patients. In 2013 the Greek and other European HCV Guidelines recommend treatment allocation in G1 naïve patients according to the IL28B genotype or the RVR profile. Local studies indicate that the IL28B-CC and the RVR (+) rates are approximately 30%. The objective of this study was to implement this guidance and examine whether triple therapy with PegIFNa-2a+RBV and the two protease inhibitors, Boceprevir or Telaprevir, constitutes a cost-saving option for the treatment of naïve G1 patients in the Greek health care setting. **METHODS:** For the needs of this analysis, a cost-consequence model was utilized, to compare the costs incurred when: i) patients with IL28B CC aplotype (30%) were treated with SoC (PegIFN alfa-2a + RBV) and patients with IL28B non-CC aplotypes (70%) were treated with triple therapy and ii) all patients are treated with triple therapy. The economic inputs are based on official and publically available sources while the clinical inputs are taken from published clinical trial results. The number of patients treated per year was provided by local bibliography. **RESULTS:** The total cost to treat 509 naïve patients with triple therapy was €13,8 million compared to €10.9 million to treat based on IL28B allocation, maintaining the same SVR rate of 70% for either of the treatment strategies. **CONCLUSIONS:** This personalized approach based on a baseline predictor of response such as the IL28B profile was proven to be a cost-saving resource allocation choice compared to the option of treating all treatment naive patients with triple therapy, providing SVR rates of 70% and a constrain of cost for the Greek health care system of €2,9 million/year (aprox.25%).

PGI26

COST-EFFECTIVENESS OF EARLY VERSUS DELAYED HEPATITIS C VIRUS (HCV) TREATMENT WITH TELAPREVIR/PEGYLATED INTERFERON ALPHA/RIBAVIRIN TRIPLE THERAPY IN ADULTS AGED 40+ IN FRANCE

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OBJECTIVES: To assess the cost-effectiveness of treating HCV infection (genotype 1) with telaprevir/pegylated interferon alpha/ribavirin (TPR) at METAVIR fibrosis stage F2 ("early") versus delaying treatment until progression to F3 ("delayed") from the French health care perspective. **METHODS:** A Markov model tracked the HCV+ French population aged 40+ over a lifetime horizon to compare outcomes of early versus delayed treatment. Model health states are defined by fibrosis stage (F0-F4) and complications of advanced HCV including decompensated cirrhosis, hepatocellular carcinoma, liver transplant, and death. During each 1-year cycle, individuals may remain in the current health state, respond to treatment or progress, at probabilities determined by disease status, age at infection, current age, gender, and treatment received. Transition probabilities, treatment efficacy, health-state utilities, resource utilization and costs were derived from published literature and standard French sources. Costs and outcomes were discounted at 4.0% for 30 years and 2% thereafter. Cost-effectiveness was assessed as incremental cost per life year gained (LYG) and QALY gained. **RESULTS:** An estimated 203,644 French residents aged 40+ years are diagnosed with HCV in 2013. Treating with TPR at F2 versus F3 is projected to result in 135,240 versus 113,728 individuals treated, at an incremental lifetime cost of €654.65M from the French health care perspective. Early treatment avoided 2,205 HCV-related deaths and saved 11,384 life-years, and 17,599 QALYs, at a cost of €57,506/LYG and €37,197/QALY gained. Results are most sensitive to efficacy parameters, time horizon, and discount rates and least sensitive to diagnosis and treatment parameters. **CONCLUSIONS:** Treating HCV-infected individuals at F2 is expected to results in better clinical outcomes but at higher cost compared to delaying treatment until the individual progresses to F3. Earlier treatment with TPR should be considered as an efficient choice by the French health care system based on its estimated incremental cost-effectiveness ratio of €37,197/QALY gained.

PGI27

COST-EFFECTIVENESS OF LINACLOTIDE COMPARED TO ANTIDEPRESSANTS IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME WITH CONSTIPATION IN SCOTLAND

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OBJECTIVES: Presently, linaclotide is the only EMA approved therapy indicated for the treatment of irritable bowel syndrome with constipation (IBS-C). This study sought to determine the cost-effectiveness of linaclotide compared to antidepressants for the treatment of adults with moderate to severe IBS-C who have previously received antispasmodics and/or laxatives from the perspective of the Scottish National Health System (NHS). **METHODS:** A Markov model was created to estimate costs and QALYs over a 5-year time horizon from the perspective of NHS Scotland. Health states were based on treatment satisfaction (satisfied, moderately satisfied, not satisfied) and death. Transitions between states were based on satisfaction data from the linaclotide pivotal studies (MCP-103-302 and LIN-MD-31) and Scottish general all-cause mortality statistics. Treatment costs were calculated from the British National Formulary. NHS resource use and disease-related costs for each health state were estimated from Scottish clinician interviews in combination with NHS Reference costs. Quality of life was based on EQ-5D data collected from the pivotal studies. Costs and QALYs were discounted at 3.5% per annum. Uncertainty was explored through extensive deterministic and probabilistic sensitivity analyses. **RESULTS:** Over a 5-year time horizon, the additional costs and QALYs with linaclotide were £659 and 0.089, resulting in an incremental cost-effectiveness ratio of £7,370 per QALY versus antidepressants. Results were most sensitive to health state transitions probabilities, NHS resource use assumptions and health state utilities. Threshold analyses showed that the effectiveness of linaclotide would have to be at least 11% lower than the base case to exceed a willingness-to-pay threshold (WTP) of £20,000 per QALY. Based on the probabilistic sensitivity analysis, the likelihood that linaclotide was cost-effective at a WTP of £20,000 per QALY was 74%. **CONCLUSIONS:** Linaclotide is a cost-effective treatment for adults with moderate to severe IBS-C who have previously received antispasmodics and/or laxatives.

PGI28

COST-EFFECTIVENESS OF HEPATITIS C VIRUS (HCV) TREATMENT WITH TELAPREVIR/PEGYLATED INTERFERON ALPHA/RIBAVIRIN TRIPLE THERAPY VERSUS WAITING FOR NEW REGIMENS IN FRANCE

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OBJECTIVES: To assess the cost-effectiveness of treating chronic HCV infection (genotype 1) with currently available telaprevir+pegylated interferon alpha/ribavirin (TPR) compared to waiting for new regimens with improved efficacy (hypothetical treatment assumed) currently in development from the French health care perspective. **METHODS:** A Markov model tracked the adult naïve HCV+ French population over a lifetime horizon. Model health-states are defined by METAVIR fibrosis stage (F0-F4) and complications of advanced HCV (decompensated cirrhosis, hepatocellular carcinoma, liver transplant, and death). During each 1-year cycle, individuals may remain in the current health-state, respond to treatment or progress, at probabilities determined by disease status, age at infection, current age, gender, and treatment received. Individuals were eligible for treatment in F2-F4. Transition probabilities, treatment efficacy, health-state utilities, resource utilization and costs were derived from published literature and standard French sources. The efficacy of a new hypothetical treatment regimen was based on currently published results; cost for the new treatment was assumed at €50,000 for a full treatment (excluding PR backbone). **RESULTS:** A treatment lag of 1, 2, and 3 years resulted in 142,777 individuals, 140,417 individuals, and 137,930 individuals being treated by the new regimen, respectively, versus 145,010 with immediate TPR treatment. The new treatment option resulted in additional life years saved (range 11,230-27,536), QALYs gained (range 12,528-29,359), and prevented more HCV-related deaths (range 3,839-5,756). Total costs incurred were higher for the new regimen versus TPR, from the health care perspective. ICERs were €58,294.49/QALY, €73,295.59/QALY, and €107,403.02/QALY gained for a 1, 2, and 3 year treatment lag, respectively. **CONCLUSIONS:** These findings suggest waiting for new regimens currently in development should not be the most efficient choice to be considered by French Health care system. Waiting for new treatments should yield better clinical outcomes, but with higher costs and ICERS that may be challenging for the payer.

PGI29

CROHN'S DISEASE: AN ECONOMIC ASSESSMENT OF BIOLOGICAL DRUGS IN ITALY

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OBJECTIVES: This study had a dual objective: verify the improvements in quality of life (QoL) due to biological drugs administration and evaluate their cost-effeffectiveness versus the standard steroid-based therapy in Crohn's Disease (CD). High-cost biological drugs' efficacy is well-established, but they still lack of cost-effectiveness studies. **METHODS:** A survey was prepared with clinicians and pharmacoeconomists and administered in 9 centers in Italy. The questionnaire was set up to detect QoL through a Visual Analogue Scale and EQ-5D and to assess patients' profile (age, gender, job) and clinical features (time-to-first diagnosis, current and at-diagnosis Montreal classification, current and at-diagnosis treatments, past surgical procedures, hospitalizations). Collected data were then used in a statistical regression model and an economic assessment complete of probabilistic sensitivity analysis was performed comparing costs and utilities of the considered treatments. **RESULTS:** A total of 348 questionnaires were collected, giving back a

population with a mean age of 42, 52% male, 58% actively working, 52% undergone surgical interventions, and 66% being already administered previous therapies. The mean number of outpatients visits was 4.15/year, with 0.23 hospitalizations/year. At diagnosis, the 55% of patients were treated with steroids, while only the 3% with biological drugs. At the time of survey administration, the 9% of patients were treated with steroids, and the 50% with biological drugs. The statistical model showed a significant QoL improvement due to biological drugs therapy of about 6%. The economic assessment showed biological drugs to be cost-effective only in more severe settings of patients (€ 26.000 – 38.000 /QALY), but not in mild and moderate CD (€ 58.000 to 328.000 /QALY). **CONCLUSIONS:** The results of the analysis, based on simulation models and real practice data, are consistent with evidences from other countries and thus biological drugs can be considered a good health care investment in severe cases of CD.

PGI31

IS THE USE OF ESOMEPRAZOLE IN GASTROESOPHAGEAL REFLUX DISEASE A COST-EFFECTIVE OPTION IN POLAND?

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OBJECTIVES: To compare the cost-effectiveness of therapy of different forms of GERD with esomeprazole and other proton pump inhibitors (PPIs) in Poland. **METHODS:** Results of clinical trials with esomeprazole in comparison with equivalent doses of other PPIs in the treatment of erosive esophagitis (EE - 6 RCTs), non-erosive reflux disease (NERD – 1 RCT) and GERD maintenance therapy (2 RCTs) were systematically reviewed. Meta-analysis was conducted as appropriate, relative risk values were calculated. Cost data derived from Polish Ministry of Health and pharmacies in Wroclaw. Cost effectiveness ratios and incremental cost effectiveness ratios were assessed for 100 patients. **RESULTS:** In the treatment of EE esomeprazole was significantly more effective than other PPIs. For 4 weeks therapy ICER values (esomeprazole 40 mg vs. omeprazole 20 mg and pantoprazole 40 mg) were 614 PLN and 906.33 PLN respectively if original and generic esomeprazole products were taken into account and 118.22 PLN and 162.67 for generics. For 8 weeks therapy ICER values (esomeprazole 40 mg vs. omeprazole 20 mg, lansoprazole 30 mg and pantoprazole 40 mg) were: 430.45 PLN, 329.47 PLN and 325.33 PLN (for generics and original esomeprazole) and 1869.58 PLN, 2677.89 PLN and 1812.67, respectively for generics. Differences in effectiveness of NERD therapy with esomeprazole and other PPIs were not statistically significant. The replacement of pantoprazole 20 mg with more effective esomeprazole 20 mg in the 6-month maintenance therapy was associated with a marginal cost of 3078.01 PLN (only generics included) and 4590.91 PLN (for original esomeprazole and generics) respectively. **CONCLUSIONS:** 1) For 4 and 8 weeks therapy of EE esomeprazole has to be recognized as a cost-effective option. 2) In the NERD treatment the choice of PPI should be based on the price of medicament. 3) The use of esomeprazole in GERD maintenance therapy is associated with a very high ICER.

PGI32

COMPARATIVE ECONOMIC ANALYSIS OF RETREATMENT STRATEGIES FOR HCV GENOTYPE 1 PATIENTS IN RUSSIA

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OBJECTIVES: To assess the cost-effectiveness of retreatment with pegylated interferon and ribavirin in combination with boceprevir of HCV genotype 1 patients, who failed to respond to previous treatment, in comparison with absence of retreatment and retreatment with pegylated interferon and ribavirin. **METHODS:** We performed cost-effectiveness analysis. Based on the published data we modeled the number of long-term unfavorable outcomes of HCV (liver cirrhosis, hepatocellular carcinoma and death) in the hypothetic cohort of HCV genotype 1 patients following one of three retreatment strategies: "no treatment" (NT), "peginterferon+ribavirin" (PR) and "peginterferon + ribavirin + boceprevir" (PRB). We have evaluated direct medical costs for a short-term (only cost of HCV retreament) and for a long-term (costs of medical care for adverse outcomes) periods for all strategies. Costs were estimated on the basis of average price for the drugs and reimbursement rates for medical services in the compulsory medical insurance system. Incremental cost-effectiveness ratio (ICER) for PR and PRB strategies vs NT were calculated as additional cost per unfavorable outcome avoided. **RESULTS:** It is expected that in hypothetic cohort of 10000 HCV genotype 1 patients 58,1% would fail to respond to the treatment. The estimated costs of retreatment for this group were EURO 69,07 mln in case of PR strategy and EURO 235,58 mln for PRB. The cumulative number of unfavorable outcomes of HCV during 25-year period would be 5075 cases for NT strategy, 4262 for PR and 2012 for PRB. The long-term costs of NT strategy were EURO 205,35 mln, EURO 168,37 mln in case of PR strategy and EURO 81,4 mln for PRB. ICER for PR strategy was EURO 44532 and for PRB - EURO 36379 per unfavorable outcome avoided. **CONCLUSIONS:** The use of PRB strategy is efficient as it allows reducing the number of unfavorable outcomes of HCV at a lesser cost.

PGI33

COST-UTILITY ANALYSIS OF LINACLOTIDE IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME WITH CONSTIPATION IN BELGIUM

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OBJECTIVES: Linaclotide is the first drug that received EMA approval in the management of irritable bowel syndrome in its constipation form (IBS-C). We aimed at estimating the cost-utility of linaclotide, compared to standard of care (SoC) in Belgium. **METHODS:** The analysis was conducted using data from a 6-month randomized trial of linaclotide 290µg once daily (N=401) versus placebo (N=403), which provided monthly EQ-5D measures, treatment duration, adverse events (diarrhoea) and responder status (abdominal pain/discomfort improvement ≥ 30% from baseline). Belgian EQ-5D tariffs were used to estimate utilities and trapezoidal rule to estimate QALYs. A Delphi panel including 6 general practitioners and 5 gastroenterologists provided the resource use for IBS-C patients in different treatment phases: controlled with 2nd line or new drug else non-responders. Patient-level costs were applied using first-order Monte-Carlo simulation (gamma distribution function; per treatment arm and responder status; health care payer perspective). A stopping rule was implemented at 4 weeks for linaclotide non-responders. A non-parametric bootstrap with 1000 replications was performed. The 2012 Belgian GDP per capita (€34,000) was used as willingness-to-pay threshold. **RESULTS:** The responder rate at 4 weeks was 54.6% with linaclotide vs. 35.5% with SoC. There was on average 0.0129 QALYs gained per linaclotide patient vs SoC at 6 months (0.385 vs. 0.372), with an incremental cost of €95 (€1,376 vs. €1,280). The incremental cost-effectiveness ratio of was €7,364/QALY. The diarrhoea costs were higher with linaclotide (+€19.4) while savings were observed in clinical management (-€132.2) compared to SoC. Using a willingness-to-pay threshold of €34,000/QALY, 66% of the simulations were cost-effective. **CONCLUSIONS:** Due to improvements in abdominal pain/discomfort complaints in patients receiving linaclotide, savings were generated in the clinical management of IBS-C compared to SoC. Using the GDP per capita as willingness-to-pay threshold, linaclotide seems a cost-effective alternative to today SoC of IBS-C in Belgium.

PGI34

COST-EFFECTIVENESS OF CAPSULE ENDOSCOPY (PILLCAM®) IN THE DIAGNOSIS OF SMALL BOWEL CROHN'S DISEASE

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OBJECTIVES: Capsule endoscopy (CE) is a minimally invasive endoscopic technology that uses a disposable capsule containing a small camera to monitor and diagnose disorders of the gastrointestinal tract such as Crohn's disease and obscure gastrointestinal bleeding. This study examines cost-effectiveness of CE (PillCam®, Given Imaging) for the diagnosis of small bowel Crohn's disease in Australia. **METHODS:** A modelled cost-utility analysis of CE vs. no CE followed by empiric treatment is performed. The population under consideration consists of patients with a clinical suspicion of Crohn's disease despite non-confirmatory results with prior endoscopic/radiologic tests. Due to a lack of alternative diagnostic options, many of these patients currently receive empiric treatment, whereby a diagnosis is achieved based on long-term response to therapy for Crohn's disease. CE increases the proportion of patients who receive a confirmed diagnosis for Crohn's disease or for other bowel conditions (represented by irritable bowel syndrome in the model), thereby allowing more patients to promptly receive a correct treatment and thus improving the down-stream treatment effectiveness. The administration of correct and effective treatment, as aided by CE, thus produces additional QALYs and potential cost savings, which are captured by the current model. The model has a 12-month time horizon and takes the perspective of Australian health care system. **RESULTS:** CE is estimated to produce 0.057 additional QALYs over the 12-month period. The additional cost of CE is in part offset by cost savings arising from the improved treatment selection. The incremental cost-effectiveness ratio (ICER) is estimated to be $23,672 per additional QALY. **CONCLUSIONS:** The current model suggests CE is highly cost-effective. Importantly, the target patient population currently experience a unique and special unmet clinical need because the currently funded endoscopic/radiologic technologies are unable to provide a confirmed diagnosis. The evidence for cost-effectiveness clearly supports that CE represents good value for money.

PGI35

THE COST-UTILITY OF FIDAXOMICIN AS COMPARED TO CURRENT STANDARD TREATMENT IN THE MANAGEMENT OF CLOSTRIDIUM DIFFICILE INFECTIONS IN BELGIUM

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OBJECTIVES: Clostridium difficile infection (CDI) is one of the most common hospital acquired infections in industrialised countries. CDI is responsible for severe morbidity, partly driven by the high proportion of patients experiencing a recurrence after an initial successful response to treatment. In Belgium, CDI incidence and mortality has more than doubled between 1998 and 2007. The aim of this study was to assess the cost-utility of fidaxomicin as compared to current standard treatment for managing CDI in Belgium. **METHODS:** A Markov model with a 1-year time horizon and 10-day cycles was developed to compare fidaxomicin, metronidazole and vancomycin in patients with all CDI and two subpopulations (severe CDI and first recurrence of CDI). Clinical data from two pooled published phase-3 trials (fidaxomicin vs. vancomycin) were used along a mixed treatment comparison of fidaxomicin vs. metronidazole. Treatment paths and data input were approved during an advisory board. Costs of first episode and recurrent CDI hospitalizations were taken from the IMS Hospital Disease Database. Cost per quality-adjusted life-year (QALY) gained was calculated from the health care payer perspective. **RESULTS:** The model showed cost savings and QALY gained versus vancomycin and metronidazole. Fidaxomicin versus an average of these comparators delivered benefits for all CDI patients (-1,100€; 0.008 QALY), for severe CDI (-1,300€; 0.009 QALY) and for first recurrence CDI (-1,500€; 0.009 QALY). One-way sensitivity analyses revealed that time horizon and the odds ratio of recurrence with fidaxomicin had most affect on the results. Applying a cost-effectiveness threshold of €30,000 per QALY gained, probabilistic sensitivity analysis showed acceptable cost-effectiveness in 80% of all CDI cases. **CONCLUSIONS:** Based on the available clinical data the model showed that fidaxomicin dominates vancomycin and metronidazole generating additional QALYs with cost-savings not only in patients with all CDI, but also in subpopulations with severe CDI or a first recurrence.

PGI36

THE COST EFFECTIVENESS OF PEGINTERFERON ALFA AND RIBAVIRIN FOR THE TREATMENT OF HEPATITIS C IN CHILDREN AND YOUNG PEOPLE

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OBJECTIVES: To assess the cost-effectiveness of peginterferon α-2a and peginterferon α-2b in combination with ribavirin compared to best supportive care (BSC), for the treatment of chronic hepatitis C virus (HCV) in children and young people aged 3 to 17 years. **METHODS:** A Markov state-transition economic model of chronic HCV in children and young people was developed that extrapolated the impact of sustained virological response (SVR) on life expectancy, quality-adjusted life expectancy and lifetime costs. The model was adapted from one previously developed for adults. A systematic review was conducted of the clinical effectiveness of the treatments, and the health related quality of life for patients with hepatitis C. Uncertainty was explored through probabilistic and deterministic sensitivity analyses. **RESULTS:** Seven studies were identified that were relatively small and of generally poor quality. Estimates of SVR were similar for peginterferon α-2a (60%) and peginterferon α-2b (58%), whilst the SVR for no treatment was assumed to be zero. From this model, peginterferon alfa (α-2a or α-2b) in combination with ribavirin was more effective and cheaper than BSC. Sensitivity analyses suggest that the results were generally robust to all changes to the structural assumptions and input parameters. The model results were most sensitive to changes to the discount rate, time horizon, SVR and baseline fibrosis of the cohort. **CONCLUSIONS:** Treatment of children and young people with peginterferon alfa (α-2a or α-2b) and ribavirin may be an effective therapy. Peginterferon alfa (α-2a or α-2b) in combination with ribavirin is cost-effective compared with BSC. However, the available evidence is of poor quality. The views expressed in this paper are those of the authors and do not necessarily represent the views or policies of the UK HTA programme or Department of Health.

PGI37

COST-UTILITY ANALYSIS OF TELAPREVIR IN COMBINATION WITH PEGINTERFERON ALPHA AND RIBAVIRIN IN PREVIOUSLY UNTREATED PATIENTS WITH CHRONIC HEPATITIS IN A ROMANIAN SETTING

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OBJECTIVES: To estimate the cost-effectiveness in Romanian setting of triple therapy with Telaprevir and Peginterferon/Ribavirin (TVR+PR) compared with PR alone in previously untreated patients with hepatitis C virus (HCV) infection from the third payer - National Health Insurance Agency (NHIA). **METHODS:** We used the published data of efficacy from large international trials and published Markov models to estimate the cost-effectiveness of this new HCV serine protease inhibitor (telaprevir) using the specific local cost and epidemiological data. The superior results shown by Jacobson IM et all in ADVANCE trial - (Telaprevir for previously untreated chronic hepatitis C virus infection) for telaprevir - 75% sustained virologic response compared with 44% for PR alone. The discount rate was 3% for both cost and efficacy. Cost were extracted from NIHA tarrifs, Minister of Health drugs price catalog and from previous published data. The reference patient was a 45-year-old male with chronic liver disease due to chronic HCV infection. Time horizon was set patient life time. The clinical outcomes and Utilities for all health states were taken from ADVANCE phase-3 trial. The comparator was Peginterferon 2alfa with ribavirin. The effectiveness was measured in quality-adjusted life years (QALY). The cost of secondary drug reactions were not included in the model. **RESULTS:** Incremental cost effectiveness ratio (ICER) for telaprevir in combination with PR compared to PR alone was 23291 €/1 gained QALY. **CONCLUSIONS:** As in Romania HTA is only at the beginning, health authorities has to evaluate the most cost-effective strategy to follow for treatment of patients with chronic hepatitis as ICER of telaprevir in combination with PR compared with PR alone is reaching or is above the level recommended by Word Health Organisation as upper threshold (3 GDP/capita – Romania's GDP/capita is 6200Euro). Further CUA should be performed, including for guided therapy and treatment designated to previous treated patients.

PGI38

THE CURRENT MANAGEMENT AND COSTS OF IRRITABLE BOWEL SYNDROME WITH CONSTIPATION IN BELGIUM: A 2-ROUND EXPERT SURVEY

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OBJECTIVES: Patients suffering from irritable bowel syndrome (IBS) with constipation (IBS-C) receive laxatives as first line therapy. In spite of these laxatives most of them experience failure. We aimed at describing the current management and its costs of Belgian IBS-C patients who failed first line treatment. **METHODS:** A 2-round Delphi panel was conducted including general practitioners (GP) and gastroenterologists. The type and frequency of medical resources used per year as second-line IBS-C therapy (consultations, exams/tests, drugs, hospitalizations) were collected, reflecting the expert's own practice in the first round and finding a Belgian consensus in the second round. Two patients' profiles were defined: second line current management and third line management in case of second line failure. Unit costs (2012 INAMI/RIZIV tariffs) were assigned to the resources used to calculate a cost per patient-year and a range based on the distribution of experts' answers. **RESULTS:** Eleven experts participated (6 GPs/5 gastroenterologists). The drugs prescribed in second line were laxatives (71.4%, mainly osmotics), spasmolytics (72.2%), pain killers (11.5%) and antidepressants (6.0%). There were 7.7 consultations per patient-year on average (GP: 5.3; specialists: 2.4). Emergency room visits occurred in 10.4% and diagnostic tests included thyroid function (79.1%), rectosigmoidoscopy (39.8%) and abdominal echography (36.8%). There were 0.97 IBS-related admissions to hospital per patient-year. After a second line failure, resource use increased with more laxatives (75.5%), antidepressants (24.6%) and pain killers (17.3%), 11.6 consultations (GP: 7.5; specialist: 4.1), 14.5% emergency room visits and 1.25 hospitalizations. Diagnostic tests were also more frequent (rectosigmoidoscopy: 49.3%; abdominal echography: 43.6%) except thyroid function (70.0%). The annual cost of second line was €2,114 [1,509;2,819] versus €2,920 [2,072;3,917] after second line failure. Hospitalizations accounted for about 75% of the costs. **CONCLUSIONS:** IBS with constipation leads to significant resource use and high costs certainly in case of second line treatment failure.

GASTROINTESTINAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PGI39

AGREEMENT BETWEEN CHILD AND PARENT SYMPTOM DIARY RESPONSES IN CHRONIC CONSTIPATION (CC) AND IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C): IMPLICATIONS FOR THE MEASUREMENT OF SYMPTOMS IN YOUNG CHILDREN

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OBJECTIVES: Using patient-reported and observer-reported outcome measures to assess symptoms in children is challenging. While the child is arguably the most 'valid' reporter, parents may provide more reliable responses. Our aim was to assess the agreement in child and parent ratings of CC/IBS-C symptoms collected through an electronic daily diary (eDiary). **METHODS:** Separate child and parent eDiaries were developed to assess CC/IBS-C symptoms based on concept elicitation interviews with 64 children and 75 parents. The eDiaries were completed by 36 children (aged 6-11) and 30 parents for 5-9 days prior to cognitive debriefing interviews. eDiary data were compared for five symptoms: abdominal pain, bowel movement (BM) frequency, stool form/consistency, straining and rectal pain during defecation. **RESULTS:** There were moderate to high levels of agreement (children/parents selecting the same level of response on a given day) for all items, including 66.9% agreement for BM frequency; 70.2% for stool form and 72.5% for rectal pain. Children's reports of their 'tummy hurting' were consistent with parents seeing their child holding his/her tummy (68.5% agreement) and parents being told by the child that his/her tummy hurt (76.4% agreement). Children's reports of straining were consistent with parents observing their child making a face (60.4% agreement) and hearing their child grunt (52.3% agreement) during defecation. Across all symptoms, agreement was higher for 6-8 year old children and their parents (mean 76.9% agreement) compared to 9-11 year old children and their parents (mean 58.4%). **CONCLUSIONS:** The results present evidence of moderate to strong agreement between children's and parents' reports of core CC/IBS-C symptoms. Lower levels of agreement in ratings amongst 9-11 year old children and their parents may be due to parents being less aware of their child's symptoms.

PGI40

VALIDATING THE UNIDIMENSIONAL FATIGUE IMPACT SCALE (U-FIS) FOR USE IN CROHN'S DISEASE

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OBJECTIVES: Fatigue is usually defined as a feeling of exhaustion, lack of energy or tiredness and affects many aspects of daily living. Crohn's Disease (CD) is often associated with severe fatigue. The Fatigue Impact Scale (FIS) was developed to determine the mental and physical impacts of fatigue. It has been simplified and shortened to 22 items and shown by Rasch analysis to be unidimensional. This version is called the U-FIS. The study was designed to determine the validity of the U-FIS when used with CD patients. **METHODS:** CD patients were asked to complete the U-FIS and a subset of respondents completed it again two weeks later to assess test-retest reliability. Rasch analysis was applied to U-FIS data to determine unidimensionality. Construct validity was further assessed by relating scores on the U-FIS to those on the Crohn's Life Impact Scale (CLIQ) and the Nottingham Health Profile (NHP). **RESULTS:** A total of 158 CD patients (36.1% female; aged 16-79 years (mean: 42.4; SD 15.0)) completed the U-FIS, with 103 completing it a second time. Overall fit to the Rasch model was confirmed ($p = 0.61$) and no items misfit. Internal consistency (0.98) and reproducibility (test-retest reliability = 0.88) for the U-FIS were good. U-FIS scores correlated 0.79 with those on the CLIQ indicating the importance of fatigue to quality of life. U-FIS scores were also related as expected with NHP section scores. **CONCLUSIONS:** The U-FIS is a reliable and valid instrument for measuring fatigue in Crohn's Disease. These findings replicate those found with the use of the measure with patients who have Multiple Sclerosis. The U-FIS is valuable as it provides a holistic index of the impact of fatigue from the patient's perspective. The measure may prove valuable for use with patients who have a wide variety of chronic conditions.

PGI41

VALIDATION OF THE CROHN'S LIFE IMPACT QUESTIONNAIRE (CLIQ), THE FIRST PATIENT-REPORTED OUTCOME MEASURE SPECIFIC TO ADULTS WITH CROHN'S DISEASE

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OBJECTIVES: The study was designed to identify the final CLIQ – the first patient-reported outcome measure specific to adults with Crohn's Disease (CD) and determine its unidimensionality, reproducibility and construct validity. The measure has two scales; Activity limitations and needs-based Quality of Life (QoL). **METHODS:** CD patients were sent a package consisting of the CLIQ, the Nottingham Health Profile (NHP), the Unidimensional Fatigue Impact Scale (U-FIS) and a demographic questionnaire. A subset of respondents received a second questionnaire package 2 weeks later. Rasch analysis was applied to responses for item reduction and assessment of unidimensionality. Assessments of internal consistency, test-retest reliability and construct validity were also undertaken. **RESULTS:** The CLIQ was completed by 273 CD patients (65.6% female; aged 16-79 years (mean: 43.9; SD 15.1).

101 patients completed and returned the second package. Both scales had good overall fit to Rasch model (Chi^2 p = 0.35; Chi^2 p = 0.13 for activity limitations and QoL respectively) and unidimensionality of the scales was confirmed. No evidence of DIF by age or gender was found and the scales had good coverage of the measurement constructs. Internal consistency was 0.91 for the QoL scale and 0.93 for Activity limitations. Good reproducibility was observed (QoL 0.91, Activity limitations 0.89) and both scales were able to distinguish between self-perceived disease severity and general health status groups (p<.01). **CONCLUSIONS:** The CLIQ is the first CD-specific PRO and is truly patient-based as its content was generated directly from CD patients. It is well accepted, completed by patients and is easy to score. Both scales measure a clear unidimensional construct and generate valid total scores. The scales have good consistency, reproducibility and promising construct validity. Studies are planned to assess responsiveness. The CLIQ will prove to be an important tool for assessing Activity limitations and QoL in clinical audit, practice and trials.

PGI42

THE RELATIONSHIP BETWEEN IRRITABLE BOWEL SYNDROME WITH CONSTIPATION SYMPTOMS AND HEALTH-RELATED QUALITY OF LIFE

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OBJECTIVES: To identify symptoms significantly impacting health-related quality of life (HRQOL) and how changes in symptoms explain variability in HRQOL among adult patients with irritable bowel syndrome with constipation (IBS-C). **METHODS:** IBS-C symptom and HRQOL data were pooled from two Phase 3 trials (n=1602) assessing efficacy and safety of linaclotide, a guanylate cyclase-C agonist approved for adult treatment of IBS-C in the US and moderate to severe IBS-C in Europe. IBS-C symptoms measured included abdominal (bloating, cramping, discomfort, fullness, pain) and bowel (spontaneous bowel movement [SBM] and complete SBM [CSBM] frequency, stool consistency, and straining) symptoms. HRQOL measures included: a disease-specific Irritable Bowel Syndrome-Quality of Life questionnaire (IBS-QOL), and generic HRQOL measures, the EuroQol-5D (EQ-5D) and Short Form-12 (SF-12). Analysis of variance evaluated relationships between Week 12 change from baseline in IBS-C symptoms and HRQOL, controlling for demographics and baseline HRQOL. **RESULTS:** Changes in IBS-QOL overall score were most significantly impacted by changes in abdominal fullness, cramping, and straining (beta coefficients: -1.1, -1.3, -1.7, respectively). The full model explained nearly half of the changes in IBS-QOL (R-Square: 0.42). Changes in EQ-5D were primarily driven by changes in abdominal bloating, cramping, and straining (beta coefficients: -0.009, -0.009, -0.011, respectively, R-Square: 0.49). Changes in SF-12 physical and mental component summaries (PCS and MCS) were best explained by changes in bloating, cramping, and straining (beta coefficients: -0.41, -0.34, -0.53, respectively; R-square: 0.42), and abdominal fullness and CSBM frequency (beta coefficients: -0.59 and 0.26, respectively; R-square: 0.35), respectively. **CONCLUSIONS:** Improvements in abdominal cramping and straining at Week 12 compared to baseline were associated with improvements in HRQOL as measured by the IBS-QOL, EQ-5D and SF-12 PCS. Improvements in abdominal bloating and fullness, and increases in CSBMs were also associated with HRQOL improvements. Targeting improvement in specific IBS-C symptoms may result in increased patient HRQOL.

PGI43

THE IMPACT OF TYPE OF LIVER CONDITIONS ON THE PATIENTS' HEALTH RELATED QUALITY OF LIFE

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OBJECTIVES: Liver diseases (LDs) have a high impact on morbidity, mortality and health-related quality of life (HRQoL). LDs may have different impact on patients' HRQoL. The aim of our study was to evaluate HRQoL in the major liver conditions: hepatitis B(HBV), hepatitis C(HCV), cirrhosis(compensated and decompensated), hepatocellular carcinoma(HCC), autoimmune hepatitis(AIH), primary biliary cirrhosis(PBC), primary sclerosing cholangitis(PSC), NAFLD/NASH, patients in the liver transplant list and post-transplant. **METHODS:** A naturalistic, prospective, multicenter study has been conducted to generate and validate a set of health care outcomes indicators for the major liver conditions. LDs patients (age>18 years) were enrolled in 3 major Italian medical centers and are still being followed up (median f-up:13 months). Within this study, socio-demographic, clinical and HRQoL were collected using the EQ-5D-3L. The HRQoL data was analyzed dividing the patients in sub-groups according to the most recently diagnosed and most severe condition. **RESULTS:** We enrolled 3,217 patients, 64.8% male, aged 19-91 (median=61) years; 95.0% of them filled in the EQ-5D at baseline visit. Patients in the HCC group were 22.6%; while in the AIH group were 1.6%. The highest percentage of problems in Mobility dimension (39.2%) was reported by decompensated cirrhosis sub-group, the highest percentage in Self-care (22.6%) and Usual Activities (47.1%) by patients in liver transplant list, in Pain/Discomfort (59.2%) by AIH and in Anxiety/Depression (57.8%) by PBC. The HBV sub-group reported the best HRQoL with a mean EQ-5D VAS of 77.8; while AIH and listed for liver transplant patients reported the worst HRQoL levels (mean EQ-5D VAS=67.7 and 63.5, respectively). **CONCLUSIONS:** our study shows how HRQoL is different between LDs and how it is negatively related with the clinical severity. Understanding the different impact of LDs on the patients' HRQoL could help physicians and decision makers to better estimate the burden of these conditions and to improve the quality of care.

PGI44

ECONOMIC AND QUALITY-OF-LIFE BURDEN OF MODERATE TO SEVERE IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C) IN SPAIN: INTERIM ANALYSIS OF THE IBIS-C STUDY

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OBJECTIVES: The IBIS-C study, currently ongoing, is the first to assess the burden of IBS-C in 6 European countries (France, Germany, Italy, Spain, Sweden, UK) . We present an interim analysis of the retrospective data from Spain. **METHODS:** This is an observational, retrospective-prospective (±6-months(m)) study in patients diagnosed in the last five years of IBS-C (Rome-III criteria) of moderate-to-severe degree (IBS-Symptom Severity Score(IBS-SSS)≥175). Quality-of-life(QoL) was assessed with the EuroQoL-5D(EQ-5D) and IBS-QoL. **RESULTS:** We included 46 patients (62% severe, mean(±SD) 44.6±12.2 years, 83% women, time since diagnosis 2.8±3.6 years). According to IBS-SSS, 94% had abdominal pain in the last month (62% of time) and 85% abdominal distention. Other prevalent symptoms were: constipation (96%), abdominal discomfort (72%) and bloating (59%). Mean IBS-QoL was 46±23, on a scale 0-100 (worst QoL), and the most affected domains were "food avoidance" (mean:64) and "health worry" (60). Mean EQ-5D was 51±20, on a scale 0-100 (best QoL), and 93% and 70% of patients, respectively, reported problems in pain/discomfort and anxiety/depression. In the previous 6m, 83% of patients consulted a primary care physician, and 89% a specialist (mostly a gastroenterologist)(mean(95%CI):2.8(1.4-4.3) and 2.0(0.9-3.1) visits, respectively). 20% of patients required emergency department visits or hospitalization (mean stay:1.3(0.6-1.9) days). 76% of patients underwent a diagnostic test (mean:2.1(1.3-2.9) tests). 89% of patients took medication (63% prescription drugs and 54% OTC medications), 26% received complementary therapies. The mean direct costs per patient for the National Health System(NHS) were €1,025/6m(549-1627) and the mean costs for the patient were €200/6m. 17% of patients had sick leave(mean:3.5 leaves; mean duration:58 days) and 46% had productivity losses(mean:49 hours). Mean indirect costs were €991/6m. Total costs amounted to €2216/6m. **CONCLUSIONS:** Moderate-to-severe IBS-C has a great impact on health care resource utilization and productivity of patients, and the results suggest significant costs to the NHS and society. QoL can be severely affected.

PGI45

HEALTH-RELATED QUALITY OF LIFE (HRQL) IN CHRONIC HEPATITIS C (CH-C) PATIENTS TREATED WITH SOFOSBUVIR CONTAINING INTERFERON-FREE REGIMENS

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OBJECTIVES: Interferon-containing regimens for treatment of CH-C are associated with substantial side effects and significant impairment in HRQL. The aim of this study is to evaluate the effect of Interferon-free regimens on HRQL. **METHODS:** Three validated HRQL instruments, namely, Medical Outcomes Study-Short Form 36 (SF-36), CLDQ-HCV (Chronic Liver Disease Questionnaire-HCV) and FACIT-F (Functional Assessment of Chronic Illness Therapy-Fatigue) were administered to previously untreated CH-C patients (N=201) treated with interferon-free regimen (Sofosbuvir+Ribavirin) at baseline, during, and after treatment. Patients were randomized to receive 16 weeks of active treatment or 12 weeks of active treatment followed by 4 weeks of blinded placebo. Historical data for interferon containing regimens were available for all these questionnaires. **RESULTS:** Small decrements in most of the domains of all HRQL metrics were noted at weeks 4, 12, and 16 of active treatment regardless of the study arm (maximum observed decrements in HRQL summary scores between 3.3% and 8.8% compared to baseline, p<0.05). There were no differences between the study arms at all time points (p>0.05). These decrements were substantially better than historical data available for interferon-containing regimens (between 10.4% and 15.2% for the same scores, p<0.0001). By week 4 of follow-up after treatment, some of the social and emotional well-being-related domains of FACIT-F improved significantly compared to their own baseline (by 4.9-6.0%, p<0.05). At the end of 12-week follow-up, all those domains as well as domains of CLDQ-HCV (activity, emotional, worry, systemic domains) further improved (by 3.8-11.2%, p<0.05), while physical and functional well-being-related domains of FACIT-F and SF-36 returned to their baseline levels or improved moderately (by 3.1-8.3%, p<0.05). **CONCLUSIONS:** The impairment in HRQL in CH-C patients treated with an interferon-free regimen is minimal and diminishes soon after the end of treatment. This interferon-free regimen is associated with substantially better HRQL as compared to interferon-containing regimens.

GASTROINTESTINAL DISORDERS – Health Care Use & Policy Studies

PGI46

SYSTEMATIC LITERATURE REVIEW IN MODERATE TO SEVERE ULCERATIVE COLITIS

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OBJECTIVES: Ulcerative colitis (UC) is a chronic inflammatory bowel disease. The objective of this systematic literature review (SLR) was to examine the evidence on the efficacy and safety of all available pharmacological interventions for moderate to severe UC. **METHODS:** A systematic literature search using a predefined strategy was performed in Medline®, EMBASE®, Medline-In-Process, Cochrane Library and BIOSIS from 1966 to 2013, to identify randomized controlled trials (RCTs) concerning the efficacy and safety of available treatments in adult patients with moderate to severe UC. Studies reporting on mild-moderate UC patients were included if they reported results for the moderate subgroup separately. No language restrictions were applied to the search. **RESULTS:** A total of 4344 abstracts were screened based on the predefined selection criteria, of which 4279 were excluded. In total, 65 publications, reporting results from 65 RCTs were included (49 double blind),

examining aminosalicylates (n=23), corticosteroids (n=10), immunosuppressants (n=15), biologics (n=16) and kinase inhibitors (n=1). Baseline patient characteristics, study design and outcomes were extracted, including: adverse events (AE) (reported in n=24 studies), serious AE (n=25), deaths (n=23), clinical remission (n=49), clinical response (n=33) and mucosal healing (n=11). Eleven different disease activity scales and four different endoscopic scales were used. The mean age of included patients ranged from 27 to 51, and the percentage of males from 28.6% to 87.5%. Due to large differences and different scales used for reporting efficacy it is not feasible to report the range across different scales. Safety endpoints were also reported inconsistently. The results per outcome are presented in a narrative way per treatment class. **CONCLUSIONS:** A comprehensive SLR performed which identified 65 RCT reporting on the efficacy and safety of pharmacological treatments in moderate to severe UC patients. Differences in patient population, disease severity, disease activity scales and trial duration are explored and presented.

PGI47

HOW THE PRICING STRATEGY OF 2ND GENERATION HCV DIRECT ANTIVIRAL AGENTS CAN AFFECT THE NUMBER OF TREATED PATIENTS IN ITALY AND THE NATIONAL DRUG BUDGET

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OBJECTIVES: To assess the impact of new HCV drugs pricing strategy on the number of potential treated/cured patients and on the Italian Healthcare Service budget, using a simplistic model to design different scenarios for second generation direct antiviral agents (DAAs). **METHODS:** We calculated the HCV drugs budget and the number of patients for setting a base case by summing a) AIFA values for HCV dual therapy drugs to assess the number of patients currently treated; b) triple therapy number of patients estimated from AIFA budget (210.000.000€ in total). We performed budget scenarios on two variables: 1) pricing strategy of more effective DAAs; 2) total HCV drugs budget. We calculated the number of treated and responder patients, considering only genotype 1 HCV to maintain a comparability between base case and future scenarios with new DAAs. **RESULTS:** The number of patients to be cured with stable budget vs base case are: 1) 9.000 (+56% vs. base case) with parity price vs. triple therapy; 2) 7.500 (+30% vs. base case) in case of a 20% premium price that would allow 8.300 patients to be treated. Assuming to double the allocated budget from payers (420.000.000€) and to reduce the new DAAs price by a 20%, 25.000 patients will be treated and 22.500 (+291% vs. base case) will be cured. **CONCLUSIONS:** This simplified analysis shows that more effective drugs can significantly increase the number of patients who could be treated and cured. In order to support these results, efforts from both payers (higher budget) and pharma companies (lower prices) are needed.

PGI48

EXPLAINING THE INCREASED HEALTH CARE EXPENDITURES AMONG INDIVIDUALS WITH CO-OCCURRING CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND GASTROESOPHAGEAL REFLUX DISEASE: A COST-DECOMPOSITION ANALYSIS

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OBJECTIVES: The objective of this study is to examine health care expenditures associated with Gastro-esophageal Reflux Disease (GERD) among elderly with Chronic Obstructive Pulmonary Disease (COPD) and understand the explanatory factors associated with incremental expenditures associated with (GERD). **METHODS:** The study utilized retrospective cross-sectional design. Data were extracted from multiple years (2006-2009) of the Medicare Current Beneficiaries Survey (MCBS). The analytical sample consisted of community dwelling elderly individuals with COPD (n = 3,821) identified using appropriate International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. The key independent variable was defined as presence or absence of GERD. T-tests and ordinary least squares regressions (OLS) on log-transformed total health care expenditures were performed to analyze the association between health care expenditures with GERD among individuals with COPD. Blinder-Oaxaca decomposition analysis was performed to estimate contribution of factors towards explaining the excess health care expenditures. **RESULTS:** Among elderly individuals with COPD, the annual average health care expenditures were higher for those with GERD ($36,793 ± $1,387) as compared to those without GERD ($24,722 ± $800). Individuals with GERD had poorer health status, low physical activity profile, and higher rates of obesity. Furthermore, the rates of depression and anxiety were significantly higher among individuals with GERD compared to those without GERD. A decomposition technique revealed that nearly 30.9% of the incremental health care spending associated with GERD was due to the differences in characteristics such as Charlson's comorbitity score (17.5%), perceived health status (7.13%) and depression (5.85%). **CONCLUSIONS:** Our findings highlight the burden of comorbid conditions among those with COPD and GERD. This study reinforces the need to modify the care-delivery model from single-disease care approach to integrated/ multiple diseases care approach to manage the complex comorbid diseases, which may ultimately reduce the excess health care expenditures.

PGI49

DISPENSATION CHANNELS OF ANTI-TNFS IN INFLAMMATORY BOWEL DISEASE

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OBJECTIVES: In The Netherlands, the funding for some high cost drugs and particularly biologics was transferred in 2012 to hospital pharmacy dispensation channel. A European study forecast (2012-2016) shown hospital dispensation as a very effective policy to reduce budget impact of branded biologics and increase savings related to biosimilars. Two biologics (anti-TNFs) are indicated for Inflammatory Bowel Disease (IBD) in EU with different mode of administration: infliximab (Intravenous) and adalimumab (Subcutaneous). The objective of this study was to compare the dispensation channel of anti-TNFs used in IBD across European (EU) top 5 countries. **METHODS:** We analyzed dispensation conditions using IMS data from 2011 and official local official websites, France (Haute Autorité de Santé and Health insurance drugs database), Italy (Agenzia Italiana del Farmaco), Spain (Ministerio de Sanidad Servicios Sociales e Igualdad), Germany (Gemeinsamer Bundesausschuss), United Kingdom (Department of Health). **RESULTS:** In UK, Spain, Italy, both infliximab and adalimumab dispensation were restricted to hospital channel. In Germany, both infliximab and adalimumab can either be dispensed through retail and hospital channels. In France, adalimumab was available either in hospital and retail channels under exceptional status, and infliximab was dispensed through hospital channels only. The differences across countries could not be related to products labels as they are all approved under European Medicines Agency (EMA) centralized procedure. **CONCLUSIONS:** It is unlikely that the gaps observed are only related to differences in health care services organization but rather budget constraint like in UK, Italy and Spain. In Germany and France, the two leading EU pharmaceuticals markets this is not yet the case. Hospital dispensation channel of biologics and biosimilars is a new way to generate savings mainly through tenders.

PGI50

PAEDIATRIC GASTROENTERITIS: DISEASE BURDEN, COST AND LOSS OF PRODUCTIVITY OF MALAYSIAN AND VIETNAMESE PARENTS

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OBJECTIVES: The cost of paediatric gastroenteritis is poorly documented in Asia. This analysis reports findings of a survey on disease burden, cost and productivity loss caused by paediatric gastroenteritis in Malaysia and Viet Nam. **METHODS:** A survey was conducted between August 2012 and April 2013 targeting respondents in public spaces in Hanoi and Bac Giang, Viet Nam and Klang Valley, Malaysia. The surveys were self-administered and collected information on demographics, disease burden, cost and productivity loss. Descriptive analysis was conducted to report the overall findings using STATA SE 11.2. **RESULTS:** Survey questionnaires were completed by 245 and 307 respondents from Malaysia and Viet Nam, respectively. Over 90% of the respondents were parents of children below 10. Overall, 69% reported that their children experienced gastroenteritis requiring physician visits and 28% reported episodes requiring hospital admissions. Differences were noted in the treatment seeking patterns between the two countries. These differences influenced cost and productivity loss to the families of affected children. In Malaysia, a large proportion of parents (41.2%) reported hospitalisation cost to be more than USD 350 whereas in Viet Nam, a majority (74.6%) reported hospitalisation cost less than USD 34. Among these, 52.9% and 30.5% of Malaysian and Vietnamese parents paid out-of-pocket for hospital admission, respectively. The majority reported days off work of 2 to 5 days, however more parents in Viet Nam (23.7%) required greater than 6 days off work to care for their affected child compared to Malaysia (3.9%). **CONCLUSIONS:** Gastroenteritis has an impact on cost and productivity loss to parents of affected children in Malaysia and Viet Nam. However, there were several differences noted likely due to differences in GDP, health system and cultural factors.

PGI51

INFLAMMATORY BOWEL DISEASES IN ITALY: INCIDENCE TRENDS AND PATIENTS' CHARACTERISTICS

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OBJECTIVES: To assess the impact of inflammatory bowel diseases (IBD) in the Italian general population: incidence and time trends from 2003 to 2009, as well as population characteristics. **METHODS:** A retrospective observational study was conducted in Lombardy, an Italian region with about 10 million of inhabitants, using health care administrative databases of the national health care system (HS) which provides universal coverage. The main administrative databases were integrated in a data warehouse called DENALI using probabilistic record linkage. New cases of Crohn's Disease (CD) and Ulcerative Colitis (UC) were identified in the adult population between January 1, 2003 and December 31, 2009. Annual age-standardized incidence rates were computed separately for CD and UC using the population living in Lombardy at 2001 census. Moreover we evaluated patients' baseline main characteristics, coexisting chronic conditions and survival at December 31, 2009. **RESULTS:** The annual incidence rate per 100,000 person-years of IBD was 15.6 (95%CI 15.2-15.9); UC and CD incidences were 9.7 (9.4-10.0) and 5.9 (5.7-6.1) respectively. Incidence rates of both diseases were higher in men than in women. CD incidence was highest in subjects aged 20-24 (9.2, 95%CI 8.1-10.2) and decreased with age, while UC incidence was stable in the 20-65 year-old population. No time trends in UC and CD incidences were observed from 2003 to 2009, both in the whole study population and in gender and age-specific subgroups. The mean age at CD diagnosis was 44 years (±16.6 sd), which was lower than that at UC diagnosis (46 ± 16.6, $p<0.0001$). During a mean follow-up time of 3.4 years (± 2.0) 2.2% of IBD patients died. **CONCLUSIONS:** Our study provides updated estimates on current epidemiology of IBD in Italy. IBD incidence in Lombardy is lower than in northern Europe and the data confirm that UC incidence is higher than that of CD.

SENSORY SYSTEMS DISORDERS – Clinical Outcomes Studies

PSS1

INDIRECT COMPARISON OF THE EFFECT OF BIOLOGICS IN PATIENTS WITH PSORIASIS; A META-ANALYSIS OF RANDOMIZED, DOUBLE BLIND CLINICAL TRIALS IN BAYESIAN FRAMEWORK

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OBJECTIVES: The main aims of this systematic review were to identify all relevant literature on clinical efficacy for biological medications in patients with psoriasis and to conduct an up-to-date meta-analysis. **METHODS:** The following comparators were considered for this analysis: adalimumab, etanercept, infliximab, and ustekinumab. A MEDLINE search was conducted until March 2013. The Cochrane Highly Sensitive Search Strategy was applied to identify randomized controlled publications and was combined with 'psoriasis' MeSH terms and drug names. Randomized, controlled, clinical trials with adults with moderate-to-severe psoriasis where the full paper can be obtained were included. Evidences were combined in a mixed treatment comparisons in a Bayesian framework. Efficacy was measured by the 75% and 90% improvement of Psoriasis Area Severity Index (PASI) at three months were analysed. **RESULTS:** Nineteen trials were included in this indirect comparison; treatment arms with off-label dosages were excluded. Each biologic showed significantly more favourable effect than placebo with respect to any level of PASI response. Significantly more patients on infliximab treatment met PASI75 endpoint than on etanercept, adalimumab or ustekinumab, combined odds ratios (95% confidence intervals) were 5.34 (2.29-12.50), 7.49 (3.31-16.92) and 3.64 (1.62-8.20) respectively. Similarly, significantly more patients on infliximab treatment met PASI90 endpoint than on adalimumab or etanercept, odds ratios were 6.12 (1.07-34.86) and 7.78 (1.02-59.01). No significant differences in terms of PASI75 and PASI90 improvements were observed between adalimumab, etanercept or ustekinumab. **CONCLUSIONS:** All biologics demonstrated statistically significant improvements compared to placebo. This review also showed that infliximab was significantly more efficacious than other biologics.

PSS2

COMPARATIVE EFFECTIVENESS OF PEAK AND TROUGH EFFECTS OF BIMATOPROST 0.03%/TIMOLOL 0.5% PRESERVATIVE-FREE FIXED COMBINATION FOR THE TREATMENT OF OPEN-ANGLE GLAUCOMA AND OCULAR HYPERTENSION

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OBJECTIVES: To evaluate the comparative effectiveness of bimatoprost 0.03%/timolol (BTFC) 0.5% preservative-free (PF) fixed combination solution in single dose vials (BTFC PF) for the treatment of glaucoma/ocular hypertension (OHT) compared to alternative combination therapies accounting for fluctuations in intraocular pressure (IOP). **METHODS:** A systematic review was conducted to identify randomised controlled trials investigating efficacy of combination therapies for the treatment of glaucoma/OHT; where efficacy is defined as IOP change from baseline. Maximum and minimum changes in IOP were used as a representation of peak and trough effects of medication. Prostaglandin/prostamide analog and timolol monotherapy trials were also included as key connectors. A Bayesian mixed treatment comparison (MTC) analysis was used to synthesise the resulting evidence base. Supportive probability of best and rankogram summary analysis were used to position treatments within the network based on efficacy. **RESULTS:** A total of 136 studies met the pre-determined MTC inclusion criteria in total; representing 24 unique treatment arms. BTFC PF was numerically superior to all treatments (monotherapies and combination therapies; preserved and PF therapies) in lowering IOP efficacy in both peak and trough analyses. This superiority was statistically significant ($p<0.05$) for 18/23 comparisons in both analyses. Lack of evidence is the likely reason for non-significance in remaining comparisons. The probability of the BTFC formulations (preserved or PF) being the best treatments in the network was 0.94 (94% chance) in the peak analysis and 0.90 (90% chance) in the trough analysis; BTFC PF specifically had a 57% chance in the peak analysis and 62% chance in the trough analysis. No other treatments had >6% chance. Overall ranking of BTFC PF and BTFC preserved in terms of IOP-lowering efficacy was 1st and 2nd respectively. **CONCLUSIONS:** BTFC PF showed the greatest clinical efficacy of any combination- or mono-therapy in reducing IOP from baseline in patients with glaucoma and/or OHT.

PSS3

BASELINE CHARACTERISTICS AND VITREORETINAL INTERFACE FEATURES IN PATIENTS WITH VITREOMACULAR TRACTION AND MACULAR HOLE FROM THE MIVI-TRUST CLINICAL PROGRAM

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OBJECTIVES: There is limited published evidence on demographic and vitreoretinal interface (VRI) characteristics of patients with vitreomacular traction (VMT), including when associated with macular hole (VMT+MH). Establishing insights into the characteristics of untreated VMT patients may contribute to a better understanding of the burden of VMT disease. The objective of our analysis is to describe baseline patient characteristics and VRI features in patients with persistent VMT included in the phase 3 ocriplasmin studies. This analysis reports on VMT patients without MH (VMT) and VMT patients with MH (VMT+MH). **METHODS:** Two randomized, double-masked, placebo-controlled trials designed to determine efficacy and safety of ocriplasmin for the treatment of VMT comprising of 652 patients (VMT n=499; VMT+MH n=153). Baseline characteristics included patient demographics (age, gender); eye-disorder characteristics (time since diagnosis, visual acuity (VA) in study eye (SE); VA in non-study eye (NSE), presence of pseudophakia and/or ERM; VRI features (focal adhesion ≤1500 microns; min-max MH width), VFQ-25 composite score. **RESULTS:** Baseline characteristics for VMT vs. VMT+MH patients were respectively: 72.6 versus 68.7 years; 62.7% versus 75.8% female. Time since diagnosis: 268 days versus 62 days; VA: SE 66.8 versus 55.9, NSE 73.5 versus 77.8. Pseudophakes: 38.7% versus 20.9%, concomitant ERM: 46.3 % versus 15.8%. The majority of VMT patients presented with focal adhesion ≤1500 microns (69%) while VMT+MH patients presented with a min-max hole width of 272.7 microns. VFQ-25 composite score: 78.0 vs. 80.3. **CONCLUSIONS:** Baseline characteristics of the MIVI-TRUST ocriplasmin patient population show differentiations between patients with persistent VMT versus those with associated MH. This analysis establishes the representativeness of the MIVI-TRUST patient population in the context of clinical practice.

PSS4

ATOPIC DERMATITIS: EVALUATION OF 2 DIFFERENT DRUG RELATED MANAGEMENTS

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OBJECTIVES: Atopic Dermatitis (AD) is a chronic relapsing skin condition and one of the most common skin diseases worldwide. Nowadays, the prevalence of AD is estimated to be between 5%-and-30% in children. AD onset is commonly before 5years old in children. Therapeutic treatments include topical corticosteroids (CS) and long-term emollients as first-line therapy, followed by topical calcineurin inhibitors. Emollients represent one of the cornerstones of treatments for patients with AD. The aims of this study were to compare the drug related management and the drug related costs between children with AD treated by at least an emollient (composed-of-Glycerol [15 gr], Vaseline [8 gr] and liquid-paraffin [2gr] per 100 gr) and children not treated by emollient. **METHODS:** This was a retrospective analysis of data extracted from the "Disease Analyzer™" database, including anonymized data from medical files of the patients seen by a representative sample of FrenchGP. Children with AD diagnosed before 1 year old were tracked for 12-months after the date of diagnosis. Only children monitored at least 1 year after the diagnosis were included in the analysis. Costs of AD treatments were calculated from a societal perspective. **RESULTS:** 49 children with AD were treated by the emollient (group 1) and 59 were not (group 2). 59.2% of children of group 1 were treated by CS *vs* 72.9% in group 2; the same trend was found for the prescription of antiseptic (24.5%-*vs*-27.1%) and antibiotic (10.2%-*vs*-13.6%). On the contrary, healing was more prescribed in the emollient group (32.7%-*vs*-25.4%). Average annual cost of prescribed dermatological drugs was estimated to be 139.8 € in the emollient group and 146.4 € in the other group. **CONCLUSIONS:** These preliminary results suggest that CS, which may have negative effects (skin fragility, infection, addiction and impact on growth), are less prescribed in the emollient group. Studies considering larger samples are warranted to confirm this trend.

PSS5

BASELINE PATIENT, OCULAR FEATURES AND MANAGEMENT OF A PATIENT POPULATION DIAGNOSED WITH VITREOMACULAR TRACTION: AN OBSERVATIONAL STUDY IN FLANDERS

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OBJECTIVES: Limited data is published on baseline characteristics of patients diagnosed with vitreomacular traction (VMT) or different macular hole (MH) stages. Aim of our study was to describe the baseline patient and ocular characteristics, and the management of patients diagnosed with diseases of the vitreomacular interface. **METHODS:** This was an observational study with retrospective design. The study sample included patients from a large tertiary care ophthalmology center in Flanders, who had at least 1 outpatient visit at the study center between July 2009 and May 2013. Patients presented with or without visual symptoms and were examined using optical coherence tomography (OCT) in both eyes. Patients diagnosed with other retinal diseases were excluded from this study. This analysis reports on the VMT cohort only. **RESULTS:** The study sample included a total of 509 patients of which 156 patients (191 eyes) presented with VMT. Mean (SD) age was 72.8 (9.8); 59% were female. Majority (73%) was referred by an ophthalmologist for symptoms of general vision loss (60%) and/or metamorphopsia (23%). Mean follow-up was 1.64 years. Eyes in which a vitrectomy was performed (n=41) presented with worse visual acuity (VA) compared with eyes managed through observation (0.43 versus 0.55; p=0.029). However, VA in fellow eye was significantly better in eyes managed with vitrectomy (0.7 versus 0.56, p=0.039). Metamorphopsia (61% versus 37%, p=0.005) and concomitant ERM (20% versus 9%, p=0.049) were significantly more prevalent in eyes managed through vitrectomy compared with observation. **CONCLUSIONS:** In a real-life population, visiting the outpatient clinic of a large tertiary care ophthalmology center, 31% of patients presented with VMT. Patients were predominantly managed though observation. Worse visual acuity of fellow eye, and presence of metamorphopsia or ERM were significantly associated with occurrence of vitrectomy.

PSS6

CHILDREN WITH ATOPIC DERMATITIS: MONITORING A FRENCH COHORT OVER A NINE-YEAR PERIOD

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OBJECTIVES: To assess the diseases associated with AD or that take over during the years following the diagnosis of the infant and to calculate the annual cost of treating these children. **METHODS:** The cohort includes infants with AD who have undergone consultation with their general practitioners between the beginning of 2000 to the end of 2003. The data gathered through the IMS database was entered by general practitioners, enabling tracking of patients. The tracking period was started after diagnosis. Only infants who were monitored for a minimum of one-year were included. A control group comprising infants without AD and who were monitored for at least a year was created. **RESULTS:** A total of 723 infants who met the criteria outlined were identified. In the first year following their birth, infants with AD had significantly more concomitant disorders, particularly respiratory disorders (85% vs. 76%), and asthma (8.9% vs 4.6%) or other types of dermatosis (46.9% vs. 28.2%) among others. During the nine-years of monitoring, the children of the AD cohort consumed more dermatological products than the children of the control-group did in terms of emollients or topical corticosteroids. As well, the AD group consumed more antiseptic products than the control group did in the first year (27.6% vs 14%). Children with AD were observed to consume more anti-asthma drugs, with a peak occurring at age 4. **CONCLUSIONS:** From an epidemiological perspective, this study

was in line with current data. Pulmonary symptoms call for vigilance in monitoring children. Chronic ocular inflammation sometimes is the cause of long-term cataracts in patients with atopic disorders. Early ocular symptoms found in this cohort must be specified and suggest that an opthamological follow-up may be required in some cases. In addition, the abnormally high consumption of antiseptics - and also often the source of irritation - raises concerns about children's treatment.

PSS7

BURDEN OF ACTINIC KERATOSIS IN GERMANY-RESULTS OF A LITERATURE RESEARCH

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OBJECTIVES: Actinic keratoses (AK) are dermatological conditions with the risk-potential becoming squamous cell carcinoma (SCC). Descriptions of AK-epidemiology and cost-of-illness are currently necessary when submitting an AMNOG dossier for an AK-product in Germany. **METHODS:** To describe AK-epidemiology a targeted literature research was conducted in PubMed in 2012, using the search terms (epidemiology OR incidence OR prevalence). To find relevant cost-of-illness information the following search terms were used (cost OR costs OR burden OR econom* OR pharmacoeconom* OR financ* OR budget OR reimburs* OR (resource NEAR (use OR utilization))). Both searches were combined with AND ((actinic OR solar OR senil*) AND (keratos* OR cheilitis)) AND Germany. PubMed research was supplemented by additional searches in guidelines and the World Wide Web for publications in German/English. **RESULTS:** The screening of the epidemiology results (36 in PubMed) identified two relevant publications of four studies investigating AK-prevalence in Germany (Schäfer epub ahead of print 2012, Lichte 2010). An additional search for the German phrase "nicht melanozytäre Hautkarzinome" identified a publication on the cost-benefit of skin-cancer-screening, including data on prevalence of AK (Guther 2011). The study results demonstrate a prevalence range between 2.0% and 7.4% with increasing prevalence by age. So far no cost-of-illness data of AK were identified for Germany (5 hits in pubmed). In an expert survey from Augustin and Kornek (2012) one important cost-factor was seen in the progression of AK into SCC and its prevention might reduce treatment cost and burden of disease for patients. Citation tracking of this expert-survey identified an additional prevalence-study in Germany (prevalence 2%, Augustin 2011). **CONCLUSIONS:** No data of AK-incidence in Germany are available. Prevalence data of AK in Germany have a broad range from 2.0% - 7.4%. Cost-of-illness data are needed for Germany to demonstrate the cost saving aspect of AK-prevention as seen in cost-of-illness studies of other countries.

PSS8

PREVALENCE AND RISK FACTORS OF ACTINIC KERATOSES

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OBJECTIVES: In Europe only few and inconsistent data on the prevalence and treatment of Actinic Keratoses (AK) are available. Objective of this study was to determine the prevalence of AK in Germany, to identify potential predictors and to estimate the number of AK cases treated in dermatologic practices. **METHODS:** In a multiple-source-approach, prevalence was assessed from whole-body-examinations in a cohort of 90.800 employees and from nationwide statutory health insurance (SHI) data of 2008. c) The number of cases documented in dermatological offices was estimated from statistics of a SHI Physicians Association. **RESULTS:** Standardized prevalence of AK from dermatological examinations was 2.7%; the rate increased with age (11.5% in the group 60-70 years) and was higher for men (3.9%) than for women (1.5%). Significant associations were also identified for skin phototype I, sunburns in childhood and solar lentigines. Vitiligo and a history of melanoma were also but not significantly associated with AK. In the SHI data analysis standardized AK prevalence was 1.8%. Age-specific rates were below 1.5% up to 60 years and rose to 8.2% (13.2% in men) in the group 80-89 years. The prevalence from these large data sets - which is at the lower limit of studies from other countries – suggests about 1.7 Mio. estimated AK cases in Germany. In 2011 AK accounted for 8.3% of the hundred most frequently treated dermatological outpatient diagnoses. The proportion of AK cases has risen almost continuously over the last 10 years. Estimated annual number of AK cases documented by dermatologists in Germany is about 1.7 Mio. **CONCLUSIONS:** AK is a frequent condition in higher age groups and more prevalent in men; a relevant need for health care evident. Predictors and risk factors for AK are easy to identify in the population, which could also help to detect groups with special need for preventive measures.

SENSORY SYSTEMS DISORDERS – Cost Studies

PSS9

THE BUDGET IMPACT OF INTRODUCING RANIBIZUMAB IN ENGLAND AND WALES FOR THE TREATMENT OF VISUAL IMPAIRMENT DUE TO CHOROIDAL NEOVASCULARIZATION SECONDARY TO PATHOLOGIC MYOPIA

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OBJECTIVES: To evaluate the budget impact of introducing ranibizumab. **METHODS:** Cumulative costs were assessed using an open cohort model with a 5-year time horizon and NHS perspective. The number of eligible patients was based on: the estimated prevalence of pathologic myopia (PM) in the population >40 years old (1.2%); the incidence of choroidal neovascularization (CNV) in patients with PM (0.98%); the proportion of patients eligible for pharmacotherapy (81%) and bilateral disease prevalence (5.5%). Treatment and diagnosis rates were estimated at 80% and 83–86% respectively. Treatment frequency was based on RADIANCE trial data. The model compared two scenarios. In the 'with ranibizumab' scenario, the proportion of eligible patients treated with ranibizumab was estimated as 7% at year 1, increasing to 32% at year 5; the proportion receiving verteporfin photodynamic therapy (vPDT) fell from 93% to 68%. In the 'without ranibizumab' scenario, only vPDT was administered. Costs of treatment, administration, monitoring, bilateral disease and management of recurrences were included. **RESULTS:** An estimated 2045 patients were eligible for treatment at year 1 and 2119 at year 5. In the 'with ranibizumab' scenario, 143 patients received ranibizumab at year 1, increasing to 678 at year 5; 1902 patients received vPDT at year 1 and 1441 at year 5. 'With ranibizumab' annual costs were higher in years 1–2 than 'without ranibizumab' costs. During years 3, 4 and 5, cost savings occurred with ranibizumab (£3867, £121 584 and £232 467, respectively), owing to lower total costs of treatment and monitoring than with vPDT. The total 5-year saving 'with ranibizumab' over 'without ranibizumab' was £227 086. **CONCLUSIONS:** Treating visual impairment due to CNV secondary to PM with ranibizumab rather than vPDT is estimated to provide significant cost savings in England and Wales over 5 years.

PSS10

PHARMACOECONOMIC ASSESSMENT OF RANIBIZUMAB IN THE TREATMENT OF THE DIABETIC RETINOPATHY IN THE RUSSIAN FEDERATION

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Diabetic retinopathy (DR) is one of the main reasons of vision loss. Traditional treatment provides insufficient control of disease and adverse events. New drug ranibizumab usage in treatment of DR opens new opportunities in treatment of DR. **OBJECTIVES:** To provide pharmacoeconomic assessment of ranibizumab in DR treatment in the Russian Federation. **METHODS:** Comparative modeling cost-effectiveness (CEA) and budget impact (BIA) analyses based on clinical trials results were conducted. CEA with 1 year time horizon for basic group patients and BIA with 5 year time horizon for high risk vision loss patient group. CEA considered only direct costs (DC), while BIA dealt with both DC and indirect costs (IC). 1 EURO = 40 RUB. **RESULTS:** Annual total costs (TC) per patient (PP) for ranibizumab treatment (8 injections on the average) approached 9786 EURO. Annual TC for LC treatment were 440 EURO PP. Ranibizumab provides 6,1 letters vision improvement on the average, while LC – 0,8 letters. Cost-effectiveness ratio (CER) for ranibizumab was 1604 EURO per letter, for LC CER was 550 EURO per letter. ICER was 1764 EURO per additional letter. Second scenario included DR patients going blind in 5 years on LC treatment, while on ranibizumab treatment they could keep their eyesight. TC over 5 years for ranibizumab treatment (13 injections on the average) were 15225 EURO PP. TC over 5 years on LC were 27327 EURO PP, including IC due to vision loss – 25250 EURO. BIA results have shown that ranibizumab treatment for high-risk vision loss DR patients group provided 9 616 EURO (discounted at 3,5%) cost-saving PP in comparison with LC treatment. **CONCLUSIONS:** Ranibizumab is highly effective costly treatment that demands additional consideration for administration in common DR patient group, while it seems to be cost-saving in DR patient group of high-risk vision loss.

PSS11

EVALUATION OF THE HERPES ZOSTER IMPACT AS COMORBIDITY FACTOR IN 5 PATHOLOGIES FRENCH HOSPITAL CARE AMONG ADULTS AGED 50 AND OLDER

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OBJECTIVES: To evaluate the impact of Herpes Zoster (HZ) as associated diagnosis on hospitalizations for an other main health problem, using 3 evaluation criteria: length of stay, number of death and cost from the national health insurance perspective. **METHODS:** The hospitalizations of people aged 50 years and more were selected from the French national hospital database (PMSI) 2011 using ICD 10 diagnosis code: HZ (B02*) in associated diagnosis (DAS), and excluding codes of immunosuppressive conditions (D8* or B20*-B24*). The 5 main categories of diseases leading to hospitalization distribution allowed us to select, in decreasing order of importance: circulatory (I0*-I5* & I7*-I9*), respiratory (J0*-J9*), digestive (K0*-K9*), osteo-articular systems (M0*-M9*), and diabetes (E1*). For each of the 5 categories, a retrospective case-control has been realized. The cases are defined by hospitalizations with HZ in DAS and controls were hospitalizations without HZ in DAS matched on age and sex to the cases. Statistical non parametric analyses (Wilcoxon-Mann-Whitney) in each of the five categories have been realized to evaluate the difference in length of stay, death rate, and cost. **RESULTS:** In each of the five categories, cases presented a statistically significant length of stay compared to the controls. Median differences varying of 3 days for osteo-articular system (+50%) to 6 days for digestive system (+300%). None difference in the death rates has been observed. The study also demonstrated a statistically significant cost of cases compared to the controls median differences varying of 857€ for circulatory system (+25%), 922€ for osteo-articular system (+26%), 945€ for respiratory system (+26%), 987€ for diabetes (+39%), and 2011€ for digestive system (+126%). **CONCLUSIONS:** When present as an associated diagnosis in hospitalizations of people 50+ for other medical reasons, HZ significantly increases the length of stay at hospital and subsequent economic burden for the French health system.

PSS12

SPECTACLE INDEPENDENCE AND VISION-RELATED QUALITY OF LIFE IN CATARACT SURGERY PATIENTS FOLLOWING IMPLANTATION OF A MULTIFOCAL INTRAOCULAR LENS

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OBJECTIVES: The aim of this study was to compare spectacle independence and vision-related quality of life following implantation of a multifocal intraocular lens (IOL: ReSTOR®) or monofocal IOLs. **METHODS:** This prospective observational study involved 206 cataract surgery patients (median age 71 years, range 51–90 years) receiving either the multifocal IOL or monofocal IOLs. The primary outcome measures were the proportion of patients with a postoperative improvement in uncorrected visual acuity of 0.1 logMAR or better, the proportion of patients achieving spectacle independence, and vision-related quality of life assessed using the

5-dimension National Eye Institute Refractive Error Quality of Life (NEI-RQL)-42 scale; expenditure on spectacles was also measured. **RESULTS:** The proportion of patients with a postoperative improvement in visual acuity of 0.1 logMAR or better was significantly higher with the multifocal IOL than with monofocal lenses (45.7% vs. 2.1%, respectively; P<0.0001), as was the proportion of patients achieving spectacle independence (73.3% vs. 25.3%, P<0.0001). At 6 months, the group difference in NEI-RQL-42 scores for dependence on correction significantly favoured the multifocal IOL (mean difference 37.3, 95% confidence interval 28.7–46.0, P<0.0001), but there were no significant differences between the groups in scores for the other four dimensions (near vision, appearance, limitation in activity, and satisfaction with correction). The mean costs of spectacles in patients with multifocal or monofocal IOLs were €154.42 and €267.21, respectively, for lenses and €66.59 and €74.35, respectively, for frames. **CONCLUSIONS:** Compared with monofocal IOLs, the multifocal IOL resulted in greater spectacle independence and lower expenditure on glasses. These findings are consistent with those of a previous economic modelling study, which showed that the use of this lens resulted in significant cost savings due to a reduced need for spectacles.

PSS13

COSTS COMPARISON OF CUTANEOUS DRUG REACTIONS TREATMENT DIVIDED BY DIAGNOSIS GROUPS

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OBJECTIVES: The aim was to analyze the total direct costs of treatment of cutaneous drug reactions (CDR) from health care provider and public payer perspective divided by diagnosis groups. **METHODS:** We analyzed retrospectively data from 164 patients (57 men, 107 women) hospitalized in the Department of Dermatology, Military Medical Institute in Warsaw (from 2002 to 2012) due to CDR. Total direct costs from the public payer and health care provider were calculated for different diagnoses (based on ICD 10 codes). The analysis was based on data derived from the patients' medical charts, daily medication logs, and cost data provided by the hospital organization and accounting department. The services paid by National Health Fund (NHF) were grouped based on ICD-10 and DRG system. For the purpose of the analysis the hospitalization costs were calculated based on the prices for medical services established by the NHF on the basis of a contract with the selected health institution. **RESULTS:** In the study group 3 CDR groups were identified: J38-severe skin disease (generalized rash) J39-large dermatological diseases (erythema multiforme) J49-gentle dermatological diseases (urticaria). From NHF perspective the most expensive procedure is J 38 – 962 € per patient (1€ = 4.24 PLN), the lower cost is for J39 and J 49 (476€ and 331€ respectively). From health care provider's perspective the total direct costs equal: J38 – 630 €, J 39 – 552 €, J49 – 375€. Differences in costs could be due to high costs of the clinically severe diseases treatment incurred by the provider while according to the NHF, these units are classified as large dermatological diseases and thereby direct treatment costs are much lower than real provider's costs. **CONCLUSIONS:** The analysis results suggest taking into consideration reclassification of the services by NHF or better estimation of DRG groups by the public payer.

PSS14

COSTS OF PREVALENCE-BASED CENTRAL RETINAL VEIN OCCLUSION (CRVO) IN THE UNITED KINGDOM

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OBJECTIVES: The societal costs associated with CRVO are little known. Only a few studies report on the burden of retinal vein occlusion, the resource use and cost of CRVO. No specific burden of illness study is available that describes the situation in the UK. The purpose of this study was to create a model that enabled the calculation of the societal costs of CRVO in the UK. **METHODS:** The health care utilisation inputs for the model were derived from a survey conducted among UK ophthalmology experts. The model included parameters that contribute to the costs of illness of CRVO and is based on the prevalence of CRVO in the UK. These were direct and indirect costs including drug treatment, non-drug treatment (e.g. grid laser photocoagulation and pan retinal photocoagulation), monitoring of the disease, adverse events, lost productivity, transportation and the cost of blindness. **RESULTS:** In the UK, the average annual contribution from each patient to the overall cost of CRVO was calculated to £14,692. The annual cost for the UK society was estimated to be almost £700 million. The main part of the cost, 42%, was from monitoring of the disease. Also, 20% was from the cost of blindness, 16% from the drug treatment and 15% from treatment of adverse events. **CONCLUSIONS:** Despite CRVO being an uncommon disease, the annual costs to the UK society are substantial. The total burden of CRVO is most sensitive to changes in the cost associated with interventions, with the number of hospital visits, ophthalmoscopy examinations and the number of optical coherence tomography (OCT) procedures as the dominating factors. By reducing the cost and/or the number of interventions by 25%, the overall burden of CRVO decreases from £14,692 to £13,147 per patient, which corresponds to a societal saving of almost £73 million per year.

PSS15

SYSTEMATIC LITERATURE REVIEW OF ECONOMIC BURDEN OF CHRONIC PLAQUE PSORIASIS

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OBJECTIVES: Psoriasis is a significant economic burden to both patients and payers in terms of direct and indirect costs. Previous systematic reviews have been limited with regards to geographical region of assessment and type of economic outcomes reported. Hence, the objective of this systematic review is to provide a global comprehensive understanding of the direct and indirect economic burden of psoriasis. **METHODS:** A systematic literature search was conducted and studies were identified from PubMed and conference proceedings. Studies published in English language between January 2001 and May 2013, and reporting direct and indirect economic burden of psoriasis were identified using search strategies. A total of 1,181 abstracts were screened by two researchers; any discrepancy was resolved by a third researcher. **RESULTS:** Forty studies (34 primary articles and 6 conference abstracts) from 12 countries including 19 from the US, 4 from Canada, 3 from Germany, 2 each from Italy, The Netherlands and the UK, 1 each from Australia, Brazil, Israel, Spain, Sweden and Switzerland, and 2 multinational studies met the inclusion criteria. Overall, 27 studies assessed direct costs, 3 studies assessed indirect costs, and 10 studies evaluated both. Major contributors of direct costs included medication costs, office visits, hospitalization costs and monitoring costs. Productivity loss, patient and caregiver work days lost, and restricted activity days were key drivers of indirect costs. Among the European countries, the most recent studies reported an annual total cost (direct and indirect cost) per patient of €11,928 in Sweden, €8,372 in Italy, and €2,866 - €6,707 in Germany based on treatment type. In US and Canada, the annual direct and indirect economic burden of psoriasis was $1.4 billion and CDN$1.7 billion respectively. **CONCLUSIONS:** Costs associated with chronic plaque psoriasis are high in many countries indicating a continued need for new treatments.

PSS16

CANADIAN BURDEN OF CHOROIDAL NEOVASCULARIZATION SECONDARY TO PATHOLOGIC MYOPIA: BASELINE CHARACTERISTICS OF PATIENTS

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OBJECTIVES: To identify the real world standard of care, treatment patterns, medical history, resource use and costs of patients with choroidal neovascularization (CNV) secondary to pathologic myopia (PM) in Canada. **METHODS:** With enrollment still ongoing, 85 patients with Myopic CNV were recruited by ophthalmologists and retina specialists from 16 centres across Canada to participate in this retrospective, multicenter study. Medical records covering at least one year of follow up data from the CNV diagnosis, and up to two years, were analyzed to gather all information related to Myopic CNV. **RESULTS:** Data from 67 study participants was analyzed. Patients had a mean age of 55.4 years (range: 27 – 80 years) at the time of their PM diagnosis (CNV affected eye), and 56.0 years (range: 29 - 82 years) at the time of their first lifetime CNV episode. The analysis showed that 71.6% of participants were female, 71.6% were Caucasian, 61.2% had subfoveal CNV in the affected eye and 31.3% had more than one lifetime CNV episode reported. Based on their visual acuity at the time of CNV diagnosis at the beginning of the chart review period, they were grouped by the Snellen score of the affected eye into 7 groups: 20/32-20/20 (n=5), 20/50-20/32 (n=5), 20/80-20/50 (n=15), 20/125-20/80 (n=12), 20/200-20/125 (n=2), 20/320-20/200 (n=7) and <=20/320 (n=21). The approximate mean Snellen score was 20/160 in the affected eye and 20/63 in the fellow eye. The proportion of patients that had both eyes affected with PM was 58.2%. **CONCLUSIONS:** Information on Myopic CNV is very limited in the literature. The baseline characteristics of Canadian patients presented here are aligned with other few data available in the public domain. This is the first study worldwide investigating the burden of Myopic CNV and the final results, will help us better understand this debilitating disease.

PSS17

COSTS OF INCIDENCE-BASED CENTRAL RETINAL VEIN OCCLUSION IN FRANCE

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OBJECTIVES: Retinal vein occlusion (RVO) is the most common retinal vascular disorder with the potential for significant vision-related morbidity. The societal costs associated with CRVO are little known. Only a few studies reports on the burden of retinal vein occlusion or the resource use and cost of Central Retinal Vein Occlusion (CRVO). No specific burden of illness study is available that describes the situation in France. The purpose of the current study was to create a model that enables study of the societal costs of CRVO in France. The perspective of the model was prepared from a societal perspective. **METHODS:** The input for health care utilisation input, were derived from a client survey conducted among French clinical experts in ophthalmology. An incidence-based model was constructed, which included the following parameters: direct and indirect costs, including treatment with drugs, non-drug treatments (e.g., grid laser photocoagulation and pan retinal photocoagulation), monitoring of the disease, adverse events, lost productivity, transportation and the cost of blindness. **RESULTS:** In France the incidence of people suffering from CRVO was estimated to 10,471 (2011). The average annual contribution from each patient to the overall cost of CRVO was calculated to 11,434€. The yearly direct and indirect costs were estimated to app. 120mill Euros. The contributing factors driving the cost of CRVO, in France, are, cost of blindness 29%, drug treatment cost 26%, cost of adverse events 25% and cost from monitoring 14%. **CONCLUSIONS:** Despite CRVO being a uncommon disease, the annual costs to the French society, based on the incidence of CRVO, are substantial. The cost of blindness account for 26% of the total annual costs indicating that there is a potential for reducing those costs with improved treatment options in CRVO.

PSS18

COSTS OF BEST SUPPORTIVE CARE IN THE TREATMENT OF MODERATE-TO-SEVERE PSORIASIS IN THE UNITED STATES

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OBJECTIVES: To describe the best supportive care costs of psoriasis patients following discontinuation of conventional systemic or biologic therapy. **METHODS:** Adult patients with ≥ 2 psoriasis diagnoses (from office visits) with continuous insurance

coverage ≥ 6 months before (baseline period) and ≥ 12 months post-index date were selected from the MarketScan Commercial and Medicare Claims database (2005-2009). The index date was defined as the last day of conventional systemic or biologic drug coverage. Discontinuation was defined as no systemic or no biologic treatment for ≥ 12 consecutive months from the last day of systemic or biologic prescription coverage. Patients were classified as having discontinued from a biologic if there was evidence of biologic drug use during the baseline period; otherwise they were defined as having discontinued from non-biologic systemic therapy. Twelve-month average costs following discontinuation were reported. **RESULTS:** A total of 4,720 psoriasis patients met the selection criteria; 67.4% discontinued from non-biologic systemic therapy and 32.6% from biologic therapy. Over the 12-month period following discontinuation, total costs were $10,577 (SD: 19,910) and $9,001 (SD: 16,401) for biologic and non-biologic discontinuers, respectively (p=0.004). Outpatient and medication costs were significantly higher for the biologic discontinuers compared to the non-biologic discontinuers ($5,283 vs. $4,449, p= 0.003, and $2,738 vs. $2,470, p= 0.022, respectively). There was no statistically significant difference in hospital/ER costs ($2,556 vs. $2,083, p= 0.214, respectively). Outpatient costs accounted for approximately 50% of total costs for both cohorts. **CONCLUSIONS:** This study suggests that outpatient costs account for a substantial proportion of health care costs in psoriasis patients who discontinued from systemic or biologic therapy. Patients who had discontinued from biologic therapy incurred significantly higher outpatient and medication costs compared to patients who had discontinued from conventional systemic therapy.

PSS19

AN INNOVATIVE METHOD: APPLICATION OF NEGATIVE PRESSURE WOUND THERAPY IN THE TREATMENT OF CHRONIC LEG ULCERS – MEDICAL AND HEALTH ECONOMICS ASPECTS

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OBJECTIVES: Chronic leg ulcers without healing tendency present a serious public health and socio-economic issue. Rationally combinig causal and conservative treatments with innovative methods, it would be beneficial to improve the effectivity of wound treatment, thus reducing its financial impacts. The aim of study was to investigate the cost of conservative treatment and an innovative Negative Pressure Wound Therapy (NPWT). **METHODS:** The authors present cases of dermatological patients with severe, chronic leg ulcers of various etiologies resistant to conservative therapy (Patients-1: fasciitis necrotisans; Patients-2: ulcer associated with chronic venous insufficiency; Patients-3: pyoderma gangrenosum), thus comparing the costs of conservative treatment (social insurance subsidies on bandages) and NPWT (not financed by social insurance) in each patient. Furthermore, the authors compare costs of NPWT cases with other cases (Patient-4: fasciitis necrotisans; Patient-5: ulcer associated with chronic venous insufficiency; Patient-6: ulcer associated with rheumatoid arthritis), in which no NPWT was applied thus far due to financial reasons. (1USD$=225 HUF, Hungarian Forint). **RESULTS:** Social insurance subsidies on bandages/patient (USD) in treatment period: Patient-1.: $1324; Patient-2.: $15495; Patient-3.: $412; Patient-4.: $11376; Patient-5.: $10557; Patient-6.: $7306. Cost of NPWT/patient and proportion of social insurance subsidies on bandages/patient: Patient 1.: $1405 (106%); Patient 2.: $667 (4.3%), Patient 3.: $778 (188.9%). The cost of NPWT is relatively high, however, NWPT-treated leg ulcers have healed compared to cases receiving conservative treatment, which can be attributed to NPWT stimulating wound healing. **CONCLUSIONS:** Treatment of the disease resulting leg ulcer – causal therapy combined with NPWT – is beneficial in wound healing, reducing high costs of wound treament, shortening the time of wound healing, improving the patient's quality of life. Application of NPWT in specialized centers of wound treatment and financing by social insurance would be recommended for cases not responding to conservative treatment in Hungary.

PSS20

DIFFERENTIAL DIAGNOSIS OF LEG ULCERS – MEDICAL AND HEALTH ECONOMICS ASPECTS

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OBJECTIVES: Incidence of chronic leg ulcers without healing tendency exceeds 1% among adults and 3-5% among people over 65 years. The burden of diseases caused by wounds without healing tendencies can only be estimated. Complications of chronic wounds are severe, life-threatening. Total social insurance subsidies on bandages in Hungary is 22-26 million USD/year. Using case studies the authors emphasize the importance of (differential) diagnosis, mistakes of wound treatment affecting healing and increasing costs of treatment, in contrast to therapy costs. **METHODS:** The authors present leg ulcer cases of various etiologies referred to the dermatological clinic, seeking mistakes of wound treatment, examining social insurance subsidies on bandages, based on bandage prescriptions. Patients 1-4.: Ulcus cruris due to chronic venous insufficiency; Patient 5.: Leg ulcer caused by lymphoedema; Patients 6-8.: Ulcerous malignancies treated as leg ulcers; Patient 9.: Ulcus cruris+myeloproliferative disease; Patient 10.: Bilateral leg ulcers resulting from cardial decompensation and diabetes mellitus. (1USD$=225 HUF, Hungarian Forint). **RESULTS:** Social insurance subsidies (USD) on bandages per patients and mistakes in wound therapy: Patient 1.: $1857; Patient 2.: $1639; Patient 3.: $1787; Patient 4.: $53329, lack of compression therapy and lymphatic massage; Patient 5.: $12.567, lack of lymphatic massage; Patient 6.: $213; Patient 7.: $294; Patient 8.: $2143, lack of correct diagnosis; Patient 9.: $2993, no treatment of concomitant hematologic disease; Patient 10.: insufficient therapy of co-morbidities: diabetes, obesity, cardial decompensation. **CONCLUSIONS:** Modern treatment of leg ulcers mainly aims at determining primary causes, treating diseases causing wound healing disorders, namely causal therapy. Inefficient wound treatment is costly, application of modern bandages without principles, not treating co-morbidities and treating on inadequete levels cause financial problems to both the patient and the social insurance. Introducing professional guidelines for wound treatment, shortening "patient paths" and establishing centers of wound treatment would be recommended in Hungary.

PSS21

THE COST-EFFECTIVENESS OF INTRAVITREAL AFLIBERCEPT (IVT-AFL) IN TREATING NEOVASCULAR AGE-RELATED MACULAR DEGENERATION IN AN ITALIAN SETTING

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OBJECTIVES: In Italy, standard treatment care of patients with neovascular ("wet") age-related macular degeneration (wAMD) is currently performed with ranibizumab (RBZ) on as-needed basis (PRN). The objective of this study was to assess the cost-effectiveness of intravitreal aflibercept (IVT-AFL), administered every other month vs. RBZ PRN treatment, in the Italian treatment setting. **METHODS:** A Markov model was built to compare IVT-AFL compared to RBZ PRN in wAMD. Health states were based on visual acuity in the better-seeing eye. In the model, patients may remain in the same status (same visual acuity), progress to another status or die. A proportion of patients may also discontinue treatment monthly or upon becoming blind. Parameters were estimated from two randomized phase III studies VIEW 1/VIEW 2, published literature or expert opinions. Analyses were performed from the Italian Healthcare perspective, using a 20-year time horizon (starting age was 77 years). The simulation model calculated costs (drug, administration, monitoring, vision impairment and adverse events), quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs), all discounted at 3% annually. Deterministic and probabilistic sensitivity analyses (SA) were performed to test the robustness of the results. **RESULTS:** IVT-AFL costs 30,852€ compared with 33,636€ for RBZ PRN; QALYs totaled 2.651 for IVT-AFL and 2.638 for RBZ-PRN respectively. IVT-AFL is associated with less cost and more QALYs gained than RBZ-PRN and hence dominates RBZ PRN. Deterministic SA showed that the results were most sensitive to changes in efficacy and time horizon, while probabilistic SA showed that 90% of the iterations fell within the cost-effectiveness threshold deemed acceptable for Italian Payers (for example €40,000). **CONCLUSIONS:** Results indicate that, within the Italian treatment setting, attainment of maximal visual gains via IVT-AFL is cost-saving that means less costly and more effective (more QALYs gained) compared to RBZ PRN.

PSS22

COST-EFFECTIVENESS OF RANIBIZUMAB FOR THE TREATMENT OF VISUAL IMPAIRMENT DUE TO CHOROIDAL NEOVASCULARIZATION SECONDARY TO PATHOLOGIC MYOPIA IN THE UNITED KINGDOM

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OBJECTIVES: To evaluate the cost-effectiveness of ranibizumab compared with verteporfin photodynamic therapy (vPDT) for the treatment of patients with visual impairment due to choroidal neovascularization (CNV) secondary to pathologic myopia (PM). **METHODS:** A Markov model with a 3-month cycle length and health states defined by best-corrected visual acuity (BCVA) was developed from the UK health care provider perspective. A lifetime time horizon was applied, and future costs and outcomes were discounted at 3.5%/year. Baseline characteristics were derived from the phase 3 RADIANCE study; year 1 health state transitions and treatment frequency were based on the RADIANCE study and a vPDT study (VIP). Treatment was given beyond year 2 only in cases of mCNV recurrence (6%/year). Existing literature was used to estimate BCVA transitions beyond 12 months. Health states were based on the visual acuity of the study eye, which could be each patient's better-seeing eye (BSE) or worse-seeing eye (WSE). BSE utility values came from a published source. **RESULTS:** The mean lifetime cost of ranibizumab treatment was slightly lower than the cost of vPDT. Ranibizumab was associated with higher lifetime quality-adjusted life-years (QALYs) than vPDT (relative gain of 0.43), reflecting higher utility values and reduced mortality with ranibizumab. Ranibizumab therefore dominated vPDT. Ranibizumab had a 100% probability of being cost-effective compared with vPDT at a willingness-to-pay threshold of £20 000 per QALY. The model was sensitive to the number of ranibizumab injections in year 1. Ranibizumab remained cost-effective even when the mean number of ranibizumab injections increased from 3.5 (base case) to 12 and the mean number of vPDT treatments remained constant (3.4) in year 1. **CONCLUSIONS:** Ranibizumab is less costly and is associated with a gain in QALYs relative to vPDT for the treatment of patients with visual impairment due to CNV secondary to PM in the UK.

PSS23

COST-EFFECTIVENESS OF BIOLOGIC THERAPIES FOR THE TREATMENT OF MODERATE TO SEVERE PSORIASIS IN THE UNITED KINGDOM

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OBJECTIVES: To evaluate the cost-effectiveness of biologic treatments for moderate to severe psoriasis in the UK. **METHODS:** A decision model similar to those utilized in NICE appraisals TA103, TA134, TA146, and TA180 was constructed consisting of 2 distinct periods, the trial and treatment periods. Clinical efficacy was estimated during the trial period based on the relative probabilities of achieving Psoriasis Area and Severity Index (PASI) response (50/75/90) obtained via a network meta-analysis of 15 randomized controlled trials of adalimumab, etanercept, infliximab, and ustekinumab. Weight-based dosing was calculated for infliximab and ustekinumab to reflect licensed use. Only patients who achieved PASI 75 response in the trial period continued into the treatment period. Treatment benefits were determined by the relationship between predicted PASI response and the EQ-5D health utility measure. Costs (2011 British pounds) were assessed from a UK National Health Services perspective and included drug acquisition, administration, monitoring and hospitalization

costs. Drug acquisition cost for ustekinumab reflected the manufacturers' UK Patient Access Scheme. Incremental cost-effectiveness ratios (ICERs) were calculated and treatments were ranked relative to supportive care. One-way sensitivity analyses, using alternative plausible values for key parameters, explored uncertainty in the results. **RESULTS:** Infliximab provided the most additional quality-adjusted life-years (QALYs) vs. supportive care (0.186) followed by ustekinumab (0.174) and adalimumab (0.169). In the base case, adalimumab was the most cost-effective biologic (£19,082/QALY vs. supportive care), followed by ustekinumab (£20,964/QALY), etanercept 25 mg BIW (£26,580/QALY), etanercept 50 mg BIW during the trial period followed by 25mg BIW (£28,719 per QALY), and infliximab (£46,844 per QALY). ICERs for ustekinumab and infliximab compared with adalimumab were £87,625 and £332,015, respectively. Adalimumab remained the most cost-effective in the majority of the sensitivity analyses. **CONCLUSIONS:** In this decision-model analysis, adalimumab was the most cost-effective biologic treatment for moderate to severe psoriasis in the UK.

PSS24

A COST-EFFECTIVENESS ANALYSIS OF INGENOL MEBUTATE GEL FOR THE TREATMENT OF ACTINIC KERATOSIS: A SCOTTISH PERSPECTIVE

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OBJECTIVES: Ingenol mebutate gel is a recently developed, topical, 2 or 3 days patient-administered AK therapy. The objective was to compare the cost-effectiveness of ingenol mebutate gel with diclofenac gel and other available therapies for the first-line treatment of AK in adult patients, from the perspective of the National Health Service (NHS) in Scotland. **METHODS:** A cost-utility analysis was conducted using a decision tree approach to calculate the costs and benefits of different treatment strategies for AK over a 12-month time horizon. Data on the relative efficacy of treatment was derived from a systematic review of RCTs and a subsequent mixed-treatment comparison (MTC). Utility scores and resource use data were obtained from published sources. Due to the uncertainty surrounding the impact of AEs on HRQoL and costs, AEs were modelled in a scenario analysis. **RESULTS:** In the primary comparison, ingenol mebutate 150 mcg/g gel and 500 mcg/g gel were associated with ICERs of £44 and £114 per QALY gained, respectively compared with diclofenac (3%) for 8 weeks and £36 and £74, respectively compared with diclofenac (3%) for 12 weeks. In the secondary comparisons, ingenol mebutate 150 mcg/g gel and 500 mcg/g gel were associated with ICERs of £47 and £134, respectively compared with 5-FU/salicylic acid (0.5%/10%) cutaneous solution and dominated cryotherapy (i.e. were cheaper and more effective). Ingenol mebutate 150 mcg/g gel and 500 mcg/g gel were cheaper and less effective than 5-FU (5%) cream. Ingenol mebutate 150 mcg/g gel, but not ingenol mebutate 500 mcg/g gel, was cost-effective assuming a decision making willingness-to-pay threshold of £20,000/QALY (for one additional QALY gained, there would be an incremental cost of £26,525 incurred for 5-FU (5%) cream vs ingenol mebutate gel). **CONCLUSIONS:** Ingenol mebutate gel is a fast-acting, convenient and, relative to most comparators, cost-effective therapy for the first-line treatment of AK.

PSS25

COST EFFECTIVENESS OF ANTI-OXIDANT VITAMIN + ZINC TREATMENT TO PREVENT THE PROGRESSION OF INTERMEDIATE AGE RELATED MACULAR DEGENERATION TO ITS WET FORM. A SINGAPORE PERSPECTIVE

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OBJECTIVES: To determine if providing high dose anti-oxidant vitamins + Zinc treatment to intermediate Age Related Macular Degeneration (AMD) patients aged 40-79 years from Singapore is cost effective in preventing progression to Wet AMD. **METHODS:** We estimated the number of AMD patients aged 40 to 79 years (Category 3 and 4) in the Singaporean resident population. This hypothetical cohort was followed for 5 calendar years to determine the number of patients who would progress to wet AMD given the following four treatment scenarios: a) Vitamins +Zn followed by Ranibizumab (as needed) for wet AMD; b) Placebo followed by Ranibizumab (as needed) for wet AMD; c) Vitamins + Zn followed by Bevacizumab (monthly) for wet AMD; and d) Placebo followed by Bevacizumab (monthly) for wet AMD. Costs were estimated for the above scenarios from the providers' perspective and cost effectiveness was measured by cost per disability adjusted life year (DALY) averted with a disability weight of 0.22 for wet AMD. Crude annual mortality rate was incorporated into the model. **RESULTS:** Over 5400 patients could be prevented from progressing to Wet AMD cumulatively over five years if preventive anti-oxidant vitamins +Zn treatment were prescribed. Vitamins + Zn followed by ranibizumab (as needed) or bevacizumab (monthly) was cost effective compared to placebo followed by either drug (cost per DALY averted: $1885.8 - well within the threshold suggesting it is cost effective). However, bevacizumab (monthly 1 injection) alone was cost effective. Cost savings as a result of prescribing anti-oxidant vitamins +Zn were $ 46.7M for ranibizumab arm over 5 years. **CONCLUSIONS:** Prophylactic treatment with high dose anti-oxidant vitamins + Zn for intermediate AMD patients, followed by ranibizumab for patients who progressed to wet AMD was found to be cost-effective. These findings have implications for intermediate AMD screening, treatment and health care planning in Singapore.

PSS26

COST-EFFECTIVENESS ANALYSIS OF LINEZOLID AND VANCOMYCIN IN PATIENTS WITH COMPLICATED SKIN AND SOFT-TISSUE INFECTIONS CAUSED BY METHICILIN-RESISTANT STAPHYLOCOCCUS IN PORTUGAL

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OBJECTIVES: Methicillin-resistant Staphylococcus aureus (MRSA) complicated skin and soft-tissue infection (cSSTI) is an infection associated with high health expenditure for the Portuguese National Health Service (NHS). A decision analytic model was adapted to the Portuguese setting to evaluate the cost-effectiveness (CEA) of linezolid *vs.*vancomycin in MRSA cSSTI. **METHODS:** Published Bayesian evidence synthesis results were used to populate efficacy parameters of the model. Resource utilization and MRSA prevalence rates were obtained through an expert panel of Portuguese clinicians and costs from published sources were applied to resource units. Analyses were done from the Portuguese NHS perspective. Both univariate and probabilistic sensitivity analyses were performed to test the robustness of model results. **RESULTS:** Average cost per patient for linezolid and vancomycin treatments were 15,195€ and 17,345€ respectively. Average effectiveness gained with linezolid treatment was 0.002QALYs. Average saving obtained with linezolid treatment was 2150€ per patient. **CONCLUSIONS:** Linezolid is a dominant strategy compared to vancomycin: less costly and more effective. Compared to vancomycin, linezolid is expected to result in lower total costs that offset its higher acquisition cost in cSSTI in Portugal.

PSS27

ECONOMIC EVALUATION OF RANIBUZUMAB FOR THE TREATMENT OF MYOPIC CHOROIDAL NEOVASCULARIZATION IN CANADA

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OBJECTIVES: To assess the cost-effectiveness of ranibizumab compared to verteporfin in photodynamic therapy (vPDT) for the treatment of myopic choroidal neovascularization (mCNV) from the Canadian health care and societal perspectives. **METHODS:** A Markov model was used to follow a cohort of 55-year old patients with mCNV over a lifetime horizon. The model included 8 health states based on best corrected visual acuity (BCVA) and an absorbing death state. Patients were allowed to remain in their current health state, or transition to other health states or death every 3 months. Results from the RADIANCE trial were used to inform the first year transitions for patients receiving ranibizumab, and the first 3 months for those on vPDT. The VIP trial was used to estimate month 4-12 transitions for vPDT. Patients transitioned according to natural progression from year 2 onwards. Health state utilities were derived from a Canadian utility study and published sources. Resource use and costs were collected from clinical trials, published literature, expert opinion, and standard Canadian sources. **RESULTS:** From the health care perspective, patients receiving ranibizumab for mCNV incurred less health care costs compared to those on vPDT (cost savings of $3,939). This was achieved while accruing an additional 0.07 life years (LYs) and 0.37 quality-adjusted life years (QALYs). Thus ranibizumab dominated vPDT. Similar findings were observed from the societal perspective (cost saving of $14,217). The average BCVA score remained consistently higher with ranibizumab compared to vPDT over the entire time horizon. **CONCLUSIONS:** From a cost-effectiveness standpoint, ranibizumab dominated vPDT in the treatment of mCNV, from both Canadian health care and societal perspectives. Patients on ranibizumab realized more QALYs and LYs at a lower cost compared to vPDT.

PSS28

COST-EFFECTIVENESS OF INTRAVITREAL AFLIBERCEPT IN TREATING NEOVASCULAR AGE-RELATED MACULAR DEGENERATION IN SWEDEN

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OBJECTIVES: Monthly dosing with ranibizumab (RBZ) is needed to achieve maximal sustained visual gains in patients with neovascular ("wet") age-related macular degeneration (wAMD). In Sweden dosing is on an as-needed (PRN) basis, resulting in suboptimal efficacy. Intravitreal aflibercept dosed every 2 months (IVT-AFL) demonstrated clinically equivalent efficacy compared to RBZ monthly dosing (RBZ Q4) in a randomized clinical trial setting. We assessed the cost-effectiveness of IVT-AFL vs. RBZ Q4 and RBZ PRN real-life data, in a Swedish setting. **METHODS:** A Markov model compared wAMD treatment over two years with either IVT-AFL, RBZ Q4 or real-life RBZ PRN. Health states were based on visual acuity in the better-seeing eye; a proportion discontinued treatment monthly or upon visual acuity <20/400. Parameters were estimated from trial data, published literature, or expert opinion. Analyses were performed from a societal perspective with a lifetime horizon (starting age 77 years). The model calculated costs (drug, administration, monitoring, vision impairment, adverse events, caregiver), quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs), all discounted 3% annually. Deterministic and probabilistic sensitivity analyses were performed. **RESULTS:** IVT-AFL cost 578,400 SEK, compared with 686,600 SEK for RBZ Q4 and 565,700 SEK for real-life RBZ PRN; QALYs totaled 4.58 for IVT-AFL, 4.59 for RBZ Q4, and 4.43 for real-life RBZ PRN. Compared with real-life RBZ PRN, IVT-AFL cost 80,000 SEK/QALY gained. RBZ Q4 cost over 20 million SEK/QALY gained, compared with IVT-AFL Q8. The model was most sensitive to IVT-AFL efficacy and patient age. IVT-AFL had a 42% probability of dominating RBZ Q4 and a 100% probability of being cost-effective vs. RBZ PRN, at an assumed willingness-to-pay threshold of 500,000 SEK. **CONCLUSIONS:** Results suggest that, in Sweden, attainment of maximal visual gains via IVT-AFL is cost-effective compared with real-life RBZ PRN dosing. RBZ Q4 is not cost-effective relative to IVT-AFL.

PSS29

THE COST-EFFECTIVENESS OF BIMATOPROST 0.03%/TIMOLOL 0.05% PRESERVATIVE-FREE FIXED COMBINATION COMPARED WITH DORZOLAMIDE/TIMOLOL PRESERVATIVE-FREE FIXED COMBINATION AND 2-BOTTLE UNFIXED COMBINATIONS FOR THE TREATMENT OF PRIMARY OPEN-ANGLE GLAUCOMA IN THE UNITED KINGDOM

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OBJECTIVES: To evaluate the cost-effectiveness of bimatoprost 0.03%/timolol 0.05% (BTFC) preservative-free (PF) fixed combination compared with dorzolamide/timolol

PF fixed combination (DTFC PF), and tafluprost PF/timolol PF unfixed-combination (TTUF PF) for the treatment of primary open-angle glaucoma (POAG). **METHODS:** A cost-effectiveness and cost-utility model was developed to estimate lifetime costs and outcomes. The analysis was performed from a UK NHS perspective. No head-to-head evidence was available for BTFC PF and the comparators; therefore effectiveness estimates in terms of the mean lowering of intraocular pressure (IOP) at Week 12 were estimated using a mixed treatment comparison (MTC). Estimates of visual field progression were taken from the literature and modelled by an irreversible decrease in patients' mean deviation (MD) score in each 12-week cycle. Resource use levels for each of the health states were obtained using a clinician survey. All costs and utilities were obtained from literature or NHS cost sources. Outcomes were reported in terms of cost per mmHg IOP gained and cost per quality-adjusted-life-year (QALY). Deterministic and probabilistic sensitivity analyses were performed. **RESULTS:** The cost-effectiveness results indicated that BTFC PF dominates DTFC PF and TTUF PF, with patients treated with BTFC PF having a greater IOP reduction (1.6 mmHg) and incurring lower lifetime costs (£2,294 vs. DTFC PF, £2,919 vs. TTUF PF). The cost-utility results indicate BTFC PF dominates DTFC PF and TTUF as well with an incremental gain of 0.03 QALYs. Deterministic sensitivity analyses indicate the results are most sensitive to the rate of visual field progression. Probabilistic sensitivity analysis indicates that BTFC PF has a 98.8% probability of being cost-effective at a threshold of £20,000/QALY. **CONCLUSIONS:** BTFC PF is considered a cost-effective treatment option for the treatment of POAG when compared with DTFC PF and TTUF PF from a UK NHS perspective.

PSS30

COST-MINIMIZATION ANALYSIS OF INTRAVITREAL AFLIBERCEPT (IVT-AFL) FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION IN SPAIN

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OBJECTIVES: Anti-VEGF therapy improves visual acuity in patients with neovascular ("wet") age-related macular degeneration (wAMD). By comparing different treatment regimen scenarios, based on data from available randomized clinical studies, the objective was to compare costs for intravitreal aflibercept (IVT-AFL) treatment with Ranibizumab treatment when treating wAMD patients in a Spanish setting. **METHODS:** A Markov model, describing wAMD treatment was estimated, calculating the direct medical costs based on 2-year clinical trial data. Parameters were estimated from trial data, published literature, and expert opinion. Costs, discounted at 3% per year, were calculated over a five-year horizon. Alternative scenarios and deterministic sensitivity analyses were performed and reported. **RESULTS:** IVT-AFL, dosed every two months in Year 1 and modified quarterly dosing in year two, was least expensive, €13,519, followed by IVT-AFL every second month, for two years, €16,085. Cost of Ranibizumab monthly (RBZ Q4) regimens ranged from €17,284 (12.6 injections over two years) to €26,457 (monthly injections over two years). Results were driven by less frequent IVT-AFL dosing and monitoring. The model was most sensitive to RBZ Q4 Year 1 efficacy and Year 2 injection frequency. **CONCLUSIONS:** IVT-AFL is less expensive than Ranibizumab when treating wAMD in Spain, due to less frequent dosing with IVT-AFL and lower monitoring costs.

PSS31

COST-MINIMIZATION ANALYSIS OF MULTIFOCAL AND MONOFOCAL INTRAOCULAR LENSES IN CATARACT SURGERY IN THE CZECH REPUBLIC

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OBJECTIVES: To model the lifetime cost attributed to intraocular lenses (multifocal vs. monofocal) implantation during cataract surgery from patient's perspective. **METHODS:** The Markov model was developed with 28-day cycle length projecting life-time costs of patients undergoing cataract surgery of both eyes at 65 years. Patients move among four health states which occur after cataract surgery. Patients become independent on the spectacles or need them after cataract surgery with probabilities derived from literature. In the model, we assume that new glasses are bought by patients, who wear glasses after surgery, every three years. Patient may die from each health state with probability derived from Czech life-tables there was no difference in mortality specific for particular intraocular lenses. Resource utilization was received by an expert panel and unit costs were derived from current pricing list. Costs of cataract surgery with multifocal and monofocal lenses implantation were 1,200EUR and 9.9EUR, respectively. Mean costs of spectacles were 48.9EUR and 82.5EUR after the intervention of implanting multifocal and monofocal lenses, respectively and monthly costs of ophthalmologist visit, maintenance and service of spectacles was 0.4EUR. Discount rate of 3% was applied. One-Way Sensitivity Analysis was performed. **RESULTS:** After cataract surgery with multifocal lenses implantation, patients purchase on average by 4.4 spectacles less compare to patients undergoing monofocal intraocular lenses implantation (i.e. 5.9). The initial patient's investment of 1,190EUR into multifocal IOLs is in the lifetime horizon partially offset by saving of 364EUR attributed to lower number of new spectacles purchased and their maintenance. Costs on spectacles after cataract surgery with monofocal lenses and level of reimbursement of multifocal lenses were the biggest driver of the results. **CONCLUSIONS:** Bilateral multifocal IOL implants decrease patient's dependence on spectacles. From patient's perspective, the initial investment into multifocal lenses is partially compensated by saving of spectacles costs and its maintenance.

PSS32

A QUEBEC ECONOMIC EVALUATION FOR 36 MONTHS OF RANIBIZUMAB FOR THE TREATMENT OF DIABETIC MACULAR EDEMA

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OBJECTIVES: The value of ranibizumab monotherapy and laser combination therapy compared to laser photocoagulation was assessed within the framework of a cost-utility analysis from the Quebec health care and societal perspectives. **METHODS:** A Markov model followed a cohort of patients with diabetic macular edema over a lifetime time horizon. The model included 8 heath states as defined by best-corrected visual acuity and one absorbing state for death. All transition probabilities in Year 1 were based on the RESTORE trial. For Years 2 and 3 data from the RESTORE Extension trial was used to inform ranibizumab monotherapy and combination therapy transition probabilities. For laser photocoagulation, Years 2 and 3 transition probabilities were based on data from DRCR.net trials. From Year 4 onwards, all transition probabilities were based on the natural history of disease. Health state utilities were derived from the literature (for the best-seeing eye) and a Canadian utility study in RVO patients (for the worse-seeing eye). Resource use and costs were collected from published literature and standard Quebec sources. Costs and outcomes were discounted at 5% as recommended by Canadian guidelines. **RESULTS:** From the health care perspective, patients receiving ranibizumab monotherapy accrued an additional 0.40 quality-adjusted life years (QALYs) and an incremental cost of CAD$9,790, resulting in $24,345 per QALY gained. Patients receiving combination therapy accrued an additional 0.32 QALYS and an incremental cost of $11,387, resulting in $36,148 per QALY gained. At a willingness-to-pay threshold of $50,000, ranibizumab monotherapy and combination therapy had a 75.2% and 59.3% probability of being cost-effective (CE), respectively. From the societal perspective, considering costs from productivity losses, ranibizumab monotherapy and combination therapy dominated laser photocoagulation and had an 88.2% and 78.8% probability of being CE, respectively. **CONCLUSIONS:** Compared to laser photocoagulation, ranibizumab monotherapy and combination therapy for 3 years show cost-effectiveness from health care and societal perspectives.

PSS33

A COST-UTILITY ANALYSIS OF RANIBIZUMAB IN AGE-RELATED MACULAR DEGENERATION BASED ON REAL-LIFE OBSERVATIONAL DATA IN FRANCE

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OBJECTIVES: To calculate the cost-effectiveness of ranibizumab versus licensed comparators in wet age-related macular degeneration (AMD) from a French societal perspective based on real-life observational data. **METHODS:** A Markov model was developed containing 5 health states defined by visual acuity (VA) of the treated eye and a death state. The model time horizon covered 2 years of treatment followed by 8 years of best supportive care (BSC). Medical and non-medical resource use and efficacy during treatment were based on observational patient-level data with ranibizumab (LUEUR and LUMIERE studies) or verteporfin (OPV study). No observational data were available for pegaptanib. Efficacy was obtained per VA level to control for population differences in baseline VA. The base-case analysis reflects 1st line therapy. Mutual to both comparators, BSC was modelled with clinical trial placebo data and resource use estimates. Annual discount rates were 4% for costs (€ 2011) and outcomes. Utilities reflected general population preference (UK) using time-trade-off methods. **RESULTS:** Compared to verteporfin, 1st line ranibizumab provided a gain of 0.20 QALYs and avoided 0.63 years of vision impairment (Y_{VI}). The total incremental cost was €3,843. The cost-utility was €19,088/QALY, the cost per Y_{VI} avoided was €6,114. Similar outcomes were obtained when including pre-treated patients. Ranibizumab was cost-effective with a probability of 62.8% and 78.2% at willingness to pay thresholds of €20,000/QALY and €30,000/QALY respectively. **CONCLUSIONS:** Based on real-life observational studies, 2-year treatment with ranibizumab was associated with improved vision-related health outcomes and a cost-utility ratio below commonly applied willingness to pay thresholds.

PSS34

COST-EFFECTIVENESS OF SEQUENCES OF BIOLOGIC TREATMENTS FOR MODERATE-TO-SEVERE PSORIASIS IN FINLAND

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BACKGROUND: Little is known about the health-economic properties of sequences of biologics agents for the treatment of moderate-to-severe psoriasis. These are available to patients who have failed to achieve therapeutic goals on the traditional systemics such as methotrexate and ciclosporin. **OBJECTIVES:** To predict the five-year costs and health outcomes associated with different sequences of biologic psoriasis treatments (adalimumab, etanercept, infliximab, and ustekinumab), and to evaluate their cost-effectiveness from a Finnish societal perspective. **METHODS:** The Psoriasis Area Severity Index (PASI) was chosen as the main efficacy measure and results of a published meta-analysis were re-run to provide relative efficacy of the biologics in the short term. A fully stochastic Markov cohort model was developed that represents patient health in terms of PASI, Dermatology Life Quality Index (DLQI), and quality-adjusted life-years (QALY). Failure to achieve efficacy targets, serious adverse events and other reasons of withdrawal led to switch to the next treatment in the sequence, and eventually methotrexate maintenance. Costs included direct medical and related direct costs as well as productivity losses. Costs and QALYs were discounted at 3% per annum. **RESULTS:** At a willingness-to-pay threshold of EUR 50,000 per QALY gained, only four of the 60 potential sequences had non-zero probability of being cost-effective. The sequence most likely to be cost-effective was first-line ustekinumab followed by adalimumab followed by maintenance. Its incremental cost-effectiveness ratio (ICER) per QALY gained relative to the cheapest sequence (etanercept followed by adalimumab) was estimated at EUR 8,253. Some modelling assumptions tested in the sensitivity analyses may be influential in driving the results, but others, for example inclusion of an anti-TNF class effect, made

little difference. **CONCLUSIONS:** Using a sequence model of biologic therapies in psoriasis, first-line ustekinumab was found to be cost-effective in the treatment of moderate-to-severe psoriasis in Finland.

PSS35
COST-UTILITY OF PEDIATRIC COCHLEAR IMPLANTATION IN HUNGARY
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OBJECTIVES: To calculate the Cost-Utility of unilateral pediatric Cochlear Implantation in Hungary. Parallel to that, we aim to provide an assessment of currently served cases and epidemiological demand. **METHODS:** Cost accounting of direct medical costs, from public purchaser perspective, covering medical resources sacrificed for unilateral implant in 1 year children, with a 60 year life expectancy. Cost-utility is calculated based on direct costs and QALY gain retrieved from literature, both to be discounted at 3% annually. Prevalence of eligible newborns to undergo Cochlear Implantation versus served cases is reported. **RESULTS:** Draft estimation of total direct costs is 12.26 million HUF (25,288 EUR) and when discounted it would be 7.3 million HUF (24,219 EUR). This is divided into 2.1% preoperative, 53.8% operative (including cost of implant) and 44% post operative. Based on health utility reported by Cheng, discounted QALY gain ranges from 6.1 to 10.8 life years. Therefore, Cost-utility of unilateral CI would range from 679,433 HUF (2,343 EUR) to 1,204,449 HUF (4,153 EUR) per discounted QALY gain. Currently in Hungary, about 90 cases are operated per year (0.1 % of crude birth rate). From 220 to 250 new cases, 2.5 to 3 times currently served, every year (0.24 – 0.37 % of crude birth rate), would be necessary for providing equal access to care. **CONCLUSIONS:** This study provides an overview to Hungarian policy makers and other stakeholders about cost-utility, direct costs and estimated effect, and also of the possible full capacity of such costly intervention. Unilateral Cochlear Implantation appears to be reasonable if direct costs per QALY are compared to GDP in Hungary. Hungarian values are compared with international values.

SENSORY SYSTEMS DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PSS36
UTILITY AND RESOURCE USE OF AN AUSTRALIAN POPULATION OF PSORIASIS PATIENTS
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OBJECTIVES: Psoriasis is a chronic, systemic immune-mediated disorder characterised by skin and often joint involvement affecting 2.3% of the Australian population. While psoriasis has traditionally been viewed as a non-serious skin condition, it is now recognised as a systemic inflammatory disease with a growing body of evidence linking the condition with a number of serious co-morbidities. The objective of this study was to determine the burden, in terms of disutility and resource use, that co-morbidities have on patients with psoriasis. **METHODS:** A large-scale, multi-centre, cross-sectional study of Australian adults with psoriasis was conducted during 2011. The survey contained 43 questions and focused primarily on comorbidity, health care resource use and the impact of psoriasis on disutility as assessed by EQ-5D. **RESULTS:** A total of 330 patients responded to the survey. Three-quarters of respondents reported having at least two or more concomitant medical conditions, with only 8% reporting no comorbidities. Combined, joint-related conditions such as joint pain (46%) and psoriatic arthritis (28%) represented the largest proportion of medical comorbidities reported. The mean EQ-5D score for the cohort was 0.73. Utility decreased as the number of co-morbidities increased, ranging from 0.88 for patients with no co-morbidities to 0.36 for patients with 9 co-morbidities. Resource use and out of pocket expenses also increased with increasing number of co-morbidities. **CONCLUSIONS:** This study highlights the co-morbid nature of psoriasis with most respondents reporting having two or more concomitant conditions. Furthermore, based on the mean EQ-5D health status score, psoriasis has a considerable impact on patient quality of life comparable with other chronic diseases.

PSS37
PATIENT PREFERENCES REGARDING MONITORING AND TREATMENT FOR THE MANAGEMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION
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OBJECTIVES: To investigate qualitatively patient preferences for monitoring and treatment in the management of neovascular (wet) age-related macular degeneration (wAMD) in different countries. **METHODS:** The study involved 39 patients with wAMD from the UK (n=9), Canada (n=10), Germany (n=10) and Japan (n=10). Subjects participated in a 30-minute semi-structured telephone interview. Data were analysed to identify key themes and opinions. **RESULTS:** Most (74%, n=29) patients were aged ≥ 70 years, 28% (n=11) required a caregiver to attend clinic visits, and 90% (n=35) had comorbidities. Only 13% (n=5) of patients were treatment-naïve, 41% (n=16) had received ≤ 1 year of therapy and 46% (n=18) had received > 1 year of therapy. Most (92%, n=36) were currently or had previously been receiving ranibizumab; 8% (n=3) were receiving or about to initiate therapy with aflibercept. Most patients (62%, n=24) preferred monthly monitoring with treatment given as needed based on disease progression, 26% (n=10) preferred bimonthly monitoring and fixed bimonthly dosing and 13% (n=5) had no preference. Patients reported being very anxious about their sight and tended implicitly to trust their treating physician to decide on the most appropriate treatment; as a result, patients reported being highly adherent to therapy. Many patients reported appreciating the reassurance provided by frequent monitoring and were very satisfied with their current dosing regimen as chosen by their treating physician. **CONCLUSIONS:** The results of this pilot, qualitative study suggest that most patients prefer frequent monitoring with dosing based on disease progression to treat their wAMD. Understanding patient preferences will help physicians to manage their patients' disease most effectively and potentially ensure greater adherence to therapy. Further research is warranted to understand patient preferences quantitatively.

PSS38
PSORIASIS PATIENTS' TOLERANCE FOR THERAPEUTIC RISKS IN RETURN FOR SYMPTOM IMPROVEMENT IN THE UNITED KINGDOM
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OBJECTIVES: To quantify UK psoriasis patients' tolerance for serious side-effect risks associated with biologic treatments relative to the value of symptom improvements. **METHODS:** Members of a UK psoriasis patient organization were invited to complete an on-line conjoint-analysis survey which evaluated efficacy and safety features of biologic treatments for psoriasis. Patients' trade-off preferences for improvements in the severity and coverage of psoriatic lesions were elicited, as well as treatment-related risks of tuberculosis (TB), serious infections, and lymphoma. The choice pattern observed in the data was used to estimate preference weights which indicated patients' relative trade-off preferences among treatment outcomes. Preference weights were used to derive maximum levels of side-effect risks that patients would accept for various improvements in psoriasis symptoms. The DLQI was used to assess the impact of psoriasis on patients' quality of life. **RESULTS:** A total of 159 people with a self-reported physician diagnosis of psoriasis completed the survey. Mean age was 39 years and most respondents reported having psoriasis for at least 5 years. Also, the mean DLQI score was 11. Respondents would accept up to 0.39% of treatment-related risks of lymphoma for reducing the area covered by a severe lesion from 25% to 10% of their torso, and up to 0.60% if lesions were on their arms or legs.For the same improvement in symptoms, respondents would accept up to a 2.3% risk of TB or 3.3% risk of serious infections if the lesions were on their torso, and a 3.6% risk of TB or 5.2% risk of serious infections if the lesions were on their arms and legs. **CONCLUSIONS:** Psoriasis patients' tolerance for side-effect risks varies with side-effect severity and location of lesions. Estimates of patients' risk tolerance for serious side-effects indicate that patients value psoriasis symptom control further confirming that psoriasis has a significant effect on patients' quality of life.

PSS39
ATOPIC DERMATITIS IN ADULTS: DESIGN AND VALIDATION OF A SPECIFIC BURDEN QUESTIONNAIRE
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OBJECTIVES: Atopic Dermatitis (AD) is a common skin condition, even in adults. On the contrary of quality of life questionnaires, the notion of individual burden associated with a disease has been introduced to determine the "disability" in the broadest sense. The aim of the current study was to develop and validate the Atopic dermatitis Burden Scale questionnaire for Adults (ABS-A) following Classical Test Theory method (CTT). **METHODS:** The questionnaire was developed by a working group composed of individuals with expertise in PRO development, dermatologists, and patients from patients' association. Subsequently, this questionnaire was sent to 900 people with AD. ABS-A was refined via exploratory factor analysis (EFA). Internal consistency was determined by calculating the Cronbach's alpha, concurrent validity by calculating the Spearman's rank coefficient correlation between ABS-A, SF-12 and Dermatology Life Quality Index (DLQI) questionnaires. Discriminant validity was analysed according to the severity degrees of AD assessed by the Patient Oriented SCORing index of AD questionnaire. **RESULTS:** A total of 128 individuals filled out the ABS-A entirely and were then evaluated. 68.8% of them were men and almost 50% of them were aged between 35 and 64 years old. Based on the results of the EFA, 1 item was removed due to cross-loading on factors. Consequently, the questionnaire consisted of 18 items grouped into 4 domains. ABS-A showed good internal coherence (Cronbach's á: 0.89). ABS was significantly correlated to both components of the SF-12 ($r(PCS)=-0.36$, $p<0.0001$; $r(MCS)=-0.52$, $p<0.0001$). A higher coefficient correlation has been found between ABS-A and DLQI ($r=0.78$; $p<0.0001$). Significant differences between severity degrees of AD have been shown. **CONCLUSIONS:** These preliminary results suggest the validity of the ABS-A questionnaire. However, since recruitment of patients is not achieved, performing analyses of the other stages of CTT, and Confirmatory Factor analysis or Rash analysis are warranted. Comparison between both methods may be valuable.

PSS40
THE BURDEN IMPOSED BY ATOPIC DERMATITIS ON FAMILIES: CREATION OF A SPECIFIC QUESTIONNAIRE
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OBJECTIVES: The notion of individual burden, associated with the disease, has been introduced recently to determine the "disability" caused by the pathology in the broadest sense of the word (psychological-social-economic-physical). **METHODS:** The ABS questionnaire (Atopy Burden Score Q) consists of 19 items, structured around 5 components. It was distributed to a random sample of families consulting at the Necker Hospital, staying at the Avène Hydrotherapy Center, and members of the patient-association. The ABS was accompanied by SF12 and PGWBI, to confirm internal and external validation, and by the PO-SCORAD to assess the level of severity. **RESULTS:** A total of 58 Q were considered evaluable. 51% of the AD children were girls. The PO-SCORAD established the level of severity of the AD: 14%, 50% and 36% of children had mild, moderate or severe AD respectively. Internal-validity was measured by Cronbach's alpha, which is equal to 0.81, reflecting a good homogeneity of the 19 items. The mean PGWBI score is 51.82±14.28. The score reflecting the most important deterioration is found among parents of children with severe atopy. In contrast, the scores associated with moderate and mild atopy are not correlated with severity. Families' QoL, measured using the SF12, revealed no deterioration in the physical component. The ABS score is correlated with the scores of the Q

used, thus confirming external validity. The mean score calculated from the ABS is 48.17±18.36. The score increases with the severity of the AD. A statistically significant difference is observed between the 3 severity-groups, i.e. mild, moderate and severe, with scores of 30.63, 42.55 and 62.62 respectively. **CONCLUSIONS:** The internal and external validity of our Q were confirmed. ABS is correlated with the severity of AD. Hence, we have a short, easy-to-use, validated tool for assessing the burden imposed by atopy on families. Following cultural and linguistic validation, the ABS is now available in US English, Spanish, German and Italian.

PSS41

HEMANGIOMA FAMILY BURDEN: CREATION OF A SPECIFIC QUESTIONNAIRE

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OBJECTIVES: The notion of individual burden, associated with the disease, has been introduced recently to determine the "disability" caused by the pathology in the broadest sense of the word (psychological-social-economic-physical). The aim of our study is to develop a specific questionnaire for assessing the burden on families of children with HI. **METHODS:** A "Hemangioma Family Burden" questionnaire (HFB) consisting of 22 items, The score increases with the heaviness of the burden. It was distributed accompanied by 2 validated QoL questionnaires (SF12 and PGWBI) to obtain internal and external validation **RESULTS:** A total of 58 evaluable Q were returned. One parent from each family described how they perceived the effects of the disease, which led to the creation of 6 severity groups, paired together for size reasons: "not-very-far-reaching" and "somew-hat-far-reaching"; "quite-far-reaching" and "far-reaching"; "very far-reaching" and "extremely far-reaching". Internal validity was measured by Cronbach's alpha, which is equal to 0.95, reflecting a good homogeneity of the 22 Q items. The mean scores of the physical and mental components are 54.93±5.12 and 40.49±11.28 respectively. Hence, the HFB score is correlated with these 2 components, thus confirming external validity. The mean score calculated from the HFB is 23.42±19.93. The score increases with the "severity score" of the parents. In fact, a statistically significant difference is observed between the 3 severity groups: 5.28±6.8 for those reporting the smallest extent to 41.0±18.71 for those reporting the greatest extent, and 27.7±16.96 for a moderate extent. This confirms the sensitivity of the HFB **CONCLUSIONS:** During the evaluation, internal and external validity were confirmed. The HFB is correlated with the extent felt by parents, a feeling deemed relevant because it is often the cause of consultation and demand for treatment. We now have an easy-to-use, validated IH tool for assessing the disability caused. Following cultural and linguistic validation, the HFB is now available in US English, Spanish, German and Italian.

PSS42

A SYSTEMATIC REVIEW OF PATIENT REPORTED OUTCOMES IN GLAUCOMA

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OBJECTIVES: Patient reported outcomes (PRO) are becoming useful tools for collecting and generating evidence for new medical products to show improvements in health-related quality of life (HRQoL). Glaucoma is a chronic disease with high importance for patient HRQoL. The objective of this study was to review, analyze, and understand trends in the PRO instruments used in patients with Glaucoma. **METHODS:** A systematic literature search for Glaucoma trials with PROs endpoints was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar and Cochrane. Data was collected for the study size, interventions, year, PRO instrument and results for PROs. Analysis for conducted to identify trends in commonly used PRO instruments and categorize results as positive, neutral or negative. **RESULTS:** A total of 31 studies with a total of 9819 patients were identified. In these studies there were eleven different PROs instruments were identified that were Glaucoma health perception index, Glaucoma quality of life questionnaire (Glau-QoL), Glaucoma utility index, Impact of vision impairment, Low vision quality of life questionnaire, National eye institute visual function index-19 items, National eye institute visual function index-51 items, Nursing home vision quality of life questionnaire, Quality of life and visual function questionnaire, Vision core module 1, and Vision quality of life index. The most commonly used instruments were Impact of vision impairment (used in 7 studies) and Low vision quality of life questionnaire (used in 4 studies). **CONCLUSIONS:** Patients with glaucoma have significant impairment in their QoL, hence collection of such data is important for new medical products. PRO instruments such as Impact of vision impairment and Low vision quality of life questionnaire have been commonly used to generate evidence to show which therapies improve patient QoL.

PSS43

CORRELATIONS BETWEEN CHANGES IN THE URTICARIA ACTIVITY SCORE (UAS7) AND THE DERMATOLOGY LIFE QUALITY INDEX (DLQI) FROM BASELINE TO 28 OR 40 WEEKS: COMPARISONS OF TRAJECTORIES OF CHANGE IN PATIENTS WITH CHRONIC SPONTANEOUS/IDIOPATHIC URTICARIA (CSU/CIU)

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OBJECTIVES: The UAS7 is a patient-reported measure of urticaria symptoms. Daily pruritus scores and number of hives are summed over 7 days for a weekly score. The DLQI was developed as a brief (10-item) patient-reported measure with one-week recall for routine clinical use to assess the psychosocial effects of skin disease. The objective of this analysis was to examine changes in the UAS7 with those of the DLQI to see if the DLQI could be used in a clinic visit in lieu of collecting one week of UAS7 diary data. **METHODS:** Data come from three pivotal, phase 3 clinical trials investigating the effects of omalizumab for patients with refractory CSU/CIU (publication available elsewhere). DLQI data were collected at baseline and weeks 4, 12, 24, and 40 (ASTERIA I and GLACIAL), and baseline and weeks 4, 12, and 28 (ASTERIA II). UAS7 score was reported at baseline and every four weeks but data from the same weeks as the DLQI were used for these analyses. Pooled data from all 3 studies were analysed using latent growth models to generate intercepts and slopes of change across trials for each patient, irrespective of treatment. Slopes of change were correlated to examine how closely DLQI changes mirrored UAS7 changes. **RESULTS:** Results indicated that both measures showed large improvements over the course of the trials: UAS7 and DLQI scores were high at the start of the study reflecting moderate-severe CSU/CIU (UAS7) and a very large effect on patient's life (DLQI). Correlations between changes in DLQI and changes in UAS7 by study end were 0.88, 0.85, and 0.88, indicating high correspondence between the two measures. **CONCLUSIONS:** These results suggest that collecting DLQI information in-clinic can provide an excellent indication of the weekly UAS7 score, and is more efficient for clinical practice routine in assessing CSU/CIU patients.

PSS44

ETANERCEPT PROVIDES IMPROVED QUALITY OF LIFE REGARDLESS OF THE PRESENCE OF PSORIATRIC ARTHRITIS IN MODERATE/SEVERE PSORIASIS SUBJECTS FROM CENTRAL AND EASTERN EUROPE, LATIN AMERICA AND ASIA

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OBJECTIVES: Some psoriasis patients also have psoriatic arthritis (PsA), which increases disease burden and further reduces quality-of-life (QoL). Our objective was to compare QoL of subjects with both psoriasis and PsA to those with psoriasis alone, and to evaluate improvement on etanercept (ETN) therapy in specific countries of Central and Eastern Europe, Latin America, and Asia where data are limited. **METHODS:** Patients with moderate/severe psoriasis were randomized to 50mg ETN QW (once weekly) or 50mg ETN BIW (twice weekly, weeks 1-12), followed by 50mg QW (weeks 13-24). The following post-hoc assessments were included: EuroQoL-5D (EQ-5D); Dermatology Quality of Life Index (DLQI); Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue; Hospital Anxiety and Depression Scale (HADS); Medical Outcomes Study (MOS)-Sleep; and Work Productivity and Activity Impairment (WPAI). Subjects with and without PsA were pooled across ETN groups for comparisons of changes in scores from baseline to week 24, which were based on independent sample t-tests. **RESULTS:** Of 171 subjects analysed, 64 (37.4%) had PsA. Baseline demographic characteristics and QoL measures were similar in PsA and psoriasis-alone groups. EQ-5D scores improved significantly over time with ETN treatment in both subjects with and without PsA ($P<0.0001$) with similar adjusted mean improvement in both groups after 24 weeks (0.2 vs 0.2; $P=0.6202$). Improvement in EQ-5D greater than MID (change ≥ 0.05) at week 24 was observed in a greater proportion of PsA than psoriasis-alone subjects (74.6% vs 63.8%; $P=0.174$). Significant improvements from baseline in both PsA and psoriasis-alone groups were also observed after 24 weeks in DLQI (both $P<0.0001$), FACIT (both $P<0.01$) and HADS anxiety (both $P<0.0001$) scores. Improvements of other patient-reported outcomes were also observed at weeks 24 in both disease subgroups. **CONCLUSIONS:** ETN in both dose regimens provided significant improvement in QoL measures in subjects with moderate-to-severe psoriasis, regardless of the presence of PsA.

PSS45

QUALITY OF LIFE IMPROVEMENT WITH ETANERCEPT IN PATIENTS WITH MODERATE/SEVERE PSORIASIS FROM CENTRAL AND EASTERN EUROPE, LATIN AMERICA AND ASIA

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OBJECTIVES: To assess the impact of etanercept (ETN) on quality-of-life (QoL) through 24 weeks in patients with moderate/severe psoriasis in specific countries of Central and Eastern Europe, Latin America, and Asia where data are limited. **METHODS:** Patients with moderate/severe psoriasis were randomized to 50mg ETN QW (once weekly) or 50mg ETN BIW (twice weekly, weeks 1-12), followed by 50mg QW (weeks 13-24). Patients completed the Dermatology Life Quality Index (DLQI) EuroQoL 5D (EQ-5D), FACT-Fatigue, HADS Anxiety Score, Psoriasis Subject Satisfaction Questionnaire, and Work Productivity Activity Impairment (WPAI) at baseline and subsequent visits. **RESULTS:** Of 171 patients analysed, 85 were randomised to ETN BIW and 86 to ETN 50 QW. Baseline DLQI scores were 14.8 in both treatment groups suggesting severe QoL impairment. Significant improvements in DLQI from baseline were observed at weeks 12 and 24 in both groups (all $p<0.0001$); mean improvement at week 12 for ETN BIW was greater than for ETN QW (10.8 vs 8.4, $p=0.001$), but was similar between groups at week 24 (11.0 vs 9.5, $p=0.063$). EQ-5D utility was significantly improved from baseline in both groups at weeks 12 and 24 (all $p<0.0001$), with mean improvement significantly greater for the higher dose at both time-points (week 12: 0.3 vs. 0.2, $p=0.029$; week 24: 0.3 vs. 0.2, $p=0.027$). Mean EQ-5D improvement at week 24 was greater than MID (change ≥ 0.05) in a significantly greater proportion of patients receiving BIW than QW (77.1% vs 58.8%; $p=0.013$). Improvements of other patient-reported outcomes from baseline were observed at weeks 12 and 24 in both treatment groups. **CONCLUSIONS:** At baseline, patients had severely impaired QoL, and improvement in QoL was achieved with both ETN regimens. Improvements observed with ETN BIW were significantly greater than with ETN QW for both DLQI and EQ-5D utility at week 12, but only for EQ-5D at week 24.

PSS46

QUALITY OF LIFE OF PATIENTS SUFFERING FROM EXUDATIVE AGE-RELATED MACULAR DEGENERATION AND TREATED BY INTRAVITREAL INJECTIONS AND ITS PREDICTORS: THE EQUADE STUDY

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OBJECTIVES: To assess the quality of life (QoL) of patients with an exudative Age-Related Macular Degeneration (AMD) treated by intravitreal Anti-VEGF (vascular endothelial growth factor) and determine its drivers in a real-life setting. **METHODS:** A self-reported survey was carried out among AMD patients belonging to 2 French associations. Only patients with exudative AMD and under active intravitreal anti-VEGF treatment over the last 6 months were included. Data on demographics, disease parameters, past and ongoing treatments were collected. One validated vision-specific QoL instrument was also considered: the NEI-VFQ-25. Patients were stratified into four groups of visual acuity (VA). A multivariate model was performed to identify the QoL drivers. **RESULTS:** Out of the 1,888 questionnaires mailed 32.4% were returned and 24.7% fulfilled the inclusions criteria and were fully completed for analyses. Patients' mean age was 78.0 years (SD 7.6). A total of 70.5% were women. A total of 60.4% had bilateral disease. The mean duration of symptomatic exudative AMD was respectively of 7.2 (SD 5) and 2.3 years (SD 3) for the first and the second eye. Most of anti-VEGF treated eyes (n=641) were treated for more than 1 year (77.4%). The mean annual number of anti-VEGF injections was 4.7 (SD 2.7). The mean NEI-VFQ-25 global score was 53.4 (SD 21.5). A decrease of this score was positively correlated to VA decrease (0.63;p<.0001). This correlation was observed for 11 subscales out of 12. The main risk factor associated to the lower Qol score was the worst VA category, with an odds ratio of 5.2 (CI95%[2.6-10.4];p<.0001). **CONCLUSIONS:** In a real-life survey of patients treated and followed for exudative AMD, VA decrease was the strongest factor linked to QoL worsening. Other factors such as the number of Anti-VEGF injections were not correlated to QoL in this study. Then, preservation of useful VA still remains a major concern to improve patients' QoL.

PSS47

ASSESSMENT AND CAUSAL LINK BETWEEN VISION-RELATED QUALITY OF LIFE AND GENERAL HEALTH RELATED QUALITY OF LIFE IN DRY EYE PATIENTS

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OBJECTIVES: This abstract describes attempts to evaluate the burden of dry eye disease with regards to vision-related quality of life (QoL) and the causal link to general health related quality of life. Recent increased awareness of dry eye disease (DED) by both health care professional and patients has been accompanied by improved recognition that it is a chronic disorder often requiring long-term treatment and management. DED, frequently associated with symptoms of discomfort and visual disturbance, also impairs general health status and general quality of life, including aspects of physical, social, and psychological functioning. This abstract summarizes the available research on the burden of DED and the impact on QoL. **METHODS:** The research included systematic literature search on clinical relevant DED literature based on HTA relevant requirements, in order to identify potential differences within DED. Correlations with socio- demographic characteristics, clinical parameters, and psychological status were evaluated. **RESULTS:** A relative small amount of data supporting the effectiveness of DED treatments as assessed by QoL measures exists (such as DEQLQ, IDEEL etc.). Dry eye treatments have been associated with improvements in symptoms measured by OSDI (Ocular Surface Disease Index), and in ophthalmology-disease-specific measurement of QoL, and with enhancement of patients' ratings regarding their ability to perform activities of daily life. Significant correlations were found between symptoms score and QoL scores and patient anxiety, especially depression levels which correlates to general health. **CONCLUSIONS:** Vision-related QoL in dry eye patients was correlated with general health status, especially with anxiety and depression. DED has further implication on general public health and deserves an increased attention and resources.

SENSORY SYSTEMS DISORDERS – Health Care Use & Policy Studies

PSS48

PHYSICIAN EXPERIENCE WITH RITUXIMAB TO TREAT PEMPHIGUS VULGARIS IN CANADA: A QUESTIONNAIRE-BASED STUDY

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OBJECTIVES: To examine the experience of physicians who treat patients with pemphigus vulgaris (PV) in Canada as well as the utilization and access of the drug rituximab (Rtx). **METHODS:** An online questionnaire was created in SurveyMonkey® to collect data from participants based on a convenience sample size of 10 English-speaking dermatologists. Consent was implied once the dermatologist completed the questionnaire. Non-identifying information for both dermatologists and PV patients was collected. **RESULTS:** The 10 participating dermatologists have been treating PV patients an average of 20.9 ± 10.7 (5 – 45) years in which 28.8 ± 58.3 (0 – 200) was the mean number in their practice. Experience with Rtx is based on an average of 4.1 ± 3.8 (0 – 10) years and 13.1 ± 29.2 (0 – 100) PV patients treated with Rtx. All participants answered that "failure of conventional therapy for at least six months" was the primary reason for using Rtx and that azathioprine, intravenous immunoglobulin and mycophenolate mofetil were the most popular treatments used to treat PV patients prior to Rtx. On average, it takes 3.2 ± 2.2 (0 – 6) months for a remission to be induced after Rtx treatment and 90% of the dermatologists were concerned that infections would be an adverse event. Lastly, 6.3 ± 12.3 (0 – 40) was the mean number of Rtx drug reimbursement letters that the dermatologists had written on behalf of PV patients in which 1.9 ± 2.5 (0 – 6) letters were successful in securing Rtx drug reimbursements. **CONCLUSIONS:** A recent survey of 10 Canadian dermatologists experienced with treating PV patients found that Rtx utilization is still new, disease remission is achieved within a short period of time, and the drug reimbursement process remains a barrier based on the low number of letters written by the dermatologists.

PSS49

REAL-WORLD UTILIZATION DATA OVER 4 YEARS OF RANIBIZUMAB INJECTIONS FOR THE TREATMENT OF WET AGE-RELATED MACULAR DEGENERATION IN CANADA

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OBJECTIVES: To assess the yearly frequency of ranibizumab injections for the treatment of wet Age-Related Macular Degeneration (wAMD) in two large Canadian public drug plans: Ontario Public Drug Program (OPDP) and Régie de l'assurance-maladie du Québec (RAMQ). **METHODS:** Pharmastat database (IMS Health Canada Inc.) was used to assess the mean annual number of ranibizumab injections for wAMD patients covered by the OPDP or RAMQ drug plans (1 injection was defined as 1 claim). Only wAMD treatment-naïve patients were included and the index date was defined as the date of the first ranibizumab claim. The analysis looked at monthly data from March 2008 to November 2012 for OPDP patients and from January 2008 to May 2012 for RAMQ patients and tracked the mean number of claims during the patient's first, second, third and fourth year of ranibizumab therapy. **RESULTS:** For the OPDP, the mean number of ranibizumab injections was 6.0, 5.4, 5.5 and 5.6 for year 1 (N=26,606), year 2 (N=19,466), year 3 (N=12,708), and year 4 (N=6,681), respectively. For the RAMQ, the mean number of injections was 5.4, 4.7, 5.2 and 5.7 for year 1 (N=3,457), year 2 (N=2,185), year 3 (N=1,178), and year 4 (N=349), respectively. **CONCLUSIONS:** These results suggest that many Ontario and Quebec retina specialists and ophthalmologists do not treat monthly but rather adopt an individualized ranibizumab treatment regimen to manage their patients' wAMD. In addition, these results provide information on the real-world utilization of ranibizumab in wAMD for up to four years of treatment. The analyses, conclusions, opinions and statements expressed are those of Novartis Pharmaceuticals Canada Inc., and not those of IMS Health Canada Inc.

PSS50

DEFINING THE PATIENT JOURNEY VIA CLAIMS ANALYSIS IN AN ORPHAN OPHTHALMIC CONDITION: IS THERE A STANDARD OF CARE?

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OBJECTIVES: To date, there has not been extensive study on the economics or established treatment guidelines in patients with non-infectious posterior uveitis (NIPU). Current treatment is mostly topical/systemic/injection corticosteroids, though treatment is associated with significant side effects. We undertook a secondary research analysis of MarketScan claims data to better understand the patient journey and the current treatment standard of care for NIPU patients. **METHODS:** We analyzed the MarketScan dataset to identify NIPU patients from a defined list of ICD-9 codes. We then identified patients with 30 months of continuous enrollment data, 6 months prior and 24 months post initial diagnosis. Patients were assessed for number of office visits/procedures, number of diagnostic tests, number of inpatient stays, and number and frequency of drug treatment (corticosteroids, corticosteroid injections, immunomodulators, and biologics). **RESULTS:** Of the 56 million lives in the claims dataset, 34,827 had an ICD-9 code consistent with NIPU. Of these unique patients, 33,386 were analyzed. 78.8% of patients came from the commercial dataset, 59% of patients were female, and the average age at diagnosis was 51.5 years. Prior to diagnosis, 5,775 patients were treated for NIPU at an average cost of $185.43 per patient (58.0% topical/systemic corticosteroids, 22.7% corticosteroid injections, 15.7% immunomodulators, 3.7% biologics). In the 24 months post-diagnosis, the number of treated patients increased to 11,570 patients at an average cost of $249.01 per patient (45.7% topical/systemic corticosteroids, 37.4% corticosteroid injections, 16.4% immunomodulators, 3.2% biologics). Examining each six-month period post-diagnosis, the number of treated patients decreased, but the share of treatments remained the same. **CONCLUSIONS:** Patients with NIPU are engaging the health care system and being treated for NIPU at least six months prior to an official diagnosis. Efforts should be made to better identify patients with NIPU to ensure proper diagnosis and treatment.

PSS51

WAITING TIMES AND SCHEDULING IN DERMATOLOGICAL PRACTICES IN GERMANY

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OBJECTIVES: Waiting time for medical consultation is an important quality indicator of health systems. International studies have shown that there is considerable variation of waiting time between countries. It may also vary within countries depending on the degree of emergency, indication, and way of reimbursement. Our objective was to assess practice organization and waiting times in German dermatological practices. **METHODS:** A one page questionnaire was sent to be returned anonymously by fax to 2,644 German office base dermatologists randomly selected. Included were items on organization of practice, region and specific average waiting times for selected diagnoses. The postal codes obtained from the practices were mapped to the 17 German regions of physicians association of statutory health insurance. **RESULTS:** Data sets were obtained from 681 practices. A total of 4.3% of practices rarely or never gave fixed appointments, 36.3% only gave fixed appointments. The percentage of treatment at fixed appointments varied by regions from 71.1% in Bremen and Brandenburg to 90.0% in Hessen. Moreover, private practices not being associated with the statutory health system showed a higher rate of timed appointments with 94.8% compared to 83.0%. Average waiting time in practices treating also patients with statutory health insurance is 5 weeks and thus 4 times higher compared to waiting time in practices treating private insured patients only (1.2 weeks). There was large variation in waiting time for the first appointment between different indications. Patients with acute eczema or pigmented lesions specific for melanoma were given appointments after 1.7 or 1.2 weeks, respectively; for skin cancer screening, patients had to wait for 5.7 weeks on average. There was only small geographic variation regarding this pattern. **CONCLUSIONS:** Patients with risky and acute indications are treated with low waiting times whereas patients with less threating skin diseases have to wait longer for appointments at dermatological offices.

PSS52

SAFETY IN NATIONAL CARE - REAL WORLD DATA FROM THE GERMAN PSORIASIS-REGISTRY "PSOBEST"

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OBJECTIVES: The registry "PsoBest" observes systemic therapy of moderate and severe psoriasis/psoriasis-arthritis in Germany since 2008. The registry is supported by the German society for dermatologists, the association of dermatologists, pharmaceutical manufactures, dermatologists and patients. It is located at CVderm and documents safety, effectiveness and patient benefit in routine health care. One purpose of PsoBest is to monitor the safety of systemic antipsoriatics. **METHODS:** Patients receiving first time a conventional systemic or biologic treatment are observed for 5 years, regardless of therapy switches. Standardised questionnaires for physicians and patients are compiled. Adverse and serious adverse events (AE/SAE) are coded in MedDRA and analyzed twice a year. **RESULTS:** Pharmacovigilance after 42 months on 1984 patients with 800 expositions to biologics (1196 patient years) and 1430 to systemics (1548 patient years) resulted in 187 SAE codings in 121 patients (6.1%). A total of 105 SAE were observed under biologic and 95 under conventional systemic treatment (8.9 and 4.5%, respectively). Of these, 20 SAE in 14 patients were observed in combined treatment. By system-organ-classes, general disorders and administration site conditions were observed for 2.3% of biologic (1.51 events/100 patient years) and 1.3% systemic patients (1.32 events/100 patient years). The rates for cardiac disorders were 0.92 (1.4% of patients) and 0.84 (0.9% of systemic patients), respectively. For infections and infestations the rates were 0.84 (1.3%) and 0.52(0.8%) and for neoplasms benign, malignant and unspecified (incl. cysts and polyps) 0.67 (1.0%) and 0.71 (0.8%). **CONCLUSIONS:** PsoBest provides urgently needed long-term safety data in the systemic treatment of psoriasis and psoriatic-arthritis from routine care in Germany. To date, no safety concern emerged from the registry. To raise the power for signal detection, verification, analysis and assessment, PsoBest is proactively contributing to the European surveillance of effectiveness and safety of systemic psoriasis therapy (ENCEPP-network psonet).

PSS53

AFLIBERCEPT IN NEOVASCULAR (WET) AGE-RELATED MACULAR DEGENERATION: AN ANALYSIS OF THE PAYER DECISION LANDSCAPE

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OBJECTIVES: To investigate and analyse decisions of Health Technology Assessment or national drug reimbursement agencies for aflibercept in neovascular (wet) aged-related macular degeneration, including decision outcomes, the rationale for these, the data package and any payer critique of the manufacturer approach. **METHODS:** A search of decision-making agency websites in key European markets, Canada and Australia was conducted to identify relevant decisions. Data were extracted and used to conduct a qualitative analysis of decisions. **RESULTS:** Five decisions were identified; from NICE (England & Wales), SMC (Scotland), HAS (France), G-BA (Germany) and PBAC (Australia). In all instances, the clinical and economic arguments, where applicable, were based on demonstration of non-inferiority of aflibercept to an existing therapy, ranibizumab. These arguments were supported by two key trials of aflibercept vs. ranibizumab: VIEW 1 and 2, and also indirect comparisons and network meta-analyses. In all decisions, aflibercept was either recommended for the full licensed indication or recommended with restrictions. All agencies commented that the key trials were well conducted and unbiased; however, they also state that the dosing schedule for ranibizumab did not reflect the license or clinical practice in respective markets, and it was unclear if there would be any difference in the frequency of injections between therapies in the clinical setting. Furthermore, for the economic models for NICE, SMC and PBAC, the respective agencies thought the frequency of injections and number of clinician visits for ranibizumab were overestimated. All agencies concluded that aflibercept demonstrated no additional clinical benefit over ranibizumab. For example, HAS in France granted an ASMR level V: no improvement in clinical benefit, while NICE recommended that aflibercept be used in accordance with their recommendations for ranibizumab. **CONCLUSIONS:** While aflibercept is an effective alternative therapy to ranibizumab, payers have concluded that it offers no demonstrable added clinical benefit compared with ranibizumab.

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HEALTH RELATED QUALITY OF LIFE-OUTCOME IN NATIONAL CARE - REAL WORLD DATA FROM THE GERMAN PSORIASIS-REGISTRY "PSOBEST"

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OBJECTIVES: The registry "PsoBest" observes systemic therapy of moderate and severe psoriasis/psoriasis-arthritis in Germany since 2008. The registry is supported by the German society for dermatologists, the association of dermatologists, pharmaceutical manufactures, dermatologists and patients. It is located at CVderm and records efficacy, safety, and patient benefit in routine health care. One purpose of PsoBest is to monitor health related quality of life (HrQoL) and severity of psoriasis in the process of care. **METHODS:** Patients receiving first time a conventional systemic or biologic therapeutic are observed for 5 years, independent of further treatment. Standardised questionnaires for physicians and patients are compiled. Main outcomes are severity (PASI), affected body surface area (BSA) and HrQoL (DLQI and EQ-5D). **RESULTS:** A total of 1,984 patients were enrolled up to July 2012 (60% male, mean age of 47 years); mean duration of illness was 19±14 years. Patients on biologics (n=686) tended to be male (63 v. 58%), older (48.1 v. 46.7 years) as patients on conventional systemics (n=1,298) and had a longer history of psoriasis (21.9 v. 16.8 years). The biologic cohort showed more nail involvement (64 v. 52%), signs of arthritis (47 v. 17%), higher severity (PASI: 15.6 v. 14.6; BSA: 22. v. 21.5) and lower HrQoL (DLQI: 11.7 v. 11.0; EQ-5D VAS: 50.6 v. 55.7). For the biologics cohort, mean PASI improved to 4.5 between 12 and 24 months (reduction of 70% from baseline). Moreover, HrQoL (DLQI) improved by 65% from inclusion. The conventional systemics cohort showed comparable reduction in PASI=3.1 (77%) but less improvement in DLQI= 3.1 (49%). **CONCLUSIONS:** PsoBest provides long-term real-world data on psoriasis care in Germany. The results show the high burden of psoriasis patients entering the registry and also the high quality of care and patient benefit after initiation of systemic treatment.

PSS55

RECRUTING PHYSICIANS FOR HEALTH OUTCOME AND POST-APPROVAL STUDIES: BENEFITS OF A MANAGED PHYSICIAN PANEL

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OBJECTIVES: Access to multi-country physician panels is an alternative option to recruit medical sites for health outcome or post-approval studies, compared to the conventional approach of individually recruiting clinical expert sites. The objective of our study was to assess the potential of physician panels for site recruitment. **METHODS:** In 2012, a representative survey among members of a managed physician panel (All Global's managed panel of ophtalmologists in US, UK, GER, FR, IT and SP) was conducted. The survey assessed the willingness of the physicians to participate in post-approval studies. Information about former participation in those studies and commitment to special requests for post-approval studies (e.g. ethical committee involvement, advent reporting to sponsor, security of patient's informed consent) were also collected. **RESULTS:** A total of 200 opthalmologists participated in the survey. Since no special incentive was offered for participation the response rate of more than 25% was satisfactory. 79 (39,5%) of the physicians formerly participated in clinical trials and 95 (47,5%) in post-approval studies. 54,5% of the ophtalmologists were willing to participate in future studies. More than 80% of this group was ready to ask their hospital or other legal authorities for permission to participate in studies of this kind, to report serious adverse events to the sponsor of the study and to ask patients for written informed consent. **CONCLUSIONS:** Managed physician panels are a valuable alternative option to recruit medical sites for post-approval or health outcome studies. Every second ophtalmologist from panels is experienced in this kind of studies and most of them are willing fullfil all necessary legal and quality requirements. In addition to timing and cost factors, an adavantage of physician panels is the better representation of daily medical routine-practice, adding to the epidemiological validity of respective projects.

PSS56

LYMPHEDEMA – THE LONG WAY TO DIAGNOSIS AND THERAPY

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OBJECTIVES: Clinical experience indicates that edema often remain undiagnosed. The aim of this study was to examine how much time passes between important events in the 'patient journey' and what predicts late consultation and diagnosis. **METHODS:** Sixty-five patients with secondary arm lymphedema and 161 patients with primary or secondary leg lymphedema were interviewed. The following latency times were computed: time between 1) first symptoms and first visit to physician; 2) visit to physician and diagnosis; 3) diagnosis and lymph drainage therapy; and 4) diagnosis and compression therapy. Associations of latency times with patient and clinical characteristics were analysed using t tests and multivariate linear regression. **RESULTS:** All arm edema patients had consulted a physician in the year after first symptoms at the latest, and everyone except two received the diagnosis in the following year at the latest. For secondary leg edema, the average latency until physician consultation was also short with 0.5 ± 1.8 years, and latency until diagnosis was 1.7 ± 3.8 years. In contrast, latencies in primary leg edema were significantly longer: The average time between first symptoms and physician consultation was 5.2 ± 11.0 years, and edema diagnosis was made after further 6.7 ± 11.4 years. On average, it took 13.5 years from first symptoms to lymph drainage therapy in these patients and 13.7 years until compression therapy. Predictors of late consultation and late diagnosis in primary leg edema were age<40, positive family anamnesis, and female gender. **CONCLUSIONS:** Primary leg lymphedema are diagnosed late in many cases, especially in younger women.

PSS57

ADHERENCE BY SPANISH RETINOLOGISTS TO THE GUIDANCE FOR THE MANAGEMENT OF PATIENTS WITH WET AGE-RELATED MACULAR DEGENERATION

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OBJECTIVES: To assess the adherence by Spanish retinologists to the recommendations for the management of age-related macular degeneration (AMD) published by the Spanish Society of Retina and Vitreous (SERV). **METHODS:** Non-interventional, retrospective and multicenter study, involving 59 researchers from different Spanish Ophthalmology Services that collected medical records from 346 patients aged ≥50 years and diagnosed with exudative AMD. **RESULTS:** Adherence to SERV-guidelines by Spanish retinologists was high concerning diagnostic (96.8%) and control items (98.6%) of AMD patients, slightly lower for therapeutic issues (84.4%), and much lower on patient follow-up and retreatment criteria (46.9%). When focusing on diagnostic, first symptoms indicative of wet AMD were sharp and progressive loss of visual acuity (64.7%), followed by metamorphopsia (distorted vision) (33.8%) and central scotoma (23.1%). Main diagnostic confirmatory tests were visual acuity (97.1%), OCT (93.4%), biomicroscopy (92.2%) and fluorescein angiography (71.1%). For therapeutic issues, first choice treatment was based on anti-VEGF-drugs (99.1%), mainly ranibizumab (96.8%) as a loading dose of three injections (88.1%). Main patient follow-up tests were: visual acuity tests (98.0%), optical coherence tomography (96.0%), biomicroscopy (91.9%). Most common control schemes during the first year of treatment were every-two-months (35.8%) or monthly (30.4%) visits;

while after first year of treatment, controls tend to become less frequent, mostly every-three-months (39.9%). When recurrence occurs, main retreatment criteria were: presence of macular fluid (93.5%), loss of ETDRS letters (50.5%; 68.8% with ≥5 letters), macular hemorrhage (46.3%) and increase of central-retinal-thickness (45.4%). Single injection of anti-VEGF retreatments was applied in 48.6% of recurrences, while 23.6% were not treated with anti-VEGF. **CONCLUSIONS:** A relatively high adherence to SERV guidelines was followed by Spanish retinologists regarding diagnosis, treatment and control of AMD. However, limitations have been identified on patterns of follow-up and retreatment criteria that may compromise therapeutic and clinical outcomes.

PSS58

TREATMENT PATTERNS OF RANIBIZUMAB AND AFLIBERCEPT FOR THE MANAGEMENT OF WET AGE-RELATED MACULAR DEGENERATION IN ROUTINE CLINICAL PRACTICE IN THE UNITED STATES

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OBJECTIVES: To compare the frequency of injections for ranibizumab and aflibercept for the treatment of wet age-related macular degeneration (wAMD) in a real-world setting. **METHODS:** Claims from the IMS Integrated Data Warehouse were used to identify treatment-naïve patients with wAMD receiving ≥1 prescription for ranibizumab or aflibercept between 1 November 2011 and 31 March 2012 and with a follow-up of 365 days. Patients were considered to be treatment-naïve if they had received no anti-VEGF treatment for >180 days prior to the index date. Mean number of injections received within 365 days of treatment initiation and the proportion of patients receiving 3 loading doses within 3 months were calculated and compared for patients starting therapy with ranibizumab or aflibercept. No adjustments for bilateral treatment were performed. **RESULTS:** Patient characteristics were similar for patients receiving ranibizumab (N=2,799) or aflibercept (N=117) at the index date (median age: 82 years; % male, 36%). The mean (±SD) number of anti-VEGF injections received by patients starting on ranibizumab or starting on aflibercept was similar: 5.6±3.5 and 5.4±2.8, respectively (p=0.6593). In patients continuously treated with the same agent for 12 months, the mean number of injections was also similar across ranibizumab and aflibercept: 4.9±3.4 (n=1,898) vs 5.2±2.6 (n=87), respectively (p=0.2705). Approximately two-thirds of patients with more than 3 injections received 3 loading doses within the first 3 months (ranibizumab, 65.6%; aflibercept, 64.3%). Results for patients who were treatment-naïve for 365 days were consistent with the above results. **CONCLUSIONS:** There are limited data regarding real-world treatment patterns with aflibercept for the management of wAMD. Our results suggest that in routine clinical practice patients receive a comparable number of injections in the first year of treatment with both ranibizumab and aflibercept. Analysis of data from larger patient populations and for longer follow-up is warranted when these data become available.

RESEARCH POSTER PRESENTATIONS – SESSION IV
DISEASE-SPECIFIC STUDIES

CARDIOVASCULAR DISORDERS – Clinical Outcomes Studies

PCV1

APPLICATION OF LOGISTIC REGRESSION FOR SIGNAL DETECTION AND RISK ASSESSMENT OF MACROLIDE-ASSOCIATED TORSADE DE POINTES

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OBJECTIVES: Torsade de pointes (TdP) is an identified risk for antibacterial treatment with macrolides, but the risk might vary across individual macrolides. This study evaluates the association between macrolides and TdP from the FDA Adverse Event Reporting System (FAERS). **METHODS:** Disproportionality analysis of FAERS between 1997 and 2012 was conducted for azithromycin, clarithromycin, erythromycin and Telithromycin with TdP preferred term of the Medical Dictionary for Regulatory Activities using logistic regression. Logistic reporting odds ratio (LROR) and corresponding 95% confidence intervals (CIs; LR05-LR95) are estimated for individual macrolides. Estimates are compared with Multi-Item Gamma Poisson Shrinker data mining algorithm. Estimates ≥2 yield significant safety signals. Lack of overlap between estimate-specific CIs indicates efficient approach for signal detection. **RESULTS:** A total of 318 TdP events were reported for macrolides. The majority of reports were for erythromycin (n=122) and clarithromycin (n=114), followed by azithromycin (n=74) and telithromycin (n=8). Most of events were reported for females with median age of 62.8 years. 98% of TdP were serious events (10% of those were deaths). Death contributed to 18%, 10% and 5% of serious TdP events for azithromycin, erythromycin and clarithromycin, respectively. Telithromycin didn't have death TdP reports. Significant TdP signals were identified for macrolides. LROR (LR05-LR95) were: erythromycin 48.1 (40.4-55.9); clarithromycin 15.3 (12.1-19.1); azithromycin 13.9 (11.1-17.2); and telithromycin 6.79 (3.20-13.5). Except for telithromycin, no overlap was observed between estimate-specific CIs between analysis methods. **CONCLUSIONS:** Macrolides are associated with more than expected reporting of TdP compared to other drugs and events in the database; however, the risk was highest in erythromycin and lowest in telithromycin. Fatal TdP was highest in azithromycin, and telithromycin didn't have fatal TdP. The findings show differential risk of TdP across macrolide antibiotics, emphasizing the need for monitoring cardiac rhythms in patients treated with macrolides.

PCV2

DIRECT-TO-PATIENT CONTACT AND PROACTIVE PHARMACOVIGILANCE SYSTEM: A CASE STUDY

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Post-authorization non-interventional safety studies typically enroll patients at sites and safety events are reported and collected as appropriate by site personnel during standard-of-care visits. Although this is the traditional approach, it has several practical shortcomings: infrequent or irregular standard-of-care visits; patients switching health care providers; transient nature of some safety events; treatment at non-study sites, and the lack of care-seeking for the safety events. An alternative study design that overcomes several of these shortcomings includes direct-to-patient contact (DPC) and follow-up. **OBJECTIVES:** The purpose of this study is to describe patients' short and long term management patterns including the detection and verification of events of interest by contacting patients' event treating physician (ETP). **METHODS:** This is multinational multicenter observational prospective longitudinal cohort study involving 10,600 patients in Europe and South America. Patients were enrolled at hospital and followed up by telephone by a specialized DPC unit at 6 weeks then quarterly up to 2 years after hospital discharge. Data collected include clinical outcomes, safety events of interest, economic burden and quality of life. **RESULTS:** A total of 88,276 phone calls to patients were performed, achieving a reachable rate of 88.5% and an interview successful rate of 84.6%. 87.2% of the initial sample completed the 2-year follow-up period: 5.7% of the sample died, 6.0% voluntarily withdrew and 0.9% was withdrawn to participate to a clinical trial. Only 19 patients were never reached (0.2%). In total, 2144 events of interest were detected and a medical verification from ETPs was obtained in 72.3% of the case. **CONCLUSIONS:** This study demonstrates that DPC along with a proactive pharmacovigilance system achieved very high response rates from both patients and ETPs. It represents an effective alternative methodology to collect patients data, including safety data, in real life settings.

PCV3

ANTITHROMBOTIC STRATEGIES AND ADVERSE OUTCOMES IN ACUTE CORONARY SYNDROME AND ATRIAL FIBRILLATION: A COMMUNITY STUDY

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OBJECTIVES: Atrial fibrillation (AF) is frequent in acute coronary syndromes (ACS) and impacts the need for subsequent antithrombotic treatment. However, whether associations of antithrombotic treatment with strokes, bleeding, and death differ between ACS patients with and without AF remains uncertain. **METHODS:** Olmsted County, MN residents with incident myocardial infarction or unstable angina during 2005-2010 were classified according to AF status prior to or during the index ACS hospitalization. Antithrombotic strategy at discharge was categorized into double/triple vs. no/single and warfarin vs. no warfarin therapy. Cox regression was used to examine associations between treatment and strokes, bleeding, and mortality and to test whether AF differentially impacted these associations. Models were age- and sex-adjusted and weighted for the inverse probability of the propensity score for therapy. **RESULTS:** A total of 244 of 1140 incident ACS patients had AF (ACS+AF), and of these patients, 49% were discharged on double/triple antithrombotic therapy and 33% received warfarin. In 896 ACS patients without AF, 63% were discharged on double/triple therapy and 4% on warfarin. Over a median of 4.2 years, 95 strokes, 297 bleeds, and 255 deaths occurred. Antithrombotic strategy was not associated with the risk of stroke or bleeding. Among all ACS patients, mortality was similar between strategies; however, ACS+AF patients on double/triple therapy (vs. no/single therapy) showed a trend toward a lower risk of death [HR (95% CI): 0.64 (0.41-1.02) for ACS+AF, 1.25 (0.83-1.87) for those without AF; $p_{interaction}$=0.03]. For warfarin vs. no warfarin, those with AF exhibited a lower mortality risk with warfarin [HR (95% CI): 0.46 (0.29-0.73) for ACS+AF, 2.01 (0.94-4.32) for those without AF; $p_{interaction}$<0.01]. **CONCLUSIONS:** Altogether, in community ACS patients, antithrombotic strategy is not associated with the risk of stroke, bleeding, or death. However, in the subset of ACS patients with AF, a warfarin strategy is associated with a lower risk of death.

PCV4

COMORBIDITY INFLUENCE IN THE CONTROL OF ARTERIAL HYPERTENSION

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OBJECTIVES: Determine the impact of co-morbidity in controlling arterial hypertension in clinical practice situation. **METHODS:** Cross-sectional study, conducted from retrospective review of patient records obtained from primary care. We included patients' ≥ 30 years who demanded attention during the year 2012. The main measures were: demographics, control (≤ 140/90 mmHg) blood pressure (BP), evolution time, co-morbidity (general and specific) protocol using cardiovascular events (CVE), visits and referrals to specialists. Statistical analysis and multiple linear regression for correction of the models, $p<0.05$. **RESULTS:** We recruited 900 patients (mean age 67.4 years, women: 51.1%). The 64.8% (CI: 61.7% -67.9%) of subjects had a proper control of the BP. The average duration of hypertension was 6.0 years and use 4.6 protocol entries / year. The average number of visits was 15.3 and 0.7 referrals. The years of evolution were associated with age ($r = 0.323$). The control patients showed a higher average BP of ischemic heart disease (11.1% vs. 6.9%) and CVE (19.4% vs. 14.8%), $p <0.05$. The BP control was associated with women (OR = 1.4) and the presence of CVE (OR = 1.8), $p <0.02$. The number of diagnoses (morbidity) was associated with age (ß = 0.14) and the number of referrals (ß = 0.08), $p <0.05$ (coefficient R^2= 40%). **CONCLUSIONS:** Optimal control of BP is high. The profile of these patients is women in a situation of secondary prevention.

PCV5

HIGH DOSAGES OF STATINS IN HIGH CARDIOVASCULAR RISK PATIENTS IN A REAL WORLD SETTING: TREATMENT PATTERNS AND OUTCOMES

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OBJECTIVES: International guidelines recommend the use of high dosages statins (in particular, Rosuvastatin and Atorvastatin) in high cardiovascular (CV) risk patients. The aim of this study was to assess the degree of implementation of the

recommended therapeutic strategies and clinical outcomes as a function of the therapeutic strategies in a real world setting. **METHODS:** An observational retrospective cohort analysis based on 4 Local Health Units administrative databases was conducted. High CV risk patients who filled at least one prescription for high dosages statins between January 1, 2007-December 31, 2007 (enrolment period) were included. Patients were followed-up for 24 months. Patients were defined as adherent if they had >80% of follow up period covered by drugs dispensation. To correct for potential confounders, a multivariable proportional hazards Cox regression model considering age, gender, type of statin, adherence to treatment and stay on treatment was assessed. Stay on treatment was defined as no switch or down titration during the follow up period. **RESULTS:** Among 36,327 (3% of the population) high CV risk patients, Rosuvastatin 40mg (R40) and Atorvastatin 80mg (A80) were not used (0.1% each treatment); 625 (2%) patients used R20 and 908 (2%) A40. Stay on treatment was similar across treatments: 61% for R20 and 60% for A40 (p=0.583). 2.6 (1.7-3.5) CV events per 100 patients/year for R20 and 4.4 (3.4-5.4) for A40 were observed (p=0.014). At the multivariable Cox regression analysis, risk of CV event was lower for R20, as compared to A40 (HR=0.60, 95%CI 0.39-0.91, p=0.017). Other statistically significant covariates were adherence (HR=0.50, 95%CI 0.29-0.87, p=0.015) and stay on treatment (HR=0.58, 95%CI 0.40-0.85, p=0.006). **CONCLUSIONS:** Despite guidelines recommendations, high dosages statins are poorly used in real practice. Stay on treatment was similar among those treated with R20 and A40, even though R20 showed a lower incidence of cardiovascular events.

PCV6

MODELING THE CARDIOVASCULAR EFFECTS OF SWITCHING PATIENTS FROM ROSUVASTATIN TO ATORVASTATIN

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OBJECTIVES: This analysis estimates the impact of switching from rosuvastatin to atorvastatin on cardiovascular (CV) events. **METHODS:** Using the Archimedes model, a discrete-event simulation, we evaluated a simulated population of 50,038 patients aged 45–70 years with dyslipidemia and adherent to rosuvastatin. The virtual population was created based on matched biomarker profiles of patients in the National Health and Nutrition Examination Survey (NHANES). Statin treatment models were based on data from published studies, including STELLAR, JUPITER, CARDS, ASCOT, and TNT. Patients were started on a rosuvastatin dose based on their LDL-C and ATP-III goal. Treatment prevalence was calibrated to match distributions of statin use observed in U.S. pharmacy claims data. In the experimental arm, patients switched to twice the mg atorvastatin dose as their rosuvastatin dose at their first follow-up visit (no switching occurred in the control arm). Patients were monitored for 5 years, during which time they received regular visits, with the opportunity to increase their dosage if they were above their LDL-C goal. Rate of first occurrence of MI, stroke, or CV death (MACE) for each arm was estimated. **RESULTS:** After 5 years, when all patients switched to atorvastatin, 4.8% fewer patients reached goal, and mean LDL-C increased by 7.1 mg/dL. The 5-year relative risk of MACE was 1.117 (95% CI 1.098–1.135), and the number needed to harm (NNH) to incur one additional MACE was 262, favoring rosuvastatin. For diabetics, the relative risk of MACE was 1.128 (95% CI 1.096–1.159), and the NNH to incur one additional MACE was 195, indicating greater risk for diabetics. The results were insensitive to assumptions of adherence rates and LDL-C goal values. **CONCLUSIONS:** In this simulation, switching from rosuvastatin to atorvastatin led to fewer patients attaining LDL-C goal, higher mean LDL-C values, and greater risk of MACE over 5 years.

PCV7

RIOCIGUAT FOR THE TREATMENT OF PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH): RESPONDER ANALYSIS OF WHO FUNCTIONAL CLASS III PATIENTS FROM THE PATENT-1 STUDY

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OBJECTIVES: Indications for PAH medications vary between countries, and products may have restricted reimbursement based on policies limiting treatment to WHO functional class (FC) III patients. In the PATENT-1 study, the novel soluble guanylate cyclase stimulator riociguat significantly improved 6-minute walking distance (6MWD) and a range of secondary endpoints in patients with PAH. This subgroup analysis of PATENT-1 investigated the proportion of FC III/IV patients achieving threshold criteria. **METHODS:** PATENT-1 was a double-blind, randomized Phase III study in which patients with PAH received 12 weeks' oral treatment with placebo, an individual titration of riociguat (up to 2.5 mg tid), or a capped titration of riociguat (up to 1.5 mg tid). Increase in 6MWD ≥40 m, 6MWD ≥380 m, cardiac index (CI) ≥2.5 L/min/m^2, pulmonary vascular resistance (PVR) <500 dyn·s·cm^{-5}, mixed venous oxygen saturation (SvO_2) ≥65%, FC I/II, absence of clinical worsening events, and NT-proBNP <1800 pg/mL were chosen as positive response criteria based on studies showing their prognostic relevance at baseline and after targeted therapy. **RESULTS:** At baseline, 241 patients were in FC III/IV (FC IV n=4) across the three treatment groups, and similar proportions met selected criteria in the riociguat individual titration (n=141) and placebo groups (n=61). At Week 12/last visit, the proportion of patients fulfilling these criteria was higher in the riociguat individual titration group than the placebo group for all parameters: increase in 6MWD ≥40m (44% vs 15%), 6MWD ≥380m (49% vs 36%), CI ≥2.5 L/min/m^2 (75% vs 43%), PVR <500 dyn·s·cm^{-5} (52% vs 27%), SvO_2 ≥65% (68% vs 35%), FC I/II (33% vs 23%), absence of clinical worsening events (99% vs 90%), and NT-proBNP <1800 pg/mL (84% vs 64%). **CONCLUSIONS:** In this population of predominantly FC III PAH patients, riociguat increased the proportion fulfilling criteria defining a positive response to therapy.

PCV8

PATIENT REPORTED OUTCOMES ASSSESMENT OF THAI CHRONIC STABLE ANGINA PECTORIS(CSAP)

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OBJECTIVES: A pilot test to assess patient-centered outcomes in daily management of coronary artery disease at cardiology clinics in Thailand. **METHODS:** A Delphi method was used for development of PRO questionnaire assessing along with ivabradine treatment from randomly selected CSAP patients under the Health Authorities' pharmacovigilance monitoring program. A 15-items short-form health survey with 5 response choices adopted with permission from validity-tested PRO used in medical outcomes study in Thai patients, four health dimensions included general, physical, social function role limiting and mental health dimensions with 1, 6, 5 and 3 items each respectively. Standardized scoring was calculated with the lowest(0) to highest(100). Field tests among healthy volunteers performed.The reliability test employed inter-item and intra-item consistency using Cronbach's alpha coefficient. All 15 items of survey were evaluated at initiation and after four months clinical intervention. The treatment acceptability was further assessed from patient interviews. **RESULTS:** Of 162 patients randomly selected for PRO evaluation, 85(53%) was men, all patients mean(SD) age of 67.3(11.7) years whom 97(59.5%)was >65 years, 9(5.5%) was smokers and 81(49.7%) had a Body Mass Index ≥25 kg/m^2. Forty-three (26.4%) of patients had previous intervention and 63(39%) had heart failure(HF). The internal consistency of the score for all 15 items, for physical, social function role limiting and mental health dimensions, reflected Chronbach's alpha coefficient of 0.888, 0.771, 0.702 and 0.807 at baseline. After 4-month, Cronbach's alpha coefficient were of 0.735, 0.715, 0.661 and 0.519. All mean scores(SD) of these four health dimensions, were significantly improved from 47.59(11.50) to 54.91(9.45), from 50.33(12.11) to 54.91(10.42), from 39.53(10.35) to 52.68(10.32) and from 45.88(17.08) to 54.88(18.49) respectively (P<0.001). **CONCLUSIONS:** This pilot development confirms reliability of 15-items short-form health survey, score is consistent overtime. Thai CSAP patients who were prescribed ivabradine reported a highly significant improvement in quality of life including all health dimensions general, physical, social function role limiting and mental health. Patient-reported outcomes questionnaires could be recommended alongside clinical treatment.

PCV9

ATTAINMENT OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL GOALS IN PATIENTS AT VERY HIGH CARDIOVASCULAR RISK IN THE UNITED KINGDOM: RESULTS FROM A GENERAL PRACTICE POPULATION STUDY

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OBJECTIVES: European guidelines support LDL-C goals based on an individual's absolute cardiovascular (CV) risk and have established a goal of <70 mg/dL in very high CV risk patients. The objective of this study was to estimate the proportion of individuals that attain these goals and assess the determinants of any observed variation. **METHODS:** Patients in The Health Improvement Network (THIN) UK general practice database with an LDL-C measurement during 2011 and at very high risk of CV risk events were identified and further categorized as recent acute coronary syndrome (ACS, within 6 months pre LDL-C measurement), prior coronary events, stroke, and peripheral vascular disease (PVD). Lipid-lowering therapy (LLT) was categorized as high-potency statin, standard-potency statin, non-statin LLT, and no LLT. **RESULTS:** In total, 25,535 patients met the inclusion criterion. Median (inter-quartile range [IQR]) age was 71 (62 to 79) years, 63.5% were male, and median (IQR) LDL-C was 108 (83 to 139) mg/dL. Across the total cohort, 6.3%, 61.3%, 17.8%, and 14.6% had evidence of recent ACS, prior coronary events, stroke, and PVD. Patients with LDL-C < 70 mg/dL within these categories were 18.9%, 13.5%, 14.5%, and 11.4%. Across the total cohort, 16.0%, 52.5%, 0.5%, and 31.0% were on high-potency statin, standard-potency statin, non-statin LLT, and no LLT. Patients with LDL-C < 70 mg/dL within these LLT categories were 18.3%, 15.4%, 11.6%, and 8.5%. **CONCLUSIONS:** In a large, contemporary cohort of very high CV risk patients, few achieved the optimal LDL-C goal of <70 mg/dL. One third were not on any LLT, <20% were on high-potency statin, and >80% of those receiving high-potency statins were not at LDL-C goal. These data suggest the need for ongoing efforts to improve prescribing of appropriate LLT as well as identifying new therapies to improve goal attainment among very high CV risk patients.

PCV10

VENOUS THROMBOEMBOLISM IN GYNAE-ONCOLOGY PATIENTS POST SURGERY – IS TINZAPARIN PROPHYLAXIS AN EFFECTIVE ANTICOAGULANT?

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OBJECTIVES: Venous thromboembolism (VTE) is a relatively common post-operative complication in cancer patients associated with high mortality rates. Gynae-oncology patients are predisposed to developing VTE due to the presence of a number of high risk factors. Current thromboprophylactic protocols for LMWH dosage and duration may be insufficient as a significant percentage of VTEs in gynae-oncology patients occur despite LMWH prophylaxis. The aim of this study is to investigate the anticoagulant (anti-Xa) activity of Tinzaparin prophylaxis in the immediate post-operative period in gynae-oncology patients. **METHODS:** All patients attending St. James's

Hospital with suspected gynaecological malignancy and who fulfilled the inclusion criteria were recruited for the study. All patients with BMI less than 35 received Tinzaparin (4500 IU) once daily injection while those with BMI more than 35 received a higher dose (7500 IU). Two days post surgery; venous blood samples were collected for anti-Xa analysis 4 hours post Tinzaparin injection. **RESULTS:** The majority of patients received Tinzaparin of 4500 IU. The mean anti-Xa level in the malignant group was 0.191 IU/ml while in the benign group the level was 0.1740 IU/ml. There was no difference between the two groups. In the malignant group, the number of cases with peak anti-Xa levels below 0.1IU/ml was slightly higher than in the benign group. One patient with malignant disease developed VTE, in the immediate postoperative period and showed a low peak anti-Xa level (0.06IU/ml). **CONCLUSIONS:** The results of this study show that Tinzaparin prophylaxis provides adequate peak anti-Xa levels in the majority of gynae-oncology patients post surgery and is unlikely to be responsible for the high rates of VTE in cancer patients in the immediate post operative period. Larger studies are required to confirm this.

PCV12

IMPACT OF PILL-SPLITTING TRAINING ON DRUG PHYSIOCHEMICAL PROPERTIES, COMPLIANCE AND CLINICAL OUTCOMES IN ELDERLY POPULATION: A CROSS-OVER COHORT STUDY

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OBJECTIVES: Pill splitting is a common problem in Hong Kong public hospitals for flexible dose adjustment and cost containment, especially for chronic diseases' treatments such as hypertension, diabetes mellitus. The current study aimed to determine the importance of education on the proper way of pill splitting for elderly in Hong Kong by exploring their habits of pill splitting, evaluating their knowledge on pill cutting and investigating the impact of improper pill cutting habit. **METHODS:** Survey was conducted on elderly taking selected drugs require splitting (Metformin, Atenolol and Amlodipine) in 5 elderly centers. The survey focuses on habits and knowledge regarding pill cutting. Elderly subjects were asked to cut 3 pills that they were currently taking in their own ways. After proper education, they were asked to cut another 3 pills with a pill cutter. The collected sample were then weighed and analyzed. The result was then compared with ideal value of half of the whole pill. **RESULTS:** From the survey, 72% of the elderly have never received any education on pill cutting. Above half consider pill cutting troublesome. About half thought that all kinds of pills can be cut without affecting the expected effect. 80% cut pills for more than one dose each time, including 44% cut pills for 7 days' doses each time. From the experiment, the results of Metformin and Atenolol show that the cut drug samples' weights deviate a lot from the ideal value (50% of the whole pill) before education. After education, the samples' weights get closer to the ideal value. However, the result of Amlodipine does not show significant difference. **CONCLUSIONS:** Education can improve the accuracy of dose in regimen require pill splitting. Elderly in Hong Kong do not receive enough education on the proper way of pill splitting from the health care giver.

PCV13

TOTAL AND LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS IN HIGH RISK PATIENTS TREATED WITH ATORVASTATIN MONOTHERAPY IN THE UNITED KINGDOM

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OBJECTIVES: European guidelines recommend statins as first-line treatment for elevated cholesterol in patients at high cardiovascular (CV) risk; however, many patients do not attain guideline-recommended goals on statin monotherapy. As atorvastatin is now generically-available and its use is likely to increase, we examined recommended total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels in high-risk patients treated with atorvastatin monotherapy in the UK. **METHODS:** In this retrospective UK general practice database study, included were patients with a prescription for atorvastatin monotherapy (IndexRx) between November 30, 2008-November 30, 30, 2011, who had evidence of coronary heart disease (CHD), atherosclerotic vascular disease (AVD), diabetes mellitus (DM), or familial hypercholesterolemia, ≥1 TC and LDL-C measurement 3-12 months post-IndexRx, and an atorvastatin prescription (to determine the daily dose) within 45 days of lipid measurements. Endpoints included proportions of patients (overall and by dose) below guideline-specific thresholds: TC<5.0, TC<4.0, and for patients with CHD/AVD+DM, TC<4.0 or LDL<2.0 mmol/L. **RESULTS:** Of 2999 high-risk patients (60.2% males, mean age 67.9 years [SD 10.6]) meeting selection criteria, 23.9, 28.2, 36.2, and 11.6% received prescriptions for 10-mg, 20-mg, 40-mg, and 80-mg atorvastatin, respectively. Further, 27.6% of patients were newly initiated with atorvastatin monotherapy at index date. Overall, mean follow-up TC was 4.08 (SD 0.80) and LDL-C was 2.08 (SD 0.65) mmol/L. The proportion of patients with TC<5.0 and <4.0 mmol/L was 88.8% and 45.8%, respectively. For those with CHD/AVD+DM, 63.7% had TC<4.0 or LDL-C<2.0 mmol/L. Generally, more patients were below lipid thresholds with higher atorvastatin doses. **CONCLUSIONS:** In UK patients at high CV risk, a substantial proportion did not achieve guideline-recommended lipid levels. Less than half of patients achieved TC<4.0 mmol/L, and only two-thirds of patients with CHD/AVD+DM were below recommended levels for either TC or LDL-C. More effective lipid-lowering strategies may be needed to achieve optimal TC and LDL-C levels in high-risk patients.

PCV14

INDIRECT TREATMENT COMPARISON AND ECONOMIC EVALUATION OF NOVEL ORAL ANTICOAGULANTS FOR THE PREVENTION OF STROKE IN PATIENTS WITH ATRIAL FIBRILLATION IN THE NETHERLANDS

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OBJECTIVES: Management with vitamin K antagonists (VKAs) has been an effective and cost-effective strategy for stroke prevention in atrial fibrillation (AF) but is associated with shortcomings. Novel oral anticoagulants (NOACs) were developed with the aims of no monitoring requirement and improved effectiveness and safety profiles. Economic evaluations require the comparison of all relevant options. However, there are no randomized controlled trials (RCTs) directly comparing these agents. In such cases, indirect treatment comparison (ITC) can be used to synthesize indirect comparative evidence. Through ITC-based evidence synthesis, the cost-effectiveness of all available NOACs for stroke prevention in AF patients may be evaluated. **METHODS:** ITC models were based on RCTs data comparing dabigratran, rivaroxaban, or apixaban with VKA treatment. Relative effectiveness was estimated for stroke/systemic embolism, intracranial hemorrhage, myocardial infarction, extracranial hemorrhage, and minor bleeding. A Markov model was developed using ITC-synthesized evidence with VKA as the baseline. Health utilities were collected from international sources whereas costs and mortality data were extracted from Dutch sources. Univariate and probabilistic sensitivity analyses (PSA) were conducted on the base-case incremental cost-effectiveness ratio (ICER). **RESULTS:** The ICERs for dabigatran, apixaban, and rivaroxaban compared to VKA were €12,146/QALY, €12,488/QALY, and €24,124/QALY, respectively. Sensitivity analysis using the upper and lower limits of the 95% confidence interval for absolute stroke risk with VKA treatment resulted in ICERs that varied drastically from dominance for VKA to being dominated by all NOACs. This is likely due to the large uncertainty observed between the baseline risk profiles of the VKA arms in the three RCTs. The options with the highest probabilities of cost-effectiveness in PSA were VKA at thresholds under €13,000/QALY and dabigatran or apixaban at thresholds above this mark. **CONCLUSIONS:** Dabigatran and apixaban were shown to be cost-effective options for AF patients in The Netherlands. However, these results were strongly influenced by uncertainty around stroke risk with VKA treatment.

PCV15

ESTIMATING THE CARDIOVASCULAR BENEFITS OF DPP-4 INHIBITORS: A SIMULATED STUDY

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OBJECTIVES: Outcomes trials are currently underway to establish the effects of DPP-4 inhibitors on major adverse cardiovascular events (MACE), but to-date no major clinical trial has published results. Using simulations, we evaluated the effectiveness of DPP-4 inhibitors in preventing MACE in two populations with type 2 diabetes, relative to the standard of care. **METHODS:** We used the Archimedes ARCHeS platform to simulate two clinical trials of virtual individuals with diagnosed type 2 diabetes (N=11,000 each). The DPP-4 class was modeled with a meta-analysis of HbA1c and weight change, pooling results from published trials. The study treatments were added-on to standard care. The first simulated trial examined subjects with elevated cardiovascular (CV) risk, based on established CV disease or multiple risk factors. The second considered individuals on metformin monotherapy with HbA1c ≥ 7%. We tracked changes in biomarkers and outcomes for 20 years. **RESULTS:** The DPP-4 class was associated with HbA1c drops of 0.66% [0.71% , 0.62%] in the elevated CV risk population and 0.71% [0.75%,0.67%] in the metformin add-on population; and a weight drop of 0.14 [0.36,-0.07] kg in both cohorts. The biomarker benefits produced a relative risk (RR) for MACE at 5 years of 0.977 [0.968, 0.986] and 0.962 [0.949, 0.975] for the elevated CV risk population and metformin add-on population, respectively. The number needed to treat to prevent one occurrence of MACE at 5 years was 327 [233,550] in the elevated CV risk population. **CONCLUSIONS:** Our simulated study suggests that DPP-4 inhibitors do not increase the risk of MACE relative to the standard of care in a population with elevated CV risk, and a representative diabetic metformin monotherapy population. This study provides insights on the long term benefits of DPP-4 inhibitors, and will support interpretation of the CV safety trial results likely to be published soon.

PCV16

INDIRECT COMPARISONS OF NOVEL ORAL ANTICOAGULANTS FOR THE PREVENTION OF STROKE IN PATIENTS WITH NONVALVULAR ATRIAL FIBRILLATION: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: Given the absence of head-to-head studies, this review summarized indirect treatment comparison studies of oral anticoagulants (OACs) for the prevention of stroke in patients with nonvalvular atrial fibrillation (NVAF). **METHODS:** Eligible English-language studies published up to May 31, 2013 were identified from electronic databases, Medline, EMBASE and Cochrane Library. Studies were included if the indirect comparison involved at least two OACs currently on the market with the common comparator warfarin. The search yielded ten published studies and one in press study was obtained. **RESULTS:** Eleven indirect comparison studies, based on data from three phase III (RE-LY, ROCKET-AF, and ARISTOTLE) and one phase II (PETRO) clinical trial, was reviewed. Six pairwise comparisons were reviewed across studies: any/all OACs vs. warfarin, apixaban vs. dabigatran 110mg, apixaban vs. dabigatran 150mg, apixaban vs. rivaroxaban, dabigatran 110mg vs. rivaroxaban, and dabigatran 110mg vs. rivaroxaban. OACs as a whole were found to have significantly better bleeding and efficacy endpoints when compared with warfarin. Apixaban and dabigatran 110mg were found to have significantly reduced risk of multiple bleeding endpoints when compared with rivaroxaban and dabigatran 150mg. Dabigatran 150mg was found to have significantly decreased risk of multiple efficacy endpoints when compared with rivaroxaban. Three studies compared discontinuation rates. Apixaban and rivaroxaban were found to have significantly lower discontinuation rates compared with both doses of dabigatran. Apixaban was also found to have a significantly lower discontinuation rate compared with rivaroxaban. **CONCLUSIONS:** Apixaban,

dabigatran and rivaroxaban appear to have better safety and efficacy profiles when compared with warfarin. Apixaban and dabigatran 110mg consistently demonstrated reduced risk of bleeding when compared with rivaroxaban and dabigatran 150mg. Dabigatran150mg demonstrated increased efficacy on multiple endpoints when compared with rivaroxaban, while discontinuation rates were increased. Head-to-head studies would help clarify any differences among these medicines for efficacy and bleeding.

PCV17

META-ANALYSIS OF SAFETY OF DABIGATRAN AND WARFARIN FOR TREATMENT OF ATRIAL FIBRILLATION

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OBJECTIVES: Atrial fibrillation (AF) is an irregular and often rapid heart rate that commonly causes poor blood flow to the body. Dabigatran and Warfarin have shown safety and efficacy for treatment of AF. The objective of this study was to conduct meta-analysis and present evidence for safety of Dabigatran versus Warfarin for treatment of AF. **METHODS:** For this meta-analysis we included randomized controlled trials (RCTs) evaluating Dabigatran for the treatment of AF. We included studies that were: (1) a RCT in humans; (2) an investigation of patients with nonvalvular atrial fibrillation; (3) an evaluation of dabigatran compared with warfarin or each other; and (4) a report of results of stroke or systemic emboli and major bleeding. A systematic literature search for dabigatran trials was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interventions, year and total bleeding events. For meta-analysis, random effects and fixed effects models were used to obtain cumulative statistics. **RESULTS:** Two RCTs with a total of 12,268 patients were identified. The pooled event rate for Dabigatran for total bleeding events was 31.9% (95% CI 31%-33%). The pooled response rate for Warfarin for total bleeding events was 35.1% (95% CI 34%-37%). The cumulative relative risk for total bleeding events with Dabigatran versus Warfarin was 0.91 (95% CI 0.89-0.93) **CONCLUSIONS:** Meta-analysis shows Dabigatran has a slightly lower rate of total bleeding events compared to Warfarin.

PCV18

EFFECT OF IVABRADINE ON THAI CHRONIC STABLE ANGINA PECTORIS PATIENTS

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OBJECTIVES: To evaluate efficacy/safety of ivabradine in chronic stable angina pectoris(CSAP) Thai patients. **METHODS:** Ivabradine 5-7.5 mg bid was prescribed to CSAP patients. Hemodynamic parameters including systolic/diastolic blood pressure(SBP/DBP) in mmHg and heart rate(HR) in beats per minute(bpm) were recorded at entry and after 1,4 months follow-up. A standardized digital device was used to monitor BP and HR. Acceptability was evaluated in patient interviews. **RESULTS:** A total of 256 patients, men/women ratio of 1.04, mean(SD) age 67.1(12.4) years, 149(58%) were >65 years old, 64(25%) and 76(29.7%) of patients had previous intervention and heart failure(HF). 127(50%)&51(20%) received beta-blockers&nitrate as initial medication. Patients' assessment was made using Canadian Cardiology Society angina pectoris classification(CCS). At entry, 34.9%, 52.2% and 10.8% of patients were found with CCS grades 3, 2 and 1. Among 76 HF patients, 35.8%, 58.2% and 6.0% were found with stage 3, 2 and 1 of NYHA classification. In overall population, mean(SD) baseline HR was 86.9(11.2) bpm and SBP/DBP 137.8(24.6)/81.7(15.9) mmHg. After 4 months, mean(SD), HR significantly reduced to 69.96(7.13)bpm ($p<0.001$) and SBP/DBP lowered to 126.5(12.9)/73.9(8.9) mmHg, while mean arterial pressure(MAP)was optimally maintained at 100.4(17.6) mmHg. The highly significant drop in mean difference(SE) HR of 16.9(0.7) was observed with 95% CI between 15.5-18.3 bpm. No significant mean difference(SE),[95% CI] SBP drop, between patients with/without HF, and with/without previous intervention of 7.32(1.17),[4.99-9.64] and 8.15(2.07),[4.02-12.2764], or 8.14(1.27),[5.61-10.67] and 7.46(0.89),[5.69-9.22] ($p=0.502$, $p=0.691$) respectively. Improvement for CCS 3 and CCS 2 angina class, reduced to 1.9% and 36.1% whereas the NYHA classification for stage 3&2 reduced to 3.2%&56.4%($p<0.001$). Common AE reported were palpitation(2.5%) and nausea(1%). **CONCLUSIONS:** Ivabradine is a well-tolerated heart rate reducing agent, effective for both chronic stable angina pectoris and heart failure. It effectively reduces elevated heart rate without affecting other hemodynamic parameters. In this Thai setting, ivabradine significantly improves CCS and NYHA classifications with minimal side effects being reported.

PCV19

EVALUATION OF THE POTENTIAL EFFICACY OF IVABRADINE IN HEALTH CARE OF THE REPUBLIC OF BELARUS

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OBJECTIVES: To determine the potential population of patients with stable angina pectoris in Belarus who need prescription of ivabradine and setting the amount of the effect of the drug in this group of patients. **METHODS:** In the research pharmacoeconomic Markov model of ivabradine application in patients with stable angina, national surveillance data, analysis of literature have been used. Patients with stable angina after revascularization, patients with contraindications to beta-blocker use, not applying the dihydropyridines and having a contraindication to ivabradine use have been used to determine the target population. The number of prevented or postponed events – PPE - (nonfatal myocardial infarction and unstable angina, cardiovascular death, the number of surgical revascularization) has been calculated. For the potential efficacy of ivabradine use in patients with stable angina and heart rate $\geq$ 70 bpm calculating the data about efficacy in accordance with the results of the Beautiful study were used **RESULTS:** The total number of patients with stable angina pectoris in Belarus in 2011 was 242943. The total number of patients with stable angina who have indications for ivabradine was 17559 people. The number of prevented cases of non-fatal myocardial infarction and unstable angina was 244 cases per year. The number of prevented cases of cardiovascular death was 95 cases per year. The number of prevented cases of surgical revascularization was 260 cases per year. **CONCLUSIONS:** The analysis allowed to identify Belarusian patients in need of ivabradine use by estimating the size of the target group of patients with stable angina and elevated heart rate for whom antianginal therapy is inadequate or impossible and who need an ivabradine prescription and potentially could make the most effective reaction to the therapy.

PCV20

EVIDENCE THRESHOLDS IN THE ABSENCE OF EFFECTIVE ALTERNATIVES: THE CASE OF INTERMITTENT COMPRESSION IN CRITICAL LIMB ISCHEMIA

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OBJECTIVES: Intermittent pneumatic compression (IPC) is proposed as an adjunct to medical care for people with critical limb ischemia (CLI) who are unsuitable for revascularisation. Given the lack of treatment options for these patients, a safe therapy that can be shown to provide even a modest clinical improvement may make a significant contribution to the management of this condition. This research aims to synthesise and critically appraise the evidence supporting the use of this technology in this cohort. **METHODS:** A systematic review of the clinical effectiveness of IPC in non-reconstructable CLI was performed. Medline, Embase and trial registries were searched for randomised controlled trials (RCTs), non-randomised controlled trials (nRCTs) and controlled before-and-after (CBA) studies comparing IPC plus medical care to medical care only. **RESULTS:** No RCTs or nRCTs were identified. Two CBA studies, both with a high risk of bias, found that IPC was associated with improved limb salvage and wound healing (OR 7, 95% CI 1.82 to 26.89, $p<0.05$ for both outcomes) as well as improved quality of life scores in bodily pain (mean difference [MD] 32.7, 95% CI 29.4 to 36.0, $p<0.05$) and physical functioning (MD 18.8, 95% CI 14.1 to 23.6, $p<0.05$). Improvements were also reported for initial and absolute claudication distances (MD 26.9m, 95% CI 21.7 to 32.1, $p<0.05$; MD 52.9m, 95% CI 42.2 to 63.6, $p<0.05$, respectively). No serious adverse events were reported. **CONCLUSIONS:** Despite some promising results there is a lack of high-quality evidence demonstrating the effectiveness of IPC in addition to medical management in non-reconstructable CLI. Where findings are equivocal a question arises as to the minimum level of evidence required to support the introduction of a technology when no effective alternatives exist. Competing interpretations of the balance of risks and benefits between different stakeholders in the decision-making process in these circumstances are discussed.

PCV21

EFFECTS OF EXCESS USE OF CORONARY ANGIOGRAPHY AND ITS ASSOCIATION WITH MORTALITY RATES, HEALTH CARE COSTS AND HOSPITAL QUALITY IN TURKEY

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OBJECTIVES: To evaluate excess use of coronary angiography prior to coronary artery bypass graft (CABG) surgery and its association with mortality, health care costs and hospital quality in Turkey. **METHODS:** MEDULA, a nationwide integrated system shared between general health insurance and health care providers in Turkey was used to analyze coronary angiography utilization. Patients age 18–99 years who underwent CABG surgery between April 1, 2009 and October 1, 2010 were identified and assigned to "standard-therapy" or "excess-use" groups based on whether they had one or more coronary angiography, respectively, within 3 months of the first CABG diagnosis date (index date) during the identification period. Survival rates and annual health care costs of patients in the coronary angiography standard-therapy and excess-use groups were compared using propensity score matching. The empirical Bayes approach was used to combine mortality and hospital volume for quality index. Chi-squared tests were used to assess the relationship between hospital quality and excess use of coronary angiography excess use. **RESULTS:** From a total of 20,126 identified patients, 7.27% underwent excessive coronary angiography procedures, at average annual costs that were 9.7% higher than patients with a single angiography ($p<0.01$). Operational mortality associated with excessive use was significantly higher as well (7.4% vs. 5.4%, $p<0.02$). Use of coronary angiography across cities and hospitals varied. Patients who underwent cardiac surgery in high-quality hospitals were less likely to have excessive angiography use than those in low-quality hospitals (7.0% vs. 9.5%, $p<0.01$). **CONCLUSIONS:** In Turkey, excess use of coronary angiography prior to CABG surgery is associated with higher operational mortality, higher expenditures and lower hospital quality.

PCV22

ANTICOAGULANT USE IN HOSPITALIZED PATIENTS WITH ACUTE VENOUS THROMBOEMBOLISM IN THE UNITED STATES

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OBJECTIVES: To examined anticoagulant use and associated factors in hospitalized patients with acute venous thromboembolism (VTE) in the US clinical practice setting. **METHODS:** Adult VTE patients were selected from the linked MarketScan and Hospital Drug database in an inpatient setting between 07/01/2006-12/31/2011. The first hospitalization with a diagnosis of VTE was designated index hospitalization (IH). Patients were required to have at least 6 months continuous enrollment and

have no VTE diagnosis in the 6 months prior to IH. Parenteral and oral anticoagulants used during IH were identified. Multivariate logistic regression was used to examine factors associated with anticoagulant use. **RESULTS:** A total of 957 VTE patients were eligible for the study. Mean age was 62.8 years, and 45.1% were male. Mean length of stay was 8.7 days. During index hospitalization, 45.4% patients were treated with parenteral anticoagulants (PA) and warfarin, 24.6% with warfarin only, and 13.6% with PA only. Among patients treated with PA, low molecular weight heparin accounted for 93.4%. Chemotherapy (OR=2.24), respiratory disease (OR=1.44), and pulmonary embolism (PE) vs deep vein thrombosis (DVT) (OR=1.42) were significantly associated with PA use, while prior stroke (OR=0.43) and renal disease (OR=0.58) were associated with less likelihood of PA use. DVT plus PE vs DVT (OR=3.87), obesity (OR=2.57), chemotherapy (OR=2.23), and PE vs DVT (OR=2.19) were significantly associated with warfarin use, while bleeding history (OR=0.41), diabetes (OR=0.64), and heart disease (OR=0.67) were associated with less likelihood of warfarin use. **CONCLUSIONS:** Less than half of VTE patients during hospitalization were prescribed PA and warfarin, 25% warfarin only, and 14% PA only. Clinical factors including VTE type, stroke and bleeding history, comorbid respiratory disease, diabetes, heart disease, obesity, and chemotherapy were associated with anticoagulant use. Further research needs to examine characteristics and health outcomes of patients who did not receive parenteral anticoagulants during hospitalization.

PCV23

THE USE OF ORAL ANTICOAGULATION DRUGS FOR STROKE PREVENTION IN NONVALVULAR ATRIAL FIBRILATION IN FRANCE, ITALY, GERMANY, SPAIN AND THE UNITED KINGDOM: IS CURRENT PRACTICE CONSISTENT WITH THE 2012 ESC RECOMMENDATIONS?

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OBJECTIVES: The REACT AF study investigated the outcomes and management associated with stroke prevention treatments in patients with non-valvular atrial fibrillation (NVAF) in Europe. This analysis assessed 1) the use of oral anticoagulation drugs (OACs) and 2) whether current practice is consistent with the 2012 European Society of Cardiology (ESC) recommendations. **METHODS:** We conducted an observational retrospective cohort study of patients with NVAF in the *Longitudinal Patient Database (CEGEDIM)* in France, Italy, UK, Spain and Germany. The analysis included patients >=18 years old, with AF diagnosis, and without rheumatic valvular disease or prosthetic valves. Patients had to be in the database for ≥1 year before date of 1st visit (index date) during the inclusion period (May 2010-April 2012). We calculated patients' CHA_2DS_2-VASc score at index date for untreated patients and at the time of the current OAC initiation for treated patients. We evaluated patients' requirement for stroke prevention therapy based on the 2012 ESC recommendations and calculated the percentage of patients for whom treatment initiation and OAC use were consistent with recommendations. **RESULTS:** In France 53% of the OAC patients (total=16,329) were treated consistently with the 2012 ESC recommendations (treatment requirement and choice of OAC); 46% in Germany (total=13,468), 58% in Spain (total=12,357); 39% in Italy (total=22,447); and 36% in the UK (total=19,956). The percentage of patients (CHA_2DS_2-Vasc> 1, if not alone due to female gender) not receiving the required treatment (either not treated or treated with a non-recommended OAC) was 36% in France; 48% in Germany; 34% in Spain; 52% in Italy; and 48% in the UK. **CONCLUSIONS:** The study findings indicate there is a discrepancy between current practice regarding OAC prescribing and the 2012 ESC recommendations. Special attention must be given to time of treatment initiation and choice of OAC to correctly follow ESC recommendations.

PCV24

ADHERENCE TO TREATMENT AND PERSISTENCY IN PATIENTS TREATED WITH VKA IN FRANCE, ITALY, GERMANY, SPAIN AND THE UNITED KINGDOM

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OBJECTIVES: This study investigated the outcomes and management associated with stroke prevention treatments in patients with non-valvular atrial fibrillation (NVAF) in Europe. This analysis estimated persistence and adherence to treatment with VKA. **METHODS:** We conducted an observational retrospective cohort study of patients with NVAF in the *Longitudinal Patient Database (CEGEDIM)* in France, Italy, the UK, Spain and Germany. The analysis included patients >=18 years old, with AF diagnosis, treated with VKA and without rheumatic valvular disease or prosthetic valves. Patients had to be in the database for >=1 year before date of 1st visit during inclusion period (May 2010/April 2012). We estimated persistence (time to VKA discontinuation) as the time from first prescription to last prescription before discontinuation, defining discontinuation as switch or absence of renewal within 3 months, using the Kaplan-Meier method. We measured adherence to treatment by the Medication Possession Ratio (MPR) during the inclusion period. **RESULTS:** Median time to treatment discontinuation was 0.78 year in Germany (n=6,386), 1.00 year in Italy (n=8,774), 1.34 years in France (n=9,184), 1.99 years in Spain (n=7,526), and 1.92 years in the UK (n=7,731). Persistence at 5 years was 12% in Germany, 20% in Italy, 24% in France, 26% in Spain, and 25% in the UK. Concerning adherence the mean MPR was 0.54 in Spain, 0.56 in Italy, 0.57 in France, and 0.59 in Germany. There was insufficient data to estimate adherence in the UK. **CONCLUSIONS:** MPR >=0.80 is used to define good adherence. The results show adherence to treatment with VKA is low in the countries studied. Results were consistent across countries, which suggest that low adherence is not country specific. Low adherence to treatment with VKA can affect the maintenance of patients within recommended range of INR, and therefore may increase the risk of stroke.

PCV25

ANTICOAGULATION TREATMENT WITH VKA IN FRANCE, ITALY, GERMANY, SPAIN AND UNITED KINGDOM. RESULTS FROM THE REACT AF STUDY

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OBJECTIVES: This study investigated the outcomes and management associated with stroke prevention treatments in patients with non-valvular atrial fibrillation (NVAF) in Europe. The primary objective of this analysis was to assess the management of patients treated with vitamin K antagonists (VKA). **METHODS:** We conducted an observational retrospective cohort study of patients with NVAF in the *Longitudinal Patient Database (CEGEDIM)* in France, Italy, the UK, Spain and Germany. The analysis included patients >=18 years old with recorded AF diagnosis, treated with VKA, and without rheumatic valvular disease or prosthetic valves prior to the index date (date of 1st visit during inclusion period – May 2010 - April 2012 - , or date for first AF diagnosis, if this falls during this period. Only patients with >=1 year of data were included to ensure adequate data availability. Using recorded INR measures, we estimated the average time within therapeutic range (TTR), INR between 2 and 3 for patients eligible to apply the Rosendaal Method. **RESULTS:** In France 1,110 patients were assessed, in Germany 1,208, in Italy 1,230, & the UK 2,702. Insufficient data were retrieved in Spain (n=12). INR was measured 9.6 times/year in France, 9.5 times/year in Germany, 9.8times/year in Italy, and 13.1 times/year in the UK. In France, 48% of the patients had TTR >=70% of their time; in Germany, 44%; in Italy, 46%, and in the UK, 65%. **CONCLUSIONS:** Treatment outcomes with VKAs, in particular stroke and bleeding, depend on maintaining patients' INR values within recommended range. The results show that the majority of patients in France, Germany and Italy, & 1/3 of patients in UK did not achieve recommended TTR and therefore were at increased risk of stroke or major bleeding. Further research is needed to demonstrate the correlation between these estimates and stroke and major bleeding rates within countries.

PCV26

PHARMACOEPIDEMIOLOGICAL STUDY OF HMG COA REDUCTASE INHIBITOR PRESCRIBING: IMPACT OF GENERIC PRESCRIBING ON COST

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OBJECTIVES: To investigate the prescribing of hypolipidaemic agents with specific emphasis on the effect of generic prescribing on HMG-CoA reductase inhibitor (statin) costs. **METHODS:** A retrospective, cross-sectional pharmacoepidemiological study was conducted on 2011 medical insurance claims data in South Africa. **RESULTS:** A total of 4805 patients (56.88% males) were prescribed 38373 hypolipidaemic agents. The average age of patients was 56.07 (SD=13.32) years. Statins accounted for 93.85% of all prescriptions and 83.44% of cost, followed by fibrates (3.61% of prescribing frequency and 7.72% of cost). Simvastatin was the most frequently prescribed statin (accounting for 62.59% of all prescriptions), followed by atorvastatin (17.04%) and rosuvastatin (11.68%). Simvastatin was also the active ingredient with the lowest average cost per product of R46.43. Simvastatin was prescribed under 16, atorvastatin six and pravastatin four different trade names. Fluvastatin, lovastatin and rosuvastatin only had one trade name under which they were prescribed. Only one cholesterol absorption inhibitor drug was prescribed (ezetimibe) accounting for 1.64% of prescriptions. This product had the highest average cost per prescription of R416.37. Other hypolipidaemic agents prescribed accounted for only 0.89% and consisted of the combination of ezetimibe and simvastatin, and cholestyramine. The fibrates constituted 3.61% of prescribing, with most prescriptions for bezafibrate. Dosages for the statins were investigated and it was found that the average Prescribed Daily Doses (PDDs) were generally lower or in agreement with the Defined Daily Doses (DDDs). The average PDD of simvastatin was 23.70 (DDD=30 mg), pravastatin 25.35 mg (DDD=30 mg), lovastatin 26.31 mg (DDD=45 mg), atorvastatin 20.91 (DDD=20 mg) and fluvastatin 57.29 mg (DDD=60 mg). **CONCLUSIONS:** There are a variety of generic equivalents available for the statins on the South African market. It was clear that products with more generic equivalents had a lower average cost per prescription compared to the innovator products.

PCV27

USE OF CALCIUM CHANNEL BLOCKERS IN SERBIA IN THE PERIOD FROM 2007 TO 2011 YEAR

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OBJECTIVES: Calcium channel blockers are drugs of first choice in the treatment of hypertension. The aim of this study was to analyze the consumption of calcium channel blockers in Serbia in the period from 2007 to 2011 year. **METHODS:** The data about the use of drugs were taken from the Agency for Drugs and Medical Devices of the Serbia. **RESULTS:** The most frequently used drug from this group with mainly vascular effects was amlodipine. During this observed five years the consumption of amlodipine is in steadily increased. In 2007. it was 21.25DDD/1000 inh/day, at the end of 2011. year the consumption was 72.97DDD/1000 inh/day. On the second place in drug consumption in the same group of drugs was nifedipine. Contrary to amlodipine, nifedipine recorded a decline in consumption. From the calcium channel blockers with direct cardiac effects the most frequently used drugs were verapamil and diltiazem. The consumption of verapamil in the observed years was uneven. At the and of 2011. consumption of this drug was reduced by 50%. The consumption of diltiazem in observed five years is in constantly decreasing. **CONCLUSIONS:** In Serbia, in the observed period the consumption of calcium channel blockers been uneven. In 2010 and 2011 the consumption of calcium channel blockers marks a positive trend. This research was supported by Provincial Secretariat for Science and Technological Development, Autonomous Province of Vojvodina project No 114-451-2458/2011 and by Ministry of Science, Republic of Serbia, project no 41012.

PCV28

USE OF DIURETICS IN SERBIA IN THE PERIOD FROM 2007 TO 2011 YEAR

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OBJECTIVES: Diuretics are drugs of first choice in the treatment of hypertension. The aim of this study was to analyze the consumption of diuretics in Serbia in the period from 2007 to 2011 year. **METHODS:** The data about the use of drugs were taken from the Agency for Drugs and Medical Devices of the Serbia. **RESULTS:** The use of diuretics during the observed period in Serbia is quite small and it ranged from 5 to 6% of the total consumption of all drugs from the C group. Furosemide was the most frequently used diuretic. In the five year period furosemide consumption ranged from 33-55% of the total consumption of all diuretics. The second largest consupmtion during first four years of the study is belonged to the indapamide. Indapamide consumption in the fifth year was at the fourth position. At the third position in drug consumption in the first four years was hydrochlorothiazide. Use of hydrochlorothiazide in 2011 took second place. Spironolactone has occupied the fourth position in the first four years. During the last years of the period spironolactone occupied the third position. Consumption of all other diuretics was small. **CONCLUSIONS:** In Serbia, in the observed period, consumption of diuterics is two to three times lower in comparison with the consumption of diuretics in Norway and Finland. This research was supported by Provincial Secretariat for Science and Technological Development, Autonomous Province of Vojvodina project No 114-451-2458/2011 and by Ministry of Science, Republic of Serbia, project no 41012.

PCV29

USE OF BETA BLOCKING AGENTS IN SERBIA IN THE PERIOD FROM 2007 TO 2011 YEAR

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OBJECTIVES: Beta blocking agents are drugs of first choice in the treatment of hypertension. The aim of this study was to analyze the consumption of beta blocking agents in Serbia in the period from 2007 to 2011 year. **METHODS:** The data about the use of drugs were taken from the Agency for Drugs and Medical Devices of the Serbia. **RESULTS:** During the observed period in Serbia the consumption of selective beta blocking agents were dominant. The most frequently used drug from this group was metoprolol. During this five years the consumption of metoprolol is in steadily decreased. In 2007. it was 37.73 DDD/1000 inh/day, at the end of 2011. year the consumption was 22.13 DDD/1000 inh/day. On the second place in drug consumption in the same group of drugs was atenolol. Atenolol also recorded a decline in consumption. On the third place in drug consumption was bisoprolol. At the beginning of 2007. consumption of this drug was very small, gradually grew and reached its maximum in 2011. From the unselective beta blocking agents the most frequently used was propranolol and his consumption in the observed years was constant. **CONCLUSIONS:** In Serbia, in the observed period the consumption of beta blocking agents been mostly constant. From all drugs in C07 group the most frequently used group of drugs was C07AB. This research was supported by Provincial Secretariat for Science and Technological Development, Autonomous Province of Vojvodina project No 114-451-2458/2011 and by Ministry of Science, Republic of Serbia, project no 41012.

PCV30

THE HUMANISTIC AND ECONOMIC BURDEN OF VENOUS THROMBOEMBOLISM IN PREGNANT WOMEN: A SYSTEMATIC REVIEW

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OBJECTIVES: To systematically review the humanistic and economic burden of pregnancy-related venous thromboembolism (VTE). **METHODS:** Pubmed, Cochrane Central Register of Controlled Trials, Econlit, Science Direct, JSTOR, Oxford Journals and Cambridge Journals were searched using combinations of a considerable number of relevant words. Humanistic studies published from January 2000 to December 2012 were eligible for inclusion in the review. The reference lists of all relevant papers retrieved from the original search were manually screened to identify additional studies. The identified studies were independently reviewed by two reviewers against pre-determined criteria. A quality assessment of the selected studies was also conducted by using standard methods. The data of selected studies were extracted onto a data extraction form and consequently synthesized. **RESULTS:** Twenty studies were included in our review. The overall pregnancy-related VTE incidence rate per 1,000 deliveries ranged between 1 and 1.72. This rate was higher in the postpartum period compared to the antenatal period. Events were spread across the 3 trimesters, with the majority of events occurring in the third trimester of pregnancy. Limited data is available on mortality due to pregnancy-related VTE, with one study reporting an overall mortality rate of 1.1/100,000 deliveries due to pregnancy-related VTE. Recurrence rate was found to be higher in the postpartum period compared to the pregnancy period. Poorer quality of life (QoL) was identified in women with pregnancy-related VTE in comparison to their counterparts with no VTE. Data regarding the economic burden of VTE in this specific population was lacking. **CONCLUSIONS:** The present systematic review showed that women are under a substantially increased risk of VTE events during pregnancy and VTE strongly affect their QoL. Despite the expected economic burden imposed by the pregnancy-related VTEs, no relevant studies were found. Therefore, further research is required to evaluate the humanistic and economic burden of VTE in pregnant women.

PCV31

IN-HOSPITAL AND LONG-TERM MORTALITY AND MORBIDITY BURDENS IN PATIENTS WITH ACUTE CORONARY SYNDROMES

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OBJECTIVES: To describe current real-world data on in-hospital/long-term mortality and morbidity outcomes in patients in the western world with acute coronary syndromes (ACS). **METHODS:** We conducted a review of publications from international registries: GRACE (Global Registry of Acute Coronary Events) and GRACE expanded (both worldwide); GRACE UK-Belgium; and EuroHeart survey II/III (Europe/Mediterranean basin). The most recent data on in-hospital/long-term outcomes were stratified by ACS type: ST-elevation myocardial infarction (STEMI) and non-ST elevation Acute Coronary Syndromes (NSTE ACS), which includes unstable angina (UA) and the non-ST elevation myocardial infarction (NSTEMI). **RESULTS:** In-hospital mortality rates were 4.6–7.8% in STEMI patients, 2.2–5.9% in NSTEMI patients, and 0.8–2.7% in UA patients. At 6 months post-discharge, mortality rates were 4.5–4.8% in STEMI patients, 6.2% in NSTEMI patients, and 3.6% in patients with UA. These rates increased to 19%, 22%, and 18% in STEMI, NSTEMI, and UA, respectively, at 5 years post-discharge. The most common morbidities were in-hospital congestive heart failure (STEMI, 11–15%; NSTEMI, 6.1–10%; and UA, 6%) and in-hospital myocardial (re)infarction (STEMI, 2–2.8%; and NSTE-ACS, 1.7–2.4%). Six months post-discharge myocardial (re)infarction rates were 2% in STEMI patients and 2.9% in NSTE-ACS patients, which are lower than previously reported in clinical trials. **CONCLUSIONS:** Despite current treatments, a substantial proportion of patients with ACS still suffer death and serious morbidities in the acute phase of the disease and longer term. Further research is needed to improve acute and long-term therapies.

PCV32

INTERRUPTION/BRIDGING OF VKA TREATMENT OF PATIENTS WITH ATRIAL FIBRILLATION: ANALYSIS OF INCIDENCE AND CLINICAL OUTCOMES BASED ON A GERMAN CLAIMS BASED DATA SET

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OBJECTIVES: For patients with atrial fibrillation (AF) undergoing a surgery, guidelines recommend the interruption of VKA-treatment combined with LMWH/UFH bridging. As a result, patients may be placed at higher risk for thromboembolic events during this time. This study investigates the incidence of such perioperative management situations and describes clinical event rates. **METHODS:** Claims data from a large German statutory health insurance (period 01/01/2007-31/12/2011) was analysed. AF-patients who started VKA-treatment within this period and continued ther-apy until 31/12/2011 were included. VKA-interruption/bridging was assumed when the patient was admitted to a hospital due to an inpatient surgical procedure (case 1) or the patient experienced an outpatient surgery, combined with an outpatient prescription of a LMWH/UFH within 10 days after surgery (case 2). Clinical events of interest were cardiovascular (strokes, TIA, embolism, myocardial infarctions) and bleedings leading to inpatient hospitalization. Daily event rates during regular VKA usage days were compared to those 5 days before/30 days after surgery ("interruption/bridging days"). **RESULTS:** 41,170 patients were included (mean age 74.8 years; 50.8% male; average CHA2DS2-VASc score 5.2). 11,695 (28.4%) VKA-patients experienced a hospital admission due to a surgery (case 1). 464 patients (1.1%) experienced an outpatient surgery with outpatient LMWH prescription (case 2). Overall (both cases) potential interruption/bridging occurred 0.24 times per person-year. The daily cardiovascular/bleeding event risk during potential VKA-interruption/bridging was about 10fold/25fold higher than during a regular VKA-usage day (0.08%/0.21% vs. 0.0078%/0.0083%, vs. ($p<0.0001$)). About half of the bleedings were coded by treating physicians as due to anticoagulation therapy. **CONCLUSIONS:** Periods in which VKA-interruption/bridging due to surgery was required frequently occur during the VKA-treatment of AF patients. The cardiovascular/bleeding event risk of VKA-patients is significantly higher during such periods compared to periods of regular VKA-treatment. Whether this is due to VKA-interruption/bridging or the surgical procedures themselves needs to be analysed in future.

PCV33

USING A CAUSE-OF-DEATH-BASED MORTALITY MODEL TO IDENTIFY THE INDIVIDUALS WHO WOULD BENEFIT MOST FROM PRIMARY PREVENTION WITH STATINS

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OBJECTIVES: To explore the use of a cause-of-death-based mortality model to identify those individuals most likely to benefit from taking statins for primary prevention of cardiovascular disease (CVD). **METHODS:** A cause-of-death-based, deterministic Markov model of all-cause mortality was developed. The baseline population average mortality rates for CVD, COPD, other respiratory disease, and cancer were adjusted by referencing individual risk factor values to population averages. Risk factors that were used as model inputs included cigarette consumption per day (CPD), systolic blood pressure (SBP), body mass index (BMI), total cholesterol (TC), and high density lipoprotein (HDL). A total of 11,520 scenarios were modelled encompassing all combinations of high and low values for these risk factors, in men and women, and younger (35 years) and older (65 years) age categories. **RESULTS:** Using an arbitrary threshold for a meaningful clinical benefit of 6 months' increased life expectancy per 10 years of treatment, individuals who are on the cusp of benefiting from statin therapy include: men aged 35 with SBP of 150 mmHg, BMI of 20 kg/m^2, smoking 15 cigarettes per day, with a TC:HDL ratio of 3.5; men aged 70 with SBP of 140 mmHg, BMI of 20 kg/m^2, smoking 10 cigarettes per day, with a TC:HDL ratio of 2.8; women aged 35 with SBP of 135 mmHg, BMI of 20 kg/m^2, smoking 15 cigarettes per day, with a TC:HDL ratio of 4.2 or higher; and women aged 65 with SBP of 140 mmHg, BMI of 30 kg/m^2, who are non-smokers, with a TC:HDL ratio of 4.2. **CONCLUSIONS:** The model facilitates decision-making about when to start preventive treatment and highlights that this is a multi-dimensional problem that renders rules-of-thumb inadequate in determining who most benefits from therapy.

PCV34
THE EFFECTIVENESS OF STATINS IN THE TREATMENT OF CARDIOVASCULAR DISEASE: CROSS-SECTIONAL STUDY WITH PAIRED GROUPS FROM ELECTRONIC PATIENT RECORDS
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OBJECTIVES: Electronic Patient Record has proven useful to assess the benefits, harms and costs in the real world. To describe the association between the use of statins and cardiovascular events in patients with myocardial ischemia by means an Electronic Patient Record (ePR) as the basis for a retrospective cohort study. **METHODS:** To evaluate the association between the use of statins and cardiovascular events, we conducted a cross-sectional study with patients in the ePR of the Heart Institute (InCor) - University of São Paulo Medical School. Patients were considered for the period between 2004 and 2012 and evaluated in terms of the association between the use of statins with prevalence of percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) and inpatient mortality. A total of 46,757 patients were randomly selected and matched for gender, age group (18-49/50-59/60-69/>70), and category of cardiovascular disease diagnosis, being from three ICD-10 groupings, I20-I25/I63-I69/G45/I70. The pairing resulted in two groups, each of them with 14,654 patients, a group with prescription of statin (SG) and a group for comparison (CG) without statin. **RESULTS:** A total of 67.4% of the patients registered in the ePR used statins. The presence of reverse causality, very common in cross-sectional studies, was observed in patients submitted to revascularization procedures. Revascularization was made present in 14% of CG versus 42% of SG, which is justified by the drug administration for care of patients undergoing those procedures. Mortality was 5.8% in CG and 4.7% in SG, with prevalence rates of 80%. The absolute reduction in the prevalence of death between groups was 1.1% ($^{95\%}$CI:0,6-1,6%) in favor of the use of statins. **CONCLUSIONS:** Statins were not prescribed to approximately one third of the patients, the use of statins was higher in patients undergoing revascularization procedures and, was also associated with a 20% reduction in the occurrence of mortality.

CARDIOVASCULAR DISORDERS – Cost Studies

PCV35
BUDGET IMPACT ANALYSIS OF ROUTINE GENTAMICIN-COLLAGEN IMPLANTS FOR THE PREVENTION OF SURGICAL SITE INFECTION (SSI) IN HIGH RISK CARDIOTHORACIC SURGERY PATIENTS
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OBJECTIVES: The SSI rate after cardiothoracic surgery is estimated at 7.3% by the UK Health Protection Agency (HPA) for high risk patients. This represents a burden on resources, through greater risk of in-hospital mortality and increased length of hospital stay (mean 22.1 extra days for deep SSI). Treatment guidelines recommend IV antibiotic prophylaxis before surgery; however a challenge in high-BMI and diabetic patients (high risk) is the inability of systemic antibiotics to sufficiently penetrate target tissue. It is however estimated that 40%-60% of SSIs are avoidable, with clinical data supporting additional use of local gentamicin-collagen for SSI prevention. The purpose of this study was to examine the budget impact case from a UK NHS perspective of routinely administering gentamicin-collagen local prophylaxis against SSI in high risk patients undergoing cardiothoracic surgery. **METHODS:** A literature review was undertaken regarding gentamicin-collagen efficacy in reducing SSI in cardiothoracic patients, NHS costs of SSI, and annual UK cardiothoracic patient numbers. The SSI rate in cardiothoracic surgery was obtained from HPA data. Findings were incorporated into a decision tree budget impact model to analyse potential savings from routine use of gentamicin-collagen in high risk cardiothoracic patients. **RESULTS:** Considering a cohort of 3710 high-risk cardiothoracic patients, annual NHS costs of SSI are £2,164,316. Administration of two gentamicin-collagen implants to each high risk patient would cost £200 per patient. Assuming a 59% reduction in SSI; this would prevent 197 sternal wound infections, with direct savings of £1,590,882 per year, a net saving of £229 per cardiothoracic surgery patient. **CONCLUSIONS:** Significant NHS and hospital trust savings may be achievable through routine use of gentamicin-collagen implants in high risk cardiothoracic surgery patients. A conservative estimate of high-risk patient numbers was used in the analysis, suggesting the scope for budgetary savings could exceed reported findings.

PCV36
EVALUATION OF TELEMEDICINE PROGRAM (ITHACA): INNOVATION IN THE TREATMENT OF ARTERIAL HYPERTENSION INCREASING THE COMPLIANCE AND ADHERENCE IN THE SECOND YEAR OF ITS IMPLEMENTATION (2011-2012)
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OBJECTIVES: To evaluate effectiveness of an interventional strategy (disease management program (DMP)) supported by a telemedicine platform in patients with mild/moderate hypertension. **METHODS:** Quasi-experimental design, paired data with control group (1:2, patients were matched by age and gender). Study population and follow-up period: patients from 6 primary care centers in Badalona (Barcelona, Spain) were followed-up during 2011 and 2012. Study groups: intervention group (telemedicine program) and control group (usual clinical practice). The intervention consisted on establishing a permanent channel of interaction with the patient (telemedicine platform) and providing the patient with educational materials, clinical monitoring, SMS, phone calls, etc. Main measures: Demographic, co-morbidity, anthropometric and biochemical parameters, adherence to treatment, blood pressure control (BP: 140/90 mmHg), associated health care management costs and satisfaction surveys to professionals and patients. Statistical significance:p<0.05. **RESULTS:** A total of 750 patients were included (intervention group n=250, control group n=500). Mean age was of 64.2 years old 52.1% of patients were women. The control group was selected to show an optimal comparability in terms of demographic and morbidity measures between the two groups. The intervention group showed better compliance (87.9% vs. 71.4%, p=0.001). BP control was 52.5 vs. 53.1% (p=NS) initially and 63.2% vs. 55.6% at the end of the study (p<0.001) for the intervention group vs. control, respectively. The follow-up average cost per patient and year was € 377.9 vs. € 442.4, p<0.001 (reduction in intervention group: 66 €). 82% of health care professionals and 91% of patients were satisfied with the DMP. **CONCLUSIONS:** The DMP has improved adherence to treatment and BP control and has reduced health care management costs. If the study results were extrapolated to the overall population of Badalona, a potential saving of 1.7 million per year would be achieved.

PCV37
BUDGET IMPACT ANALYSIS OF APIXABAN FOR THE PREVENTION OF VENOUS THROMBO-EMBOLISM IN PATIENTS UNDERGOING ORTHOPEDIC REPLACEMENT SURGERY IN ITALY
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OBJECTIVES: Venous thromboembolism (VTE) is a common cardiovascular condition, frequently leading to severe complications and requiring high-cost health care interventions. New oral anticoagulants (nOACs) have demonstrated to be efficacious and safe in VTE prevention of patients undergoing total hip replacement (THR) and total knee replacement (TKR). This analysis is aimed present article aims to evaluate its economic impact in the perspective of the Italian SSN. **METHODS:** We conducted a budget impact analysis to estimate clinical outcomes and economic consequences associated to the reimbursement of apixaban in the prevention of VTE as a consequence of major orthopedic surgery, over a three-year time horizon. The analysis compared two alternative scenarios, with apixaban either reimbursed (Scenario B) or not reimbursed (Scenario A) by the Italian SSN. Only direct health care costs have been considered. **RESULTS:** According to market assumptions, it is estimated that 1.2%, 3.7%, and 6.5% of THR patients, and 1.2%, 3.8% and 6.7% of TKR patients, would be treated with apixaban over the first three years since launch. The introduction of apixaban, at the estimated daily cost of €2.48/die, would translate into a budget impact of €14.3 mln, €45.5 mln, and €81.4 mln at years 1, 2 and 3 since launch, respectively. This expenditure would be more than offset by savings, due to: i) reduction of prescriptions of alternative treatment options (other nOACs, low-molecular weight heparins, fondaparinux); ii) reduction of the economic burden attributable of CV complications of VTE. Finally, Scenario B resulted slightly favourable compared to Scenario A, leading to economic savings for about €50 thousands over three years. **CONCLUSIONS:** Reimbursement of apixaban does not determine a budget impact increase for Italian SSN, and offers an additional option to prevent high-cost event provoked by VTE. Its usage may be considered fully sustainable from a pharmacoeconomic viewpoint.

PCV38
ASSESSMENT OF THE BUDGETARY IMPACT OF IMPROVING THE USE OF EVIDENCE-BASED MEDICINE IN THE TREATMENT OF PATIENTS WITH HEART FAILURE AND LEFT VENTRICULAR DYSFUNCTION IN ENGLAND
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OBJECTIVES: Heart failure places a significant burden on the resources of the NHS. The aim of this study was to compare from a budgetary perspective the current treatment of patients with heart failure and left ventricular dysfunction with an estimate of what could be achieved if the use of evidence-based medicine was optimised in accordance with national guidance. **METHODS:** Quality and Outcomes Framework prevalence and Hospital Episode Statistics data 2011/12 were analysed to determine the number of hospital admissions associated with patients with a diagnosis of heart failure for each Clinical Commissioning Group (CCG) and GP Practice in England. These data were adjusted for patients with left ventricular dysfunction who were in sinus rhythm and hospitalisation costs were applied. This was combined with the cost associated with the current use of evidence-based medicine to determine the total cost associated with this condition. This was compared with an estimate of total costs (hospitalisation and medication) if patients received the levels of evidence-based therapy, and outcomes, reported in the SHIFT trial. SHIFT was chosen as the largest and most recent contemporary trial in heart failure and left ventricular dysfunction, which reflects the optimal use of recommended therapies. Data for each CCG and GP practice in England is available via a model presented in Microsoft excel® or Apple numbers®. **RESULTS:** Increasing the use of evidence-based therapy to the levels achieved in the SHIFT trial can potentially release estimated funding of up to £175m for the population of England, £810,000 for a CCG with a population of 250,000 and £32,000 for a GP practice with a list size of 10,000. **CONCLUSIONS:** If the use of evidence-based therapy for patient's heart failure and left-ventricular dysfunction is increased from current levels, significant improvements in terms of patient outcomes and the use of NHS funding can be achieved.

PCV40
A BUDGET IMPACT ANALYSIS TO ESTIMATE THE ECONOMIC IMPACT OF DRUG ELUTING BALLOON FOR THE TREATMENT OF PERIPHERAL VASCULAR DISEASE
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OBJECTIVES: Drug Eluting Balloon (DEB) is a promising alternative for the treatment of patients with peripheral arterial disease, due to the potential reduction in re-intervention rates and cost-savings compared to other technologies commonly used. The objective of this analysis was to assess the economic impact of DEB and other endovascular therapies for patients with femoral-popliteal disease. **METHODS:** A budget impact model was developed to compare the relative impact in Italy of four different index procedure treatments (PTA with regular balloons, DEB, bare metal stents (BMS) and drug eluting stents (DES)) based on the

repeat procedure rates (TLR - target lesion revascularization) over 1 year. The model was developed from a Italian national health care system (NHS) perspective with a 5-year time horizon. A systematic literature review was carried out on TLR rates in patients with femoral-popliteal disease treated with one of the four treatment choices. Costs associated to each treatment are derived from the average DRG tariffs used for peripheral angioplasty procedures. A decision analytic model was developed to estimate total costs over 12 months of index procedures and possible revascularizations. **RESULTS:** Pooled 12-month TLR rates show clear patients benefit with DEB compared to PTA (8,6% vs 28,6%) and non-inferiority of DEB vs DES (9,4%) and BMS (11,5%). Total Italian DRG payments for index and repeat interventions (based on TLR rates estimation) across treatments showed that DEB was the least costly treatment strategy over 1 year, with saving of almost €1,000 per patient with DEB vs PTA. Based on these per-patient savings, the potential total savings amounted to approximately €2 million for an assumed annual increase of 5% in DEB adoption rate over 5 years. **CONCLUSIONS:** The analysis suggests clear patient benefit for DEB. Despite initial higher investments, DEB represents a cost-saving alternative to other technologies according to the NHS perspective.

PCV41

BUDGET IMPACT ANALYSIS OF RIVAROXABAN IN THE PREVENTION OF STROKE IN NON-VALVULAR ATRIAL FIBRILLATION PATIENTS IN ITALY

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OBJECTIVES: In Italy about 500,000 non-valvular atrial fibrillation (NVAF) patients have a major unmet medical need as they do not receive adequate anticoagulation therapy for stroke prophylaxis: many patients receive antiplatelet therapy, even when the guidelines recommend vitamin-K antagonists (VKA), or are not treated at all or have international normalized ratio inadequate control despite treatment with VKA. The purpose of this study was to perform a budget impact analysis of rivaroxaban - a novel oral anticoagulant (NOAC) - in NVAF patients with the highest unmet medical need from the Italian health care system (SSN) perspective. **METHODS:** Two scenarios were compared within a three-year timeframe: the actual scenario, where patients are treated according to current clinical practice (46% with VKA, 38% with antiplatelets, 17% non-treated) and a scenario where Rivaroxaban is present with increasing market shares. The event risks (ischemic and haemorrhagic stroke, systemic embolism, myocardial infarction and bleedings) were retrieved from the ROCKET-AF trial or from a network meta-analysis. Resource consumption was computed using mean regional tariffs. Since Rivaroxaban price is not officially published, the daily cost used ranges from €2.10 (price of the first NOAC approved in this indication in Italy) and the lowest Rivaroxaban price available in Europe (€1.94). The results of the analysis are displayed as a total costs difference between the two scenarios. **RESULTS:** A reduction in the total number of events and costs at SSN charge is shown since the first year from rivaroxaban introduction. The increase in pharmaceutical expenditure is offset by savings from a lower number of events to treat and absence of routine coagulation monitoring. **CONCLUSIONS:** The introduction of rivaroxaban in the national scenario is beneficial because it will provide a substantial reduction in the disease burden for patients and in costs for the SSN.

PCV42

COMPARISON OF DABIGATRAN ETEXILATE VERSUS WARFARIN, ASPRIN & NO TREATMENT FOR STROKE PREVENTION IN ATRIAL FIBRILLATION IN ENGLAND, UNITED KINGDOM, OVER 5 YEARS

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OBJECTIVES: To estimate the number of clinical events and costs of these events for dabigatran etexilate (dabigatran) versus a combination of warfarin, aspirin and no treatment for stroke prevention in atrial fibrillation (AF) patients in an England, UK, setting over 5 years. **METHODS:** An interactive model was built in Microsoft Excel to calculate the following: • Total number of AF patients eligible for dabigatran • Number of clinical events for dabigatran, warfarin, aspirin and no treatment patients over a 5 year time horizon. Clinical events included were stroke (ischaemic, haemorrhagic, systemic embolism); major bleeding (intracranial and extracranial); all cause mortality; acute myocardial infarction • Total costs of clinical events for each treatment. The total cost per day for dabigatran is £2.20 per day; warfarin is £1.18; aspirin is £0.09; no treatment is £0.00. Warfarin had a TTR of 55% (from Jones et al 2005); aspirin and no treatment clinical event rates were from Roskell et al (2010). Dabigatran data was from the RE-LY trial **RESULTS:** The model estimates there are 822,527 patients with AF in England, of which 78% are eligible for dabigatran (641,571). After 5 years, patients treated with dabigatran versus 80% with warfarin; 10% aspirin; 10% no treatment are associated with: 1) 27,357 fewer strokes (16,938 fewer ischaemic storkes); 2) 14,413 fewer major bleeding events; and 3) An increase of £268,167,861 in drug budget; however there is an overall cost saving of £11,240,201. The overall cost saving is predominantly driven by savings in disability following stroke. **CONCLUSIONS:** Study indicates that due to a superior clinical profile, dabigatran may more than offset the increase drug budgets, resulting in cost savings, if used preferentially versus warfarin, aspirin or no treatment.

PCV43

COMPARISON OF DABIGATRAN ETEXILATE VERSUS WARFARIN FOR STROKE PREVENTION IN ATRIAL FIBRILLATION IN IRELAND OVER 5 YEARS

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OBJECTIVES: To estimate numbers of clinical events (strokes, major bleeds, acute myocardial infarctions and deaths) and health care costs over a five year period in Ireland following a switch of antithrombotic therapy for atrial fibrillation (AF) from warfarin to dabigatran. **METHODS:** A model was built in Microsoft Excel and included an estimate of the number of Irish patients diagnosed with AF and eligible for treatment with dabigatran. It is assumed that all diagnosed AF patients eligible for oral anticoagulation currently receive warfarin and that all patients switch to dabigatran in Year 1, regardless of International Normalised Ratio (INR) control amongst warfarin patients. Differences in numbers of clinical events expected to occur based on a patient's antithrombotic treatment were estimated by applying event rates from literature sources. Costs were estimated from a HSE perspective and included costs of clinical events, disability costs and medication costs. **RESULTS:** A total of 28,332 Irish patients are estimated to have been diagnosed with AF and are eligible for dabigatran. Switching these patients from warfarin to dabigatran may avoid: 657 strokes; 792 major bleeds; 1,437 deaths. By Year 5, cumulative dabigatran drug costs were estimated at €7,670,870. Cost savings due to clinical events avoided amounted to €2,894,743 and savings on disability costs at €5,563,349, giving a total cost saving with dabigatran of €787,223. **CONCLUSIONS:** Use of dabigatran as compared to warfarin for stroke prevention in AF in the Irish setting may avoid a significant number of clinical events and result in overall cost savings.

PCV44

ECONOMIC BURDEN OF VENOUS THROMBOEMOBLISM ACROSS PATIENT POPULATIONS: A LITERATURE REVIEW

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OBJECTIVES: To conduct a literature review on the economic burden of venous thromboembolism (VTE) (encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE)) and related complications. **METHODS:** Eligible English-language studies published post-1990 were identified from electronic databases (Medline, EMBASE and Cochrane Library: accessed December 2012) and conference proceedings with no restriction on geographical location or patient population. All costs are reported in US$ adjusted to 2013 levels. **RESULTS:** Twenty-nine studies met eligibility criteria: United States (n=17), Canada (n=2), Australia (n=1), South America (n=1) and Europe (n=8). The estimated annual cost of VTE treatment is in excess of $2 billion in the USA and Europe and $153 million in Australia. This figure rises to $15.6–$34.8 billion in the US and to $1.78 billion in Australia on inclusion of complications, productivity loss and other societal costs. The cost of treating PE per patient ($12,567-$20,488) is higher than that of treating DVT ($2,912-$13,299). Hospitalisation is the main cost driver for VTE treatment, accounting for 56%-89% of all treatment costs. For patients with cancer, costs were 30-50% higher for those with VTE compared with those without VTE. VTE-related complications incur additional costs including: bleeding (up to $23,963 per patient with a major bleed); recurrent VTE (up to $18,122 per patient); post-thrombotic syndrome (increase of up to 75% in treatment cost); chronic thromboembolic pulmonary hypertension (up to $6,708 per patient); and heparin-induced thrombocytopenia (up to $18,779 per patient). **CONCLUSIONS:** Incident VTE events and related complications are associated with significant economic burden across several patient populations. Treating PE may cost up to five times more than treating DVT, with hospitalisation reported as the major cost driver of VTE treatment. Effective and convenient therapies associated with both a reduced incidence of bleeding and complications are required to further reduce the cost burden associated with VTE.

PCV45

PHARMACOECONOMIC ASPECTS OF ACTOVEGIN AND SOLCOSERYL IN THE TREATMENT OF RUSSIAN PATIENTS WITH ACUTE CEREBROVASCULAR ACCIDENTS

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OBJECTIVES: To assess the cost-effectiveness of actovegin and solcoseryl in the treatment of Russian patients with acute ischemic stroke and predict potential budget impact of the implementation of actovegin in routine clinical practice. **METHODS:** The pharmacoeconomic model was developed based on the data from Russian clinical trial performed by A. Fedin et al. (2000). Two groups of patients (100 persons each) hospitalized with acute ischemic stroke were included in the model. The first group of patients received conventional therapy + actovegin and the second group received conventional therapy + solcoseryl. Based on the reported by A. Fedin et al. time-dependent mortality reduction in actovegin-treated patients (mortality rate was 7% in patients started actovegin within the first 6 hours after stroke onset, 10% – in those started actovegin within the first 24 hours, 14% – in those started actovegin after more than 24 hours, and it was much higher in the control group – 21%) cost-effectiveness ratios (CERs) and indicator of economic rationality of costs of previous periods (IRPP) were calculated and compared. **RESULTS:** Estimated CERs varied from 46,348.82 to 50,121.40 RUB per one survivor in the actovegin group and from 50,900.56 to 53,585.17 RUB per one survivor in the solcoseryl group. Inefficient expenditures (IRPP) varied from 301,730.83 RUB to 603,461.67 RUB in the actovegin group, and were 873,453.57 RUB in the solcoseryl group. **CONCLUSIONS:** The study has demonstrated the preferred cost-effectiveness profile of actovegin as compared to solcoseryl in patients with acute ischemic stroke.

PCV46

PHARMACOECONOMIC BENEFITS OF CITICOLINE IN THE TREATMENT OF ACUTE ISCHEMIC STROKE IN RUSSIA

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OBJECTIVES: To assess the cost-effectiveness of citicoline in the treatment of Russian patients with acute ischemic stroke and identify potential budget impact of the implementation of citicoline in routine clinical practice. **METHODS:** The pharmacoeconomic model was developed based on the data of meta-analysis performed by A. Davalos et al. (2002). Two groups of 100 patients each were included in the model: the first group of patients received conventional therapy and the second group (active treatment group) additionally received citicoline. It was assumed that citicoline was given to patients in the active treatment group in the following way: during the first

10 days since acute stroke onset, 2,000 mg was administered intravenously; from day 11 to the end of the treatment periods (74 days), 1,000 mg was administered per os. The time horizon adopted in the model was 12 weeks. Based on the data on effectiveness of citicoline in complete patient recovery after 3 months reported by A. Davalos et al., the cost-effectiveness ratios (CERs) were calculated and compared. **RESULTS:** Estimated CERs were 513,099.20 RUB per one patient recovered in control group and 435,368.00 RUB per one patient recovered in citicoline group. Furthermore, the costs of rehabilitation of patients were lower in the citicoline group as compared to control group, cost savings were estimated to be about 1,719,610.00 RUB. **CONCLUSIONS:** The study has demonstrated that the treatment of acute ischemic stroke with citicoline was more cost-effective and had the potential to reduce the rehabilitation expenses.

PCV48

REMOTE PATIENT MONITORING IN CRT-D RECIPIENTS MAY REDUCE USE OF HOSPITAL-BASED CARE

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OBJECTIVES: Heart failure (HF) is a costly disease imposing a substantial health burden which affects 1-2% of Europeans. Hospital readmission for HF is a common occurrence with 25% of all patients readmitted within 30-days following initial hospitalization. Reducing readmission is an important component of managing HF costs and increasingly being targeted with health care policy reforms. The objective of this study is to examine how remote patient monitoring (RPM) may affect health care costs following the placement of a CRT-D device for patients with HF through the use of a simulation model. **METHODS:** The analysis was an individual patient event-based simulation from a US payer perspective based on a sample of patients from RAPID-RF, a multi-center prospective single-arm registry which enrolled 889 patients who received a CRT-D and RPM system (LATITUDE® Boston Scientific). The modeled population consisted of patients that had at least one alert for weight change, atrial tachycardia or ICD shock with a subsequent intervention (N=128). The population was limited to this subset to focus on the costs of changes in management due to RPM. A non-RPM control group was created by cloning each trial patient and simulating their response in the absence of RPM to the conditions that triggered each alert in the trial over one year using a decision tree which computed rates of hospitalization and physician contacts based on literature data. Event and hospitalization costs were estimated per Medicare (CMS) national average payment. **RESULTS:** RPM reduced total costs after the index procedure by $323/patient driven by a reduction in costs related to hospitalization admissions. The decrease in hospital admission cost was partially offset by RPM's increase in physician visits and telephone counseling. **CONCLUSIONS:** RPM has the potential to shift HF-related care from an inpatient setting to office-based care, resulting in cost savings to national payers.

PCV49

DABIGATRAN ETEXILATE IN PREVENTION OF STROKE FOR NONVALVULAR ATRIAL FIBRILLATION PATIENTS IN TURKISH HEALTH CARE SETTING; A STUDY ON COST CONTAINMENT OF SOCIAL SECURITY INSTITUTION (SSI)

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OBJECTIVES: Analysis of cost containment of SSI via use of Dabigatran Etexilate (150MG) versus current standard of care (Warfarin) in prevention of stroke for non valvular atrial fibrillation patients in Turkish health care setting. **METHODS:** All calculations are performed for a group of 1000 patients in each treatment arm per year (Treatment arms; Dabigatran 150MG & Warfarin 5MG – results are represented as "cost per patient per day"). Available clinical data is analyzed for calculation of event costs in each treatment arm (RE-LY study). Local costs of events are included from local literature. Microsoft Excel (2007) is used for calculations and construction of data tables. **RESULTS:** Direct cost of SSI (indirect costs are not included in this analysis) is calculated in each treatment arm. Difference of daily medication cost between Dabigatran Etexilate and Warfarin treatments is +3.12 TL/Day*Patient however, this difference is calculated as -3.34 TL/Day*Patient when medication cost is combined with total treatment cost (costs of thromboembolic&adverse events, INR monitoring, impairment). Dabigatran Etexilate offers a cost containment (saving) of 0.22 TL/Day*Patient in prevention of stroke for non valvular atrial fibrillation patients in Turkish health care setting. **CONCLUSIONS:** Limitation of this study is covering only direct cost data due to lack of local literature on indirect costs. Further analysis may be performed by non-interventional studies, which will define cost containment data via real life cost and effectiveness values. This study demonstrates that Dabigatran Etexilate treatment may sustain cost containment (saving) via reduction of direct cost of SSI with respect to current standard of care, in prevention of stroke in patients with atrial fibrillation in current Turkish health care system.

PCV50

COST SAVING AFTER SUTURELESS REPLACEMENT IN AORTIC VALVE STENOSIS: RESULTS FROM A PROPENSITY-MATCHED SCORE ANALYSIS IN GERMANY

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OBJECTIVES: New sutureless aortic valve prostheses reduce the surgical time. Objective of this study is to asses if shorter operative times may also result in improved patient outcomes and the impact on the hospital costs. **METHODS:** Records of 547 patients that underwent aortic valve replacement with a bioprosthesis from March 2009 and May 2013 were identified. Based on a propensity score analysis 2 groups (Sutureless and Sutured) with 82 matched pairs were created from the 112 patients received a Perceval sutureless bioprosthesis and the 435 patients received a sutured valve. Hospital and follow up outcomes, resources consumption was recorded and compared between groups. Analysis was performed according the National Health Care system perspective. **RESULTS:** Preoperative characteristics and risk scores of the 2 groups were comparable. Hospital mortality was 3.7% in Sutured and 2.4% in Sutureless (p=0.65). Aortic cross-clamp, cardiopulmonary bypass time and operation time were 20%, 23% and 16% shorter in Sutureless (each one p<0.001).Sutureless required less blood transfusion (1.2±1.3 vs 2.5±3.7 units, p=0.005) with a similar incidence of postoperative bleeding (2 patients vs 5, p=0.221). Sutureless had a shorter intensive care unit stay (2.0±1.72vs 2.8±1.3 days, p<0.001), a shorter hospital stay (11.4±3.9 vs 17.3±13.7 days, p<0.001) and a shorter intubation time (9.5±4.6 vs 16.6±6.4 hours, p<0.001). A neurological event was recorded in 3 sutureless patients and in 6 sutures (p=0.248). Sutured has an higher incidence of postoperative atrial fibrillation, pleura effusions and respiratory insufficiency (p 0.015, 0.024 and 0.016, respectively). Reduced risk of post operative complication resulted in a dramatic reduction of resources consumption in the sutureless group allowing a saving of 50% of the complication related resource use. **CONCLUSIONS:** Shorter procedural times resulting from sutureless aortic valve replacement are associated with better outcomes and lower costs. Sutureless valve may be considered as the first-line treatment for patients underwent aortic valve replacement with a bioprosthesis.

PCV51

TRENDS IN THE COST-EFFECTIVENESS OF STROKE CARE

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OBJECTIVES: To assess the annual average costs and quality adjusted life years (QALYs) of stroke services in the UK before and after the introduction of the National Stroke Strategy (period: 2006-2011). **METHODS:** Data from the South London Stroke Register (SLSR) from 2006 to 2011 were used to populate a discrete event simulation (DES) model. Parameters, such as daily probability of survival and length of stay, included in the model were calculated by using Cox proportional hazard model and multivariate regression methods respectively. Barthel Index was used as proxy for measures of quality of life. Treatment costs were introduced in the model in order to calculate the total costs based on resource usage. The model simulated the stroke care delivery from stroke onset with 10-year follow up. Average cost and QALYs were calculated for every year from 2006 to 2011. **RESULTS:** The average total costs per treating a stroke patient decreased from £30,745 to £27,086 between 2006 and 2011 (p-value for trend < 0.001). This is mainly as a result of savings achieved in the inpatient phase due to a shorter LOS and a higher proportion of patients with mild disability. Per patient QALY's also increased from 2.2 to 3.1 during the same period (p-value for trend < 0.001), this is due to a higher proportion of patients having access to better organised stroke care. **CONCLUSIONS:** This study has demonstrated that stroke services in the UK have improved their value for money over time with constant gains in efficiency. The use of DES together with SLSR data allows the testing of the costs and outcomes of a whole stroke provision system or components of it and provide opportunities for retrospective (as done in this study) as well as prospective analysis (in the case of health technology assessment studies).

PCV52

DISCRETE EVENT SIMULATION MODEL OF PRIMARY PREVENTION OF STROKE: BENEFITS OF INCREASING COVERAGE TO UNSERVED PATIENTS

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OBJECTIVES: To assess the impact of a hypothetical increase in the stroke primary preventive care coverage in the UK. Productivity gains, using resource utilization as proxy, and monetary benefits were calculated. **METHODS:** Data from the South London Stroke Register (SLSR) from 2009 to 2011 were used to create a hypothetical cohort to populate a discrete event simulation (DES) model. The model simulated the stroke care delivery from primary preventive stroke care until discharge from stroke unit or general medical ward. Primary preventive care was defined as taking medications to control hypertension, high-cholesterol and also anticoagulants in patients with atrial fibrillation in order to prevent strokes. Treatment costs were introduced in the model in order to calculate the total costs based on resource usage. Hypothetical scenarios consisting in 10% incremental increase of primary preventive care for high-risk factors were tested. The reduction of strokes was given by relative risk reduction ratios extracted from clinical trials. **RESULTS:** Our findings indicate that for every 10% increase in the number of patients undergoing primary prevention treatment the number of strokes would be reduced by 1.2%. In a scenario where 50% of the untreated patients receive primary prevention 7,232 strokes would be reduced per year. For the same scenario, 47 hyper acute beds, 359 acute beds and 47 general medical ward beds could be saved in average. In total this would yield in £42.2 million of savings in the inpatient phase of stroke care. **CONCLUSIONS:** Our findings suggest that by enhancing primary prevention of stroke care in the UK, significant benefits can be achieved in terms of reductions in resource consumption and monetary savings as a result of averted strokes. The generation and analysis of these retrospective hypothetical scenarios, using real-world evidence on stroke, help evaluate policy choices in stroke care in the UK.

PCV53

THE BURDEN OF RESISTANT HYPERTENSION IN 5 EUROPEAN COUNTRIES

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OBJECTIVES: Greater than 40% of Europeans over age 25 have hypertension, and 10% of those have medication resistant hypertension (RHT). In EU5 (France, Germany, Italy, Spain, UK) that results in 9.4 million persons with blood pressure above goal, despite treatment with 3+ medications. These patients have a greater than 30% risk of cardiovascular disease (CVD) over 10 years and an increased risk of end-stage renal disease (ESRD). This analysis sought to quantify the burden of RHT

in EU5, a subject about which nothing has been published to date. **METHODS:** A burden of illness model was constructed to examine the impact of RHT in EU5, specifically the incremental incidence, mortality and direct medical costs of CVD, which includes: coronary heart disease (CHD), congestive heart failure (CHF) and stroke. Framingham risk equations which included a coefficient for treatment resistance and SCORE risk charts were used to estimate the risk of CVD for patients with and without RHT. Transition probability data were taken from the literature to estimate the risk of death from CVD events, subsequent CVD events and ESRD. Direct costs for these events and their long-term consequences were taken from the literature and from country-specific drug and acute inpatient costs. **RESULTS:** The total direct medical cost of RHT in EU5 is estimated to be €3.9 billion in 2013. This does not include the cost for drugs to treat RHT, or other costs such as lost productivity not directly borne by the health care system. RHT will contribute to 188,000 cases of CHD, 57,400 strokes, 31,500 CHF and 1,400 ESRD and 30,000 deaths in 2013. **CONCLUSIONS:** The burden of RHT due to the increased incidence of CVD and ESRD is high. Reducing the incidence of CVD and ESRD through better blood pressure control should be a priority for health care decision makers.

PCV54

RETROSPECTIVE COSTING STUDY TO ESTIMATE BURDEN OF HEART FAILURE IN SPAIN

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OBJECTIVES: To analyze and estimate resource utilization and associated costs, one year following an acute episode of heart failure (HF) in Spain. **METHODS:** Patient-flow data after index hospitalization for acute HF (AHF) were obtained from EAHFE database, an emergency (ER)-based registry containing records of all AHF patients treated in 29 Spanish hospitals (over 5,800 cases). Estimated medical resource utilization data during patients' ER and other wards stay, hospitalization, and first-year follow-up was collected from medical specialists through questionnaire. AHF episodes and hospitalizations incident rates were estimated through literature review and disease statistics in official sources. Cost data was retrieved from Spanish Pharmacists official sources and a national health care costs database (Euros, 2013). To assess uncertainty, sensitivity analysis was carried out. **RESULTS:** A total of 111,803 annual hospital admissions are estimated in Spain (2013). 92% of patients suffering an AHF episode are discharged alive and of these 90% survive the first month; 23% of these patients are discharged directly from ER, while the majority of those who are hospitalized, are admitted to Internal Medicine (53%) or Cardiology (17%) wards. On an average, patients are re-admitted 0.41 times within 1 year. Total direct costs in the first year following an AHF episode averages €6,822, of which 88% are incurred in hospital, with drugs and diagnostic tests accounting for less than 5% of all hospital costs. Follow-up costs, in average, split equally between drugs and outpatient visits/tests, but vary widely depending on local HF protocols. Extrapolation of results to the Spanish population suggests that the total burden of HF is more than €542 million per year. **CONCLUSIONS:** Treating HF patients within Spain is resource intensive. Costs are primarily incurred in hospital and are mostly driven by the length of stay.

PCV55

THE BURDEN OF ILLNESS OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: A MANAGED CARE PERSPECTIVE IN THE UNITED STATES

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OBJECTIVES: Chronic thromboembolic hypertension (CTEPH) is associated with considerable morbidity and mortality. The objective of this study was to describe the burden of illness in patients with CTEPH. **METHODS:** Data for this study came from a large commercial claims database. CTEPH patients were identified based on having >2 medical claims for either primary pulmonary hypertension (ICD-9 code:416.0) or chronic pulmonary heart disease (ICD-9 code:416.8), history of pulmonary embolism in the past one year (ICD-9 code:415.1, V12.51, 38.7; CPT-4 codes:36010, 37620, 75825, 75940; HCPCS codes:C1880) and either one claim for right heart catheterization or one claim of echocardiogram and diagnosed by a pulmonologist/cardiologist within 12 months of the medical claim. Demographic variables were extracted at a patient level from administrative files and economic variables, which included health care utilization and costs for outpatient, inpatient, emergency and pharmacy services came from the respective medical and pharmacy claim files and summarized at a per-patient-per-month (PPPM). Five controls were randomly picked and matched to each CTEPH patient on demographic characteristics. Incremental burden of CTEPH was estimated using non-parametric statistical tests between controls and CTEPH group. All costs were adjusted to 2012 base year using consumer price index. **RESULTS:** A total of 191 CTEPH patients were identified and matched to 955 controls. CTEPH group had significantly higher ($p<0.001$) PPPM health care utilization compared to the matched control across all drivers: outpatient (3.1 vs. 1.5), inpatient (0.13 vs. 0.02), emergency room (0.16 vs. 0.04), and pharmacy services (4.5 vs. 2.6). The increase in utilization translated in higher ($p<0.001$) total PPPM incremental costs of $5,007 in the CTEPH group with inpatient ($3,909 vs. $332) and pharmacy costs ($607 vs. $180) being as much as twelve and three times greater compared to controls. **CONCLUSIONS:** Health care resource use and costs for CTEPH patients is high from a managed care perspective.

PCV56

THE BURDEN OF ILLNESS OF PULMONARY ARTERIAL HYPERTENSION: A MANAGED CARE PERSPECTIVE IN THE UNITED STATES

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OBJECTIVES: Pulmonary arterial hypertension (PAH) is a progressive disease resulting in high health care resource use and costs. The objective of this study was to estimate the burden of illness in PAH patients. **METHODS:** Data came from a large commercial claims database. PAH patients were identified based on having >2 medical claims for primary pulmonary hypertension (ICD-9 code:416.0), and either one claim for right heart catheterization or one claim of echocardiogram and diagnosed by a pulmonologist/cardiologist within 12 months of the medical claim. The first medical claim during this period served as in the index date with 12 months prior to this event as baseline and 12 months post as follow-up period. Demographic variables were extracted at a patient level from administrative files and economic variables, which included health care utilization and costs for outpatient, inpatient, emergency and pharmacy services came from the respective medical and pharmacy claim files and summarized at a per-patient-per-month (PPPM). Five controls were randomly picked and matched to each PAH patient on demographic characteristics. Incremental burden of PAH was estimated using non-parametric statistical tests between controls and PAH group. All costs were adjusted to 2012 base year using consumer price index. **RESULTS:** A total of 2,245 PAH patients were identified and matched to 11,225 controls. PAH group had significantly higher ($p<0.001$) PPPM health care utilization compared to the matched control across all drivers: outpatient (2.6 vs. 1.5), inpatient (0.08 vs. 0.02), emergency room (0.1 vs. 0.04), and pharmacy services (4.2 vs. 2.6). The increase in utilization translated in higher ($p<0.001$) total PPPM incremental costs of $3,193 in the PAH group with inpatient ($1,665 vs. $345) and pharmacy costs ($790 vs. $178) being as much as five times greater compared to controls. **CONCLUSIONS:** Health care resource use and costs for PAH patients is high from a managed care perspective.

PCV57

COSTS OF ACUTE HEART FAILURE IN FRANCE

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OBJECTIVES: To describe the incidence and profile of patients hospitalised for acute heart failure (AHF); to assess the trajectories of patients before and after hospitalization; and to estimate the cost of AHF inpatients stays. **METHODS:** Patients with AHF were identified over a 5-year period (2006 - 2010) from the French PMSI (Programme de Médicalisation des Systèmes d'Information), a national disease-related group inpatient database. The PMSI database contains data related to all private and public hospital stays in France (about 20 millions/year). Heart failure was identified with the ICD-10, code I50. **RESULTS:** The numbers of patients hospitalised at least once per year for AHF increased from 144,043 in 2006 to 158,623 in 2010. These numbers lead to incidence rates of 2.28‰ in 2006 and 2.45‰ in 2010. The proportion of patients aged ≥75 increased from 71.0% in 2006 to 74.3% in 2010. Half of patients were male. The mean number of comorbidities was 9.6 in 2010. The mean length of stay was 9.5 days and 12.6 days per year (2010), as mean re-hospitalization for AHF within the same year was 22%. The mean annual number of AHF hospitalisations per patient was 1.3. The mean cost for an AHF hospitalisation in the acute setting was 4,713€ in 2010. The mean annual cost for all hospitalisations occurring for a patient hospitalised at least once in a year (2010) for AHF was 6,253€. Mean costs per hospital stay was higher if the patient died during hospitalisation (5,722€ vs. 4,627€, $p<0.001$). Extrapolation to the whole country leads to a yearly cost of nearly a billion of euros (991 millions). **CONCLUSIONS:** Incidence of AHF hospitalisation increased in the recent years. This analysis highlighted the high economic hospital burden of AHF in France.

PCV58

DISEASE BURDEN OF ISCHEMIC STROKE ALONG FIRST YEAR POST-STROKE IN SPAIN

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OBJECTIVES: Stroke has catastrophic consequences resulting in death or disability in 80% of patients and representing a substantial burden on the health care system, as well as on patients, family, and society. Stroke is considered as the 2nd cause of burden of disease in Europe and ischemic stroke (IS) represents a high percentage of total strokes. The objective of the present study was to analyze the first year post-stroke burden of IS in Spain. **METHODS:** We performed an observational, multicenter, naturalistic and prospective study that included 16 hospitals (stroke units of National Health System hospitals) of 16 Spain regions. We took into consideration consumption of health care resources, social burden, productivity lost and health-related quality of live of patient and caregiver during the first year post-stroke. **RESULTS:** A total of 321 stroke patients were recruited. Mean age 72 years, 54.8% male. Basal NIH stroke scale was 9.11 and 28.9% presented moderate-high disability. 291 (90.7%) patients presented IS. Overall 1-year cost per IS was 27,596.53€. Direct health care costs were 8,623.35€ (31.25%), direct intrahospital health care costs supposed 69% (5,926.21€) of these costs. Direct non-health care costs were 18,377.75€ (66.59%), of which 16,515.09€ (59.84%) were informal care costs. Productivity lost was 595.43€ (2.16%). **CONCLUSIONS:** IS were the majority of total strokes in the study and represent a high burden on health care system and society, mainly due to hospitalization and informal care costs. Intrahospital costs were double than the published DRGs in Spain. Other diseases like Alzheimer or dementia represent a lower burden than stroke.

PCV59

FOLLOW-ON HEALTH CARE COSTS IN PATIENTS WITH ACUTE CORONARY SYNDROME (ACS)

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OBJECTIVES: To review published estimates of post-acute-care costs over one year in patients with acute coronary syndrome (ACS). **METHODS:** Using the Medline and

Embase databases, we identified published reports of direct health care costs in ACS patients in the US; we limited attention to studies published in English between January 1, 2003 and July 30, 2012. Reference lists of all such studies also were scanned to identify additional sources. We abstracted information from all relevant reports on costs of recurrent events (e.g., myocardial infarction [MI], stroke, ACS-related readmissions) and cardiac procedures, as well as costs of cardiac-related outpatient visits and pharmacotherapy and total health care costs, in the year following ACS onset. As appropriate, estimates were converted to 2011 US dollars, using the medical-care component of the US Consumer Price Index. **RESULTS:** A total of 16 studies were identified that met all selection criteria. For persons with private health insurance coverage, estimated cost per recurrent event was lowest for bleeding ($7951) and highest for MI (range = $17,081 - $20,348); the cost of ACS-related admissions ranged from $6818 to $34,089. For Medicare beneficiaries, cost per recurrent event was lowest for other cardiovascular events ($4542 - $14,360) and highest for MI ($10,082 - $11,347); the cost of ACS-related admissions was $13,683. Mean total health care costs for patients with private insurance coverage ranged from $21,319 to $40,062 in the year following ACS onset; similar estimate was identified for Medicare beneficiaries. **CONCLUSIONS:** Costs of follow-on care are high in patients with ACS, due to recurrent events, revascularization, and routine follow-on care. In general, costs were higher for patients with private health insurance coverage than those with Medicare coverage.

PCV60

PATIENT-LEVEL COSTS OF CARDIOVASCULAR EVENTS AND PROCEDURES: HOW ROBUST IS THE EVIDENCE?

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OBJECTIVES: Few studies have undertaken a global review of major cardiovascular conditions and events. This review summarizes the current literature for costs of: major cardiovascular diseases/events (angina, myocardial infarction, heart failure, stroke/transient ischemic attack, peripheral arterial disease); revascularization (coronary, cerebral, or peripheral); coronary heart disease mortality; and cerebrovascular mortality. **METHODS:** A systematic search of the scientific literature from 2007 through 2012 was conducted. English language articles reporting per-patient average direct medical costs of any cardiovascular event of interest in any country were included. Cost-effectiveness studies and primary prevention interventions were excluded. Cost of the event including initial hospitalization ("acute cost") and any re-hospitalizations or post-event follow-up ("follow-up cost") along with methodologies of each study were abstracted. **RESULTS:** A total of 176 articles representing 30 countries were abstracted. Coronary revascularization (N=46), stroke (N=43), and heart failure (N=31) articles were heavily represented. Acute cost estimates varied widely for all conditions/events (2013 USD): angina ($1,004-8,380); myocardial infarction ($570-$31,321); coronary revascularizations ($240-$129,747); heart failure ($536-$28,176); stroke ($577-$167,378); cerebral revascularizations ($7037-$57,884) peripheral arterial disease ($1241-23,144); peripheral revascularizations ($2297-$129,865); coronary heart disease inpatient mortality ($7,030-$25,556); cerebrovascular disease inpatient mortality ($6,197-$40,141). Similarly, wide variation was found for follow-up cost estimates, based on time horizons that range from 30-day re-hospitalization to the remainder of life post-initial event. The majority of studies were specific to the United States; for countries other than the US, cost estimates for each event were much less robust. Methodological differences between articles limit comparability of costs. **CONCLUSIONS:** Though estimates vary, the significant economic burden of these cardiovascular events is evident. A lack of robust literature in some conditions and countries combined with significant heterogeneity of study design and reporting makes comparison of cardiovascular event costs difficult. New research should identify a representative sample using study designs that allow for comparability.

PCV61

COSTS IN PATIENTS ALONG FIRST YEAR POSTSTROKE IN SPAIN

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OBJECTIVES: Atrial Fibrilation (AF) 5-folds stroke risk, which results in death or disability in 80% of individuals and the one-year mortality approaches 50%. The objective of the present study was to determine first year post-stroke costs in patients with or without AF. **METHODS:** We performed an observational, multicenter, naturalistic and prospective study that included 16 hospitals (stroke units of National Health System hospitals) of 16 Spain regions. We took into consideration all costs related to stroke: direct health care costs (inpatient and outpatient), societal cots (formal and informal care), and indirect costs (productivity lost) during the first year post-stroke. **RESULTS:** A total of 321 stroke patients were recruited, 291 (90.7%) with ischemic stroke (IS) and 30 (9.34%) with intracraneal hemorraghe (ICH); 160 with and 161 without AF. The mean age was 72±13 years, 54.8% was male, basal NIH stroke scale was 9.11±6.79 and 28.9% presented moderate-high disability. The overall cost per year was 27,711.10€. Direct health care costs: 8,491.22€ (30.64%), intrahospital costs were 68.8% (5,838.41€) of direct health care costs. Direct non-health care costs were 18,643.50€ (67.3% of total costs), and informal care supposed 89.5% of these costs. Indirect costs were 576.39€ (2.1% of total costs). ICH costs were higher than IS costs (28,895.04€ vs 27,596.53€). AF costs were higher than non AF but only formal care costs were statistically significant. The most explicative variables were age, male sex, NIH stroke scale, arterial hypertension comorbidity, and exitus along study. **CONCLUSIONS:** Stroke and its consequences represent an important use of health care and social resources during first year post-stroke, total costs of stroke represent more than 5% of public health care costs in Spain. Several studies from other countries showed similar health care costs but lower informal care costs, which where more than two-thirds of total costs in our study, with a very high burden over the family or informal carer.

PCV62

A COMPARISON OF THE ECONOMIC BURDEN AND HEALTH CARE UTILIZATIONS OF VETERAN PATIENTS DIAGNOSED WITH HYPERTENSION IN THE UNITED STATES

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OBJECTIVES: To compare the economic burden and health care utilizations of U.S. veteran patients diagnosed with hypertension. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration Medical SAS datasets from October 1, 2008 to September 30, 2012. Patients diagnosed with hypertension were identified using International Classification of Disease 9th Revision Clinical Modification (ICD-9-CM) diagnosis codes 401.x, 402.xx, 403.xx, and 404.xx, with the first diagnosis date designated as the index date. A comparison group of patients without hypertension but of the same age, region, gender and index year were identified and matched by baseline Charlson Comorbidity Index. The index date for the comparator group was randomly chosen to reduce selection bias. Patients in both groups were required to be at least 18 years old, and have continuous medical and pharmacy benefits 1 year pre- and 1 year post-index date. Study outcomes, including health care costs and utilizations, were compared between the disease and comparator groups using 1:1 propensity score matching. **RESULTS:** A total of 2,422,810 patients were included in the hypertension and comparison cohorts. After 1:1 matching, a total of 748,857 patients were matched from each group, and baseline characteristics were well-balanced. Patients diagnosed with hypertension utilized more health care resources for inpatient (8.21% vs. 1.01%, p<0.01), emergency room (ER) (12.78% vs. 3.60%, p<0.01), physician office (99.43% vs. 39.45%, p<0.01), outpatient visits (99.61% vs. 40.14%, p<0.01), and pharmacy visits (85.51% vs. 35.66%, p<0.01). The disease group also had higher patient expenditures for inpatient ($2,568 vs. $289, p<0.01), ER ($121 vs. $30, p<0.01), physician office ($2,541 vs. $767, p<0.01), outpatient visit ($2,844 vs. $853) and pharmacy visits ($544 vs. $191, p<0.01) than the comparison group. **CONCLUSIONS:** Results suggest that patients diagnosed with hypertension incurred significantly higher health care utilizations and costs compared to those without.

PCV63

THE COSTS OF SURGICAL AORTIC VALVE REPLACEMENT IN FRANCE

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OBJECTIVES: Surgical aortic valve replacement (sAVR) represents the gold standard for treatment in patients who require valve replacement therapy. However, the risks and costs are not uniform across all patients. We have examined the national hospital costs database of France to detail the variability of outcomes and costs in an attempt to allow improved decision making when deciding on appropriate interventions. **METHODS:** The Programme de Médicalisation des Systèmes d'Information (PMSI) hospital database for 2010 was examined and all discharge records retrieved for patients undergoing aortic valve replacement. In addition to the discharge costs information on hospital length of stay, mortality and Charlson risk score were also obtained. **RESULTS:** The mean cost for all 12,512 recorded sAVR procedures (defined as Groupe homogène de maladies (GHM) codes 05C02 and 05C03) in 2010 was €19,029 (median €17,349). Overall hospital mortality was 5.94% but increased to 26.06% depending on severity level and GHM code. Corresponding total costs increased if patients died prior to discharge by €11,007 and €9,200 for 05C02 and 05C03 respectively but also differed by severity, generally increasing together with mortality up to a maximum mean of €42,063. Hospital length of stay (LoS) also varied by severity levels with means of between 10.74 and 27.91 days dependent on severity. **CONCLUSIONS:** The costs and outcomes of sAVR vary enormously and a single point estimate cannot be used to adequately to reflect them. Therapeutic choices must be tailored to the individual patient and has the potential to generate substantial cost reductions for the payer by avoiding mortality and reducing LoS. We present this in the context of new treatment options for aortic valve replacement.

PCV64

ECONOMIC IMPACT OF STROKE EPISODE IN PATIENTS PREVIOUS DIAGNOSED WITH ATRIAL FIBRILLATION IN PRIVATE HEALTH SYSTEM IN BRAZIL

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OBJECTIVES: Evaluate the costs of patients with known diagnosis of atrial fibrillation who received medical care related to stroke episodes, under the Private Healthcare system perspective. **METHODS:** A retrospective evaluation of a database with 3 million individuals was conducted to identify patients diagnosed with Atrial Fibrillation (AF) using the International Classification of Diseases version 10 (ICD10) I48 code (Flutter and atrial fibrillation) between 2009 and 2010. From the identified cohort, patients presenting the following codes: ICD10 I64, I63, I66 and I69, were further analyzed from 2009 to 2012. Costs associated to the episodes such as medications, exams, procedures, hospitalizations and others were evaluated. **RESULTS:** From 1898 patients presenting the AF diagnose identified in the database, 66 Presented a diagnosis of stroke. The 66 patients cost BRL 2,325,250.61 to the supplemental health service, being BRL 2,193,185.50 spent with 21 patients hospitalizations due to stroke. **CONCLUSIONS:** If not controlled, AF may impose a significant morbidity due to increased susceptibility for thromboembolic events such as stroke and its complications, causing important spending beyond hospitalizations and other significant direct and indirect costs to the private health care system.

PCV65

COST ANALYSIS FOR PATIENTS HOSPITALISED FOR HEART FAILURE IN GERMANY

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OBJECTIVES: To calculate treatment costs for patients hospitalised for heart failure (HF) and analyse associated medical resource utilisation in a real-life care setting. **METHODS:** The study was designed as a retrospective medical record review of a cohort of 478 patients diagnosed and hospitalised for HF (as the primary diagnosis for hospitalisation with ICD-10 codes I11, I13 and I50 meeting the inclusion and exclusion criteria of RELAX-AHF, a randomised, placebo-controlled phase III-trial in acute HF) in three German hospitals. Costs and medical resource utilisation for HF treatment were extracted from datasets according to §21 KHEntgG (Hospital Reimbursement Act) and patient medical records from the full year of 2011. Costs of HF treatment were determined according to the cost calculation scheme of the German Institute for the Hospital Remuneration System (InEK). A multivariate regression model was developed to detect incremental effects. **RESULTS:** The mean cost per hospital stay was 3,518 € [3,203 €; 3,833 €; 95%CI 315 €]. Differences in costs between male and female patients were not significant. The mean length of stay (LOS) was 8.55 days [8.0; 9.1; 95%CI 0.55] with in-hospital mortality being 5.4% (26 of 478 patients). A total of 637 different active pharmaceutical agents and agent combinations were used. The percentage of patients treated with loop diuretics was 84%. About 8% of patients received nitrates (all formulations). The regression model showed a positive correlation for treatment costs with LOS and the amount of daily drug doses. **CONCLUSIONS:** This analysis highlights that HF is a condition that imposes considerable costs to the German health care system. Data suggests that there is a high use of diuretics and a low use of nitrates in a real-life care setting.

PCV66

COST-EFFECTIVENESS ANALYSIS OF APIXABAN VERSUS DABIGATRAN FOR PREVENTION OF STROKE IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION IN SPAIN

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OBJECTIVES: To assess the cost-effectiveness of apixaban vs. dabigatran in stroke prevention in patients with non-valvular atrial (NVAF) fibrillation in Spain. **METHODS:** A Markov model was developed, with cycles of 6 weeks, throughout the patient's life and 10 health states. The analysis was made from the Spanish National Health System (NHS) and the societal perspective. The safety and efficacy of the drugs was obtained from a meta-analysis of pairwise indirect comparisons. Drug costs, (apixaban: 5 mg twice daily (BID); dabigatran: 110 mg BID or 150 mg BID), NVAF complications and disease management costs were obtained from Spanish sources. An annual discount rate of 3.5% for costs and health outcomes was applied. **RESULTS:** In a cohort of 1,000 patients with NVAF, apixaban could avoid numerous complications versus dabigatran during their lifetime (24 ischemic strokes and 28 related deaths vs. dabigatran 110 mg; 11 ischemic strokes, 29 bleedings and 19 deaths vs. dabigatran 150 mg). The use of apixaban was associated with 0.126 life years (LYG) and 0.107 quality-adjusted life-years (QALYs) gained when compared to dabigatran 110 and 150 mg, respectively. Apixaban was estimated to generate more costs per patient vs. dabigatran 110 mg from the NHS perspective (139 €) but overall savings could arise from the societal perspective (-524 €), with a cost per QALY gained of 1,299 € for the NHS. Apixaban was dominant (more effective and less costly than dabigatran 110 mg) from the societal perspective. The cost per QALY gained, from the NHS and societal perspective, compared with dabigatran 150 mg BID was 6,591 € and 10,676 €, respectively. Deterministic and probabilistic sensitivity analyses confirmed the stability of these results. **CONCLUSIONS:** Results suggest that apixaban is cost-effective versus dabigatran for the prevention of stroke in patients with NVAF in Spain.

PCV67

APPLICATION OF NEW FRENCH GUIDELINES FOR ECONOMIC EVALUATIONS: A COST-EFFECTIVENESS ANALYSIS OF APIXABAN IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION IN FRANCE

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OBJECTIVES: To evaluate the cost-effectiveness of apixaban in the prevention of stroke in patients with non-valvular atrial fibrillation (NVAF) from a French payer perspective. **METHODS:** A Markov model was developed in accordance to the new French guidelines of the Commission for Economic Evaluation and Public Health (CEESP) that also recommends applying efficiency frontier. A hypothetical cohort of patients with NVAF, 70 years old eligible for stroke preventive treatment (CHADS2≥1) was simulated over lifetime. Clinical events modeled included strokes, systemic embolism, intracranial hemorrhage, other major bleeds, clinically relevant non-major bleeds and myocardial infarction. Treatment efficacy and bleeding data was obtained from ARISTOTLE. Efficacy data are from published indirect comparisons. Acute medical costs of stroke and hemorrhage were obtained from a dedicated analysis of the French national hospitalization database (PMSI). Long-term medical costs and utility data were derived from the literature. Univariate and probabilistic sensitivity analyses (PSA) were also performed to assess the robustness of the model projections. **RESULTS:** Three strategies were strictly dominated: aspirin, dabigatran 110mg, and dabigatran in sequential dosages. Two others were extendidly dominated: rivaroxaban and dabigatran 150mg. The efficiency frontier was constructed by connecting the remaining strategies: warfarin and apixaban. Apixaban resulted in an incremental additional cost of 2,870€ and an incremental QALY of 0.189, corresponding to an ICER of 15,157€/QALY versus warfarin. The PSA indicated that the probabilities for apixaban being cost-effective versus warfarin were respectively 80% and 90% at the informal willing-to-pay thresholds of 30,000€ and 50,000€. Sensitivity analysis identified stroke risk with apixaban and intracranial hemorrhage risk with warfarin as the variables most influencing the results. **CONCLUSIONS:** Apixaban may be the most economically efficient alternative to warfarin in NVAF patients eligible for stroke prevention in France. All other strategies are dominated. However, uncertainty surrounding these results should be investigated through real life data.

PCV68

SCREENING STRATEGIES FOR HEART FAILURE IN PATIENTS WITH TYPE 2 DIABETES: ASSESSING COST-EFFECTIVENESS IN THOSE AGED 60 YEARS OR OVER

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OBJECTIVES: Heart failure is quite common in elderly patients with type 2-diabetes. Screening could potentially improve health outcomes at acceptable costs through early detection and adherence to current prescription guidelines. Based on a prospective study the cost-effectiveness of different screening strategies to detect heart failure in patients aged 60 years with type 2-diabetes was assessed. **METHODS:** Data obtained from our prospective study and literature were used in a Markov model with a lifetime horizon to evaluate the incremental cost-effectiveness ratio of five increasingly extensive screening strategies. Differences in survival rates estimated by the Seattle Heart Failure Model between patients with undetected versus detected heart failure, induced by medication use, were used to adjust input parameters for health states related to undetected heart failure. Estimates for costs, utilities, and transition probabilities were additionally adjusted to age and NYHA class. Scenario analyses were performed to evaluate the impact of screening age and medication prescription and effectiveness. Probabilistic sensitivity analysis was performed to assess robustness of the results. **RESULTS:** For both men and women usual care (no screening) had the highest probability of being cost-effective when the willingness to pay (WTP) was small. For WTP values in the range of €4,600/QALY-€27,000/QALY for men and €5,200/QALY-€40,000/QALY for women evaluation of the electronic medical record and symptoms had the highest probability of being cost-effective. For higher WTP values echocardiography was the preferred strategy. For all screening strategies cost-effectiveness improved if prescription of heart failure medication was optimal or screening was started at the age of 70 years. **CONCLUSIONS:** Screening for heart failure through evaluation of electronic medical record and symptoms has favorable cost-effectiveness and echocardiography may also be acceptable at higher WTP values. The benefits from screening could be much larger than currently identified when test outcomes would more often lead to proper medication prescription.

PCV69

COST-EFFECTIVENESS ANALYSIS OF APIXABAN VERSUS RIVAROXABAN FOR PREVENTION OF STROKE IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION IN SPAIN

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OBJECTIVES: To assess the cost-effectiveness of apixaban versus rivaroxaban in the prevention of stroke in patients with non-valvular atrial fibrillation (NVAF) in Spain. **METHODS:** A Markov model was developed to simulate the evolution of NVAF patients throughout their lifetime. Cycle's length was 6 weeks and 10 health states such as stroke, bleeding and other cardiovascular complications were defined. Drug's safety and efficacy outcomes were obtained from a meta-analysis of pairwise indirect comparisons. The analysis was made from the Spanish National Health System (NHS) and the societal perspective. Apixaban and rivaroxaban pharmacological costs were calculated according to their recommended doses (5 mg twice daily (BID) and 20 mg once-a-day (QD), respectively). The cost of NVAF complications and disease management were obtained from Spanish sources. An annual discount rate of 3.5% for costs and health outcomes was applied. **RESULTS:** Model results illustrate that 1,000 patients with NVAF treated with apixaban during their lifetime could avoid numerous complications versus rivaroxaban (9 strokes, 10 intracranial bleedings, 1 systemic embolism, 32 major bleedings, 52 clinically relevant non major bleedings and 12 related deaths). The use of apixaban was associated with 0.062 life years (LYG) and 0.049 quality-adjusted life-years (QALYs) gained when compared to rivaroxaban. Due to the lower expected mortality of patients, apixaban generated more costs per patient vs. rivaroxaban from the NHS perspective (115 €), but savings would arise from the societal perspective (-241 €). Incremental cost-effectiveness ratio results were 1,855 € per LYG and 2,347 € per QALY gained for the NHS analysis. Apixaban was dominant (more effective and less costly than rivaroxaban) from the societal perspective. Deterministic and probabilistic sensitivity analyses confirmed these results. **CONCLUSIONS:** According to this analysis, apixaban is a cost-effective treatment compared with rivaroxaban for the prevention of stroke in patients with NVAF in Spain.

PCV70

REANALYZING USING BAYESIAN METHODS AND UPDATED DATA THE COST-EFECTIVENESS ASSUMPTIONS OF CAROTID ARTERY STENOSIS TREATMENTS

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Henriksson reported that surgery plus medical management can be considered cost effective as a treatment of asymptomatic carotid stenosis in 65 year-old men. He assumed a surgery relative risk reduction of 65.5%, or approximately an absolute risk reduction (ARR) of 8% in this population. However, data for the comparator arm (medical management alone) were dated and did not reflect efficacies of current medical therapies. **OBJECTIVES:** To analyze using Bayesian methods, asymptomatic carotid stenosis clinical trial data, and more current medical therapy data the probability of achieving this 8% ARR and an incremental cost per QALY of approximately $50,000 (US, inflated - 2013 dollars). **METHODS:** The outcome of interest from the clinical trials was the mean difference in the probability of any stroke or perioperative death between surgery (carotid endarterectomy [CEA]) and aggressive medical management (MM). The CEA data came from the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST). The updated medical management data came from a systematic review published in the journal Stroke (Abbott, 2009). The Bayesian analysis employed a Beta-Binomial Model. **RESULTS:** The posterior distribution of the Bayesian analysis representing the ARR of CEA versus MM had a mean of 0.008 with an essentially zero probability of achieving the Henriksson assumption of 8% ARR. Using the mean of this posterior distribution, the resulting incremental cost per QALY exceeded $500,000 in 65 year-old men – a value unlikely to be considered cost effective in any country. **CONCLUSIONS:** Bayesian analysis allows the prediction of the probability that a treatment alternative exceeds a predefined threshold. A powerful feature of Bayesian analysis is the ability to incorporate additional and/or newer data. This newer data can drastically alter assumptions about the cost effectiveness of treatment alternatives.

PCV71

COST-EFFECTIVENESS OF TRANSCATHETER AORTIC-VALVE IMPLANTATION FOR SEVERE SYMPTOMATIC AORTIC STENOSIS IN INOPERABLE PATIENTS IN THE BRAZILIAN PRIVATE HEALTH CARE SYSTEM

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OBJECTIVES: Aortic stenosis is the most common valvular heart disease in the elderly –its prevalence is estimated to be up to 5% in individuals over 75 years. Surgical replacement of aortic valve is considered the standard care and in the absence of serious coexisting conditions, the procedure is associated with low operative mortality. However, a significant proportion of patients cannot undergo surgery due to high surgical risk associated with advanced age or presence of multiple coexisting conditions. Treatment with transcatheter aortic-valve implantation (TAVI) is a therapy with potentially lower peri-procedure risk and has been used as a therapeutic option in this group considered inoperable. This study aims to develop a cost-effectiveness analysis of TAVI in patients with severe aortic stenosis who are not suitable for surgical treatment according to Brazilian Private System Perspective. **METHODS:** A Markov model was developed to compare TAVI *versus* standard therapy (drug treatment with or without aortic balloon valvuloplasty) with a 5-year time horizon. Outcomes in the model were based on safety and effectiveness (as measured by clinical outcomes of chance of successful implantation procedure and survival from PARTNER cohort B trial). Resource use included early perioperative complications (30 days) and late events. Cost data were obtained from Brazilian public lists (CMED/SIMPRO/CBHPM). Results were expressed as incremental cost-effectiveness ratio (ICER) per life years gained (LYG). Probabilistic sensitivity analysis was performed to confirm robustness of results. **RESULTS:** Compared with standard therapy with or without aortic balloon valvuloplasty, use of TAVI improves survival in 0.97 life years with an incremental cost of US$43,602, resulting an ICER of US$45,080/LYG. In an alternative scenario considering 10-year time horizon, ICER was 27,565/LYG. **CONCLUSIONS:** Use of TAVI results in improved survival with a low risk of serious adverse events, and demonstrates a cost-effectiveness profile when compared to other technologies already incorporated in Brazil.

PCV72

ECONOMIC EVALUATION OF IVABRADINE IN CHRONIC HEART FAILURE IN GREECE

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OBJECTIVES: In the SHIFT trial, ivabradine administered to chronic heart failure (CHF) patients in combination with standard therapy significantly reduced cardiovascular death and hospital admission for cardiovascular problems. An economic evaluation of ivabradine plus standard care against standard care alone, for the management CHF in patients with a baseline heart rate ≥75b.p.m. was conducted from the Greek third party-payer perspective. **METHODS:** An existing Markov model consisting of two health states for CHF NYHA classes I to IV (i.e. alive, dead) was adapted to the Greek health care setting. In each one month cycle, patients can either remain alive or die, during their life span or 29 months (i.e. within SHIFT trial period). Health state utilities were estimated from EQ-5D index scores obtained from the SHIFT clinical trial and using appropriate modeling techniques the data were extrapolated beyond the trial period. All costing data reflects the year 2013. Probabilistic sensitivity analyses (PSA) were conducted. Both cost and outcomes were discounted at 3.5% per year. **RESULTS:** Results for within trial analysis revealed that ivabradine had an incremental cost and incremental QALY of €905 and 0.05 respectively, leading to an incremental cost per QALY gained of €16,635/QALY. Ivabradine was a cost-effective alternative at a willingness to pay threshold of €36,000 per QALY gained Moreover, the cumulated lifetime analysis showed incremental cost of €2,792 and incremental QALY of 0.28. The ICER for ivabradine was calculated to be €9,986 per QALY gained. The PSA showed that the likelihood of ivabradine plus standard therapy being cost-effective at a threshold of €36,000/QALY was found to be 96% in both within trial and lifetime analysis. This result is driven by a reduction in mortality and hospitalisations and the associated costs of care. **CONCLUSIONS:** Ivabradine added to standard care could be a cost-effective treatment for the treatment in CHF patients in Greece.

PCV73

COST-EFFECTIVENESS ANALYSIS OF RIVAROXABAN IN SECONDARY PREVENTION OF ACS IN SWEDEN

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With 7 million deaths per year, ischaemic heart disease is the leading cause of mortality worldwide. In Acute Coronary Syndrome (ACS), the vast majority of fatal cardiovascular events occur after hospital discharge. Guidelines recommend antithrombotic treatment for secondary prevention after ACS. **OBJECTIVES:** To assess the cost-effectiveness of rivaroxaban 2.5mg BID in combination with standard antiplatelet therapy (ASA alone or in combination with a thienopyridine [clopidogrel or ticlopidine]) versus standard antiplatelet therapy alone for prevention of secondary events in ACS patients from a Swedish societal perspective. **METHODS:** A Markov model is used to capture single and multiple events, costs and utilities based on the time since index event to reflect clinical practice. For the first 2 years the model uses data from the ATLAS ACS 2-TIMI 51 clinical trial including efficacy, safety, treatment discontinuation and average patient age. After 2 years, transition probabilities were extrapolated using an exponential function method. Estimates for life expectancy, drug acquisition costs and other medical and indirect costs were derived from published Swedish sources. Cost and effects are discounted at 3.0%. Univariate and probabilistic sensitivity analyses were conducted with an assumed willingness to pay (WTP) threshold of SEK 500,000. **RESULTS:** For the base case scenario, incremental life time costs are estimated at SEK 10,000.44 (€1,156), incremental QALYs at 0.14, and incremental cost per QALY at SEK 71,245.76 (€8,236). Univariate sensitivity analyses indicate that the results are sensitive to changes in the cost of rivaroxaban and baseline utility value. At an assumed WTP of SEK 500,000, rivaroxaban in combination with standard antiplatelet therapy is expected to be cost-effective. **CONCLUSIONS:** From a Swedish societal perspective, secondary prevention with rivaroxaban 2.5mg BID in combination with standard antiplatelet therapy can be considered a cost-effective option for patients with ACS. Sensitivity analyses demonstrated that the results are robust.

PCV74

COST-EFFECTIVENESS ANALYSIS OF APIXABAN IN THE TREATMENT OF ATRIAL FIBRILLATION IN MEXICO

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OBJECTIVES: The most common cardiac arrhythmia (atrial fibrillation, AF) increases the risk of morbidity and mortality. We estimated the health and economic consequences of the use of apixaban compared with warfarin reducing the risk of stroke in patients with AF, from the perspective of the Instituto Mexicano del Seguro Social (IMSS). **METHODS:** We performed a cost-effectiveness analysis using a Markov model (17 health states, six-week cycles), which simulates patients treated with warfarin (fixed dose: 5mg/day) or apixaban (10mg/day). Patients enter the model at age 70 and remain there until death (disease-related or according to Mexican life tables). Safety, efficacy and utilities were extracted from published sources. The costs of warfarin and AF-related clinical events were extracted from IMSS sources. The cost of apixaban was provided by the manufacturer. Costs are expressed in US$, 2013 and a 5% per-year discount rate was applied. Years of life and quality adjusted life years (QALYs) gained were the health outcomes. Univariate and probabilistic sensitivity analyzes were performed. **RESULTS:** The model estimated 7.645 life years and 5.454 QALYs in the apixaban arm, which means 0.147 and 0.160 gained life years and QALY's, respectively (regarding warfarin). The costs of apixaban and warfarin were US$14,943 and US$15,042, respectively (apixaban is a dominant alternative). Health gains with apixaban are driven by fewer event-related deaths (10/1000 patients at risk) as well as fewer hemorrhagic strokes (12) and bleeding (13 major bleeds, 41 clinically non-major bleeds) compared to warfarin-treated patients. Treatment costs are driven by drug acquisition cost (apixaban) and monitoring cost (warfarin). **CONCLUSIONS:** Apixaban is more effective and safer than warfarin reducing the risk of stroke associated with AF, as well as bleeding events. To achieve this improvement, no additional economic resources need to be invested, which makes apixaban a cost-saving intervention in the context of the IMSS.

PCV75

COST-EFFECTIVENESS OF APIXABAN VERSUS STANDARD OF CARE FOR THE PREVENTION OF STROKE: AN ANALYSIS OF PATIENTS WITH ATRIAL FIBRILLATION IN GREECE

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OBJECTIVES: Apixaban is an oral anticoagulant that has demonstrated a superior clinical profile compared to warfarin and aspirin in the management of patients with non-valvular Atrial Fibrilation (NVAF) and at least one additional risk factor for stroke. The objective of the present analysis was to assess the cost-effectiveness of apixaban against warfarin and aspirin for the prevention of stroke in patients with NVAF in Greece. **METHODS:** A Markov model that evaluated clinical events, quality adjusted life expectancy and costs for patients treated with apixaban and warfarin or aspirin (VKA-suitable and

VKA-unsuitable, respectively) formed the basis of the analysis. Clinical events (ischemic strokes, hemorrhagic strokes, intracranial hemorrhages, other major bleeds, clinically relevant non-major bleeds, myocardial infarctions and cardiovascular hospitalizations) were modeled over a lifetime horizon based on the clinical efficacy of each comparator, as reported by two phase-III clinical trials (ARISTOTLE and AVERROES). Resource use with regards to patient monitoring was elicited via an experts' panel (cardiologists & internists). Cost calculations reflect the local clinical setting, and followed a third-party payer perspective (Euros, year 2013, discounted at 3%). **RESULTS:** Apixaban was projected to reduce the occurrence of clinical events and increase quality adjusted life expectancy compared to warfarin and aspirin (an incremental increase of 0.225 and 0.274 QALYs per patient, respectively). Taking into account costs of medications, treatment and management of events, the incremental cost-effectiveness ratio for apixaban versus warfarin and aspirin was estimated at 12,154.6 €/QALY and 5,980.6 €/QALY gained, respectively. Extensive sensitivity analyses indicated that results were robust over a wide range of inputs. **CONCLUSIONS:** Based on the results of this analysis, apixaban can be a cost-effective alternative to warfarin and aspirin for the management of VKA-suitable and VKA-unsuitable patients with NVAF, respectively, in Greece.

PCV76

TOTAL COSTS AND OUTCOMES OF DRUG-ELUTING STENT PLACEMENT WITH INTRAVASCULAR ULTRASOUND (IVUS) COMPARED WITH ANGIOGRAPHY ALONE: A COST-EFFECTIVENESS ANALYSIS FROM THE PERSPECTIVE OF THE ITALIAN HEALTH SYSTEM

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OBJECTIVES: Intravascular ultra-sound (IVUS) allows physicians to generate a superior image of coronary arteries during percutaneous coronary interventions (PCI), providing a tomographic, 360-degree view of the arterial wall from the inside, which allows a more accurate and complete assessment than is possible with angiography. The purpose of this study was to understand the cost-effectiveness of IVUS compared with traditional angiography techniques in drug-eluting stent (DES) implantation, from the perspective of the Italian health system. **METHODS:** A Markov model was developed to extrapolate the comparative costs and outcomes of a theoretical population of 1000 patients undergoing DES implantation with traditional angiography alone, or in conjunction with IVUS. The model assesses cardiac events, including revascularisations and myocardial infarctions from a health system perspective. Outcomes with and without IVUS were based on a meta-analysis by Zhang et al (2013). Because of limited clinical evidence to inform the long-term outcomes of IVUS compared with angiography, the model either assumes the benefit of IVUS is conferred only in the first year of treatment, or that the benefit is maintained permanently. **RESULTS:** Using IVUS during PCI cost an average of €542 per patient, and yields an additional 0.022 quality adjusted life years (QALYs) per patient. In a population of 1,000 patients, IVUS led to a reduction of 6.7 revascularisations and 5.9 less myocardial infarctions (MI) over the lifetime of a patient. When the revascularisation and MI benefit of IVUS is assumed to extend for the patient's lifetime, angiography with IVUS costs €38 per patient and yields an additional 0.09 QALYs over a patient's lifetime; avoiding 13.4 MIs and 12.3 revascularisations per 1,000 patients. **CONCLUSIONS:** IVUS appears to be a cost-effective addition to traditional angiography in DES placement in Italy, with the increased upfront cost of IVUS offset by reduced cardiac events in IVUS-treated patients over time.

PCV77

COST-EFFECTIVENESS OF APIXABAN VERSUS OTHER NEW ORAL ANTICOAGULANTS FOR THE PREVENTION OF STROKE: AN ANALYSIS OF PATIENTS WITH ATRIAL FIBRILLATION IN GREECE

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OBJECTIVES: Apixaban, dabigatran (150 mg BID and 110 mg BID) and rivaroxaban are three novel oral anticoagulants (NOACs) currently approved for stroke prevention and systemic embolism in non-valvular atrial fibrillation (NVAF) patients. The objective of this analysis was to assess the cost-effectiveness (CE) of apixaban against other NOACs for the prevention of stroke in patients with NVAF in Greece. **METHODS:** A Markov model that evaluated clinical events, quality adjusted life expectancy and costs for patients treated with apixaban or other NOACs formed the basis of the analysis. Clinical events (ischemic strokes, hemorrhagic strokes, intracranial hemorrhages, other major bleeds, clinically relevant non-major bleeds, myocardial infarctions and cardiovascular hospitalizations) were modeled for a lifetime horizon. Due to lack of head-to-head comparisons, efficacy and safety data was derived from an indirect treatment comparison (ITC). The key pivotal trials, ARISTOTLE, ROCKET-AF and RE-LY, all included warfarin as a comparator therefore allowing for an ITC. Resource use with regards to patient monitoring was elicited via a panel of experts (cardiologists & internists). Cost calculations reflect the local clinical setting and followed a third-party payer perspective (Euros, year 2013, discounted at 3%). **RESULTS:** Apixaban was projected to reduce the occurrence of clinical events and increase quality-adjusted life expectancy and costs of treatment compared to other NOACs. Taking into account costs of medications, treatment and management of events, the incremental cost-effectiveness ratios for apixaban 5 mg BID versus dabigatran 150 mg BID, dabigatran 110 mg BID and rivaroxaban 20 mg QD were estimated at 15,403€/QALY, 4,955€/QALY and 10,130 €/QALY gained, respectively. Extensive sensitivity analyses indicated that results were robust over a wide range of inputs. **CONCLUSIONS:** Based on the results of this analysis, apixaban can be a cost-effective alternative to other NOACs, for the prevention of strokes in patients with NVAF in Greece.

PCV78

PHARMACOECONOMIC EVALUATION ACCEPTABILITY OF CLOPIDOGREL VERSUS ACETYLSALICYLIC ACID IN PATIENTS WITH CARDIOVASCULAR DISEASE FOR STROKE PREVENTION IN UKRAINE

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OBJECTIVES: The results of many clinical trials demonstrate the benefit of long-term antiplatelet therapy in reducing the risk of cardio- and cerebrovascular complications. Both acetylsalicylic acid (ASA) and clopidogrel are effective, but have potentially serious side effects, and clopidogrel is more expensive than ASA. The purpose of the study is to evaluate the pharmacoeconomic acceptance of clopidogrel versus ASA in patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease to prevent non-fatal stroke and death rate according to the clinical trial CAPRIE from Ukrainian perspective. **METHODS:** Outcomes of the clinical study CAPRIE, modeling "decision tree" and analysis "cost-effectiveness" were used. **RESULTS:** The results of the clinical trial CAPRIE study showed, that clopidogrel is more effective versus ASA for reducing the risk of nonfatal stroke: absolute risk reduction is -2.7%. Model "decision tree" was built using the probabilities of events (nonfatal stroke and death) from the study CAPRIE. Direct costs were calculated taking into account the costs of antiplatelet therapy, of nonfatal stroke treatment (drugs, diagnosis, patient's stay in hospital) and the cost of rehabilitation after stroke. Indirect costs are not taken into account because the patients were of retirement age (62.5 years old). As a result of calculations it was found, that antiplatelet therapy with clopidogrel is more expensive and more effective (2 additional lives saved per 1000 patients over 1.91 years) compared with ASA. Due to the threshold of society "willingness to pay" per 1 life saved, or 1 QALY, use of clopidogrel as antiplatelet agent in patients with cardiovascular disease is economically profitable for Ukraine. **CONCLUSIONS:** The use of clopidogrel as an antiplatelet agent in patients with cardiovascular disease to prevent nonfatal stroke compared to the ASA is economically profitable for Ukraine.

PCV79

AN ANALYSIS OF THE COST EFFECTIVENESS OF LEFT ATRIAL APPENDAGE CLOSURE FOR THE PREVENTION OF STROKE IN PATIENTS WITH ATRIAL FIBRILLATION AND ABSOLUTE CONTRAINDICATIONS TO WARFARIN THERAPY

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OBJECTIVES: Stroke and its associated disability costs the European Union an estimated €62 billion per year. Warfarin is the mainstay for stroke prevention in atrial fibrillation (AF), but many patients have absolute contraindications to this drug. The Watchman device for left atrial appendage closure (LAAC) received CE mark for stroke prevention in AF patients with contraindications to warfarin. This analysis sought to estimate the cost effectiveness of treating warfarin-ineligible AF patients with LAAC as compared to standard aspirin therapy. **METHODS:** A Markov model was developed comparing clinical outcomes and total costs between patients treated with LAAC or aspirin over 5 and 10 years based largely on clinical outcomes from the Aspirin and Plavix Registry (ASAP) and ACTIVE trials. Clinical events included ischemic stroke, TIA, systemic embolism, bleeding, and acute myocardial infarction as well as procedure-related events. Germany was chosen as the country of analysis because of its unique DRG for the LAAC procedure. Acute costs were taken from German DRGs and long-term disability costs were taken from the Berlin Acute Stroke Study. Sensitivity analysis was performed on clinical and cost inputs; the model was most sensitive to changes in the rate of ischemic stroke. **RESULTS:** LAAC demonstrated a benefit in terms of ischemic strokes and mortality avoided. The cost per ischemic stroke avoided was €91,020 and €24,722 at 5 and 10 years, respectively. The cost per life year gained for LAAC versus aspirin was €22,694 at 5 years and decreased to €5,859 at 10 years. **CONCLUSIONS:** LAAC is a cost-effective alternative to aspirin therapy in patients with contraindications to warfarin. Cost offsets achieved with LAAC become considerably more pronounced over time. This analysis highlights the importance of considering the lifetime costs of stroke prevention in AF, especially as the probability of both stroke and bleeding increases with patient age.

PCV80

COST-EFFECTIVENESS OF RIVAROXABAN IN THE PREVENTION OF STROKE IN NON-VALVULAR ATRIAL FIBRILLATION PATIENTS IN ITALY

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OBJECTIVES: To perform a cost-effectiveness analysis of rivaroxaban (once-daily) in the prevention of stroke and systemic embolism of patients with non-valvular atrial fibrillation (NVAF) and in patients sub-groups from the perspective of the Italian health care system (SSN). **METHODS:** A Markov model was developed with a lifetime timeframe where a hypothetic NVAF patients' cohort is treated with Vitamin-K antagonists (VKAs), antiplatelet drugs (ASA) or no therapy. Patients remain stable or progress towards other health states (ischemic or hemorrhagic stroke, myocardial infarction and bleedings) until death. The base case compares rivaroxaban with VKAs. In subgroup analyses, rivaroxaban is compared with patients at highest unmet medical need: 1. VKA patients with poor INR control, 2. patients under ASA or 3. not treated. Clinical data were derived from ROCKET-AF trial or a network meta-analysis. Utility data were retrieved from published literature. Health care resources consumption was valued using average regional tariffs in Italy. Since rivaroxaban price is not officially published, the price of the first novel oral anticoagulant approved in this indication in Italy was considered. Model outcomes are expressed in terms of incremental cost per quality adjusted life year (QALY) gained (ICER). Univariate and probabilistic sensitivity analyses were performed **RESULTS:** In the base case, rivaroxaban showed to be cost-effective compared to VKA with an

ICER of €11,000/QALY which is below the threshold deemed acceptable from Italian payers (25.000€-40.000€). In the subgroups analyses, rivaroxaban demonstrated to be a dominant strategy (more effective and less costly). Sensitivity analyses showed the robustness of the results. **CONCLUSIONS:** Rivaroxaban is a cost-effective alternative to VKA and is cost-saving for the SSN in the treatment of NVAF patients at highest unmet medical need.

PCV81

COST-EFFECTIVENESS OF DABIGATRAN ETEXILATE FOR THE SECONDARY PREVENTION OF RECURRENT DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM IN THE UNITED KINGDOM

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OBJECTIVES: To estimate the cost-effectiveness of dabigatran etexilate (dabigatran) for the secondary prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE) from the perspective of the UK National Health Service. **METHODS:** A Markov model was developed to estimate costs and outcomes over the lifetime of a cohort of patients receiving either dabigatran (150mg given orally, twice daily) or placebo for 6 months after having completed 6 to 18 months of anticoagulation treatment for a DVT or PE. Modelled events included recurrent DVT and PE, major bleeding (including long-term disability from intracranial haemorrhage), clinically relevant non-major bleeding, myocardial infarction, unstable angina, pulmonary hypertension, severe postthrombotic syndrome, and death. Efficacy and safety parameters were based on the RE-SONATE study; the period of follow-up was 6 months with an extension to 18 months. Probabilities of recurrent DVT and PE after trial follow-up were based on a prospective cohort study of 1,626 patients followed-up for a median of 50 months and were assumed to be equivalent in both treatment groups. Utility estimates were based on EQ-5D data collected in dabigatran trials and published literature. The mean duration of therapy was based on the RE-SONATE study; other costs were based on NHS Reference Costs and published literature. Costs and outcomes were discounted at 3.5% per annum. Univariate and probabilistic sensitivity analyses were performed. **RESULTS:** In the base-case analysis, mean total costs for dabigatran and placebo patients were £7,147 and £7,520 respectively; mean QALYs were 13.089 and 13.070 respectively. Dabigatran was dominant; the probability of cost-effectiveness at a willingness-to-pay threshold of £20,000 per QALY was 63%. In univariate sensitivity analysis, dabigatran was dominant in all analyses. **CONCLUSIONS:** This analysis suggests that dabigatran is likely to be cost-saving compared to placebo for the secondary prevention of DVT and PE in the UK.

PCV82

A HEALTH ECONOMIC EVALUATION OF FENOFIBRIC ACID IN COMBINATION WITH STATINS IN THE PREVENTION OF CARDIOVASCULAR DISEASE IN TAIWANESE MIXED HYPERLIPIDEMIA PATIENTS

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OBJECTIVES: Statins are the standard treatment for cardiovascular disease (CVD) prevention however, with limited effect on triglyceride (TG) and high-density lipoprotein-cholesterol (HDL-C) in mixed hyperlipidemia. Fenofibric acid (FA) is approved for co-administration with statins to reduce TG and increase HDL-C in patients with mixed hyperlipidemia at goal for LDL-C with statins. This study assesses the cost-effectiveness of FA combined with low (LDS) or medium (MDS) dose statins versus low, medium or high (HDS) dose statins alone in the prevention of CVD in Taiwanese patients with type 2 diabetes and mixed hyperlipidemia. **METHODS:** A 5-health-state Markov model for diabetic patients with mixed hyperlipidemia already treated with statin (TG:250mg/dl; HDL-C:35mg/dl; LDL-C:115mg/dl; TC:200mg/dl) was developed, using a lifetime horizon with annual cycles. PROCAM (first event) and Framingham (subsequent event) risk equations were used. Effects on TG, HDL-C and TC for each comparator were derived from pooled simvastatin, atrovastatin and rosuvastatin trials. Drug and event costs were based on official national databases. Annual discounting (5%) was applied to outcomes and costs. Incremental cost (€) per Quality of Life Gained (QALYG) was calculated from the Taiwanese Bureau of National Health Insurance perspective. **RESULTS:** Compared to LDS and MDS, treatment with FA+LDS resulted in higher costs (€2,225; €1,676) but more QALYG (0.311; 0.064), resulting in an incremental cost-effectiveness ratio of €7,161/QALYG and €26,375/QALYG respectively. Compared to HDS, FA+LDS costs were lower with slightly less QALYG (ICER: €183,490/QALYG). Compared to FA+MDS, FA+LDS was dominant with lower costs (-€900) and higher QALYG (0.004). Sensitivity analyses showed robustness of the results. The probability for FA+LDS being cost-effective (< GDP threshold €45,400) is 100% for both, LDS and MDS. **CONCLUSIONS:** In this specific mixed hyperlipidemia population, FA+LDS is likely to be a cost-effective alternative to LDS or MDS alone, potentially allowing for lower statin doses in preventing CVD.

PCV83

COST-EFFECTIVENESS OF STATINS FOR PRIMARY PREVENTION IN NEWLY DIAGNOSED TYPE 2 DIABETES PATIENTS IN THE NETHERLANDS

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OBJECTIVES: Statins reduce the risk of cardiovascular events in patients with diabetes. The aim of this study is to determine whether statin treatment for primary prevention in newly diagnosed type 2 diabetes is cost-effective, taking non-adherence, baseline risk, and age into account. **METHODS:** A cost-effectiveness analysis was performed using a Markov model with a time horizon of 10 years. The baseline 10-year cardiovascular risk was estimated in a Dutch population of primary prevention patients with newly diagnosed diabetes from the Groningen Initiative to Analyse Type 2 Diabetes Treatment database (GIANTT), using the UKPDS risk engine. Statin adherence was measured as pill days covered (PDC) in the IADB.nl pharmacy research database. Cost-effectiveness was measured in costs per quality-adjusted life-year (QALY) form the health care-payers' perspective. **RESULTS:** For an average patient aged 60 at diagnosis, statin treatment was highly cost-effective at around €2,300 per QALY. Favourable cost-effectiveness was robust in sensitivity analysis. Differences in age and 10-year cardiovascular risk showed large differences in cost-effectiveness from more than €100,000 per QALY to almost being cost saving. For the average patient aged 40 at diabetes diagnosis, statin treatment for primary prevention was not cost-effective. **CONCLUSIONS:** Despite the non-adherence levels observed in actual practice, statin treatment is cost-effective for primary prevention in patients newly diagnosed with type 2 diabetes. Due to large differences in cost-effectiveness according to different risk and age groups, the efficiency of the treatment could be increased by targeting patients with relatively higher cardiovascular risk and higher ages.

PCV84

DEVELOPMENT OF NOVEL IMAGING TESTS TO SELECT PATIENTS FOR INDIVIDUALIZED THERAPIES: ARE THEY WORTH FURTHER INVESTMENT?

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OBJECTIVES: Patients with a recent transient ischemic attack (TIA) or minor ischemic stroke who receive medicines have a 10-year risk of about 16% for any recurrent stroke. Non-invasive molecular imaging technologies are currently being developed to improve individual stroke risk prediction. We estimated the potential lifetime cost-effectiveness of a novel imaging test for stroke prediction in an early stage of development. **METHODS:** Decision modelling was used to estimate the potential value of an add-on test that could identify which patients with a recent TIA or minor ischemic stroke should undergo surgery instead of receive medicines. The comparator was patient management according to Dutch guidelines. Test sensitivity and specificity were varied from 0-100% and its cost was set at €350. Different age- and gender-specific subgroups were examined to see how much cost-effectiveness varied. **RESULTS:** A perfect add-on test (100% sensitivity and specificity) for 60-year-old men appears to be cost-effective versus Dutch guidelines, with an estimated 0.61 QALY gain, €3,986 cost increase, and an incremental cost-effectiveness ratio (ICER) of €6,534/QALY gained. A test with sensitivity=60% and specificity=100% increases both health (0.14 QALYs) and costs (€2,888), resulting in an ICER of €20,338/QALY gained. Similarly, a test with sensitivity=100% and specificity=60% increases both health (0.29 QALYs) and costs (€5,784), resulting in an ICER of €19,946/QALY gained. **CONCLUSIONS:** An imaging test that improves risk prediction and therefore treatment decisions for patients with a recent TIA or minor ischemic stroke has the potential to optimize cost-effectiveness by reducing the risk of recurrent stroke. However, reduced sensitivity or specificity of the test reduces its cost-effectiveness versus the Dutch guidelines. Developers must consider if the minimum level of accuracy required to be cost-effective is close to the maximum capability of the test. Model-based analyses are valuable in facilitating decisions about investments in the further development of a test.

PCV85

PERSONALIZED TREATMENT IN HEART FAILURE DISEASE MANAGEMENT IMPROVES OUTCOMES AND REDUCES COSTS

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OBJECTIVES: At the population level, disease management programs (DMPs) for heart failure (HF) have proven to be effective in increasing quality-adjusted survival and reducing the rate of hospital readmission. However, a systematic assessment as to whether these outcomes could still be improved upon by tailoring the content and structure of such DMPs to the risk profile of the individual patient has not yet been conducted. Using data from a previously conducted randomized controlled trial, the purpose of this study was to explore the clinical and health economic consequences of assigning different DMPs to different risk categories of HF patient. **METHODS:** The analysis was conducted alongside the COACH study, in which 1023 patients were randomly assigned to one of three DMPs: care-as-usual (routine follow-up by a cardiologist), basic additional support by a nurse specialized in HF management (HF-nurse), and intensive additional support by an HF-nurse. The Subpopulation Treatment Effect Pattern Plot (STEPP) methodology was applied to graphically establish suitable cut-offs for stratifying patients into different risk categories based on their predicted 18-month mortality risk. Separate cost-effectiveness analyses were subsequently performed within each of these strata to determine per risk category the DMP that would be optimal in terms of survival time and costs. **RESULTS:** Based on the STEPP analysis, a cut-off of 0.17 was selected to classify 346 (33.8%) patients as low risk and 677 (66.2%) patients as high risk. At a threshold value of €10,000 per life-year, this resulted in an 82.9% probability that intensive support would be optimal for low-risk patients and an 83.6% probability that basic support would be optimal for high-risk patients. **CONCLUSIONS:** Assigning different DMPs to different risk groups of patient improved outcomes and reduced costs. Tailoring the content and structure of such programs to the risk profile of the individual patient seems therefore desired.

PCV86

THE COST-EFFECTIVENESS OF DABIGATRAN AND THE OPPORTUNITY COST OF DELAYED SUBSIDISED ACCESS IN AUSTRALIA

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OBJECTIVES: Dabigatran was recommended by the Pharmaceutical Benefits Advisory Committee (PBAC) in March 2011 for the treatment of non-valvular atrial fibrillation (NVAF) but was not listed on the Pharmaceutical Benefits Scheme (PBS) for over two years. This analysis examines the cost-effectiveness of dabigatran and the opportunity cost of delayed reimbursement from a societal perspective. **METHODS:** This analysis estimated the costs for dabigatran compared with warfarin and a mixed comparator (warfarin/aspirin/untreated) reflective of current

practice. A societal perspective incorporated the following indirect costs: formal and informal long term care costs for stroke, productivity losses associated with stroke and carers, and productivity, out of pocket and travel costs associated with INR testing in both metropolitan and rural settings. The opportunity cost of a delayed dabigatran PBS listing was estimated over a 2 year period. Estimates were derived using the economic model presented to the PBAC. **RESULTS:** When incorporating a societal perspective, dabigatran was cost saving versus both warfarin and the mixed comparator. Dabigatran is estimated to save an average of $2,011 and $3,994 per patient per year for patients in metropolitan and rural settings respectively compared with current practice. In the more than two years since the initial PBAC recommendation of dabigatran it is estimated over 150,000 patients have been denied affordable access to treatment, resulting in $47.9 million in costs to Medicare, $5.2 million in patient out of pocket costs and 470,000 hours of lost productivity due to avoidable INR testing. Importantly, 4,059 strokes and 902 resultant deaths could have been avoided in this time compared to current practice. **CONCLUSIONS:** Dabigatran is a cost-effective treatment for stroke prevention in patients with NVAF in Australia and is cost saving compared to current therapy (warfarin, aspirin and no treatment) when a societal perspective is taken.

PCV87

COMPREHENSIVE OVERVIEW: EFFICACY, TOLERABILITY AND COST-EFFECTIVENESS OF IRBESARTAN

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OBJECTIVES: Hypertension represents a major health problem, affecting more than 1 billion adults worldwide. Irbesartan, an angiotensin II receptor blocker, is considered to be a highly effective treatment in the management of hypertension. Therefore this study aims to evaluate the efficacy, safety and tolerability profile, as well as the cost-effectiveness of irbesartan in the treatment of hypertension. **METHODS:** A review of the literature was conducted using the electronic databases Medline, Cochrane and HEED of search terms relating to irbesartan efficacy, tolerability and cost-effectiveness and the results were synthesized. **RESULTS:** Findings from the present analysis show that irbesartan either as monotherapy or in combination with other agents can have significant reductions in Blood Pressure, both systolic and diastolic, when compared to other alternative treatment options. Irbesartan was also found to have a renoprotective effect, independent of its blood pressure lowering effect in patients with type 2 diabetes and nephropathy. Irbesartan also delayed onset of end-stage renal disease (ESRD) and reduced the cumulative incidence of ESRD. Furthermore, Irbesartan demonstrated an excellent safety and tolerability profile. Overall adverse event incidence with irbesartan was comparable with other antihypertensive drugs. Most common adverse events were headache, fatigue and dizziness. In terms of economic analyses, compared to other antihypertensive therapy alternatives, irbesartan increased life expectancy and lead to substantial cost savings. **CONCLUSIONS:** Evidence indicates that treating patients with hypertension alone or with type II diabetes and nephropathy, can control hypertension, prolong life and reduce costs, in relation to other existing alternatives.

PCV88

INDIVIDUALLY TAILORED ELASTIC COMPRESSION THERAPY FOR THE PREVENTION OF POST THROMBOTIC SYNDROME

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Post thrombotic syndrome (PTS) is a chronic condition that develops in up to 50% of patients after deep vein thrombosis and is characterized by debilitating complaints of the leg. Two randomized controlled trials (RCT) showed that elastic compression stocking (ECS) therapy for 2 years after DVT reduces the PTS incidence by approximately 50%. A recent management study showed that tailored duration of ECS therapy on individual patient characteristics may result in a reduction of ECS therapy of 18 months for 50% of patients with an even lower incidence of PTS. However, these results may be biased. **OBJECTIVES:** To explore the cost-effectiveness of individually tailored ECS therapy (IND) compared with a standard duration of 2 years ECS therapy (STANDARD), from a health care perspective in order to inform the design of an RCT comparing the two treatment options. **METHODS:** A decision-analytic probabilistic Markov model with lifelong time horizon was used. Health states in the model are: No PTS with stocking, No PTS without stocking, Mild to moderate PTS, Severe PTS, and Death. Transition probabilities, costs, and utilities were obtained from literature. The incidence of PTS was taken from the trials (STANDARD: 2-year incidence 24.5%) and the management study (IND: 2-year incidence 21.1%). The delta for non-inferiority of a future RCT was determined, and uncertainty was assessed in value of information analyses. **RESULTS:** Based on current evidence IND saves €2,292 and gains 0.14 quality adjusted life years (QALY) per patient compared to STANDARD. This result is however highly uncertain, and future research is valuable. The savings of IND amount to €306 when assuming equal incidence of PTS. If PTS incidence is 7% higher in IND, the treatment seizes to be cost-effective. **CONCLUSIONS:** Based on current limited evidence, IND may dominate STANDARD. Future research is worthwhile, and may be informed by this modeling study.

PCV89

THE COST-EFFECTIVENESS OF SCREENING FOR SILENT ATRIAL FIBRILLATION AFTER ISCHAEMIC STROKE

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OBJECTIVES: Prolonged brief intermittent arrhythmia screening has been suggested to substantially improve detection of silent paroxysmal atrial fibrillation (AF) in patients with a recent ischemic stroke/TIA. The purpose of this study was to estimate the cost-effectiveness of two screening methods for detection of silent AF, brief intermittent long-term ECG recordings at regular time intervals and short-term 24-hours continuous ECG (Holter-ECG) and to compare them to a no screening alternative in patients with a recent ischemic stroke. **METHODS:** The long-term (20 year) costs and effects of brief intermittent long-term ECG recordings at regular time intervals and short term continuous ECG are estimated with a decision analytic model combining the result of a clinical study and epidemiological data. The structure of a cost-effectiveness analysis was used in this study. The short term decision tree model analyzed the screening procedure until the onset of anticoagulant treatment. The second part of the decision model follows a Markov design simulating the patients for 20 years. **RESULTS:** Continuous 24 h ECG recording was dominated by intermittent ECG due to lower sensitivity and higher costs. The base case analysis compared intermittent-ECG screening with no screening of patients with recent stroke. The implementation of the screening program on 1000 patients resulted in 10,9 avoided strokes and the gain of 29,2 life years or 22,7 QALYs and cost savings of €55 000. **CONCLUSIONS:** Screening of silent AF by intermittent ECG recordings in patients with a recent ischaemic stroke is cost-effective use of health care resources saving costs, lives and quality of life.

PCV90

ISSUES WITH COST-EFFECTIVENESS MODELLING OF DIAGNOSTIC TESTS – CASE STUDY OF ISCHAEMIC CARDIOMYOPATHY

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OBJECTIVES: To estimate the cost-effectiveness of diagnostic pathways for assessing patients with ischaemic cardiomyopathy to identify patients with viable myocardium with a view to revascularisation. **METHODS:** A decision analytic model was developed to estimate the cost-effectiveness of diagnostic strategies for assessing patients with ischaemic cardiomyopathy. The different diagnostic pathways were applied to a hypothetical cohort of patients with ischaemic cardiomyopathy and the probability of successful identification of viable myocardium and non-viable myocardium was determined by the accuracy of the diagnostic pathway. It was assumed that patients diagnosed with viable myocardium would be managed promptly by revascularisation and that the patients diagnosed with non-viable myocardium would be on medical therapy. The model assigned each patient a risk of death and rehospitalisation depending upon whether they are truly viable and whether they had revascularisation or not. Each patient then accrued lifetime QALYs. Health care costs were also accrued through measuring diagnostic costs and treatment costs, depending on the pathway and their treatment status. **RESULTS:** All the diagnostic pathways are cost-effective when compared with no testing at current NICE threshold, this suggests that all the current services for diagnosing viable myocardium are a cost effective use of NHS resources irrespective of the diagnostic pathway used. For services that need to decide the most cost-effective strategy starting from scratch, then Stress CMR is the most cost-effective strategy. **CONCLUSIONS:** There are a number of issues with abstracting the data for cost-effectiveness modelling of diagnostic tests. For example, the diagnostic accuracy depends upon the type of index test, gold standard test and threshold used. Furthermore, the benefits of treatments after diagnosis are not always clear and might be linked to the type of diagnostic test. Appropriate caution needs to be taken when evaluating diagnostic tests.

PCV91

ECONOMIC EVALUATION OF IVABRADINE FOR CHRONIC HEART FAILURE NYHA II TO IV CLASS WITH SYSTOLIC DYSFUNCTION IN IRELAND

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OBJECTIVES: Ivabradine is approved by the European Medicine Agency for the treatment of Chronic Heart Failure (CHF) NYHA II to IV class with systolic dysfunction in patients in sinus rhythm and whose heart rate is $\geq$ 75 bpm, in combination with standard therapy including beta-blocker therapy or when beta-blocker therapy is contraindicated or not tolerated. The study objective was to perform a cost-effectiveness analysis of ivabradine based on the outcomes of the SHIFT clinical trial from the perspective of the Irish Health Service Executive (HSE). **METHODS:** A six health state Markov model with health states for CHF NYHA classes I to IV, alive, and dead was adapted to the Irish health care setting. The economic evaluation compared the cost-effectiveness of ivabradine in combination with standard therapy versus standard therapy alone. A lifetime horizon was chosen in the base case analysis. Costs and effects were discounted at 4% per year. Deterministic and probabilistic sensitivity analyses were performed. Health state utilities were estimated from EQ-5D index scores obtained from the SHIFT clinical trial. The base case analysis was based on heart failure outcomes and associated costs. **RESULTS:** When used in addition to standard therapy, ivabradine increased discounted health care costs by €2169 for a 0.23 QALY gain, resulting in an incremental cost per QALY gained of €9,426. In no case of the deterministic sensitivity analysis did the cost per QALY gained increase above €20,000. The probability of the cost-effectiveness of ivabradine at a willingness to pay threshold of €45,000 per QALY gained was estimated to be approx. 100%. **CONCLUSIONS:** When used in addition to standard therapy, based on heart failure outcomes and associated costs, ivabradine had an incremental cost per QALY gained of €9,426 with an approximately 100% probability of being cost-effective at a willingness to pay threshold of €45,000 per QALY gained.

PCV92

THE COST-UTILITY OF CATHETER-BASED RENAL DENERVATION AS COMPARED TO CURRENT STANDARD OF CARE FOR RESISTANT HYPERTENSION IN BELGIUM

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OBJECTIVES: Hypertension affects 41% of male and 31% of female adults in Belgium; 13% of these are believed to be refractory to standard hypertension treatment (uncon-

trolled with ≥ 3 different classes of antihypertensive therapy). Catheter-based renal denervation (RDN) is a novel, minimally invasive therapy for treatment-resistant hypertension. The aim of this study was to assess the cost-utility of RDN as compared to current standard of care (SoC) for refractory hypertension in Belgium. **METHODS:** A lifetime state-transition, Markov model was used, with health-states encompassing possible long-term consequences of hypertension: stroke, myocardial infarction, angina, heart failure, end-stage renal disease. Risk equations were used to calculate the risk of events with changing systolic blood pressure (SBP). Reductions in SBP following RDN vs. SoC pertain to the results of the Symplicity HTN-2 randomized controlled trial. The underlying modeled cohort was defined similar to the same trial: mean baseline SBP 178 mmHg, mean age 58 years, 34% with diabetes mellitus. Costs pertained to published economic evaluations or public tariffs and reflected the Belgian payer perspective. Costs and health outcomes were discounted at a rate of 3%, and 1.5% respectively. **RESULTS:** Projected lifetime costs were 21,743€ and 24,558€ in the SoC and RDN arms respectively, while total projected life years were 16.43 and 17.23. RDN increased patients' quality of life with 0.93 quality-adjusted life years (QALYs) vs. SoC. This resulted in an incremental cost-utility ratio (ICUR) of 3,020€/QALY. Results were most sensitive to changes in SBP reductions, and the cost of RDN procedure, but remained under a willingness to pay (WTP) threshold of 20,000€/QALY. Probabilistic sensitivity analyses showed acceptable cost-effectiveness in 100% of cases, under a WTP threshold of 20,000€/QALY. **CONCLUSIONS:** Results of these analyses suggest that, under the current model settings, catheter-based RDN procedure could be a cost-effective strategy for resistant hypertension in Belgium.

PCV93

COST-EFFECTIVENESS ANALYSIS OF ATORVASTATIN COMPARED TO SIMVASTATIN IN THE PREVENTION OF CARDIOVASCULAR DISEASES IN THE CZECH REPUBLIC

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OBJECTIVES: To assess the impact of atorvastatin compared to simvastatin use in the Czech Republic on cardiovascular diseases (CVD), Life-Years Gained (LYG) and Quality-Adjusted Life Years (QALY), based on the real proportional consumption of both statins in particular strengths (10 mg, 20 mg, 40 mg). **METHODS:** Life-time cost-effectiveness Markov cohort model was developed with 1 year cycle length and 5 health sates, i.e. Alive without CVD, Alive with experience of CVD, Non-fatal CVD, Fatal CVD and Death. The probability of transition among health states were derived from Framingham equations or from SCORE equations (probability of the first non/fatal CVD), Czech life-tables (background mortality) and international cohort studies (probability of subsequent CVD). Patients enter the model with base-line risk characteristics: age, proportions of males, diabetics, smokers, level of systolic blood pressure and cholesterol (total and HDL) level. The efficacy data for particular statin and its strength were derived from latest meta-analyses. Drug acquisition costs of atorvastatin 10 mg and 20 mg were 10% higher compared to simvastatin 20 mg and 40 mg. The costs of fatal, non-fatal CVD and one-year follow-up after CVD were 1,410 EUR, 1,460 EUR and 580 EUR. Probabilistic sensitivity analysis (PSA) using a willingness to pay (WTP) threshold equal to 1 times GDP per capita (14,300 EUR) was applied. **RESULTS:** Over a life-time horizon, atorvastatin compared to simvastatin provides 8.14 QALYs vs. 8.07 QALYs, 11.33 LYG vs. 11,24 LYG, 44.8% vs. 46.3% of non-fatal CVD and 28.2% vs. 29.4% of fatal CVD. The increment of total costs was 330 EUR for atorvastatin, ICER for atorvastatin vs. simvastatin was then 4,720 EUR/ QALY. **CONCLUSIONS:** The use of atorvastatin generates 0.07 QALYs more compared to simvastatin per patient in the Czech Republic. There is a 98.5% probability of atorvastatin being cost-effective at the selected WTP.

PCV94

NOVEL ORAL ANTICOAGULANTS VERSUS WARFARIN – A BUSINESS CASE ANALYSIS

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OBJECTIVES: The decision on whether to use more expensive novel oral anticoagulants (NOACs) or invest resources for quality improvement of warfarin therapy requires inputs of both clinical and economic outcome analyses. Outcomes of NOACs comparing to warfarin therapy at various levels of patient-time in therapeutic range (TTR) in patients with atrial fibrillation were examined from health care provider's perspective. **METHODS:** A Markov model was designed to compare life-long economic and treatment outcomes of warfarin and NOACs in a hypothetical cohort of 65-year-old atrial fibrillation patients with $CHADS_2$score 2 or above. Model inputs were derived from clinical trials published in literature. Outcome measure was incremental cost per quality-adjusted life-year (QALY) gained (ICER). **RESULTS:** Expected cost and QALYs of NOACs were USD96,602 and 9.957, correspondingly, in base-case analysis. Using USD50,000 as the threshold of willingness-to-pay per QALY, NOACs therapy was cost-effective when TTR of warfarin therapy was 60%, or monthly cost of warfarin management increased by 1.5-fold or above to achieve 70% TTR. Warfarin therapy was cost-effective when TTR of warfarin was 70% with no increment in monthly cost of care, or when TTR reached 75% with monthly cost of warfarin care increased up to 2.5-fold. At TTR 60%, 70% and 75%, NOACs was cost-effective when monthly drug cost was <USD208, <USD135-200 and <USD96-160, respectively. 10,000 Monte Carlo simulations showed NOACs to be cost-effective in 77.2%, 52.7% and 31.7% of time at TTR of 60%, 70% and 75%, respectively. **CONCLUSIONS:** Acceptance of NOACs as cost-effective was highly depended upon drug cost, anticoagulation control for warfarin, and anticoagulation service cost.

PCV95

SCREEN OR NOT TO SCREEN FOR PERIPHERAL ARTERIAL DISEASE: GUIDANCE FROM A DECISION MODEL

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OBJECTIVES: Asymptomatic Peripheral Arterial Disease (PAD) is associated with greater risk of acute cardiovascular events. American heart association and American college of cardiology clinical practice guidelines recommend low dose aspirin to reduce the cardiovascular events and mortality in PAD patients. As asymptomatic PAD often remains undiagnosed, opportunities for secondary prevention are missed in primary care. Therefore, there is a clinical need of early detection of asymptomatic PAD and to initiate the appropriate preventive treatment. United States preventive services task force's recommendation against screening is heavily criticized and expansion of the evidence base for PAD screening is recommended in 2011 in a focussed update of the guidelines. This study aims to determine the value of PAD screening using ankle brachial index test in high risk individuals using decision analytic modelling. **METHODS:** A Markov model was developed to evaluate the cost effectiveness of selective PAD screening in high risk individuals followed by preventive treatment compared to no screening and no preventive treatment. The analysis was conducted from the societal perspective using a lifetime time horizon. To address the parameter uncertainty, probabilistic sensitivity analysis was performed. **RESULTS:** Screening and preventive treatment of identified PAD patients with low dose aspirin is a dominant strategy producing higher mean quality adjusted life years per patient for a lower lifetime cost. The cost effectiveness acceptability curves show that 100% simulations favour screening followed by preventive treatment at a willingness to pay threshold of 400 Euros. **CONCLUSIONS:** This decision analysis suggests that the targeted screening and secondary prevention of cardiovascular events in the identified patients, is a highly cost effective public health intervention. This study results may provide one of the building blocks of evidence expansion for advocating PAD screening and to promote its more widespread use to detect and treat PAD patients.

PCV96

COST-EFFECTIVENESS OF INCREASING STATIN ADHERENCE FOR PRIMARY AND SECONDARY PREVENTION IN COMMUNITY PHARMACIES

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OBJECTIVES: Therapy persistence is important to achieve optimal clinical benefits of statin therapy. The aim of this study was to determine the cost-effectiveness of pharmaceutical care in community pharmacies, aimed to increase persistence with statin therapy for both primary and secondary prevention of cardiovascular events (CVEs). **METHODS:** The effectiveness of the Dutch pharmaceutical care program MeMO on improving statin therapy persistence was measured in 500 patients and compared to 502 control patients. Time-investments of the program were also collected. Markov models with lifelong time-horizons were developed to estimate the influence of the program on CVEs: stroke, myocardial infarction (MI), revascularization and mortality. The efficacy of statins, taken from large clinical trials in primary and secondary prevention, were adjusted for therapy persistence. A Dutch health care provider's perspective was adopted for the analysis and probabilistic sensitivity analyses were performed. **RESULTS:** Patients in the MeMO program had a lower risk for non-persistence, RR = 0.50 (0.40-0.63), the effect was similar in primary and secondary prevention. In a cohort of 1,000 patients, 60% of whom had a history of CVE, the MeMO program resulted in a reduction of 8 non-fatal strokes, 2 fatal strokes, 16 non-fatal MIs, 7 fatal MIs and 14 revascularizations. Additional medication, disease management and intervention costs in the MeMO program were €375,000; the cost-savings due to reduced CVEs were €450,000. Thus, the MeMO program resulted in 83 quality-adjusted life-years (QALYs) gained and cost-savings of €75,000. Clinical benefits and cost-savings were highest in the secondary prevention population. **CONCLUSIONS:** Pharmaceutical care in community pharmacies can improve statin therapy persistence, resulting in more optimal prevention of CVEs. The MeMO program resulted in considerable clinical benefits and overall cost-savings. Persistence and adherence improving programs in community pharmacies may provide good value for money and health care insurers should consider reimbursing these activities in The Netherlands.

PCV97

COST-EFFECTIVENESS ANALYSIS OF IVABRADINE IN CHRONIC HEART FAILURE IN THE POLISH SETTING

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OBJECTIVES: To estimate cost-effectiveness of ivabradine used in treatment of chronic heart failure in Poland, using model based on individual patient data from pivotal SHIFT trial adapted using contemporary real-life epidemiology, treatment pattern and cost country-specific data. **METHODS:** Economic model based on SHIFT trial was originally developed for the UK setting and published. Based on the model, in November 2012 NICE gave its positive guidance for the analysed technology in line with EMA registered indication, acknowledging a range of conservative assumptions. Current study utilizes the NICE model populated with most recently published local data. General mortality was estimated from Polish life tables for the year 2010. Unit cost and expected rate of hospitalizations on standard treatment was based on publication in Polish Heart Journal. Standard treatment cost was based on official listing of reimbursed drugs. Average cost of ivabradine (5mg and 7.5mg, 56 tabs) was based on popular drug database (Kamsoft, April 2013). Exchange rate of National Bank of Poland 1 EUR=4.1759 PLN was applied (May 2013). **RESULTS:** At current pharmacy price (55.60 EUR / 56 tabs), incremental cost-utility ratio for ivabradine on top of standard treatment vs standard treatment alone is estimated at 10 230 EUR / QALY, well below the official cost-effectiveness threshold defined at 3*DGP *per capita* (25 336 EUR). Sensitivity analysis revealed that in order to exceed the cost-effectiveness threshold, price would have to be increased to 113.60 EUR (+104%). **CONCLUSIONS:** Conservative analysis shows that ivabradine used on top of standard treatment (ACE inhibitor, beta-blocker, MR antagonist, ±diuretics) in

patients suffering from chronic heart failure is a highly cost-effective health technology in the Polish setting, according to the criterion defined in Reimbursement Law. Robustness of this finding is demonstrated by the fact that cost-effectiveness is retained even at a price double vs base-case.

PCV98

STATIN COST-EFFECTIVENESS IN PATIENTS WITH PREVIOUS CORONARY HEART DISEASE: A SYSTEMATIC REVIEW OF THE COST-EFFECTIVENESS ANALYSIS DERIVED FROM SINGLE RANDOMISED CLINICAL TRIALS

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OBJECTIVES: Large randomized clinical trials (RCT) evidenced the benefits of statins in reducing major cardiovascular events in patients with established coronary heart disease (CHD). These multinational trials are likely to provide internally valid evidence. Cost-effectiveness analysis based on single trials costs and effects are common and represent the potential net benefit of an intervention in a well-controlled environment. The aim of this study is to systematically review the cost-effectiveness studies based on statins single trials in patients with previous CHD. **METHODS:** We searched to identify all literature relating to the cost-effectiveness of statins in the secondary prevention in patients with established CHD. Only studies with the effectiveness data extracted from a single RCT and clinical outcomes such as quality assessment, mortality or cardiovascular events rate were included. The cost per QALY was classified according to the WHO, following three categories of cost-effectiveness, Highly cost-effective, Cost-effective and Not cost-effective, adjusted with GDP per capita based on purchasing power parity (constant 2005 international USD). **RESULTS:** Twenty-one studies were included in the final analysis, covering a period range from 1996 to 2009. 7 large RCTs represented the origin of efficacy data. Most of studies assumed a full compliance, the Markov models were used in 11 out 21 studies. Time horizon ranged from 5 years to time life, with 10 years being the predominant choice. 9 studies performed a cost-utility analysis and showed the average cost per QALY, 8 of them classified as highly cost-effective and 1 cost-effective. Cost per QALY was sensitive for drug price, time horizon and event rates, 6 of this models models worked with composite endpoints. **CONCLUSIONS:** Statins are highly cost-effective in patients with CHD when effect size came from single well designed RCTs. Models heterogeneity and composite endpoints can decrease the robustness of the results.

PCV99

THE COST-EFFECTIVENESS OF CATHETER ABLATION AS FIRST-LINE TREATMENT

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OBJECTIVES: It has been suggested that radiofrequency catheter ablation could take priority over antiarrhythmic drugs as first-line treatment of paroxysmal AF, due to better efficiency, and fewer serious side effects. The objective of this study was to evaluate the cost-effectiveness of treating paroxysmal atrial fibrillation with radiofrequency catheter ablation as first-line treatment. **METHODS:** A decision-analytic Markov model was developed to study long-term effects and costs of catheter ablation compared to antiarrhythmic drugs as first-line treatment. **RESULTS:** Small, positive clinical effects were found in the overall population, a gain of an average 0.06 quality-adjusted life years (QALYs) to an incremental cost of €3033, resulting in an incremental cost-effectiveness ratio of €50 570/QALY. However, the incremental cost-effectiveness ratio of a 45-year-old patient was approximately €3434/QALY, while a 65-year-old costs €108 937 per QALY. **CONCLUSIONS:** Radio-frequency catheter ablation as first-line treatment is a cost-effective strategy for younger patients with paroxysmal atrial fibrillation. However, the cost-effectiveness of using catheter ablation as first-line therapy in older patients is uncertain, and in most of these cases antiarrhythmic drug therapy should be attempted before catheter ablation.

PCV100

ACTIVE-IMPLANTABLE CARDIAC DEVICES: IS THERE ROOM FOR COST SAVINGS IN PORTUGUESE HOSPITALS?

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OBJECTIVES: Portugal is facing an economic crisis that demands a tight control over all hospitals' expenditures, namely with medical devices, whose market price is not yet regulated or documented. This study aims to describe the number and value of the Active-Implantable Cardiac Devices (AICD) bought by Portuguese hospitals in 2011, as well as to quantify potential savings that can be obtained shifting utilisation from higher to lower prices. **METHODS:** In February 2012, 42 hospitals were asked by INFARMED – National Authority of Medicines and Health Products, IP, about the number, type and value of the AICD acquired, using an ad-hoc developed software. Potential savings analysis was performed at two levels: AICD sub-groups (according to Portuguese Medical Device Nomenclature) and individual device reference. Within each level, three cost-minimization scenarios were conceptualized based on the minimum price reported (scenario 1), the average between the average price and the minimum one (scenario 2) and the average price (scenario 3). **RESULTS:** During 2011, 73.8% of the hospitals enrolled (n=31) bought AICD, comprising 16,815 devices, at a cost of 40,217,411 euros. In numbers, the most common AICD were pacemakers (44.8%), whereas cardioverter-defibrillators were related to a higher expenditure ratio (51.5% of total cost). Based on the AICD sub-groups analysis, the potential savings were 14.5 million euros in scenario 1 (44.1% of total cost), 7.4 million euros in scenario 2 (22.5%) and 1.8 million euros in scenario 3 (5.3%). Following this scenario order, the device reference approach estimated savings of 6.2 million euros (18.8%), 3.4 million euros (10.3%) and 1.1 million euros (3.3%), respectively. **CONCLUSIONS:** Significant potential savings were found, being greater when analysing AICD subgroups, assuming equal efficiency and safety for all devices within these clusters. Despite scenario 1 higher savings, scenario 2 seems the most realistic and feasible, when trying to accomplish a sustainable health care system.

PCV101

COST ANALYSIS OF ALPROSTADIL (PROSTAVASIN®) AS TREATMENT FOR PATIENTS WITH PERIPHERAL ARTERIAL DISEASE STAGES III AND IV COMPARED WITH LUMBAR SYMPATHECTOMY IN MEXICO

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OBJECTIVES: Peripheral arterial disease is associated with significant adverse outcomes, especially in patients with critical limb ischemia (CLI; stages III and IV). At 6 months, the risk of amputation is 35%, and mortality 20%. In patients unsuitable for interventional therapy, treatment with prostanoids may help reduce the risk of adverse outcomes. We aimed to assess the average cost of alprostadil (prostaglandin E_1) as treatment for patients with CLI compared with lumbar sympathectomy from the perspective of The Mexican Social Security Institute (IMSS). **METHODS:** In a clinical trial, alprostadil and lumbar sympathectomy showed similar response rates (Petronella P, et al. Nutr Metab Cardiovasc Dis 2004;14:186–92).Therefore, we conducted a cost minimization analysis based on the direct medical costs of alprostadil (40 µg twice-daily or 60 µg once-daily) administered over 28 days versus lumbar sympathectomy. Relevant costs included acquisition and infusion for alprostadil, and surgical procedure besides hospitalization (9 days) for lumbar sympathectomy. Unit cost for infusion was assumed to be equivalent to an emergency visit at first level of care at IMSS; unit cost of the surgical procedure and standard hospital stay (per day) correspond to the official values for these items at the second level of care at IMSS. UCB Pharma provided the cost for alprostadil. All costs are in 2013 Mexican pesos (MXN; 12.88 MXN = 1 USD, 17.23 MXN = 1 Euro). **RESULTS:** Costs per patient would be lower with both alprostadil 40 µg twice-daily ($59,640) and alprostadil 60 µg once-daily ($37,884) than with lumbar sympathectomy ($66,084), leading to savings of $6,444 (9.8%) and $28,200 (42.7%), respectively. Alprostadil use remained cost-saving versus lumbar sympathectomy in most of the scenarios evaluated through sensitivity analysis. **CONCLUSIONS:** These results suggest alprostadil is a cost saving intervention when compared with lumbar sympathectomy for patients with CLI from the Mexican public health care perspective.

PCV102

THE COST-EFFECTIVENESS OF APIXABAN COMPARED TO WARFARIN, ASPIRIN, RIVAROXABAN AND DABIGATRAN IN IRELAND

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OBJECTIVES: The objective of this pharmacoeconomic evaluation was to determine whether apixaban, compared to warfarin, dabigatran and rivaroxaban in patients suitable for vitamin K antagonists (VKA), or to aspirin in VKA-unsuitable patients, is a cost-effective treatment for the prevention of stroke or systemic embolism (SE) in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors. **METHODS:** A Markov model was constructed consisting of 18 health states, using a 6-week cycle length and a lifetime time horizon. Baseline characteristics were taken from a 2011 GPRD study. Clinical inputs were derived from a network meta-analysis of the efficacy and bleeding outcomes from the three warfarin-controlled trials ARISTOTLE, RE-LY and ROCKET-AF, and the single aspirin-controlled trial AVERROES. Local unit costs and utility data were assigned to the appropriate model health states to calculate total Quality-Adjusted Life Years (QALYs) and costs. Univariate and probabilistic sensitivity analyses (PSA) were conducted. **RESULTS:** Apixaban was associated with an ICER vs warfarin of €11,087. Against the less-commonly used anti-coagulants, apixaban was cost-effective against each at the €45,000 willingness-to-pay threshold. Apixaban provided more QALYs than all other therapies. Compared to warfarin, apixaban produced savings in avoided cost of stroke, intracranial haemorrhage, INR monitoring, and bleeding. Apixaban was cost-effective across all patient subgroups of INR control (centre Time in Therapeutic Range) and $CHADS_2$ stroke risk categories 1 and 2. One-way sensitivity analyses, scenario analyses, and probabilistic sensitivity analyses confirmed that the findings were robust to changes in key parameters. The probability that apixaban was the most cost-effective therapy at a willingness-to-pay threshold of €45,000 per QALY was 93% and 100% in the VKA-suitable and VKA-unsuitable populations, respectively. **CONCLUSIONS:** Apixaban can be considered cost-effective for the prevention of stroke and SE in people with non-valvular AF, at a threshold of €45,000/QALY, under standard decision rules.

PCV103

ECONOMIC EVALUATION OF APIXABAN FOR THE PREVENTION OF STROKE IN ATRIAL FIBRILLATION IN THE NETHERLANDS

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OBJECTIVES: Stroke prevention is the main goal in treating patients with atrial fibrillation (AF). Treatment with anticoagulants, such as vitamin-K antagonists (VKAs; e.g. warfarin and cumarines), was demonstrated to be an effective strategy. However, even though VKAs are the current standard therapy recommended by different guidelines, the significant risk of bleeding and the requirement for a regular monitoring are limiting its use. Apixaban is a novel oral anticoagulant (NOAC) associated with significantly lower hazard rates for stroke/systemic embolism, major hemorrhage and discontinuations, compared to VKAs. This study evaluated the cost-effectiveness (CE) of apixaban compared to VKAs in the base-case analysis and alternatively to other NOACs for stroke prevention in non-valvular AF patients in The Netherlands. **METHODS:** A global Markov model developed by United BioSource Corporation was modified to reflect the use of oral anticoagulants in The Netherlands. The model used efficacy data from a published indirect treatment comparison of NOACs and cost data from Dutch costing studies as inputs. Following health states were included in the model: non-valvular AF, primary and recurrent ischemic and hemorrhagic stroke, systemic embolism, myocardial infarction, intracranial hemorrhage, other major and non-major bleedings, treatment

discontinuations and death. Main outcomes were quality adjusted life years (QALY) and costs. Univariate and probabilistic sensitivity analyses (PSA) were conducted on the incremental cost-effectiveness ratio (ICER). **RESULTS:** In the base-case analysis, apixaban treatment compared to VKAs has an ICER well below an informal minimal willingness-to-pay threshold of €20,000/QALY for The Netherlands (i.e. around € 7,000/QALY). PSA showed that the results of the base-case analysis were quite robust. Potentials exist for apixaban to be dominant over the other NOACs, rivaroxaban and dabigatran depending on hazard ratios, risks for complications and local price levels. patients in The Netherlands. **CONCLUSIONS:** In patients with AF, we found apixaban to be a cost-effective option in The Netherlands, compared to VKAs.

PCV104

A SOCIETAL PERSPECTIVE COST-UTILITY ANALYSIS OF RIVAROXABAN COMPARED WITH ENOXAPARIN SODIUM IN PATIENTS UNDERGOING TOTAL HIP OR TOTAL KNEE REPLACEMENT SURGERY

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OBJECTIVES: Several cost-effectiveness analyses exist that compare rivaroxaban with enoxaparin sodium as thrombosis prophylaxis in patients undergoing total hip replacement (THR) or total knee replacement (TKR) surgery. However, none of these refers to a societal perspective, and thus indirect costs have so far not yet been included. The objective of this research was to conduct a cost-utility analysis from the German societal perspective, based on a life-time horizon. **METHODS:** A decision-tree was used to calculate the short term consequences of treatmentby classifying whether subjects experienced a deep a vein thrombosis, a pulmonary embolism, a major bleeding, death due to the surgery, or no event. Furthermore, we designed a Markov model to quantify the long-term consequences. The main health effect was based on the RECORD 1 and RECORD 3 trials. A semi-micro simulation approach was applied to reflect the age and gender distribution of the target population. Probabilistic, deterministic and structural sensitivity analyses were performed to assess the robustness of the results. **RESULTS:** Rivaroxaban dominated enoxaparin sodium in the case of TKR. This dominance was robust within sensitivity analysis. In contrast, the point estimate of the cost-effectiveness ratio in the case of THR was €867,018 per quality-adjusted life year (QALY). However, there was a wide variation within the probabilistic sensitivity analysis: the dots were substantially scattered over three quadrants of the cost-effectiveness plane. Compared to previous analyses, the selection of effectiveness data seems to have a significant impact of the results. **CONCLUSIONS:** Rivaroxaban was found to dominate enoxaparin sodium after TKR, whereas the evidence regarding THR is unclear. Results were similar to previous analyses from the third-party payer perspective.

PCV105

TELEMONITORING AFTER DISCHARGE FROM HOSPITAL WITH HEART FAILURE – COST-EFFECTIVENESS MODELLING OF ALTERNATIVE SERVICE DESIGNS

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OBJECTIVES: To estimate the cost-effectiveness of home telemonitoring (TM) or structured telephone support (STS) strategies versus usual care for adults recently discharged (within 28 days) after a heart failure (HF) exacerbation in England and Wales. **METHODS:** A Markov model was used to evaluate a) STS via human to machine (HM) interface, b) STS via human to human (HH) contact, and c) TM, against d) usual care. Given heterogeneity in the interventions, cost-effectiveness analysis was performed using bottom up costing scenarios regarding costs of devices, monitoring and medical care to deal with alerts. Costs and quality adjusted life years (QALYs) over a 30 year (patient lifetime) horizon were estimated based on monthly probabilities of death and monthly risks of hospitalisations (HF-related complications or other causes) estimated from clinical effectiveness parameters computed using a network meta-analysis of randomised controlled trials. **RESULTS:** Base case monthly costs per patient were: £27 for usual care, £119 for STS HM, £179 for STS HH and £175 for TM. TM was the most cost-effective strategy in the scenario using these base case costs. Compared with usual care, TM had an estimated incremental cost effectiveness ratio (ICER) of £9,552/QALY, whereas STS HH had an ICER of £63,240/QALY against TM. STS HM was dominated by usual care. Probabilistic sensitivity analysis (PSA) showed 44% chance of TM being cost-effective at a willingness to pay threshold of £20,000 per QALY, with STS HH 36%, STS HM 18% and usual care 2%, respectively. Scenario analyses performed using higher costs of usual care, higher costs of STS HH and lower costs of TM do not substantially change the conclusions. **CONCLUSIONS:** Cost-effectiveness analyses suggest TM was an optimal strategy in most scenarios, but there is considerable uncertainty in relation to clear descriptions of the interventions and robust estimation of costs.

PCV106

LIFETIME COST-EFFECTIVENESS OF ISOLATED AORTIC VALVE REPLACEMENTS ASSOCIATED WITH THE MINI-INVASIVE IMPLANTATION OF A NEW SUTURELESS AND COLLAPSED VALVE IN FRANCE AND UNITED KINGDOM

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OBJECTIVES: Mini-invasive aortic valve replacement (MiAVR) has several advantages over full sternotomy (FS), mainly less surgical trauma, decreased blood loss, lower mortality and faster recovery. Perceval S is an aortic valve which is implanted without need for suturing and a collapsed profile, thus allowing a significant reduction of cross-clamping times, an independent risk factor for worse outcomes, allowing to expand the pool of operable patients with MiAVR. **METHODS:** A patient-level simulation model fully coded in WinBugs was updated and extended to predict lifetime effectiveness and costs of isolated AVR procedures associated with this new valve in France and UK, as compared to traditional valve implants, from the cost perspective of the third party payer. Unit costs and health state-specific utilities were retrieved from official and literature sources. Two price scenarios were evaluated, one in which the sutureless valve is sold at the double, and one at the triple price of its comparator. Future costs and outcomes are discounted at a yearly 3.5% rate. **RESULTS:** In the first cost scenario, the model predicts that on average MiAVR with Perceval S instead of traditional sutured valves in FS would yield incremental 0.29 LYs (0.20 QALYs) and savings for about 3,000 € and 3,250 £, in France and UK, respectively. In the second cost scenario, Perceval S in MiAVR still remains dominant, with savings for 550 € and 740 £, in France and UK, respectively. Deterministic threshold analysis indicates that the sutureless valve would retain acceptable cost-effectiveness (at willingness-to-pay thresholds of 30,000€ and 20,000£ per QALY) as long as its price does not exceed 5.6 and 4.9 times that of the traditional valve, in France and UK, respectively. **CONCLUSIONS:** The sutureless valve in combination with MiAVR offers the opportunity to improve outcomes in isolated AVR at a reduced cost to the third party payers.

PCV107

COST UTILITY ANALYSIS OF SCREENING AND TREATMENT OF HYPERLIPIDEMIA IN CHINESE ADULTS AGED 45 AND ABOVE

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Serum total and LDL cholesterol levels are high (13.9% for borderline high LDL- cholesterol) and increasing in China. Hyperlipidemia is a main risk factor for cardiovascular and cerebrovascular diseases. Screening is one of the effective prevention methods; however, there has been no appraisal of the cost-effectiveness of blood lipid screening in China. **OBJECTIVES:** To determine the cost-utility of blood lipid screening and subsequent interventions versus no screening for the prevention and treatment of hyperlipidemia and its complication. **METHODS:** Cost utility analysis based on a Markov model was conducted for a cohort of Chinese adults aged 45 and abovefrom screening to death. Published clinical trials and epidemiological studies retrieved from electronic bibliographic databases; supplementary data obtained from CVD patients survey in China. Markov model simulated the long term effects of screening and no screening strategies from the aspects of cost and effectiveness. The model assumed a 30 year time horizon, and costs and benefits were discounted at 5%. The willingness-to-pay threshold is ¥100,000/QALY. Sensitivity analyses were conducted to evaluate assumptions of the model and to identify which model inputs had most impact on the results. **RESULTS:** Estimated costs for each quality adjusted life year (QALY) gained among no screening population were ¥6325.8, with cumulative costs of ¥77112 and cumulative utility of 12.19, and ¥5783.5 for screened population with cumulative costs of ¥72178 and cumulative utility of 12.48, respectively. The results showed the blood lipid screening was associated with increased QALY and potentially cost-saving as compared with no screening. Sensitivity analyses demonstrated robustness of the results. **CONCLUSIONS:** Based on this Markov model, blood lipid screening is likely to be cost-effective option compared with no screening for the prevention and treatment of hyperlipidemia and its complication among Chinese aged 45 and above.

PCV108

COST-EFFECTIVENESS OF DRUG-ELUTING STENTS VERSUS BARE METAL STENTS IN EGYPTIAN DIABETIC PATIENTS

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OBJECTIVES: Cost-effectiveness of Drug eluting stents (DES) versus bare metal stents (BMS) in Egyptian diabetic patients with chronic coronary artery disease from a patient perspective was evaluated over a time horizon of 3 years. **METHODS:** A cohort Markov process model with five health states: stent, coronary artery bypass surgery (CABG), non-fatal myocardial infarction (MI), percutaneous coronary intervention (PCI) and death was derived from published data. The transition probabilities from the index procedure to death, MI, PCI, and CABG were derived from an updated, previously published meta-analysis of RCTs comparing DES with BMS in patients with coronary artery disease. Relative risk reduction, restenosis risks, mortality rates, utilities were derived using published sources. Direct Medical costs were obtained from 4 top-rated cardiology hospitals in Egypt. All costs and effects were discounted at 3.5% annually. All costs were reported in Egyptian pounds of the financial year 2013. Deterministic sensitivity analysis was conducted. **RESULTS:** In the overall population, total costs for DES and BMS were 20,664 EGP and 11,957 EGP respectively. Total QALYs for DES and BMS were 2.26 and 2.05 respectively. The incremental cost-effectiveness ratio (ICER) for DES versus BMS was 41,616 EGP/QALY. DES is cost effective because it is less than 3 times GDP/capita in Egypt (57,566 EGP). Results between DES and BMS were most sensitive to the Mortality rate of both DES and BMS. **CONCLUSIONS:** World Health Organization recommends that interventions that cost more than 3 times GDP/capita for one Disability Adjusted Life Year (DALY) avoided should not be reimbursed. Despite DALY is different from QALY but we can assume that they are similar to be able to put a value on the outcome. DES represents a good value for money compared to BMS in Egyptian diabetic patients with chronic coronary artery disease.

PCV109

COST-UTILITY ANALYSIS OF CORONARY ARTERY CALCIUM SCORE TO GUIDE STATIN THERAPY IN PATIENTS WITH ELEVATED C-REACTIVE PROTEIN AND LOW LDL CHOLESTEROL LEVELS

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OBJECTIVES: Using statins in primary prevention is controversial given the low event rate and the difficulty to identify patients who really benefit. Coronary calcium score has been identified as a strong predictor of cardiovascular events, being recommended for risk stratification in intermediate risk individuals. This study aims to assess, from the Portuguese societal perspective, the cost-utility of determining coronary calcium score to guide the use of statins in individuals with elevated C-reactive protein and low LDL cholesterol. Three strategies are compared: no treatment, test and treat accordingly, and treat every patient with rosuvastatin 20mg. **METHODS:**

A Markov model was developed to predict the occurrence of myocardial infarction, stroke, coronary revascularization and death. The model considers a lifetime horizon and a 3.5% discount rate. Clinical inputs were derived from the JUPITER trial and from a cohort of the MESA study fulfilling JUPITER inclusion criteria. Event costs were obtained from the literature. Rosuvastatin 20mg cost incorporates a discount to reflect the introduction of generics within a maximum of 5 years. **RESULTS:** Coronary calcium score determination and subsequent primary prevention in individuals with a score exceeding 100 dominates no treatment. Implementing primary prevention in those patients with positive score, and not just those with score above 100, implies a willingness to pay around 40,000€ per QALY. Finally, primary prevention in all individuals is not cost-effective when compared to primary prevention in those with positive calcium score as it is associated with a cost per QALY of more than 600,000€. **CONCLUSIONS:** Determination of coronary calcium score is cost-effective as it allows to identify those patients that will benefit most from primary prevention. Primary prevention in patients with calcium score greater than 100 should be implemented. The implementation of this strategy in other patients with positive calcium score depends on the willingness to pay for a QALY.

PCV110

LIFETIME COST-EFFECTIVENESS OF ISOLATED AND CONCOMITANT AORTIC VALVE REPLACEMENTS IN GERMANY

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OBJECTIVES: Aortic valve replacement (AVR) is the most common heart valve operation, accounting for a conspicuous part of all valve surgery performed in the elderly. Prolonged aortic cross-clamping times are an independent risk factor. Perceval S is a new aortic valve which is implanted without need for suturing and a collapsed profile, thus allowing a significant reduction of cross-clamping times and to expand the pool of patients operable with mini-invasive aortic valve replacement (MiAVR) among isolated AVR candidates. Aim of this simulation study was to predict costs and outcomes of isolated AVR procedures associated with this new valve in Germany, as compared to traditional valve implants, from the cost perspective of the third party payer. **METHODS:** A previously published probabilistic, patient-level simulation model fully coded in WinBugs was updated with new clinical data and the evaluation extended to evaluate lifetime cost-effectiveness from the perspective of the third party payer. Unit costs and health state-specific utilities were retrieved from official and literature sources; the price of the sutureless valve is hypothesised twice as much as for traditional valves. Future costs and outcomes are discounted at a yearly 3.5% rate. **RESULTS:** The model predicts that on average the use of the Perceval S in MiAVR instead of traditional sutured valves in full sternotomy among isolated AVR candidates, would yield incremental 0.29 LYs (0.20 QALYs) per patient, with an associated saving around 3,500 €, thus representing a dominant option when compared to traditional surgical AVRs. In concomitant procedures, on average the use of the Perceval S valve instead of traditional sutured valves is expected to yield incremental 0.21 LYs (0.16 QALYs) per patient, with an associated saving of over 4,400 €, also representing a dominant alternative. **CONCLUSIONS:** Sutureless valves may improve outcomes in AVR at a reduced cost to the third party payers.

PCV111

STROKE PREVENTION IN NON-VALVULAR ATRIAL FIBRILLATION: SYSTEMATIC REVIEW OF COST-EFFECTIVENESS STUDIES

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OBJECTIVES: To conduct a systematic review of cost-effectiveness studies of newer oral anticoagulants for stroke prevention in atrial fibrillation versus warfarin and understand its implications for policy and for further research. **METHODS:** We searched DARE, Cochrane, NICE, Tufts, NHS EED, Science Direct and PubMed through May 2013 to identify studies of oral anticoagulants dabigatran, rivaroxaban and apixaban versus warfarin for stroke prevention in non-valvular atrial fibrillation in patients at a moderate-to-high risk of stroke initiating anticoagulation for/near lifetime using either a societal or health care perspective. A separate analysis was performed for ISPOR abstracts. **RESULTS:** Ten studies were identified, most based on one randomized trial per therapy, 3 reported an ICER above commonly accepted WTP levels. ICERs ranged from $9,099–$86,000 for dabigatran and $3,190–$55,757 for rivaroxaban. Apixaban was found to be cost-effective $11,400–$24,312. Upon PSA, dabigatran was cost-effective 40% to 98%, apixaban 44.1% to 60%, and rivaroxaban 2.1% to 80% of the time, for the lowest reported WTP. Variations in ICERs occurred between studies that used the same efficacy data. Key variables influencing variations include differences in costs; assumptions for INR monitoring and utilization of health care resources; and the probabilities of adverse event. Effectiveness, compliance, adverse events and INR management were derived from clinical trials. Additional data from recent abstracts reported similar trends. **CONCLUSIONS:** For this indication, novel agents seem to be cost-effective alternatives to warfarin, despite variations across countries. However, cost-effectiveness may depend on: prices of medicines in each country; the proportion of actual patients' time within the INR therapeutic range; and the actual real-world effectiveness, safety, and utilization of these therapies. More head-to-head RCTs and pragmatic trials are required. Future cost-effectiveness studies of these new therapies should be periodically repeated during the lifecycle of medicines under real-world utilization and should also incorporate budget impact analysis.

PCV112

PHARMACOECONOMIC ANALYSIS OF IVABRADINE USE IN BELARUS

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OBJECTIVES: Cost-effectiveness and cost-utility analysis of ivabradine use in patients with stable angina with left ventricular systolic dysfunction has been performed to determine economic advisability of its applying in Belarus. **METHODS:** Markov model with 12-month cycle duration and 10-year time horizon has been constructed on the basis of a systematic review of literature, national surveillance data, local health services market and drugs market estimation. Four conditions were included: stable process, non-fatal event (cardiac infraction or unstable angina), surgical revascularization, death. Number of patients with stable angina who stayed alive and QALY till the end of the last analyzed cycle of the model has been used as a measure of efficiency and utility. One-sided determinate sensitivity analysis has been conducted. Incremental values have been calculated. Direct medical expenses have been evaluated. Value of triple GDP per capita per year (10790 euro) has been used as threshold. **RESULTS:** Research showed clinical advantage of treatment scheme with ivabradine as compared to "traditional therapy" concerning the amount of patients who stayed alive by the end of the last cycle of model (7275 vs. 6421 persons in total population and 8136 vs 6993 in patients with heart rate >70 pbm) and QALY number (77635 vs. 69253 in total population and 84138 vs. 73031 in patients with heart rate >70 pbm years). The sensitivity analysis showed that in 9.09% of cases ivabradine was the prevailing technology, in 90.91% the cost per QALY did not exceed the threshold. The average counted incremental cost per QALY was 3836 Euro. **CONCLUSIONS:** The analysis showed the pharmacoeconomic acceptability of ivabradine use by patients with stable angina with left ventricular systolic disfunction and heart rate $\geq$ 70 bpm at prescription of the medication in optimal dosage which ensures minimal market value of the medication.

PCV113

LIFETIME COST-EFFECTIVENESS OF CONCOMITANT AORTIC VALVE REPLACEMENTS IN FRANCE AND THE UNITED KINGDOM

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OBJECTIVES: Aortic valve replacement (AVR) is the most common heart valve operation, accounting for a conspicuous part of all valve surgery performed in the elderly. Prolonged aortic cross-clamping times are an independent risk factor for worse outcomes. Perceval S is a new aortic valve which is implanted without need for suturing and a collapsed profile, thus allowing a significant reduction of cross-clamping times. **METHODS:** A patient-level simulation model fully coded in WinBugs was updated and extended to predict lifetime effectiveness and costs of concomitant AVR procedures associated with this new valve in France and UK, as compared to traditional valve implants, from the cost perspective of the third party payer. Two price scenarios were evaluated, one in which the sutureless valve is sold at the double, and one at the triple price of its comparator. Unit costs and health state-specific utilities were retrieved from official and literature sources. Future costs and outcomes are discounted at a yearly 3.5% rate. Uncertainty is evaluated through the incorporated probabilistic sensitivity analysis and deterministic threshold analyses. **RESULTS:** The model predicts that on average the use of the Perceval S valve instead of traditional sutured valves would yield incremental 0.21 LYs (0.16 QALYs) per patient, with an associated saving of about 5,100 € and 4,400 £ in France and UK, respectively, in the first scenario, and of 2,600 € and 1,900 £, in the second. Deterministic threshold analysis indicates that the sutureless valve would remain averagely dominant as long as its price does not exceed 4.1 and 3.8 times that of the traditional valve, in France and UK, respectively. **CONCLUSIONS:** The sutureless valve offers the opportunity to improve outcomes in concomitant AVR at a reduced cost to the third party payers.

PCV114

IMPACT OF CARDIOVASCULAR DISEASE ON LABOUR FORCE PARTICIPATION: BIVARIATE PROBIT ANALYSIS

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OBJECTIVES: Health status plays an important role in individuals' labour supply decision. Chronic diseases, such as cancer, diabetes mellitus, cardiovascular disease, mental illness and disabilities are reported to have strongest effect on individual transitions on the labour market. Among them, cardiovascular disease (CVD), in addition to being the leading cause of death, is likely to affect individuals' employment decision. The aim of this study is to investigate the impact of clinically diagnosed cardiovascular disease on labour supply, taking account of the observed and unobserved factors that influence the risk of cardiovascular disease and labour force participation. **METHODS:** Study subjects were randomly selected from Gazi University general internal medicine outpatient clinic. Demographic, health and employment status data have been compiled for five hundred and fifteen study subjects who applied to the clinic between December 2012 and February 2013. The bivariate probit method has been utilized to investigate the impact of incidence of cardiovascular disease on employment status. **RESULTS:** Empirical results indicate that cardiovascular disease have a strong negative impact on labour market outcomes, particularly for men, and that education level, gender, hypertension have significant indirect effects on labour force participation. Analysis results suggest that there is a correlation between the labour force participation and the incidence of cardiovascular disease, revealing that single equation models might be misspecified. **CONCLUSIONS:** As cardiovascular disease has a significant negative impact on employment status, public health programs need to address this issue and provide treatment strategies and prevention efforts to alleviate the destructive impact on societal productivity.

PCV115

REAL WORLD RESOURCE USE ASSOCIATED WITH TRANSCATHETER AORTIC VALVE IMPLANTATION AND CONVENTIONAL AORTIC VALVE REPLACEMENT SURGERY

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OBJECTIVES: To define hospital and post discharge-related resource use for patients undergoing Transcatheter Aortic Valve Implantation (TAVI) and conventional Aortic Valve Replacement (AVR) surgery within a single UK hospital. **METHODS:** A local

service evaluation of patients undergoing TAVI or AVR between January 2011 and May 2012 captured data until 6-months post-procedure, collected from hospital records and via a General Practitioner questionnaire. The main endpoints were mortality, hospital length of stay (LoS), discharge destination, readmission and post-discharge resource use. Subgroup analyses were performed for AVR patients aged ≥80 (AVR≥80) and with Euroscore of ≥10 (AVR≥10). **RESULTS:** Results given as means (standard deviation) for TAVI (n=51), AVR (n=188), AVR≥80 (n=48) and AVR≥10 (n=47) respectively, unless otherwise stated. Age in years was 83 (3.06), 71 (13.11), 84 (2.72), 79 (7.12), Logistic Euroscore1 was 24.74 (11.90), 8.07 (6.44), 12.01 (6.04), 16.45 (6.58) and post-operative LoS in days was 11.51 (11.16), 10.88 (10.82), 14.31 (16.66), 15.19 (17.67). For patients discharged alive, 0 of 48 (0%), 13 of 180 (7%), 6 of 46 (13%) and 4 of 44 (9%), had an unplanned cardiac-related readmission within 30-days of discharge. Time to readmission was 74.6 (52.9), 31.1 (37.2), 15.4 (10.5) and 16.7 (12.8) days. **CONCLUSIONS:** Despite TAVI being performed in an older, higher risk population the LoS is similar to AVR. Most strikingly there were no cardiac-related readmissions within 30-days for TAVI and time to first readmission was significantly longer. This evaluation suggests that TAVI is clinically appropriate and provides economic advantages in both the hospital and post discharge setting in this high risk group. Many patients undergoing TAVI are considered unfit for surgery and hence TAVI offers a treatment that delivers similar results to traditional AVR surgery without the high risk associated with surgery.

CARDIOVASCULAR DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PCV116
PERSISTENCE WITH MEDICATIONS: A DISCRETE CHOICE EXPERIMENT OF PREFERENCES AMONG HYPERTENSIVE PATIENTS

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OBJECTIVES: To examine patients' stated preferences for persisting with medications using a discrete choice experiment (DCE) and to explore the relationship with clinical, demographic and psycho-social variables. **METHODS:** A 4-attribute DCE (mild side-effects, potentially life-threatening but rare side-effects, dose frequency, treatment benefits) with 3-levels identified from literature and expert opinion was developed using a fractional factorial design. Scenarios were folded into nine forced binary choices: Which medicine would you be most likely to continue taking? The survey was translated, piloted and approved for eleven European countries. Target sample was 100≤n≤323 patients prescribed anti-hypertensives per country, recruited by posters in community pharmacies or general practices. Results were analysed in STATA using a random effects logit model. **RESULTS:** A total of 2856 patients from Austria (n=323), Belgium (n=180), England (n=323), Germany (n=265), Greece (n=289), Hungary (n=323), The Netherlands (n=237), Poland (n=323) and Wales (n=323) completed the online questionnaire. All four attributes influenced persistence with treatment (p<0.01). Patients were willing to forego chance of improvements in treatment benefits (%) in order to improve other attributes: -36.10% (95% CI: -41.24 to -32.94) for a very rare risk of life-threatening side-effects; -18.66% (95% CI: -21.51 to -16.67) for once daily dose frequency; -0.74% (95% CI: -0.85 to -0.67) to reduce the risk of mild ADR by 1%. Likelihood ratio tests showed that models controlling for clinical, demographic and psycho-social variables were significantly different from the base-case. There was limited evidence that self-reported adherence influenced stated preferences to persist. **CONCLUSIONS:** Patients were willing to trade potential benefits, harms, and convenience in responding that they would persist with treatment. Clinical, demographic and psycho-social factors influence the extent of the trade-offs between these attributes. Persistence may therefore be enhanced directly, through selection of medicines meeting preferred levels of attributes, or indirectly through targeting modifiable psycho-social factors that affect trade-off choices.

PCV117
ILLUSTRATION OF THE COMBINED EFFECT OF PATIENT'S ADHERENCE AND INDIVIDUAL BIOLOGICAL CHARACTERISTICS ON BLOOD PRESSURE

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OBJECTIVES: With the recognition that adherence is commonly imperfect, even with once daily regimen, 'forgiveness' is becoming acknowledged as an important characteristic in predicting real-world effectiveness. Forgiveness is typically reported as a group average value, ignoring person-to-person variability. Here we illustrate an alternative way of estimating and presenting information on drug forgiveness which allows the estimation of the combined effect of imperfect adherence and variable forgiveness. **METHODS:** Adherence data from 4783 patients with hypertension were used in these simulations. A projected dosing history over 365 days was obtained from each of these individual adherence profiles. Longitudinal clinic systolic blood pressure (SBP) collected from 4879 patients after drug withdrawal were analysed using non linear mixed effect models, allowing the estimation of the between-patient variability in the loss of effect (the 'offset'). Projected SBP profiles were obtained by combining each dosing history with 100 offset curves randomly sampled from the variance-covariance matrix estimated in the previous step. Re-samplings were performed in the resulting dataset using two adherence distributions described in the literature to estimate the proportion of time patients who achieved the maximal effect on SBP over a treatment period of 365 days. **RESULTS:** In the first population, 90% of the patients achieved the maximal effect during 95% of the time, whereas, in the population presenting a lower adherence, about 80 % maintained the maximal effect during 95% of the time. **CONCLUSIONS:** The impact imperfect adherence on response is mitigated by drug forgiveness. This methodology reveals the person-to-person variability in clinical effectiveness which is hidden when forgiveness is considered as a group-average quantity, and shows that the agent studied provides a reliable clinical effectiveness despite imperfect adherence. Ultimately, this approach could be used to compare drugs with different levels of forgiveness and/or regimens in the presence of non-adherence.

PCV118
TWO SIMPLE METHODS OF MEASURING ADHERENCE IN HYPERTENSIVE PATIENTS ARE PREDICTIVE OF BLOOD PRESSURE CONTROL: POOLED ANALYSIS OF 17,516 PATIENTS FROM SEVEN VALSARTAN STUDIES

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OBJECTIVES: Hypertension is a common chronic disease and risk factor for many other conditions. Despite effective treatments, few patients achieve recommended blood pressure targets. Among the variables related with poor antihypertensive outcomes, patient adherence appears to be especially influential. Adherence assessment should fit seamlessly into the clinical encounter, which requires simple methods. We evaluated whether adherence assessments through a single-item query and a visual analogue scale (VAS) are independent predictors of controlled systolic (SBP), diastolic (DBP), and combined systolic/diastolic (SBP/DBP) blood pressure (BP). **METHODS:** Pooled analysis of 17,516 patients treated with valsartan as second-line therapy from seven Belgian studies. Adherence was assessed at baseline and 90 days using two methods: a single query derived from the Basel Assessment of Adherence Scale ("Do you recall not having taken your medication sometime in the past four weeks?") and a physician-rated VAS (0-100 range). Logistic regression was used to model BP control as a function of these two measures. Controlled BP was defined as <140mm/90mmHg (<130/80mmHg for diabetics). **RESULTS:** BP control rates at 90 days were 39.3% for SBP, 59.4% for DBP, and 33.8% for SBP/DBP. 79% of patients identified as adherent under the single query reached BP control, with odds ratios of 0.66 (95%CI=0.62-0.71, p<0.001) for SBP, 0.68 (95%CI=0.63-0.73, p<0.001) for DBP, and 0.64 (95%CI=0.59-0.70, p<0.001) for SBP/DBP. Of those patients with a physician-rated VAS adherence score of 80 or more, 81% reached BP control, with odds ratios of 0.93 (95%CI=0.86-1.00, p<0.001) for SBP, 0.79 (95%CI=0.73-0.85, p<0.001) for DBP, and 0.91 (95%CI=0.84-0.99, p<0.001) for SBP/DBP. **CONCLUSIONS:** The two simple methods of measuring adherence, the single query and VAS, are independent predictors of blood pressure control. These measures can be integrated seamlessly into routine clinical practice. These findings must be validated in other health conditions and therapeutic areas.

PCV119
VALIDITY OF SELF-REPORTED DOSE OF PATIENTS USING WAFARIN IN CLINICAL PRACTICE

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OBJECTIVES: Warfarin is an oral anticoagulant used for the prevention of thrombosis, and many adjustments are needed to achieve a therapeutic INR. The dose of warfarin is important to establish an association between clinical and safety outcomes and the exposure. To evaluate the validity of the weekly dose of warfarin as reported by the patient compared to the weekly prescribed dose. **METHODS:** This study was based on an ongoing prospective cohort of new warfarin-users to assess the genetic and clinical risks associated with the effectiveness and safety of warfarin. Demographic and clinical data were collected from 219 patients who began the treatment between May 1st, 2010 and Oct. 31st, 2011 at the Montreal Heart Institute. They were followed-up each three months for a year. The primary outcome is the concordance between the reported and prescribed weekly dose of warfarin. The secondary outcome is the difference between the means of reported and prescribed warfarin weekly doses. A t-test and a Pearson correlation are used for the secondary outcome and a generalized mixed linear model with repeated measures is used for the primary outcome. **RESULTS:** Patients had a mean age of 67.7, 58.9% were men and 70.3% had atrial fibrillation. No significant difference between the means of reported and prescribed warfarin weekly dose (Pearson coefficient = 0.969). However, we observed that the correlation was weak at 3 months for patients in the low dose group and in the high dose group (Pearson coefficient = 0.806 and 0.829, respectively). Mixed linear model analysis detected no association between the covariates and the concordance. **CONCLUSIONS:** This study demonstrates that the weekly reported dose correlates well with the prescribed dose patients in a prospective cohort study. Furthermore, the effect was similar whether measured in new-onset users of warfarin and up to 12 months of use.

PCV120
EFFECTS OF THE OCCURRENCE OF A FIRST CARDIOVASCULAR EVENT ON STATIN ADHERENCE IN TYPE 2 DIABETES: A MATCHED COHORT DESIGN

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OBJECTIVES: Adherence to statin therapy is important for an effective reduction in cardiovascular events. We aimed to assess the effect of the occurrence of a first cardiovascular event on adherence rates in type 2 diabetes patients using a matched cohort design. **METHODS:** A matched cohort study was performed within the IADB. nl pharmacy database among type 2 diabetes patients, who initiated statin treatment for primary prevention. Index patients experienced a first event (index date) after initiation whereas reference patients did not. Index and reference patients were matched on gender, age at statin initiation, statin initiation date, adherence level before the index date and follow-up period. Adherence was measured as percentages of days covered and classified into: non-adherent, partial-adherent or full-adherent. Adherence rates were measured from statin initiation until the index date, and from the index date until end of follow-up, for reference patients in both cases the same follow-up period was used. Mean adherence rates between index and reference before and after were compared by the use of an independent samples

T-test. **RESULTS:** From the 855 index patients 375 could be matched to a reference patient. Mean adherence rates before the index date were 79% for both groups. After the index date, mean adherence rates were 81% for index patients and 71% for reference patients (p-value <0.001). Index patients were more likely to become full-adherent and less likely to become non-adherent. 26% of the index patients used more statins after the event than before whereas 20% used less. **CONCLUSIONS:** Patients receiving a statin are likely to become more adherent after the occurrence of a cardiovascular event during statin treatment. One in five of these patients, however, become less adherent showing there are still important health and economic benefits to achieve by tailoring the management of individual patients.

PCV121

HEALTH STATE IN PATIENTS WITH ATRIAL FIBRILLATION ON NEW ORAL ANTICOAGULANTS AS ASSESSED WITH THE NEW EQ-5D-5L QUESTIONNAIRE: PREFER IN AF REGISTRY

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OBJECTIVES: New oral anticoagulants (NOACs) have the promise to change the management of patients with atrial fibrillation (AF), and can be used in lieu of vitamin K antagonists (VKAs) or antiplatelet drugs (AP). We aimed to obtain contemporary data on the health state of AF patients under everyday practice conditions at the time of introduction of NOACs. **METHODS:** PREFER in AF is a non-interventional study that prospectively documents AF patients in terms of clinical characteristics, management, quality of life and other outcome parameters. The new EuroQol EQ-5D-5L descriptive system was applied in PREFER in AF to obtain patient-reported generic health-related quality of life information and utility scores to inform resource allocation decisions. **RESULTS:** Of the 7243 AF patients (63.1% males, mean age 71.5 ± 10.7 years), 2159 (30.0%) had paroxysmal, 1731 (24.0%) persistent, 517 (7.2%) long-standing persistent, and 2793 (38.8%) permanent AF. Comorbidities were highly prevalent. On the visual analogue scale, the mean score in 5674 patients (78.3% EQ-5D participation rate) was 67.7 ±18.4 points, with no major differences between patients on NOACs (68.4), VKAs (67.6), AP (69.7), or VKAs+AP (65.5), respectively. Problems of any severity were reported for mobility, self-care, usual activities, pain/discomfort and anxiety/depression in 50.1%, 20.7%, 45.0%, 55.4%, and 47.1%. The overall utility index was 0.85 ±0.17. The 319 patients on NOACs had the same utility index as the 182 patients without VKAs or AP (0.80 in both groups), whereas the 2937 patients on VKAs, the 342 on AP or the 425 patients on VKAs+AP had lower indices (0.77 vs. 0.77 vs. 074). **CONCLUSIONS:** Patients with AF present with reduced self-reported quality of life compared to the general population. Patients receiving NOACs had a slightly higher quality of life, possibly illustrating that this type of treatment is initially given to "healthier" populations compared to established VKA therapy.

PCV122

QUALITY OF LIFE IN PATIENTS WITH VENOUS THROMBOEMOBLISM: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: A systematic review was conducted to determine the quality of life (QoL) in patients with venous thromboembolism (VTE). VTE encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE) and may be associated with long-term complications including post-thrombotic syndrome (PTS) in up to 50% of patients following symptomatic DVT. **METHODS:** Eligible English language studies reporting QoL and utility scores for VTE (published since 1990 from any geographical location) were identified from electronic databases (Medline, EMBASE and Cochrane Library: accessed December 2012) and conference proceedings. **RESULTS:** Thirty studies (VTE=4; DVT=23; PE=3) that were eligible for inclusion were conducted in Europe (n=11), Canada (n=9), United States (n=7), or were multinational (n=3). A total of 14 unique generic (n=8) and disease-specific (n=6) instruments were reported. The generic SF-36 (n=18), and the disease-specific VEINES QoL/Sym (n=12) were the most frequently used instruments. In general, the QoL of patients with VTE was significantly impaired in all domains – physical, social and psychological – compared with the general population, measured using both disease-specific and generic instruments. QoL scores tended to improve during follow-up with the greatest improvement reported between 1–4 months following an initial event. Factors associated with poor QoL were identified: older age, obesity, female gender, comorbidities, and recurrent VTE events. Patients with PTS reported long-term worsening of QoL and functional disability compared with patients without PTS following an initial VTE event, with the impact on QoL increasing with severity of disease. However, in contrast to disease-specific QoL instruments, the impact of PTS on QoL was not consistently reported with generic questionnaires. **CONCLUSIONS:** Initial VTE events and long-term complications, such as PTS, are significantly associated with reduced patients' QoL in physical, psychological, and social domains. Disease-specific measurements should be further developed to assess the long-term impact of VTE recurrence, PTS, and bleeding associated with anticoagulant use.

PCV123

AN ANALYSIS OF EQ-5D QUALITY OF LIFE DATA FOR A COST-EFFECTIVENESS ANALYSIS OF IVABRADINE PLUS STANDARD CARE VERSUS STANDARD CARE ALONE IN CHRONIC HF

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OBJECTIVES: SHIFT examined the effect of adding ivabradine, a heart rate lowering therapy, to optimised standard therapy in chronic heart failure (HF) patients (n=6505). This study reports methods and results for an analysis of SHIFT patient quality of life data used to inform the UK cost-effectiveness analysis for ivabradine. **METHODS:** EQ-5D quality of life data were collected for patients in countries with a validated questionnaire (n=5313). EQ-5D data were analysed using regression techniques appropriate for repeated observations across individuals over time. **RESULTS:** Ivabradine was associated with a significant gain in patient quality of life (utility). Utility values were estimated to range between 0.82-0.46 [standard care, New York Heart Association (NYHA) class I-IV] and between 0.84-0.47 (ivabradine, NYHA I-IV). Hospitalisations were strongly associated with a reduction in utility, this reduction varied according to NYHA class from -0.07 (NYHA I) to -0.21 (NYHA IV). Patients with more severe heart failure symptoms (NYHA III and IV), were found to suffer a greater loss in utility given a hospitalisation than patients with milder symptoms (NYHA I and II). **CONCLUSIONS:** Ivabradine was associated with a significant improvement in quality of life. In addition, hospitalisation was found to significantly reduce patient quality of life; ivabradine is consequently expected to convey further quality of life benefits by avoiding the temporary utility loss associated with hospitalisations. Cumulatively, over a patient's life time, this may generate important gains in quality of life for ivabradine versus standard care.

PCV124

HEALTH OUTCOMES AT 6 TO 120 MONTHS SINCE HEART TRANSPLANT IN SPAIN: CLINICAL STATUS, HEALTH RELATED-QUALITY OF LIFE AND UTILITY ASSESSMENT

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OBJECTIVES: To evaluate the outcomes related to heart transplantation in adult recipients at 6±1 (Group I),12±2 (Group II), 36±6 (Group III), 60±10 (Group IV) or 120±20 (Group V) months after receiving the allograft. **METHODS:** A multicenter, cross-sectional study was conducted in different transplant units from Spain (n=14). Patients (aged >18 years) with a heart transplant (HTx) due to congestive heart failure and living with a single functioning graft were proposed to participate. Clinical status was assessed with the New York Heart Association Scale. Besides, participants completed the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the EQ-5D. Other measures of social support and caregivers' burden were also included. Differences between groups were studied (Chi-squared, Kruskal-Wallis and Mann-Whitney U with Bonferroni correction tests). Multivariate regression analyses were applied to examine the association of clinical and socio-demographic variables with questionnaires' scores. **RESULTS:** A total of 303 transplant recipients (77.9% males) with a mean age(SD) of 56.4(11.4) years were included. High levels of health-related quality of life (HRQoL) were found at all stages after transplant. However, a slight decrement was detected after 10 years since transplantation ($p \leq 0.033$). EQ-5D utility mean(SEM) scores were: Group I-0.81(0.03)-; Group II-0.82(0.03)-; Group III-0.85(0.03)-; Group IV-0.86(0.02)-; Group V-0.75(0.03)--). VAS values (EQ-5D) were close to those of the general population, with the exception of patients at 10 years since transplantation whose scores were lower. Multivariate analyses showed that this decrement in well-being was related to comorbid medical conditions, severe vascular disease of allograft and the number of hospitalizations (EQ-5D: 48.4% of explained variance, $F_{4,164}= 38.46$, $p<0.001$; KCCQ-overall functional score-: 45.0% $F_{3,198}= 54.073$, $p<0.001$). **CONCLUSIONS:** : HTx outcomes in Spain seem to be satisfactory with good achievements in HRQoL and utility scores.

PCV125

THE RELATION BETWEEN THE MODIFIED RANKIN SCALE (MRS) SCORES AND UTILITY WEIGHTS: RESULTS FROM A SURVEY AMONG COMMUNITY DWELLING LONG TERM STROKE SURVIVORS

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OBJECTIVES: The modified Rankin Scale (mRS) is frequently used in clinical studies to measure the level of disability following stroke and TIA. As the mRS is a disease-specific instrument, it can not be easily translated into preference-based utility-weights to be used in cost-effectiveness analyses (CEAs). Data on utility-weights by the mRS disability level are limited. We estimated the relation between mRS scores and utility-weights in a convenience sample of "real-world" stroke survivors. **METHODS:** During a personal interview of 148 community dwelling long-term stroke survivors attending day-care rehabilitation centers throughout Israel, we estimated the level of disability using the mRS, ranging from: no symptoms/disability (mRS=0), to severe disability (mRS=5). Patients also completed the EuroQoL (EQ-5D) questionnaire, the most commonly used instrument for obtaining utility values. Utility-weights were calculated using the EQ-5D UK tariffs. Health states may range from -0.594 to 1, where 1.0 is defined as perfect health and zero represents death. **RESULTS:** Mean age (±SD) of patients was 65.8±9.8, ranging from 28-85 years, with male predominance of 73.6%. Over 80% of patients were married, living with their spouse or family. The vast majority (92%) of patients did not work at the time of interview, mainly due to the stroke. Mean time from first stroke was 7.2±5.9 years and 1/3 of respondents experienced >1 stroke events. Mean utility-weights (±SD) were as follows: mRS 0-1(N=31), 0.748±0.231; mRS 2-3 (N=78), 0.395±0.317; mRS 4-5 (N=38), 0.055±0.277. Nineteen percent of patients had a utility-weight < 0 representing a health state considered worse than death. **CONCLUSIONS:** While utility-weights of stroke survivors with no symptoms/no significant disability (mRS 0-1), are comparable to those used in published CEAs, patients with moderate and severe disability (mRS 4-5) show

an extremely low quality of life. These findings should be considered in future planning of interventions in stroke patients.

PCV126
MEASURING HEALTH-RELATED QUALITY OF LIFE BY EXPERIENCES: THE EXPERIENCE SAMPLING METHOD
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OBJECTIVES: To determine the feasibility of using the Experience Sampling Method (ESM) to obtain accounts of the momentary experience of Health Related Quality of Life (HRQOL) and compare these to retrospective global measures of HRQOL and utilities derived from choice under uncertainty. **METHODS:** An experience-sampling study of 139 participants from three different patient groups and a control sample examined the momentary experience of HRQOL (mom-HRQOL). Global retrospective HRQOL measures were also administered. Feasibility of was determined by assessing willingness to participate in the study and by analysing the percentage of drop-outs and the number of completed beep questionnaires. Bivariate correlations between mom-HRQOL and momentary positive affect (PA), negative affect (NA) and physical symptoms (PS) for each participant were determined. Furthermore, correlations between mom-HRQOL, PA, NA and PS on the one hand and retrospective global health (EQ-VAS), the EQ-5D utility, the SF-6D utility and the TTO on the other hand were determined. **RESULTS:** The overall participation rate was low but there were no drop-outs and the number of completed beeps was comparable to other studies. For most participants, the correlation between mom-HRQOL and momentary PA, NA and PS was in the expected direction. Correlations between ESM data on HRQOL, PA, NA and PS and retrospective measures were moderate to high, with the exception of the TTO. **CONCLUSIONS:** Overall, this study extends our knowledge of the similarities and differences between ESM data on HRQOL, feelings and symptoms and retrospective measures of HRQOL, which may aid future health care research and decision making.

PCV127
PATIENTS WITH HYPERTENSION IN PRIMARY CARE IN SPAIN: MANAGEMENT, SELF-PERCEPTION AND SATISFACTION
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OBJECTIVES: EUprimecare is a European Union project aimed at analyzing the costs and quality of the different models of primary care (PC) in Europe. The aim of this paper is to analyze the management of patients with hypertension in PC services in Spain compared to other European countries, the satisfaction of these patients with PC services and their self-perceived health status. **METHODS:** Cross-sectional study. We conducted a population survey by telephone among PC users in each of the consortium countries (Germany, Spain, Estonia, Finland, Hungary, Italy and Lithuania). The questionnaire included information on sociodemographic characteristics, health status, satisfaction, utilization of PC services, and frequency of some interventions carried out by PC professionals. The survey was conducted to 431-432 PC users in each country (Ntotal = 3020). We use satisfaction, health status and sociodemographic variables to consider the situation of patients with hypertension in PC. **RESULTS:** The percentage of users of primary care services who reported having hypertension in Spain was 21.6% (N = 93), lower than the overall average (34.9%). 97% of patients resident in Spain were diagnosed by their primary care physicians versus 82.6% of the European average. The 91.4% of patients in Spain claimed to be in treatment to hypertension (EU average= 92.3%) and in 92.9% of cases the treatment was prescribed by their PC doctors (EU average= 84.5%). Only 7.5% of patients claimed that their health was poor or very poor, the lowest proportion of all countries evaluated. **CONCLUSIONS:** The patient with hypertension in Spain is diagnosed and managed by PC professionals more frequently than in other European countries. The self-perception of these patients in Spain is good and they were satisfied with the services of AP. The overall satisfaction of the patients with AP services was high but not significantly different from other countries.

PCV128
USER PREFERENCES FOR STROKE SERVICES IN WALES
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OBJECTIVES: To investigate patient and family carer preferences for stroke support services. **METHODS:** Discrete choice experiment (DCE) using a fractional factorial design, folded into nine binary choices, containing four attributes: format of service (group, individual); service provider (hospital stroke team, primary care, voluntary sector); provision of additional social and leisure activities (provided, not provided); and time to plan and make the journey (1,2,4 hours). Attributes and levels were defined by a review of policy documentation and two workshops with patients and family carers (n=8). Patients (six months post-stroke) and their family carers were recruited from four stroke-services in Wales, to complete a paper questionnaire including the DCE and validated instruments to facilitate pre-specified sub-group analyses. Data were analysed in STATA using a random effects logit model. Marginal rate of substitution (MRS) used journey time as the value attribute. **RESULTS:** A total of 144/474 (30%) eligible patients requested the questionnaire, 80 (56%) completed (mean age 70.8 years (sd 11.1). A total of 34/74 family carers who requested the questionnaire completed. All four attributes were significant for patients ($p<0.05$), only format of service and journey for carers. Patients preferred support services on an individual basis (p=0.00, MRS=128.61 minutes), with additional social and leisure activities (p=0.00, MRS=64.07 minutes). Family carers were willing to trade more journey time for services provided on an individual basis (p=0.00, MRS=273.73 minutes). Sub-group analysis showed significant differences between established (>315 days post-stroke) and early patients. Models accounting for patient health utility were significantly different ($p<0.05$). **CONCLUSIONS:** These findings complement the more descriptive summaries of a comprehensive matrix of sources of support within regions and localities (Department of Health, 2007), with which people living with stroke may interact. Exploring what patients and carers consider important in the provision of stroke support services, will ensure that service re-design is user-focused to maximum utility.

PCV129
PATIENTS PREFERENCES FOR LONG-TERM TREATMENT AFTER ACUTE CORONARY SYNDROME: A DISCRETE-CHOICE EXPERIMENT AND ANALYTIC HIERARCHY PROCESS
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OBJECTIVES: Diseases of the cardiovascular system are the main causes of death in Germany and other industrial countries. Different therapeutic approaches exist as well as several treatment options. How people who have suffered from an acute coronary syndrome, value aspects of their medical treatment is not very well analyzed until today. The objective of this empirical investigation was to evaluate patient's preferences regarding different antiplatelet medication options following an acute coronary syndrome. **METHODS:** Primary method was a Discrete-Choice-Experiment that included 6 patient-relevant attributes. Furthermore an Analytic-Hierarchy Process (AHP) was used to test the applicability of the method and to compare the results. The Discrete-Choice-Experiment (DCE) was conducted using a fractional factorial NGene-design with priors and the statistical data analysis used a random effect logit model. AHP was conducted using the eigenvalue method. **RESULTS:** The preference analysis of N=683 patients showed a clear dominance for the attribute "reduction of the risk of death" (DCE coef.: 0.803; AHP coef.: 0.402.). Rank 2 in AHP the "reduction of heart attack risk" (DCE coef: 0.464; AHP coef.: 0.272.) and in the DCE was "shortness of breath" (DCE coef.: 0.550; AHP coef.: 0.165.). The side effect of "bleeding" (DCE coef.: 0.400; AHP coef.: 0.117.) joined accordingly. The "frequency of administration" was less important in DCE and AHP (DCE coef: 0.025; AHP coef. 0,044.). **CONCLUSIONS:** The results of both methods generated an almost equal ranking of the included features. The highest value for patients within a treatment decision was the mortality reduction. The consideration of patient preferences in therapeutic decisions implies stronger patient focus and can at the same time be used for the development of effective therapies after acute coronary syndrome. The preference data generated can be used for health care decision makers and stakeholders to represent the patient's benefit at the same time.

PCV130
COMPARING THE PERFORMANCE OF THE EQ-5D-5L WITH THE EQ-5D-3L IN STROKE PATIENTS IN JAPAN
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OBJECTIVES: To assess the performance of the EQ-5D-5L Japanese version compared with the EQ-5D-3L in clinical setting targeted at patients with stroke in Japan. **METHODS:** The stroke patients were recruited from six rehabilitation hospitals in Japan. The proxy of the patients completed a questionnaire including the two versions of the EQ-5D. We tested the inconsistency, the redistribution properties, and the ceiling effect. **RESULTS:** A total 533 patients were recruited: 61% male, 15-99 (mean=67) years old. Diagnoses of patients were infarction (54.6%), hemorrhage (35.5%), and other (9.9%). The proportion of inconsistent responses (i.e., 3L responses that were at least two levels away from the 5L responses) was 3.6%. In particular the proportion in MOBILTY was 14.6%. Regarding redistribution, 52-61% of the patients answering level 2 with the 3L version redistributed their responses to levels 2 or 4 with the 5L version. A relative 3% reduction of the ceiling effect was found. **CONCLUSIONS:** Our findings suggest that the EQ-5D-5L Japanese version performs better in at least some properties analyzed. Further study is necessary to clarify other psychometric properties.

PCV131
A RETROSPECTIVE STUDY COMPARING COMPLIANCE, PERSISTENCE, AND BLOOD PRESSURE CONTROL BETWEEN FREE-DRUG AND SINGLE-PILL COMBINATION THERAPIES IN KOREAN HYPERTENSIVE PATIENTS
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OBJECTIVES: Existing evidences indicate that single-pill antihypertensive combinations (SPC) have greater rates of adherence and more effective lowering of blood pressure than free-drug combinations (FC). SPC therapy has been used in Korea for the purpose of achieving optimal blood pressure control. However it is questioned whether such existing positive evidence toward SPC from western countries can be found in the Korean population. **METHODS:** This study compared compliance, persistence and blood pressure change of SPC versus FC using the medical charts of 1,940 patients from 17 Korean general hospitals (GH1-17). The hypertensive patients with SPC or FC prescription, more than 40 years old, no history of hospitalization, visited GH1-17 from January 1, 2010 to December 31, 2011 were included. Compliance was compared using the Medication Progression Ratio (MPR), calculated as the ratio between the days medication was taken and days in a time interval. Persistence was measured as the number of days from the index date to the therapy discontinuation date. The blood pressure (BP) change was calculated as the difference between the first and the last visit. **RESULTS:** Overall compliance measured by MPR was 0.71 for the SPC group and 0.69 for the FC group, with the difference being statistically significant.

This was especially evident for SPC patients in the 40~64 year age group (0.71 for SPC, 0.69 for FC) and patients with two or more comorbidities (0.73 for SPC, 0.69 for FC) (P= 0.0011). However, no statistical significance was observed for the difference both in persistence and the BP change between the two groups. **CONCLUSIONS:** Our study suggests that compliance tends to be improved by the use of SPC compared with FC. Unlike the previous western studies, it was hard to find a significant increase in persistence or BP change with SPC therapy in this study.

PCV132

HEALTH RELATED QUALITY OF LIFE AND DEVICE-ACCEPTANCE IN PATIENTS WITH IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS AND TELEMONITORING

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OBJECTIVES: Telemedical systems (TMS) and data management for implantable cardioverter-defibrillators (ICD) promise to reduce costs and optimize patient care. Depressive symptoms are common among patients with an ICD and the health related quality of life (HRQoL) is affected by the underlying disease and the implanted device, respectively. TMS might improve the HRQoL of patients and ICDs acceptance due to closer monitoring and, thereby, an increased level of perceived safety. In this RCT, changes in the level of depression, HRQoL and ICD-acceptance over a period of six months after ICD-implantation were investigated. **METHODS:** A total of 161 patients (80.7% male; age: 64,1±14,6; 82% with coronary disease, 11% with DCM) with an ICD were randomized at the day of implantation into intervention (n=82) or control group (n=79). The intervention group was equipped with a telemonitoring-system that transferred ICD-data from the patients' home to the medical practitioner. The control group received regular care. Patients were asked to fill out three questionnaires (the generic EQ-5D, the depression specific HADS and the device specific FPAS); the follow-up period was six month, with postal surveys on a monthly basis. **RESULTS:** Nine patients dropped out before survey completion. A total of 140 patients filled out at least two sets of questionnaires and were included in the analyses. After six months the mean improvement in the HRQoL (EQ-5D-Index) in the telemonitoring group was 10.7 points compared to baseline (p=.006) while the mean change in HRQoL in the control group was 5.5 (p=.138). FPAS and HADS-D showed small but non-significant advantage for the telemonitoring group. **CONCLUSIONS:** Preliminary results suggest that TMS have the ability to improve HRQoL of patients with ICDs. Results on effects towards depression and anxiety and enhancement of ICDs acceptance are also promising. Since ICDs are used in chronic diseases a longer follow-up period seems to be required to validate the effects.

PCV133

FURTHER VALIDATION OF A NEW QUESTIONNAIRE TO MEASURE SATISFACTION WITH MEDICAL CARE IN PATIENTS WITH ATRIAL FIBRILLATION (SAFUCA) IN SPAIN

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OBJECTIVES: To assess convergent and divergent validity of a new questionnaire (SAFUCA) developed to measure satisfaction with medical care in patients with non valvular atrial fibrillation. **METHODS:** The 25-item reduced version instrument was administered along with the Treatment Satisfaction Questionnaire for Medication (TSQM), and 5 Visual Analog Scales (VAS) measuring: Health Related Quality of Life (HRQoL), Effectiveness and Overall Satisfaction assessed by the patient; and Effectiveness and Tolerability assessed by the clinician. A convenience sample of 230 patients recruited at 7 health centers (5 hospitals and 2 primary care centers) in Spain was used. Second Order Exploratory Factor Analysis (SO-EFA) and correlation with VAS scales were computed. **RESULTS:** SAFUCA dimensions correlated (p<0.001) higher with corresponding TSQM dimensions (e.g.: Effectiveness r=0.450, Convenience r=0.457, Undesired Effects r=-0.340, Overall satisfaction r=0.651), while SO-EFA made evident differences regarding the assessment of satisfaction with INR controls, interference in QoL and Medical Care. Correlation pattern between VAS scores was significantly different between primary care centers and hospitals, with a higher correlation between patient and clinician scores observed in primary care (e.g.: Effectiveness r_{PC}=0.430 vs. r_H=0.057). Similarly, correlation patterns between VAS concurrent scales and SAFUCA dimensions differed between center types. While high correlations between Effectiveness dimension and patient satisfaction VAS were observed in both cases (r_{PC}=0.521 vs. r_H=0.516), correlation of Tolerability with Undesired Effects differed between centers (r_{PC}=-0.474 vs. r_H=-0.085). **CONCLUSIONS:** The 25-item questionnaire exhibits good convergent and divergent validity values. Differences between types of health care centers in correlation patterns were meaningful and worth of further research.

PCV134

HEALTH RELATED QUALITY OF LIFE AT SIX MONTHS POST DISCHARGE IN PATIENTS WITH HEART FAILURE

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OBJECTIVES: There are few studies in Spain about outcomes at six months in terms of health-related quality of life (HRQoL) in patients hospitalized by heart failure (HF). The objective of the study was to evaluate changes in HRQoL from baseline to six months post discharge in patients with HF through three questionnaires, SF-12, EQ-5D-3L and Minnesota Living with Heart Failure questionnaire (MLHFQ). **METHODS:** This is a prospective study with 976 patients admitted by HF. Patients completed questionnaires during their hospitalization and at six months. The MLHFQ is a specific instrument which has 21 items with an overall scale, physical (8 items) and emotional (5 items) subscales. MLHFQ items are scoring from 0 (best) to 5 (worse). Total score ranges from 0 to 105, physical domain from 0 to 40 and emotional from 0 to 25. SF-12 has two dimensions, Physical Summary Score (PCS) and Mental Summary Score (MSC) which scores range from 0 (worst) to 100 (best). EQ-5D has been measured according to the Spanish tariffs by time trade-off and the visual analogic scale. We used general linear model to study gains in each dimension adjusted by baseline score, age, gender and readmissions in the previous 6 months. **RESULTS:** Mean age was 76.0 (SD=10.4), there were a 53.3% of men and 33.1% of readmissions in the previous six months. Regarding all questionnaires and dimensions, baseline status influence in gains, the worse the baseline the more the gains. Likewise men have greater gains and patients readmitted lower in all domains. Age has an influence in all domains but emotional dimension of MLHFQ and MSC of SF-12. **CONCLUSIONS:** Adjusted by baseline score and readmissions, men have greater improvements in all domains of MLHFQ, SF-12 and EQ-5D. On the other hand, the younger the patients the higher the improvement is, however age does not have any influence in psychological domains.

PCV135

INTERNATIONAL NORMALIZED RATIO (INR) MONITORING AND PERCENT TIME IN THERAPEUTIC INR RANGE (TTR) HAVE IMPACT ON PATIENT'S QUALITY OF LIFE? APPLICATION OF BETA REGRESSIONS IN A PROSPECTIVE 3 MONTHS SETTING

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OBJECTIVES: Warfarin anticoagulation is monitored using international normalized ratio (INR); specified with the narrow/wide 2.0–3.0/1.9–3.5 therapeutic target range, and converted to time in the therapeutic range (TTR, total percentage of time the INR reading is within the INR therapeutic range). We explored the impact of I) INR monitoring and II) TTR on patients' quality of life (QoL). **METHODS:** A total of 647 unselected patients visiting 3 health centres in Pirkanmaa district (31.01–11.02.2011), Finland participated to prospective study. To assess INR monitoring or TTR and QoL, Beta regressions were applied in Stata and EQ-5D-3L-based QoL (Smithson&Verkuilen transformation) 3 months after the baseline visit was the dependent variable. The covariates were $CHADS_2$(congestive heart failure, hypertension, age>75, diabetes mellitus, stroke) score, other comorbidities, baseline QoL, time difference (days) between dependent variable measurement and mean TTR time point (subgroup model), and INR monitoring (yes/no in total population) or TTR % (subgroup model). **RESULTS:** A total of 28 patients (46.43% male; means: age 73.21 years, $CHADS_2$-score 2.39, other comorbidities amount 1.71, baseline QoL 0.8334, INR tests 4.21, 66.31%/82.86% INR measurements on the narrow/wide range) had INR measurements ("warfarinization group") during the 3 months follow-up. 27 patients had calculable TTR (Rosendaal method) that was 69.29%/86.66% on the narrow/wide range. In the beta regression (N 393, +1 marginal change), $CHADS_2$-score (-0.021), other comorbidities amount (-0.030), baseline QoL (+0.350), and INR monitoring (p=0.299, -0.042, SE 0.044) predicted QoL. The mean adjusted QoL with/without INR monitoring in the warfarinization-like group was 0.794/0.836. In subgroup Beta regression including only warfarinization patients, higher TTR levels predicted lower QoL (p<0.050, +1 %-unit marginal change -0.006 [SE 0.007]; discrete change -0.284 in the wide range from 35.3% to 100.0%). **CONCLUSIONS:** INR monitoring may predict QoL loss and, surprisingly, higher TTR predicts lower QoL. Larger studies are needed to confirm the potential relationship between TTR and QoL.

PCV136

CORONARY ARTERY DISEASE, DIABETES, AND HEALTH-RELATED QUALITY OF LIFE: FINDINGS OF A COHORT STUDY FROM INDIA

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OBJECTIVES: Assess health-related quality of life (HRQoL) of patients with CAD. **METHODS:** The main observational study cohort enrolled consecutive patients admitted in ICU at tertiary care hospital and diagnosed with CAD. Demographic information, risk factors for CAD, and angiographic findings were collected. EQ-5D was administered at 1-year follow-up. EQ-5D levels were dichotomized: 'no problems' (level 1), 'any problem' (levels 2 and 3). Linear stepwise regression was used to assess predictors of all 5 health states (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). The independent variables studied include age, hypertension, diabetes, CHF, gender, prior MI, final diagnosis, MI type, and final treatment. Respondents reporting problems EQ-5D dimensions were stratified by presence of diabetes and compared. **RESULTS:** Of 960 CAD patients enrolled for the main cohort study (30% diabetic), 306 (male, 230; diabetics, 64) responded HRQoL questionnaire at 1-year. On liner regression, presence of diabetes was independent predictor of 4/5 EQ-5D HRQoL dimensions: mobility (p=0.019), problems performing usual activities (p=0.041), pain/discomfort (p<0.001); anxiety/depression (p=0.001). At 1-year, mean EQ-5D utility index score and VAS score were significantly lower for diabetes vs non-diabetics (0.76±0.13 vs. 0.83±0.15, p=0.0003 and 67.8 ± 8.8 vs. 73.6±5.4, p=0.0001, respectively) with more problems with performing usual activities (56.3% vs. 41.3%, p=0.04), pain or discomfort (51.6% vs. 17.8%, p=0.0001) as well as anxiety/depression (32.8% vs 14.9%, p=0.002). **CONCLUSIONS:** Among CAD

patients with diabetes, HRQoL was lower across all health dimensions measured by the EQ-5D; except mobility and self-care. Individualised therapeutic management programs could be considered in order to improve the HRQoL of CAD patients with diabetes.

PCV137
TRANSLATION AND CULTURAL ADAPTATION OF PATIENT PERCEPTION OF ARRHYTHMIA QUESTIONNAIRE IN POLAND
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OBJECTIVES: Patient Perception of Arrhythmia Questionnaire (PPAQ) is a disease-specific questionnaire designed to measure symptoms and health-related quality of life in patients suffering from a group of arrhythmias collectively called supraventricular tachycardias (SVT). There is no valid translation of PPAQ available in Poland, which hinders research in this area with Polish arrhythmia patients. The aim of this study was to conduct initial content validity testing through translation and cultural adaptation of the English language version of the PPAQ to the Polish language. **METHODS:** The whole project was conducted according to ISPOR Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures published in 2005. **RESULTS:** In 2011, the PPAQ was translated into Polish and cultural adaptation was performed on 20 patients with SVT (12 male, age 54.9±17.4). Issues concerning close meanings of symptom names and language-dependant gender-related distinctions were identified. The former was solved by cooperation with experts in arrhythmia and latter by incorporating patients' preferences during cognitive debriefing. **CONCLUSIONS:** The Polish translation was well accepted by patients during this translation and initial content validity testing. Issues arisen during the translation process may recur in other translations and be resolved in similar manner.

PCV138
HEALTH-RELATED QUALITY OF LIFE IN PATIENTS ALONG FIRST YEAR POSTSTROKE IN SPAIN
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OBJECTIVES: Atrial fibrillation (AF) 5-folds stroke risk, which results in death or disability in 80% of individuals and one-year mortality approaches 50%. The objective of the present study was to analyze the health-related quality of live (HRQoL) one year post-stroke in patients with or without AF and the burden of caregivers. **METHODS:** We performed an observational, multicenter, naturalistic and prospective study that included 16 stroke units from different Spanish regions. We used EQ-5D and VAS to test patients HRQoL and Zarit Burden Inventory to estimate the caregiver burden. We collected information at hospital entry for patients, 3 and 12 months post-stroke both for patients and carers through direct physician interviews. **RESULTS:** A total of 321 stroke patients were recruited, 160 with and 161 without AF. EQ-5D was completed by 274 patients - 127 with AF and 147 without AF -, and VAS by 249 - 113 with and 136 without AF -. The average utility scores of EQ-5D were 0.57, 0.62, and 0.65. We found a statistically significant difference between AF and non-AF obtained at hospital entry (p=0.029) and 12 months post-stroke (p=0.023). There were no differences between hospital visits (p=0.112). If we took into consideration the age of patients, the absence or presence of AF in EQ-5D scores, lost its significance (p=0.099). VAS average scores were 45.81, 44.15 and 45.74. VAS results showed non-significant differences neither by AF presence (p=0.396) nor time (p=0.613). Caregiver burden was higher in AF than non-AF patientes (46.47 vs 40.93 2nd visit and 45.29 vs 38.73 3rd visit) and the difference was statistically significant (p=0.007 and p=0.002). **CONCLUSIONS:** Stroke has a deep impact on patients HRQoL with no improvement over time. In the same line, caregivers also support an important burden related to stroke and specially in AF patients.

PCV140
TREATMENT SATISFACTION IN PATIENTS WITH ATRIAL FIBRILLATION ON NEW ORAL ANTICOAGULANTS AS MEASURED WITH PACT-Q2: PREFER IN AF REGISTRY
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OBJECTIVES: The great majority of patients with atrial fibrillation (AF) require anticoagulation in order to prevent strokes or other thromboembolic events. We aimed at obtaining detailed and current information on patients' satisfaction with their ongoing anticoagulation treatment. **METHODS:** PREFER in AF (The PREvention oF thromboembolic events – European Registry in Atrial Fibrillation) is a current non-interventional study performed in France, Germany, Austria, Switzerland, Italy, Spain and UK. A total of 7243 consecutive patients with ECG-confirmed AF in the previous 12 months are followed up prospectively. The 'Perception of Anticoagulant Treatment Questionnaire' is a valid and reliable instrument that allows the assessment of patients' expectations (PACT-Q1) and satisfaction regarding anticoagulant treatment, as well as patients' opinion about treatment convenience of use (PACT-Q2). **RESULTS:** A total of 5049 patients (69.7%) received antithrombotic treatment and were willing to fill out the PACT-Q2 questionnaire at baseline. 77.1% of these were on vitamin K antagonists (VKAs), 6.4% on new oral anticoagulants (NOACs), 5.2% on antiplatelets (AP) and 11.0% on VKA+AP combinations. In the "convenience" dimension, the overall score (0-100 range) was 82.9 ±17.3. The score was higher in the NOAC group (88.1 ± 13.0) compared to the VKA (82.1 ± 17.5), AP (87.0 ± 17.9) or VKA +AP groups (83.2 ± 16.8), respectively. In the "anticoagulant treatment satisfaction" dimension of the PACT-Q2, the overall score was 63.4 ±15.9. Again, this score was higher in the NOAC group (66.6 ±16.6) compared to the VKA (63.2 ±15.9), AP (63.7 ±16.8), or VKA + AP groups (62.8 ±15.0), respectively. **CONCLUSIONS:** Overall, patients on current anticoagulation achieve relatively high values on the convenience scale, but moderate values on the satisfaction scale. While differences in group size and patient characteristics need to be taken into account, patients on NOACs compared to patients on VKAs tend to rate their convenience and treatment satisfaction higher.

PCV141
CHRONIC PATIENTS' WILLINGNESS TO PAY FOR AN ALTERNATIVE DRUG WITH INNOVATIVE CHARACTERISTICS
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OBJECTIVES: Aim of the study was to investigate whether chronic patients are willing to pay an extra amount of money in order to switch to another drug that it is either on patent, more effective or simpler in dose. **METHODS:** A cross-sectional study was conducted among 1600 chronic patients suffering from diabetes, hypertension, COPD and Alzheimer. Logistic regression analysis was carried out to explore the factors that influence patients' decision on willingness to pay (WTP) for an alternative drug with innovative characteristics. **RESULTS:** Of the 1600 patients approached, 1594 responded to the survey (99.6%). A total of 40% stated that they would be willing to pay more for a patent drug, 57.5% for a more effective drug and 37.5% for a simpler in dose drug. The average additional amount per month that they would be willing to spend was estimated at 23.6€ for a patent drug, 24.1€ for a more effective drug and 21.9€ for a simpler in dose drug. Statistical analysis revealed that WTP for a patent drug was statistically significant related with the patient's income (OR,1.24;95%CI, 1.14-1.34) while WTP for a more effective or a simpler in dose drug was positively related with the patient's income (OR,1.25;95%CI, 1,13-1,39 and OR, 1,14;95%CI, 1.05-1.24 respectively) and educational level (OR,1.06;95%CI, 1,01-1.13 and OR, 1.06;95%CI, 1.01-1.13, respectively). **CONCLUSIONS:** Half of chronic patients demonstrate absolute willingness to increase spending for an innovative drug, which highlights the significance they attribute to pharmaceuticals for the management of their condition. The remaining's 50% reluctance may be attributed to the extended trust on their current pharmaceutical treatment and to the efforts and money spent in order to control their condition. However, patients with higher socioeconomic status are more likely to express WTP which reflects the economic burden imposed by chronic conditions, and the role of education in shaping patient attitudes.

CARDIOVASCULAR DISORDERS – Health Care Use & Policy Studies

PCV143
EVALUATION OF THE LENGTH OF HOSPITAL STAY FOR PATIENTS WITH ATRIAL FIBRILLATION
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OBJECTIVES: Identification of differences in the length of hospital stay for patients with atrial fibrillation (AF) with and without oral anticoagulation (OA). Longer stays of patients could lead to an economical burden for the hospital because of the Diagnosis Related Groups (DRG) system in Germany and the compensation with case-based lump sum. **METHODS:** We conducted a retrospective study using an electronic DRG benchmarking database. This database contains DRG data from 208 hospitals in Germany with over 2,800,000 inpatient cases per year. In total, 10,912,922 cases from the year 2010 to 2012 were analyzed. 661,845 cases fulfilled the inclusion criteria and were analyzed according the statistical analysis plan including matched pair analyses. **RESULTS:** Cases with AF and surgical intervention compared to cases without AF and with surgical intervention have a significantly longer pre-operation length of stay (+0.74 days) and a significantly longer hospital stay (+1.5 days). Furthermore cases with chronic AF (=AF+OA) have a significantly longer total length of stay in the hospital (+0.86 days). For the cases with AF and bleeding vs. cases without bleeding, there is no significant difference in the total length of stay, but there is a significantly longer stay of 0.82 days compared to the average length of stay in the DRG-catalogue. **CONCLUSIONS:** Patients with AF and with or without OA could be an economic burden for the hospital, because the increased length of stay in hospital leads to higher costs whereas the existing compensation diagnosis-based lump sum is not affected by increased treatment days. The new oral anticoagulants could lead to shorter stays of patients with AF by shortening the bridging periods compared to OA like vitamin K antagonists. Further studies should be conducted to figure out the causes for longer hospital stays of patients with AF.

PCV144
ADHERENCE TO WARFARIN TREATMENT IN BRAZIL: SYSTEMATIC REVIEW OF THE LITERATURE
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OBJECTIVES: To review the literature about adherence to warfarin treatment in Brazil. **METHODS:** A systematic review of the literature and a wide search in LILACS (Literatura Latino Americana e do Caribe em Ciências da Saúde) and MEDLINE (Medlars On Line) electronic databases were conducted to identify studies with the key words: "warfarin" and "Brazil". The combination of terms was used as reference for the analysis. Search was restricted to randomized controlled trials (RCT), systematic reviews, meta-analysis and prospective clinical trials (PCT). **RESULTS:** A total of 77 studies were identified, from which only 22 met inclusion criteria: 1 meta-analysis, 5 RCTs, 8 systematic reviews and 8 PCTs. Only 1 study described adherence to treatment. From a total of 229 randomized patients, 119 received warfarin. Adherence to treatment was observed in 42% (p=0.001) of patients using warfarin considering an average of 57+-18 months of follow-up, INR < 2 in 37.54 % and INR > 2 in 11.18 %. Multivariate analysis estimated that every 1% of INR <2, the risk of a thromboembolic event increases 8.4%. **CONCLUSIONS:** The systematic review of the literature showed lack of data regarding Brazilian patients under warfarin treatment. The only available study did not define adherence and it did not investigate the underlying causes of non-adherence. Thus, it is recommended the conduction of further studies in order to provide better understanding of anticoagulant therapies compliance in Brazilian patients.

PCV145

COMPLIANCE WITH PREVENTIVE RECOMMENDATIONS IN PRIMARY CARE AND RATE OF POTENTIALLY AVOIDED HOSPITALIZATIONS BY DIABETES, CHRONIC HEART FAILURE OR CHRONIC PULMONARY OBSTRUCTIVE DISEASE

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OBJECTIVES: Potentially avoidable hospitalizations (PAH) are increasing in Spain and account for more than 3% of all the discharges. One of the hypothesis to explain PAH lies on the suboptimal management of chronic disease at ambulatory level of care. In this study we aim at explaining the association between compliance with preventive recommendations in primary care and observed rate of PAH. **METHODS:** Compliance with evidence-based preventive recommendations regarding diabetes mellitus (DM), chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) was calculated for the 1,350 general practitioners of the Basque Health Service and compared with the annual (2011) observed rate of PAH between their patients' panel (mean panel≈1,500 adults; population covered=1,942,873). PAH was defined by a restrictive set of ICD-9 criteria following recommendations of the Spanish group of studies on Variability in Medical Practice. Multilevel poisson regression was used and age, sex, status socioeconomic (SSE) and hospital of reference were entered as covariates. **RESULTS:** After adjusting by all the covariates, higher compliance of recommendations such as periodical spirometry or assessment of the correct use of bronchodilator inhalers shows association with lower rates of PAH by COPD ($p<0.05$). Periodical foot care, oftalmological exam or assessment of the cardiovascular risk is non-significantly ($0.15\geq p\geq 0.05$) but consistently associated to lower rates of PAH by DM. No link was observed between compliance or recommendations for CHF and PAH due to this cause. The independent effect of the SSE was strong in all the diseases ($p<0.001$) (higher rates as privation increases). Variations regarding the hospital of reference were also observed. **CONCLUSIONS:** Adequate compliance of evidence-based recommendations limits, modestly but consistently, the incidence of PAH due to DM or COPD. The SSE and the hospital of reference explain part of the observed variability in hospitalization by chronic disease.

PCV146

VALUE CHAIN ANALYSIS FOR CARDIAC DEVICES

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OBJECTIVES: We investigated opportunities to cost-effectively improve health outcomes for patients eligible for ICD, sICD and CRT-D devices. This area was chosen because of the high cost of these devices and the significant amount of uncertainty on how to use them in a cost effective way. Also, we aimed to explore value-added services to patients and physicians, and the area appeared to have potential for this. **METHODS:** We conducted a value chain analysis. The first step was to clarify the care pathway and identify places where outcome or efficiency were poor; the second step was to prioritise the associated problems based on their importance (health/cost impact) and the feasibility of addressing the root causes in the short to medium term; the third step was to propose ways to address the priority problems and add value in the care pathway. To do this, we conducted secondary research, and primary research mainly focused on the UK (20 in-depth discussions with cardiologists, patients and manufacturers). **RESULTS:** A core issue was the lack of good evidence-based criteria to identify which patients would benefit most from the various devices. Referral to device implantation and funding were seen as below the levels expected given current clinical and HTA guidelines; the gap might even increase given the expectation that future guidelines may call for higher implantation rates. The proposed solutions focused on increasing awareness of the guidelines for more effective referral to specialist centres, supporting more flexibility in local funding, and taking advantage of the rich, continuous data that the devices themselves could provide with a view to eventually improve eligibility criteria. **CONCLUSIONS:** It is increasingly difficult to achieve health gains through new therapies. Therefore, focusing on improving referral and delivery pathways of current therapies may be quite effective at increasing health gains and/or efficiency.

PCV147

IMPACT OF SWITCHING ON HEALTH CARE COSTS AND OUTCOMES IN GENERIC DRUG POLICIES

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OBJECTIVES: Price erosion is considered the key success criterion of generic drug policies. For chronic drug therapy, however, persistence with the original drug substance is equally important. Low persistence may result in poor health outcomes, lead to increased health care costs. Our objective was to estimate the impact of switching drug therapy on health and economic outcomes as a consequence of the Hungarian drug policy in hypertension. **METHODS:** We retrieved 4-year medical records of hypertensive patients, who had at least 10 prescriptions of original losartan or losartan HCT in the 12 months prior to patent expiry. We allocated patients to 3 groups based on switching history in the 12 months after patent expiry. Group 1 patients were switched to another patented antihypertensive product without risk for generic substitution (n=953). Group 2 patients were switched to generic losartan or losartan HCT, but did not change the generic brand in 12 months (n=630). Group 3 patients were switched at least twice among different generic brands in 12 months (n=1144). We calculated the incidence of major cardiovascular events (MACE) and overall health care cost (289.42 HUF/EUR 2012 average exchange rate) in each group. **RESULTS:** Total 3-year health care costs were €9,728, €6,594, €8,227, the incidence of MACEs was 13.3%, 9.8%, 12.3% in Group 1, 2 and 3 respectively. **CONCLUSIONS:** In chronic diseases switching to generic drugs reduces health care costs. However, frequent switching among generic brands may result in negative health outcomes and increased health care costs. Suboptimal implementation of generic drug policies in chronic diseases may compromise expected benefits (i.e. same health gain at lower costs). Potential confounding factors may limit the generalizability of our conclusions.

PCV148

ASSESSMENT OF GENERIC DRUG POLICY IMPLEMENTATION BY MEASURING PERSISTENCE WITH ANTIHYPERTENSIVE DRUG THERAPIES AFTER PATENT EXPIRY

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OBJECTIVES: There are two important success criteria of generic drug policies in chronic diseases after patent expiry: price erosion and persistence. Our objective was to assess the implementation of generic drug policies on these criteria between 2007-2011 in Hungary by comparing the continuation of angiotensin receptor blockers after patent expiry of original therapies. **METHODS:** In Hungary the first generic losartan was launched in 2007; losartan HCT in 2009; valsartan/valsartan HCT in 2011. From the National Health Insurance Fund database, we selected prescription records of hypertensive patients with at least 10 prescriptions of original losartan (Group 1; n=2637), losartan HCT (Group 2; n=7598) and valsartan/valsartan HCT (Group 3; n=38098) in the last 12 months prior to patent expiry. We compared antihypertensive therapies in 12 months after the reimbursement of first generic drug in each group. Antihypertensives were categorized into preferred (continued antihypertensive therapy with same active ingredient generic drugs), and non-preferred (continuation on original drug therapy; switching to other patented drug(s) without risk for generic substitution; switching to generic drugs with other active ingredient(s); discontinuation of reimbursed antihypertensive drug therapies) policy outcomes. **RESULTS:** After patent expiry 76.2% and 68.9% of Group 1&2 patients continued the original losartan or losartan HCT therapy for 12 months, and only 3.9% and 8.5% were switched to generic losartan/losartan HCT. In Group 3, 33.6% of patients were switched to generic valsartan/valsartan HCT, 42.8% received other generic drugs or drug combinations, whilst 14.5% were switched to other patented products. **CONCLUSIONS:** Despite significant changes in the generic drug policies in Hungary in 2007, 2009 and 2011 not more than one-third of hypertensive patients changed to generic drugs during 12 months after first generic entry. These findings indicate suboptimal generic drug policy in a chronic disease with significant public health implications.

PCV149

CROSS-COUNTRY COMPARISON OF PRESCRIBING PATTERNS VERSUS PORTUGAL AND POTENTIAL COST-SAVINGS

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OBJECTIVES: To review the consumption pattern of ambulatory high expenditure therapeutic groups in Portugal following prescribing guidelines set forth by the Memorandum of Understanding; to perform a cross-country comparison of utilization patterns focusing on quality prescribing indicators identified by the EURO-MED-STAT and/or major international prescribing guidelines; and to perform a cost-saving scenario analysis if more rational European prescribing patterns were undertaken in Portugal. **METHODS:** Cross-national drug utilization study with data from seven European countries: Portugal, Denmark, England, Finland, The Netherlands, Norway and Sweden. Data from Portugal retrieved from hmR Pharmacy Sales Information System, a nationwide database with representative pharmacy dispensing data. Data from other countries was selected from published literature and/or public databases. Cost-saving analysis with assumptions: average annual cost per defined daily dose (DDD) from Portugal and simulations to measure the impact on total expenditure of international utilization patterns (DDD proportion) versus Portuguese pattern. **RESULTS:** Portugal has the highest consumption of oral antidiabetic combinations (19.3% in 2010), of Antagonists Reception Blockers (ARBs) (31% in 2009), and of rosuvastatin (22.2% in 2011). A total of 236 Million euro annual cost-savings was estimated in scenarios of more rational prescribing: 100 Million euro (58% decrease in costs of antidiabetic agents in 2010) when simulating the Dutch oral antidiabetic prescribing pattern; 106 Million euro when simulating the Danish antihypertensive prescribing pattern (20% decrease in antihypertensive costs in 2009); and 26 Million euro when simulating the UK statin prescribing pattern (13% decrease in statin costs in 2011). **CONCLUSIONS:** It is crucial to optimize prescribing patterns in Portugal, in order to achieve a more rational use of medicines and a sustained control of pharmaceutical expenditure. Besides prescribing

guidelines, health prevention / monitoring strategies, involving coordinated actions between primary care and pharmacies, are valuable resources to consider.

PCV150
A REVIEW OF THE APPLICATION OF INTERNATIONAL REFERENCE PRICING IN UKRAINE'S PILOT HYPERTENSION REIMBURSEMENT SCHEME
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OBJECTIVES: The Ukrainian government has been considering ways to improve the population's access to medicines by offering limited reimbursement access. For this purpose, the government has expressed its interest in implementing International reference pricing (IRP). The pilot hypertension programme, which introduced a system of IRP for certain hypertension drugs, was introduced in mid-2012. The government is currently looking to revise the pricing and reimbursement mechanism and to expand the list of drugs eligible for reimbursement under the scheme. This study examines the pilot hypertension programme and its impact in terms of achieving its objectives so far. **METHODS:** Secondary research focused on analysing the current pharmaceutical market and health care situation in Ukraine, with a specific focus on the hypertension market. The study then assessed the pricing and reimbursement methodology which is currently in place, the programme's objectives, and its impact on volume and value of the antihypertensives market. **RESULTS:** Hypertension was chosen for the pilot programme due to the high prevalence of the condition in the country. While, for the full year 2012, the weighted average cost per package in the antihypertensive drug segment decreased by 1.4% compared to the previous year, the volume of retail sales increased 16.8%. Furthermore, as of January 2013, the prices of these drugs had been falling every month from July till December 2012 compared to the corresponding months of 2011. **CONCLUSIONS:** With the pilot hypertension programme, the government is hoping to lower drug prices and thereby improve affordability. Considering that the pilot scheme could be followed by programmes in other therapeutic areas, including a government proposal to include IRP for insulin treatments, the structure and effectiveness of the hypertension programme, and the subsequent amendments to it, could substantially impact the development of any other potential programmes in the future.

PCV151
HOW COMPLEX IS THE COMPETITION IN REGULATED PHARMACEUTICAL MARKETS?
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OBJECTIVES: This paper constitutes an attempt at investigating processes of dynamic competition in pharmaceuticals, with reference to the nature and intensity of price competition in relation to patent expiry and different regulatory regimes. The paper uses comprehensive data on a selection of in-patent and off-patent (generic) cardiovascular medicines from IMS from the five largest European pharmaceutical markets - UK, Germany, France, Italy, Spain - to analyze the impact that pricing and reimbursement regulation and product differentiation have on market structure, diffusion and prices. **METHODS:** The paper develops a panel data model to explain the determinants of brand-name prices and generic prices both before and after patent expiry, the impact of generic entry and generic penetration on market share and prices of brand-name drugs, the competition patterns in their off-patent sector, the determinants of generic diffusion in the presence of generic competition, and the relationship between originator branded and generic prices under different regulatory regimes. The structure of the data allows these questions to be explored at molecule level and at product level. At all levels the originator and generic markets are observable. **RESULTS:** Despite the proliferation of generic policies in many countries, prices in the off-patent sector do not decline as fast as originally thought. Entry into the generic market is positively influenced by regulation through reference pricing and opportunities for product differentiation. Elements of product differentiation within generics promote diffusion, but do not reduce prices. And, health insurance does not capitalize fully on the cost advantage of generic medicines. **CONCLUSIONS:** The results suggest that the relationships between the dynamics of original drug prices, patent expiry, and generic competition are complex and differentiated across countries. The level of generic penetration remains low in some of them and a sharp contrast exists between countries.

PCV152
PRESCRIPTION PATTERNS OF ANTIHYPERTENSIVE AGENTS IN T2DM PATIENTS VISITING TERTIARY CARE CENTRE IN NORTH INDIA
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OBJECTIVES: Hypertension management is of a paramount importance in diabetic patients for cardiovascular risk reduction. Hence, we evaluated prescribing pattern of antihypertensive in T2DM (type 2 diabetes) patients and compare with existing recent guidelines. **METHODS:** A cross-sectional study involving evaluation of all T2DM patients referred to endocrinology unit at tertiary care centre for hypertension, comorbid complications, and recording prescription. Utilization of 5 different antihypertensive drug classes was compared for all patients receiving 1, 2, 3, 4, or more drugs. Logistical regression was used to assess likelihood of prescription of drugs and/or therapy for specific conditions mentioned in the guidelines. **RESULTS:** Out of 1358, T2DM enrolled patients 1186 (87%) had hypertension (males 52%, females 48%). The median duration (IQ) of hypertension diabetics was 4 (1-10) years. A total of 25% patients had controlled BP and 75% with uncontrolled blood pressure (13% isolated systolic hypertension, 6% isolated diastolic hypertension, and 55% both elevated). Overall, ACE inhibitors (ACEIs) were prescribed the highest (59%) followed by angiotensin receptor blockers (ARBs) (52%), calcium channel blockers (CCBs) (29%), diuretics (27%), and beta-blockers (14%). Overall, 55% of T2DM patients were on polytherapy, 41% on monotherapy, and 4% had no antihypertensive treatment. Polytherapy was more predominant with age, duration of diabetes, duration of hypertension, and comorbid complications. **CONCLUSIONS:** Although prescribing pattern of antihypertensive showed adherence to existing evidence-based guidelines, higher proportion of uncontrolled hypertensive patients was found.

PCV153
INITIAL ANTICOAGULATION THERAPY IN PATIENTS WITH VENOUS THROMBOEMBOLISM AND IMPAIRED RENAL FUNCTION: RESULTS OF AN OBSERVATIONAL STUDY
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OBJECTIVES: Patients undergoing initial therapeutic anticoagulation after a venous thromboembolic event (VTE) with severely impaired renal function (RI-VTE-patients) are at high risk of accumulating the anticoagulants resulting in an increased risk of bleeding events. Current guidelines/approved summary of product characteristics (SPC) recommend usage of specific anticoagulants only, monitoring of aXa-activity, and/or dose-adjustment (in the case of enoxaparin) for initial therapeutic anticoagulation of RI-VTE-patients. This study investigates the treatment of German RI-VTE-patients and evaluates whether guideline/SPC recommendations are implemented in the practice of real life care. **METHODS:** We conducted a chart review in 5 German hospitals. All VTE patients treated in these hospitals from 01/01/2007-31/12/2011 were included. RI was defined as CrCl<30ml/min. Treatment did not conform to the recommendations in guidelines/SPCs, if: a) A drug was used that is contraindicated according to the SPC; b) The recorded daily dose of enoxaparin was higher than the recommended weight-adjusted dose. **RESULTS:** Of 5,263 VTE patients identified, 709 (13.5%) cases could not be documented due to missing charts (601) or no documented creatinine serum levels (108). Of the remaining 4,554 patients (mean age ±SD 67.4 years ±15.7; 53.0% female; weight 80.2 kg ±20.0; 54.5% deep VT), 337 (7.4%) had a mean estimated GFR<30ml/min; additionally 1,630 (35.8%) had a minimum eGFR<60ml/min. In 19 (5.6%) of these cases, patients were treated with a drug not recommended for use, 21 (6.2%) did not receive any initial anticoagulation treatment and 91 (27.0%) received a higher than recommended dosage of enoxaparin. Additionally, for 22 patients (6.5%) receiving enoxaparin, no weight information was recorded and it is therefore unlikely that the dosage was adjusted correctly. **CONCLUSIONS:** VTE treatment in RI-VTE-patients differs remarkably from labelled recommendations; over-dosage of enoxaparin is common. It seems fair to assume that these patients are facing a higher risk of adverse reactions in particular bleeding events.

PCV154
ATTITUDES OF PHYSICIANS TOWARD IMPLEMENTING SHARED MEDICAL APPOINTMENTS AT NATIONAL GUARD FAMILY MEDICINE CENTERS IN RIYADH
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OBJECTIVES: To determine the attitude of physicians in three family medicine centers (FMCs) at the National Guard Health Affairs (NGHA) toward the implementation of the Shared Medical Appointment (SMA) approach compared to the current individual appointment approach. **METHODS:** A cross-sectional survey study was conducted by distributing a structured questionnaire among the 79 FMCs' physicians at NGHA in Riyadh, Saudi Arabia. The first part of the questionnaire was an introduction, the second part has requested socio-demographic information, and the third part consisted of 12 statements measuring physicians' attitude toward implementing SMA and the current individual appointment approach. Responses were measured using 5-points Likert Scale. Seventy-nine self-administered questionnaires were distributed to physicians' mail-boxes and the completed questionnaires were collected from mail-boxes at each clinic. Data collection was done from December 10 to 15, 2011. Data were entered and analyzed by the Statistical Package for Social Science (SPSS.16). Descriptive analysis was conducted using frequencies, percentages, and mean (SD). Inferential analysis was conducted using one way ANOVA and Mann-Whitney tests to detect statistically significant differences in responses. A significance level of 0.05 was used. The validity and reliability of the instrument was measured using Pearson's correlation and Cronbach's Alpha, respectively. **RESULTS:** A totla of 78 valid questionnaires were returned yielding a response rate of 99 %. The average attitude scores were 3.75 toward the SMA approach and 2.98 toward the current Individual Appointment approach. The average attitude scores were significantly different at all dimensions (Mann Whtiney P-value < 0.001) in favor of SMA except for patient privacy which was in favor of current individual appointment approach. Subgroup analysis by socio-demographic variables indicated that males and Saudi national physicians have higher positive attitude toward SMA. **CONCLUSIONS:** There is positive attitude of all physicians toward SMA compared to the current individual appointment approach. This attitude was affected by gender and nationality.

PCV155
ANALYSIS OF RE-HOSPITALISATIONS FOR STROKE AND TRANSIENT ISCHEMIA RECURRENCE AND ASSOCIATED COSTS IN THE BURGUNDY REGION IN FRANCE
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OBJECTIVES: To assess the re-hospitalisations rates for stroke (ST) and transient ischemia (TI) recurrences as well as related inpatient costs through the French national Hospitals Medical Health Information database (PMSI). **METHODS:** A retrospective hospital administrative-claims analysis was carried out based on the Diagnoses Related Groups (DRG)-data of four hospitals within the Burgundy region along the 2006-2011 period. In each of the four hospitals, three cohorts were followed up over two years. Patients were excluded if any related hospitalisation for ST or TI occurred in the preceding two-years (identification through ICD-10 diagnosis codes). One and two-year re-hospitalisations rates for ST and/or IT were calculated.

Re-hospitalisations were taken into account if they occurred after one month following inclusion and regardless of the location of the hospital at the national level. Alternatively, 'all' re-hospitalisations rates regardless the related diagnosis were also assessed. Inpatient costs were valued based on reference tariffs according to French National Social Health Payer perspective. **RESULTS:** Around 1750 patients were followed per cohort across the four hospitals starting from 2009, 2010 and 2011. One-year re-hospitalisations rates for ST and TI ranged from 2.9% to 7.1%. The median time to re-hospitalisation ranged between 1.5 to 9.3 months. Two-year re-hospitalisations rates for ST and TI ranged from 4.5% to 10.4%. Two-year re-hospitalisations rates regardless of related diagnosis in acute and/or rehabilitative settings ranged between 45.5% to 65.1%. Mean costs (+/-SD) per inpatient stay for ST and TI were 4'645€ (+/-3'821) in acute setting (2013 EUR). When excluding TI, mean costs were 5'293€ +/-4'225€. Hospitalization costs varied depending on sub-type of stroke, severity, co-morbidities and also year of costing. **CONCLUSIONS:** Such short term data on recurrence rates and inpatient costs might be useful when estimating potential benefits of any secondary prevention intervention aiming at reducing stroke relapses.

PCV156

STATINS IN CANADA: THE CASE FOR DISINVESTMENT

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OBJECTIVES: We examined the economic consequences of generic switching within the statin market for public plans in Canada between 2000 and 2012. **METHODS:** We extracted data (number of units, costs, and claims) for all statins reimbursed by Canadian public drug plans for the period 2000-2012 (sources: IMS Brogan and Canadian Institute for Health Information). **RESULTS:** Public plans paid $11.2 BN to reimburse statins for 2 MM patients between 2000 and 2012. The annual cost of reimbursing statins peaked at $1.3 BN in 2009. Generic atorvastatin was listed by public plans in 2010, and the proportion of statin reimbursement attributable to generics increased from 18% in 2009 to 75% in 2012, reflecting a 76% increase in generic switching. During the same period, the unit cost of brands and generics fell by 25% and 49%, respectively. The combined effect of increased generic switching and lower unit costs resulted in a 55% decrease in the total cost of statins, from $1.3 BN in 2009 to $582 MM in 2012. Annual savings attributable to generic switching increased 10-fold between 2000 and 2012, from $7 to $709 MM. The efficiency at which potential savings has been captured through generic switching increased from 8% to 74% from 2000 to 2012; we project that this will generate savings of ~$800 MM annually through 2015. Increasing generic switching to 100% could generate up to an average of $135 MM annually in additional savings **CONCLUSIONS:** Although substantial savings have been generated by generic switching within the statin class, increasing generic switching could generate additional savings. One strategy to capture these additional savings would be disinvestment: if branded statins were de-listed from public plans if a generic version were available, this would increase generic switching, increase the efficiency at which potential savings are captured, and increase total savings.

PCV157

ATRIAL FIBRILLATION'S BURDEN OF DISEASE IN PORTUGAL

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OBJECTIVES: To estimate the Disability Adjusted Life-Years (DALY) attributable to Atrial Fibrillation (AF) during 2010 in Portugal, including both AF and AF related stroke. **METHODS:** The analysis requires two types of data. The first is an extended set of epidemiological data, which resulted from a compilation of the prevalence and mortality data for AF and for stroke in Portugal. For the distribution of mortality by age, gender and cause of death the WHO Europe mortality database was used. The analysis also uses the results of FAMA, a study of the prevalence of AF in Portugal. Incidence rates were estimated from a review of the international literature. The second type of data concerns the relative risk (RR) of stroke for patients with AF. RR values by age group from the Framingham Study were used. Disability weights were taken from the Global Burden of Disease 2010. **RESULTS:** A total of 3863 deaths in Portugal in 2010 were related to AF, with 813 having AF listed as cause of death and the remaining 3.050 being stroke deaths attributable to AF. The AF attributable deaths are roughly 3.6% of total deaths in the country. The estimate total DALYs was 9.814 (2.251 for AF listed as the cause of death and 7.563 for stroke as cause of death attributed to AF). **CONCLUSIONS:** AF is an important cause of disease burden in Portugal. As reference, AF DALYs are roughly twice the estimated DALYs for skin cancer. AF should receive adequate attention from policy makers.

PCV158

SIMULATING THE POTENTIAL IMPACT OF IMPROVED BLOOD PRESSURE CONTROL ON CLINICAL AND ECONOMIC OUTCOMES IN RUSSIA

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OBJECTIVES: Russia faces a high burden of cardiovascular (CV) disease. Prevalence of all CV risk factors, especially hypertension, is high. Elevated blood pressure (BP) is generally poorly controlled, and medication usage is suboptimal. With a disease model simulation we assessed the impact of improved systolic blood pressure (SBP) control on the number and costs of CV events potentially averted in the hypertensive Russian population. **METHODS:** The Archimedes Model, a detailed computer model of human physiology, disease progression, and health care delivery was adapted to the Russian setting. Intervention scenarios of achieving SBP control rates (defined as SBP <140) of 30%, 40%, 50%, and 60% were simulated by modifying adherence rates of an anti-hypertensive medication combination and compared with current care (23.9% BP control rate). 100,000 hypertensive simulated individuals were modeled over a 10 year time horizon. Outcomes of major adverse cardiovascular events; stroke, myocardial infarction (MI) and CV death were reported. Direct health care costs of strokes and MIs were derived from official Russian statistics and price lists. **RESULTS:** To achieve SBP control rates of 30%, 40%, 50%, and 60%, adherence rates to the anti-hypertensive treatment program were 11.1%, 29.4%, 47.6%, and 65.9% respectively. CV death relative risk reductions were 5.0%, 13.2%, 21.4%, and 29.6%, respectively. For the current estimated 43,855,000 person Russian hypertensive population, each control rate scenario resulted in an absolute reduction of 398,097, 1,050,715, 1,703,334 and 2,355,952 CV deaths, and a reduction of 458,781, 1,210,881, 1,962,981, and 2,715,081 stroke/MI diagnoses. Averted direct costs from current care (225,781) were 12,834, 33,873, 54,913 and 75,952 million Rubles, respectively. **CONCLUSIONS:** Our simulation implies that a clinically significant number of CV events in the Russian hypertensive population may be prevented by achieving BP control through an antihypertensive drug combination. Averted costs may be re-allocated to strengthen evidence-based, preventive interventions.

PCV159

WHAT FACTORS PREDICT THE DECISION TO TREAT ACUTE CORONARY SYNDROME INVASIVELY? EVIDENCE FROM CLINICAL PRACTICE

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OBJECTIVES: To describe UK patients with acute coronary syndrome (ACS) who receive percutaneous coronary intervention (PCI) or are medically managed only (MM) and evaluate factors affecting approaches to treatment. **METHODS:** Patients registered with a general practice participating in the Clinical Practice Research Datalink (CPRD) with Hospital Episode Statistics (HES)-linked data were included if they had an ACS-related hospitalization (January 2008-December 2009). Logistic regression analyses were used to assess what characteristics at ACS-related hospitalization date were associated with PCI or MM classified at 30-days post-hospitalisation date (30DHD). **RESULTS:** A total of 10,753 ACS patients were identified (60% male, 67% aged ≥ 65, 81% had NSTEMI or UA at index date); 30DHD, 74% were MM and 26% had PCI. Factors associated with receiving PCI were STEMI at hospitalization (OR 3.73, 95% CI 3.30, 4.22); patients with previous PCI pre-hospitalization (OR 1.29, CI 1.07, 1.55) and current smokers (OR 1.16, CI 1.02, 1.32). Patients less likely to receive PCI included women (OR 0.67, CI 0.60, 0.75), those with previous ACS hospitalization (OR 0.69, CI 0.59, 0.80), those prescribed: statins 12 months pre-hospitalization date (OR 0.75, CI 0.67, 0.85), diuretics (OR 0.72, CI 0.61, 0.85), ACE inhibitors (OR 0.84, CI 0.75, 0.95), proton pump inhibitors (OR 0.86, CI 0.77, 0.96), those previously diagnosed with congestive heart disease (OR 0.54, CI 0.42, 0.71), atrial fibrillation (OR 0.67, CI 0.54, 0.83), stroke/TIA (OR 0.77, CI 0.63, 0.93) or renal disease (OR 0.82, CI 0.71, 0.95). Age and BMI were significant as continuous variables with non-linear effects. **CONCLUSIONS:** This is the first large-scale UK study using real-world data to assess socio-demographic and clinical predictors for PCI in ACS, and indicates that NSTE-ACS patients and those with comorbidities are more likely to be MM. This will be discussed in light of current treatment of STEMI and NSTE-ACS in the EU.

PCV160

THE PHARMACOECONOMIC OF CARDIOLOGY IN RUSSIA

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OBJECTIVES: To analyze the current state and the trends of pharmacoeconomic research in cardiology in Russia. **METHODS:** We have reviewed all main databases of scientific publications (PubMed, eLibrary.ru etc.) as well as individual journals, conference abstracts and web-sites for the period 2007–2013. **RESULTS:** It was found that cardiology becomes one of the most popular topics for pharmacoeconomists, partly because of its significance for public health and the growing amount of state funding for the prevention of CVD in recent years. Cardiovascular problems make up 16-25% of congress abstracts and 26% of applications for Da.Signa, the only award in pharmacoeconomics in Russia. Most publications in our analysis dealt with arterial hypertension (44%), coronary heart disease (16%) and chronic heart failure (7%). A wide range of original and generic drugs were included into these researches, however in most cases there was a prevalence of cost-efficiency analysis and modeling methods based on the results of non-Russian clinical trials and meta-analyses. Overwhelming majority of the results were published in Russian and therefore are not available for the non-Russian-speaking reader. **CONCLUSIONS:** During the last five years, a great number of pharmacoeconomic research in cardiology have been performed and published. However, there is a need of clinical trials that would consider the Russian specifics and health care standards. Pharmacoeconomic analysis should become an integral part of clinical trials, especially in case of drug therapy of myocardial infarction, stroke and other conditions, where the differences exist between the Russian and foreign practice. Some of the analyzed publications should be updated because of the recent changes in health care standards.

PCV161

THE VOLUME-OUTCOME RELATIONSHIP AND MINIMUM VOLUME STANDARDS – EMPIRICAL EVIDENCE FOR GERMANY

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OBJECTIVES: To analyze the volume-outcome relationship for patients with intact abdominal aortic aneurysm (AAA) and hip fracture (HIP) and define hypothetical minimum volume standards to assess changes in access. **METHODS:** The analysis is based on administrative data coming from the German system of diagnosis related groups of about 18.6 million hospital cases of 1780 German hospitals for the year 2007. The data includes detailed information on patient characteristics used for

risk-adjustment. Furthermore, we have a ZIP-code for each patient and the exact address for every hospital. Addresses of hospitals and the centroids of all German ZIP codes were geo-coded. For the empirical analysis, we use multiple logistic regression analysis. We supplement our analysis by showing changes in access to hospitals if a minimum volume standard is introduced. **RESULTS:** Patients with hip fracture who are treated in hospitals with less than 58 cases per year have an average probability of death of 5.1 % compared to an average mortality of 3.1 % for patients who are treated in hospitals with more than 151 cases. For patients with AAA the case volume effect is lower. However, compared to patients treated in hospitals with less than 15 cases per year, the average probability of death for patients treated in hospitals with more than 68 cases is 1.0 percentage points less. We show that minimum volume standards seem possible without compromising overall access. **CONCLUSIONS:** The estimation results suggest that around 380 deaths could have been presumably avoided, if around 20,000 patients in the smallest hospitals would have been treated in the largest hospitals instead. Furthermore, we show that minimum volume standards do not compromise overall access measured in travel times. However, to ensure an adequate access in all areas, a few "sole providers" in some regions seem necessary.

PCV162

THE SHORT-TERM IMPACT OF PARTICULATE MATTER EXPOSURE ON THE RISK OF PRESCRIPTION OF CARDIORESPIRATORY DRUGS IN ITALY

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OBJECTIVES: Drug prescriptions recorded in health care administrative databases (HADs) can be an indicator of moderate health outcomes (undetectable through hospitalization or death registries) correlated to particulate matter (PM) exposure. This study is aimed at assessing the short-term effect of PM_{10} exposure on the risk of cardiorespiratory drug prescription in Lombardy, a region in northern Italy. **METHODS:** For each resident in seven cities of Lombardy, we identified all prescriptions of selected respiratory, cardiovascular and antidiabetic treatments recorded during 2005-2006 in data warehouse DENALI, which gathers HADs of Lombardy health system. The Regional Environmental Protection Agency of Lombardy provided time-series of daily mean PM_{10} concentration. We applied a time-stratified case-crossover design matched by day of week and fitted separate Cox proportional hazard models for each respiratory and cardiovascular treatment. Confounding was accounted for using a method, which we developed, based on the time-series of prescription of antidiabetics. Analyses were replicated for delayed effects of PM up to 6 days and for warm and cold season. **RESULTS:** The study area counted 470,300 residents, requiring 655,805 prescriptions. Mean PM_{10} concentration was 48µg/m^3 (SD 32µg/m^3). Overall, we estimated that rises in PM_{10} concentration were associated with an immediate increment in the risk of prescription of inhalant adrenergics (0.32% for increments of 10µg/m^3 in PM_{10} concentration; 95%CI:0.00,0.65), antiarrhythmics (0.52%; 95%CI:0.16,0.87) and nitrates (0.51%; 95%CI:0.27,0.76). Increased PM_{10} exposure was also positively associated with the prescription of inhalant glucocorticoids during the warm season and of inhalant adrenergics, antiarrhythmics and nitrates during the cold season. **CONCLUSIONS:** The significant association that we detected between PM concentration and drug prescriptions suggests that PM exposure may impact public health not only through severe but also through moderate adverse events. Further investigation is needed and given the usual difficulty retrieving information on moderate outcomes, HADs represent a valuable data source.

PCV163

HYPERCHOLESTEROLEMIA'S BURDEN OF DISEASE IN PORTUGAL

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OBJECTIVES: To estimate the impact of hypercholesterolemia (HYP) on population health in Portugal. **METHODS:** We estimate the Disability Adjusted Life-Years (DALY) attributable to HYP in 2010. The DALY include both years lost to premature death and years lost to disability. HYP is a risk factor for Acute Myocardial Infarction (ICD 9 410), other Coronary Heart Diseases (ICD 9 411-414) and for Ischemic Stroke (ICD 9 433-434). In order to estimate the attributable fractions to HYP of the diseases considered a microsimulation approach was used by using Framingham equations on data from individual observations in the VALSIM database. A total cholesterol equal to the mean for observations above 200 mg/dL was imputed to all individuals under statin treatment. In a counterfactual scenario HYP was eliminated (reducing total cholesterol to 200 mg/dL and increasing HDL to 40 mg/dL in all cases with HYP). The resulting proportional change in the probability of events was taken as the HYP attributable fraction of the diseases studied. **RESULTS:** In Portugal the prevalence of HYP in 2010 was estimated at 55,5% of the population over 18 (56,7% male and 54,5% female). In 2010 there were 1689 deaths attributable to HYP. This number can be broken down by gender (640 males and 1050 females) or by disease (481 from Acute Myocardial Infarction, 235 from other ischemic heart disease and 974 from ischemic stroke). DALY for premature death were estimated at 7263, and DALY for disability at 8239. Of the total 15502 DALY attributable to HYP 6132 were for ischemic stroke and 9369 for coronary disease. Gender decomposition of this total was 8012 for males and 7489 for females. **CONCLUSIONS:** The analysis suggests that HYP is an important cause of disease burden in Portugal and that it should remain a major target for health policy interventions.

PCV164

UTILIZATION OF ROUTINE DATA FOR REGIONALIZED EPIDEMIOLOGY IN AUSTRIA - THE EXAMPLE OF ISCHEMIC HEART DISEASE (ICD9 410-414)

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OBJECTIVES: Monitoring the performance of the health care system requires timely and robust information highlighting the burden of disease on a regional level. The development of the performance measures over time may be attributed to changes in organization and management of the system. **METHODS:** As routine data the ATHIS 2006/2007 (a standardized health interview survey), the cause of death registry 2006 and 2007, the hospital discharge datasets from the Austrian DRG system 2006/2007 (KDok/DLD) and diagnoses for the outpatient sector derived from pharmaceutical claims data 2006/2007 (ATC→ICD) - are used to describe the burden of disease regarding Ischemic Heart Disease (ICD9 410–414) with different regional granularity. Methods and results are compared with epidemiological data extracted from a literature search on this topic. To explore the similarity of the results of these different methods of measurement a systematic review of regional correlation is being elaborated. Correlations pointing to a high analogy of the findings in spite of the differences in dimensions measured on the one hand and contra intuitive correlations on the other hand were further explored. **RESULTS:** The review of regional correlation indicates promising close links between the burden of disease derived from ATC→ICD, ATHIS and cause of death registry data. Hospital discharge data, however, show some contra-intuitive relations towards the other data sets. **CONCLUSIONS:** The use of routine data yields promising opportunities for monitoring the Austrian health care system in a timely and comprehensible way. It enables different aggregation levels regarding regions and periods and leads the way to further research addressing underlying causes for the observed regional variation. The methodology can be transferred to other areas of diseases.

PCV165

ASSESSING THE IMPACT OF ORGANIZED SCREENING FOR ABDOMINAL AORTA ANEURYSMS IN AUSTRIA – FOLLOWING EUNETHTA CORE INFORMATION

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OBJECTIVES: Abdominal Aorta Aneurysms (AAAs) refers to distension of the abdominal aorta. It is a common disease among 65+ year old people with increasing importance due to overageing of the population. Currently, AAAs in Austria are only incidentally detected and due to its asymptomatic course often overlooked therefore the impact of an organized screening program in Austria was evaluated. **METHODS:** An agent based simulation model for Austria's population was developed. Each agent represents a person which has an individual development of its aorta depending on age, sex, and smoking habits. Identification of risk factors and parameterization of the model was performed in the IFEDH project (FFG grant number 827347). The observed persons are 65 years old at simulation start and the observed time horizon is 20 years. The chosen screening strategy which is compared to current practice corresponds to the EUnetHTA scheme with an assumed 40% participation. **RESULTS:** Events like ruptures, deaths or treatment are recorded and accumulated over the whole simulation time. Additionally, because many figures of the model depend on probabilities, the point in time when patients benefit from the intervention with 95% probability is calculated. Ruptures are reduced from 786 to 531, death cases from 571 to 433 whereas the costs per life year gained are about 7500 €. Significant differences can be observed after about four years. Although incidence is much higher among men, it is remarkable that screening is more cost-effective for women due to higher risk of rupture and life expectancy. **CONCLUSIONS:** The agent based simulation model allows detailed analysis of groups with specific properties, e.g. smokers, other age groups and different screening strategies. It also allows decision makers to estimate when the impact of the intervention, in this case organized screening, can be observed or measured within the real population.

PCV166

ADDED VALUE AND FUTURE ADOPTION OF A NEW MEDICAL IMAGING TECHNOLOGY FOR INTERVENTIONAL CARDIOLOGY

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OBJECTIVES: To estimate the potential added value of an ultrasound-fluoroscopy fusion technology and to support product development and marketing positioning of the technology in interventional cardiology, using a combination of research methods. **METHODS:** Stakeholder analysis was carried out to determine the professionals involved in the adoption process. Literature search indicated which procedures could benefit most from the imaging technology. Subsequently, the current workflow and associated resource use of those procedures was compared with the expected workflow after potential technology adoption. Decision criteria to adopt the new imaging technology were evaluated with the analytical hierarchy process (AHP). Finally, a value based pricing approach was used to estimate the value of the technology to specific types of hospitals. **RESULTS:** Intervention cardiologists were identified as key stakeholders in the adoption of technology. The AHP showed that reduction in complication rates is the most important criterion for adopting a new imaging technology, whereas the purchase price seemed less important. Various procedures could benefit from the new technology, as this may shorten procedural times and facilitate communication between intervention cardiologists and imaging professionals. Value based pricing analysis showed that cost savings could be expected as a result of reduced procedure times, especially in centers of expertise with medium to high procedure volumes. **CONCLUSIONS:** The ultrasound-fluoroscopy fusion technology can provide added value in specific cardiac interventions, especially in hospitals with medium to high procedure volumes. Early assessment of potential added value and adoption criteria timely and effectively supported the product development phase. It informed various decision makers on the factors influencing the expected value of and uncertainties surrounding a future adoption of the technology.

PCV167

DIVERGENCE OF HTA DECISIONS ACROSS COUNTRIES: CASE ANALYSIS OF IVABRADINE

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OBJECTIVES: In 2012, ivabradine was centrally approved by the EMA for Chronic Heart Failure treatment. Through ivabradine NICE and HAS decisions analysis, the objective of this policy research is to illustrate the divergence of HTA decisions despite a consistent efficacy, effectiveness and economics information. **METHODS:** NICE and HAS reports were fully reviewed with a focus on decisions outcomes. Then, convergences and divergences between HAS and NICE decisions were highlighted. **RESULTS:** NICE recommended for use ivabradine for patient with NYHA class II to IV with systolic dysfunction, with sinus rhythm with a heart rate ≥ 75 bpm, in combination with standard therapy or when beta-blocker therapy is contraindicated or not tolerated, and with a left ventricular ejection fraction ≤ 35%. Decision made by NICE was mainly based on results of one subgroup defined post hoc on the request of EMA. HAS rated the actual benefit of ivabradine as important for the labelled indication, nevertheless HAS distinguishes 2 subpopulations: one with minor improvement of actual benefit - patient with NYHA class II to III with systolic dysfunction in sinus rhythm with the heart rate ≥ 77 bpm and in which beta-blockers are contraindicated or not tolerated- for the other patients, HAS stated that ivabradine does not provide improvement in actual benefit. HAS based its decision mainly on the results of one subgroup defined a priori in which ivabradine was superior to each individual components of the primary combined endpoint. **CONCLUSIONS:** While EUnetHTA attempts to provide a coordinated opinion on comparative effectiveness, HTA decisions continue to be divergent across Europe. Ivabradine NICE and HAS decisions divergences exemplify once more the inconsistency of HTA decisions and highlight the obstacle for the establishment of a jointed EUHTA body.

PCV168

QUALITY IMPROVEMENT INITIATIVES FOR PATIENTS ON WARFARIN IN PRIMARY CARE

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OBJECTIVES: The primary objective of this study was to report the clinical outcomes, i.e. routine calculation of time in therapeutic range (TTR), bleed events and thromboembolic events for patients on warfarin in a general practice following the introduction of quality improvement initiatives. A secondary objective was to estimate the cost of care of these patients managed from the perspective of the general practice. **METHODS:** Clinical data were analysed annually using a General Practice database, adapted to allow calculation of TTR for all patients prescribed warfarin for the years 2009 (baseline), to 2011 (Year 2). Decision trees were constructed to reflect typical episodes of care for patients with atrial fibrillation (AF). Resource use and unit cost data were applied to each node in the decision tree. The probabilities of events occurring were derived from the literature and expert clinical opinion. A 60% TTR was used as a reference criterion for patient outcomes. Ethical approval for the study was obtained. Analysis was performed in SPSS®. **RESULTS:** The TTR at baseline was 54%, rising to 61% in Year 1 and 63% in Year 2. One patient suffered a haemorrhagic stroke in the baseline year (TTR 71%), and in the same year there were 4 thromboembolic events. No major haemorrhagic or thromboembolic events have been recorded in the follow-up years. The median cost per patient with AF was €276 (using a median of 12 INR tests per annum). **CONCLUSIONS:** The introduction of routine assessment of TTR in the practice has resulted in a significant improvement in care as demonstrated by the rise in TTR values, and adherence to international best-practice criteria. Clinically significant outcomes on patient care are also evident with the absence of major bleed events or thromboembolic breakthrough events. The study highlights the feasibility and benefits of enhanced care at local level.

MENTAL HEALTH – Clinical Outcomes Studies

PMH1

EFFICACY OF LONG-ACTING INJECTABLE ANTIPSYCHOTIC THERAPIES IN MAINTENANCE TREATMENT OF SCHIZOPHRENIA: A MIXED TREATMENT COMPARISON (MTC) OF DOUBLE-BLIND RANDOMIZED CLINICAL TRIALS

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OBJECTIVES: Treatment with antipsychotic medication is an important element of relapse prevention in the management of schizophrenia. However, approximately 50% of patients with schizophrenia miss taking >30% of their medication, therefore the use of long-acting injectable (LAI) formulations is an important option for patients partially or non-adherent to oral formulations. This study aimed to compare LAIs in terms of efficacy and safety. **METHODS:** A systematic literature review in PubMed, EMBASE, Cochrane, PsychINFO and conference abstracts was conducted to identify relevant randomized controlled trials of LAIs in maintenance treatment in schizophrenia. Selection criteria included long-term follow-up, stable patients and minimamilly one LAI treatment arm. The primary efficacy outcome was relapse rate; rate of discontinuation due to treatment-related adverse events (AEs) was also considered in this analysis. Data on discontinuation parameters were analyzed by applying a MTC competing risks model appropriate for multinomial distribution of data using WinBUGS. **RESULTS:** Six trials (study follow-up from 24 to 53 weeks) were identified, allowing comparisons of aripiprazole (oral and LAI), risperidone LAI, paliperidone LAI, olanzapine (oral and LAI), haloperidol LAI and placebo. The total patient number was 3402, of which 534 (16%) received aripiprazole. Compared to placebo the risk of relapse was the smallest for aripiprazole LAI (mean hazard ratio [HR]=0.26, 95% confidence interval [CI] 0.12-0.50) and risperidone LAI (HR=0.29, 95% 0.05-0.83). The risk of discontinuation due to AEs was lower than placebo for aripiprazole LAI (HR=0.72) and higher than placebo for the other LAIs (paliperidone LAI: HR=5.08, risperidone LAI: HR=12.06, olanzapine LAI: HR=6.58, haloperidol LAI: HR=4.19). **CONCLUSIONS:** The MTC suggests that aripiprazole LAI is at least as efficacious in the management of relapse prevention as other LAIs with an advantage over other LAIs in terms of discontinuation due to AEs. This study provides support for formulary decision-making in the absence of head-to-head data.

PMH2

RISK OF PSYCHIATRIC AND NEUROLOGICAL DISEASES IN PATIENTS WITH WORKSPACE MOBBING EXPERIENCE IN GERMANY: A RETROSPECTIVE DATABASE ANALYSIS

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OBJECTIVES: In recent years workplace mobbing attracts notice in public and science. Victims of workplace mobbing frequently suffer from depressions, somatic symptoms, may develop alcoholism or other substance abuse disorders and show increased risk of suicidal behavior. The aim of this study was to calculate the number of patients with a workspace mobbing documentation and their diagnosis profile in general practices in Germany between 2003 and 2012 based on the data from a large epidemiological database. **METHODS:** This retrospective study analysed longitudinal routine care data collected by general practitioners in Germany (IMS® Disease Analyzer). Data from patients with notice as workplace mobbing (N=2653) and without such notice (N=2653) from 199 general medical practices in Germany (Disease Analyzer database; 01/2003 to 12/2012) were matched for age (41 ± 13 years), gender (male: 33%), health insurance (private: 5%) and retrospectively analyzed. Odds Ratio (OR; Logistic regression) for depression, anxiety, somatoform disorder, migraine and sleep disorder (follow-up: 3 years) were calculated. **RESULTS:** In 2003, 24 (projected to national level: 2448) patients were documented as mobbing victims; this number continuously increased to 429 (projected to national level: 43758) in 2012. Shares of female patients and mean age have not significantly changed from 2003 till 2012. In workspace mobbing persons there was a increased risk of depression (OR: 4.11, p<0.001), anxiety (OR: 2.76, p<0.001), somatoform disorder (OR: 3.51, p<0.001), migraine (OR: 1.41, p=0.003) and sleep disorder (OR: 2.32, p<0.001). **CONCLUSIONS:** This retrospective database analysis showed that experience of workspace mobbing was associated with increased prevalence of psychiatric and neurological problems. Further research is required to understand this complex issue.

PMH3

POINTS TO CONSIDER IN MULTIREGIONAL TRIALS USING PHQ-9: A META-ANALYSIS ON PHQ-9

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OBJECTIVES: As the cultural adaptation process of PROs (Patient Reported Outcome instruments), every version of PROs should be validated. However, little is known whether those validated PROs are identical in terms of the test performance (operating characteristics). In this study, we investigated PHQ-9 (Patient Health Questionnaire-9 for depression) using the meta-analysis. **METHODS:** We searched PubMed for studies examining diagnostic accuracy of PHQ-9. Then we extracted or retrieved 2 x 2 data from each study and meta-analysis was performed using Bivariate model (Reitsma et al. 2005). As the language versions of PHQ-9 and regions where the studies were conducted would be potential confounding factors, we performed meta-regression. Bivariate meta-analysis of the subgroup (region, language) was explored. **RESULTS:** Twenty-eight studies met our inclusion criteria. Univariate meta-regression showed that all the covariates assessed such as language, region significantly contributed to the heterogeneity of sensitivity (I^2=82.7) and specificity (I^2=92.5) among the studies. Meta-analysis of subgroup of the regions and languages was made using bivariate model; studies conducted in North America (6 studies), Europe (13 studies), or Asia & others (9 studies); LogitSe of North America, Europe and Asia& other were 1.66, 1.45, and 1.48, respectively. Logit Sp of these regions was 1.87, 1.90 and 2.22, respectively. **CONCLUSIONS:** Results suggest that operational characteristics would influenced by the regions, language version of PHQ-9. Therefore, when considering a multiregional study using PHQ-9 as screening tool, there would be a chance of some imbalance among regions. Therefore, before initiation of the clinical studies, efforts need to minimize the heterogeneity of the definite diagnosis, e.g. training to the investigators, or central diagnosis.

PMH4

RESULTS FROM THE "AUTOR" STUDY, A EUROPEAN OBSERVATIONAL STUDY IN PEDIATRIC PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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OBJECTIVES: To investigate factors associated with changes in attention-deficit/hyperactivity disorder (ADHD) symptom severity and quality of life (QoL) in patients who were responders and stable on their pharmacotherapy at study entry. **METHODS:** "AUTOR" is a European prospective, observational study investigating factors associated with ADHD severity changes during a 2-year follow-up period in patients aged 6-17 years. At baseline, patients had received the same pharmacotherapy for 3-8 months and had a Clinical Global Impression (CGI)-ADHD-Severity score of mild or lower and a CGI-ADHD-improvement score of improved/very much improved since treatment initiation. Data were collected at naturally occurring visits coinciding with observation windows (postbaseline): 0, 3, 6, 9, 12, 18, and 24 months, and ±6 weeks. ADHD symptom severity worsening was defined as a ≥2-point increase from baseline in CGI-ADHD-Severity score. The Child Health Profile-Child Edition (CHIP-CE) was used to measure QoL. Multivariate logistic regression was used to assess the association of different factors with changes in ADHD severity at any time postbaseline. Mixed-model repeated measures (MMRM) regression was used to estimate adjusted differences between treatments. Propensity scoring was used to adjust for imbalanced covariates before treatment comparisons. **RESULTS:** Data were analyzed from 704 patients (mean [standard

deviation] age 10.7 [2.75] years, 99% Caucasian, 82% male, 76% combined ADHD subtype). Variables associated with worsening severity were: baseline parental occupation (P=.003), poorer school outcomes (P<.001), and use of psychoeducation (P=.004). Initial use of nonstimulants (vs. stimulants) was associated with significant improvement on the CHIP-CE total score at 3 months and 9-24 months postbaseline. The estimated adjusted difference between treatments was –6.0 (95% confidence interval: –7.9, –4.1) at 24 months postbaseline. **CONCLUSIONS:** In this observational study, worsening of ADHD symptoms was associated with initial use of psychoeducation, parental occupation, and poorer school outcomes. Initial treatment with nonstimulants (vs. stimulants) was associated with improved QoL.

PMH5

CLINICAL OUTCOMES IN SCHIZOPHRENIA TREATED WITH DONEPEZIL IN COMBINATION WITH ANTIPSYCHOTICS

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OBJECTIVES: To assess the efficacy of a cognitive enhancer, donepezil, as an adjuvant treatment to antipsychotics on clinical outcomes of schizophrenia. **METHODS:** Systematic review with meta-analysis to obtain appropriate evidence from randomized clinical trials (RCTs) on the efficacy of donepezil plus antipsychotics versus placebo plus antipsychotics in patients diagnosed with schizophrenia for the following outcomes: general psychopathology, positive/negative symptoms, and depressive symptoms. Effect size estimates corrected for small sample size trials (Hedges' g) were calculated for parallel trials and cross-over trials. Negative values for Hedges' g denote an effect favouring the combined treatment. When needed, values for the cross-over correlation were imputed from available individual data to obtain the Hedges' g estimates. The individual estimates were pooled with a random-effects meta-analysis. **RESULTS:** Seven trials (4 cross-over, 3 parallel) were included. Four trials provided data on the Positive and Negative Syndrome Scale (PANSS) for total and general psychopathology scores. Three trials provided data for PANSS positive scores and 5 trials provided data for PANSS negative scores. Three trials provided data on depression scores. The combined treatment did not show differences in any of the assessed outcomes: PANSS total scores (g = -0.57, 95% CI = -2.11 to 0.96, I^2 = 67%); PANSS General Psychopathology scores (g = -0.20, 95% CI = -0.74 to 0.34, I^2 = 0%); PANSS positive symptoms (g = -0.06, 95% CI = -0.73 to 0.60, I^2 = 0%); PANSS negative symptoms (g = -0.43, 95% CI = -1.98 to 1.12, I^2 = 86%); depression scores (g = -0.35, 95% CI = -1.20 to 0.49, I^2 = 0%). **CONCLUSIONS:** The combination of donepezil with antipsychotic treatment does not improve clinical outcomes in schizophrenia.

PMH6

RESPONDER ANALYSIS OF FUNCTIONAL HEALTH AND WELL-BEING IN MDD: A POOLED ANALYSIS OF SF-36 RESULTS FROM THREE PHASE III TRIALS WITH LEVOMILNACIPRAN SR

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OBJECTIVES: Levomilnacipran (1S,2R-milnacipran) is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI) with approximately 2-fold greater potency for reuptake inhibition of norepinephrine than serotonin. Levomilnacipran SR is in late-stage clinical development for the treatment of major depressive disorder (MDD) in adults. A pooled analysis of Phase III studies was conducted to evaluate the effects of levomilnacipran SR treatment on functional health and well-being. **METHODS:** Pooled analysis of three double-blind, placebo-controlled, Phase III randomized clinical trials (Clinicaltrials.gov #NCT00969709, NCT00969150, NCT01034462), which included one fixed-dose (levomilnacipran SR 40, 80 or 120 mg/day or placebo) and two flexible-dose (levomilnacipran SR 40-120 mg/day or placebo) studies that included the acute version of the SF-36v2 health survey. Percentage of responders following 8-weeks of treatment (observed cases) with levomilnacipran SR or placebo were compared for each individual health domain and the Physical (PCS) and Mental (MCS) Component Summary scores based on individual patient-level responder criteria for minimally important differences. Estimates of odds ratios, 95% confidence intervals and p-values were from a logistic regression model with study and treatment as factors, baseline score as covariate and a study-by-treatment interaction term. **RESULTS:** Compared with placebo-treated patients, a greater percentage of patients who were treated with levomilnacipran SR were considered as responders. Homogeneity of OR could be assumed for the individual health domains and component summary scores except for the Bodily Pain scale (study-by-treatment interaction p-value=0.0123). Pooled OR [95%-CI] for being a responder were as follows: MCS=1.705 [1.292-2.250]; PCS=1.285 [0.972-1.700]; General Health=2.324 [1.763-3.064]; Social Functioning=1.698 [1.295-2.226]; Vitality=1.608 [1.250-2.068]; Mental Health=1.579 [1.203-2.072]; Role-Emotional=1.453 [1.121-1.882]; Physical Functioning=1.382 [1.032-1.850]; and Role-Physical=1.341 [1.005-1.788]. All OR (except PCS) were statistically significant (p<0.05). **CONCLUSIONS:** Compared with placebo, patients who are treated with levomilnacipran SR are more likely to achieve meaningful improvement in multiple domains of health as measured by the SF-36 Health Survey.

PMH7

DO POLICY MEASURES IMPACT ON COST CONSCIOUSNESS OF HEALTH CARE PROFESSIONALS?

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OBJECTIVES: To assess health care professional's judgments on economic consequences of prescribed medical interventions and their responsiveness of different health care policy measures aiming for increasing their cost-consciousness. **METHODS:** The design encompassed the nation-wide-cross-sectional hierarchical levels of health care facilities across the geographical regions. Authors used validated and standardized Likert scale of Health Economic Awareness (HEA) adjusted for local setting to evaluate health care professionals by face-to-face interviews. The questionnaire comprehended clinician'sattitudes on: Clinical-Decision-Making-Alternative-Interventions (CDMAI); Quality-of –Health-care (QHC); and Cost-Containment-Policy (CCP). This survey was conducted in two waves before and after policy intervention in 40 hospitals and primary care facilities in fifteen cities in Serbia from January 2010-December 2012. A total of 649 participants were interviewed before the intervention and 651 after the intervention. Core Republican Health Insurance Fund adopted and disseminated the package of cost containment measures through the Nation-wide pharmacoeconomic guidelines which principally targeted at prescribers. Pharmacists, physicians and dentists were examined by the scores of CDMAI, QHC, CCP and HEA. **RESULTS:** Pharmacists and dentists had a higher average score (mean±s.d.) of CDMAI by the pharmacists (1.200±0.421) and the dentists (1.195±0.560) than the score of physicians (1.017±0.453). Dentists had the highest average score of CCP (2.127±0.598) and then the score of physicians (1.976±0.529). The score of pharmacists was the lowest (1.854±0.461).There were no impacts of the interventions on the professional behaviors regarding the scores of QHQ, CDMAI, CCP, and HEA. **CONCLUSIONS:** Health economic awareness has differed substantially among of different health care professionals. Health policy measures were implemented to reduce non-cost-effective prescribing behaviors but the effects are non-clear-cut evidences. This experimental study is a pioneering effort in the wider Balkans region.

PMH8

EFFICACY AND SAFETY OF AGOMELATINE IN DEPRESSED THAI PATIENTS INCLUDING THE ELDERLY DEPRESSED POPULATION

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OBJECTIVES: To assess the efficacy and safety of agomelatine using pharmacovigilance during 12-week follow-up. **METHODS:** Agomelatine 25-50 mg was prescribed open label to patients with depressive disorders diagnosed by psychiatrists based on DSM-IV/ICD-10 criteria. Treatment options were intent-to-treat. All 480 patients, including 97 elderly patients were followed up at week 2 if dose titration was necessary. Efficacy was assessed using Montgomery-Äsberg Depression Rating Scale(MÄDRS) and clinical global impression of improvement (CGI-I) and of severity (CGI-S) scales, at weeks 2, 6, and 12. Data on adverse effects and for reports were gathered through patient interviews. **RESULTS:** Of 480 patients, 20-86 years (mean[SD] 49.6[14.5]), 247(51.5%) were men and 97(20.2%) were elderly (65 to 86; mean[SD] 71.1[5.0]). Among all patients, 225(46.9%) and 255(53.1%) were depressed with a single episode and recurrent episodes. Patients with recurrent episodes were taking various classes of antidepressants, including selective serotonin reuptake inhibitors in 328(50.9%) patients. Generalized anxiety disorder was a concurrent diagnosis in 95(24.3%) of patients. The respective mean(SD) baseline CGI-S, CGI-I, and MADRS scores of 3.90(0.68), 4.15(0.76), and 22.59(3.77) were reduced to 2.1(0.31), 1.11(0.37), and 9.19(2.03), with respective reductions in mean(SD; 95% CI) scores of 1.78(0.75;1.72-1.85), 2.98(0.78;2.91-3.05), and 13.39(4.36; 13.00-13.78). Similar efficacy was evidenced for elderly depressed patients (N=97), in whom mean(SD) MADRS score at baseline 22.37(4.79) was consistently significantly reduced to 14.61(3.04), 10.76(3.04), and 8.72(1.91) at weeks 2, 6, and 12, respectively. After 12 weeks, overall remission (MADRS score <10) was seen in 68.4% of patients with moderate to severe (MADRS >25) depression and in 73.4% of elderly depressed patients. The mild adverse events reported were dizziness(9.5%), headache(7.4%), difficulty sleeping(6.3%), and nausea(3.1%). There were no cases reported of alanine transaminase levels three times above upper limit of normal. **CONCLUSIONS:** Agomelatine has proven to be a safe and effective new antidepressant in intent-to-treat analysis of depressed, including elderly, patients in daily clinical practice in Thailand.

PMH9

COMPARATIVE EFFICACY AND METABOLIC SIDE EFFECTS OF LURASIDONE FOR THE MANAGEMENT OF ACUTE SCHIZOPHRENIA: A SYSTEMATIC LITERATURE REVIEW AND MIXED TREATMENT COMPARISON WITH FIRST AND SECOND GENERATION ANTIPSYCHOTICS

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OBJECTIVES: Second generation antipsychotics (SGA) are associated with increased risk of metabolic side effects. A systematic literature review and mixed treatment comparisons (MTC) were performed to assess the efficacy and the metabolic side effects of antipsychotics, and more especially to compare lurasidone to other widely used antipsychotics in patient with acute schizophrenia. **METHODS:** This review included short-term (≤12 weeks) randomised controlled trials (RCTs) in patients with an acute phase of schizophrenia. The literature search was based on the NICE guidelines on treatment for schizophrenia published in 2010. A systematic search in the most comprehensive medical databases of peer-reviewed articles (MEDLINE, EMBASE, CENTRAL) was conducted until June 2012 to update the evidence. In addition to lurasidone, eight comparators were considered: amisulpride, aripiprazole, haloperidol, olanzapine, quetiapine, risperidone, ziprasidone and placebo. A Bayesian ramdom effect MTC was performed on efficacy outcomes (PANSS total score and CGI-S score) and metabolic side effects (weight, triglycerides, total cholesterol level and fasting glucose level). **RESULTS:** Thirty-nine RCTs involving 12,721 patients were included. Results showed that lurasidone had similar efficacy

to others antipsychotics in terms of PANSS total score and CGI-S score and a similar effect as compared to placebo on all metabolic outcomes. The probability to have a lower impact than aripiprazole on weight increase and fasting glucose level was respectively 75.5% and 65.9%. Probabilities to have a lower impact on cholesterol level and triglycerides compared to olanzapine, quetiapine or riperidone varied from 98% to 100%. **CONCLUSIONS:** Efficacy has been demonstrated for all reviewed treatments vs. placebo, with a similar effect. Lurasidone had a similar effect as compared to placebo and a less negative impact than olanzapine, quetiapine and risperidone on weight increase, triglycerides, total cholesterol level and than olanzapine on fasting glucose level.

PMH10

RELATIVE EFFICACY AND ACCEPTABILITY OF VORTIOXETINE VERSUS MARKETED ANTIDEPRESSANTS

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OBJECTIVES: Vortioxetine (Lu AA21004) is an investigative multimodal antidepressant which demonstrated efficacy, safety and tolerability in Major Depressive Episode (MDE). The comparison of vortioxetine to marketed antidepressants guides decison makers and clinicians in their choice of treatment. The main study objective was to generate comparative evidence for the efficacy and acceptability of vortioxetine in MDE. **METHODS:** Indirect comparisons were performed by meta-regression analysis, an extension of classical random-effect meta-analyses, to compare vortioxetine to agomelatine, escitalopram, duloxetine, sertraline, venlafaxine IR/XR and vilazodone. To ensure comparability between studies, in terms of selection of patient population and exposure to treatment, only investigational drug and placebo arms from pre-registration placebo-controlled studies were included in the base case analyses. The main outcomes were efficacy, measured as the standardized mean difference between active treatment and placebo control in the change from baseline to 2 months of the primary endpoint (MADRS or HAM-D total score), and acceptability (the withdrawal rate due to adverse events) and expressed as the logarithm of the odds ratio (OR) between active treatment and placebo. Sensitivity analyses were performed with the inclusion of post-marketing authorization studies, adjustment for age/gender and on response and remission. **RESULTS:** For efficacy, treatment effect estimates and p-values for vortioxetine versus comparators were: -0.16(0.11) versus agomelatine (negative effect favours vortioxetine); 0.09(0.42) versus duloxetine; -0.05(0.70) versus escitalopram; -0.04(0.83) versus sertraline; 0.12(0.33) versus venlafaxine IR/XR and -0.24(0.11) versus vilazodone. For acceptability, all but one OR (<1) favoured vortioxetine: 1.77(0.03) versus agomelatine; 0.75(0.26) versus duloxetine; 0.67(0.28) versus escitalopram; 0.30(0.01) versus sertraline; 0.47(0.01) versus venlafaxine and 0.64(0.18) versus vilazodone. Meta-regression adjusted for age and gender demonstrated the robustness of the estimated differences between treatments, as did sensitivity analyses including post-marketing trials. **CONCLUSIONS:** Vortioxetine is a promising intervention with efficacy comparable to marketed antidepressants in MDE and a favourable acceptability profile.

PMH11

DRUG TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN AUSTRIA

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OBJECTIVES: The therapy of Attention Deficit/Hyperactivity Disorder (ADHD) with methylphenidate or atomoxetine, formerly only related to children and adolescents, is now extended to the adult population. Little is known about treatment patterns in Austria. The aim of this study was to evaluate the medication patterns of ADHD in 2012 in Austria, stratified by age and sex. **METHODS:** The data analysis refers to the accounting data of the 13 major Austrian health insurance funds, covering more than 97% of the Austrian population. Provided in a pseudonymised manner, with availability of the individual patient parameters age and sex, all dispensed medication of methylphenidate or atomoxetine is included in the descriptive analysis. The prevalence of ADHD medication is evaluated regarding age and sex. Furthermore the prescribed daily dose in relation to the defined daily dose is pointed out. **RESULTS:** A total of 9120 patients with ADHD medication in 2012 are included in the analysis (22% female). One per cent of all patients with ADHD medication is in the age cohort of under 6 years, 47% are between 6 and 13, 22% are between 14 and 17, and 30% are adults (18+). The relation between the defined daily dose (ddd) to the prescribed daily dose (pdd) shows that 86% of children and adolescents have less than 366 pdd in the whole year and only 1% has more than 732 pdd. 81% of the adults have less than 366 pdd and 6% have more than 732 pdd. **CONCLUSIONS:** While the variety of prescribed daily dose per patient is homogeneous during childhood and adolescence, this parameter spreads widely in adults. This could be an indicator of overuse or misuse. As the results reflect the prescription reality they can be used as a solid basis for further discussions, future evaluations and interventions about ADHD medication in Austria.

PMH12

TREATMENT DISPARITY AMONG PATIENTS DIAGNOSED WITH DEPRESSIVE DISORDER IN WORKING POPULATION BASED ON CLAIMS DATABASE IN JAPAN

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OBJECTIVES: Treatment disparity by gender and age among patients with depressive disorder in working population has not been examined in Japan. This study examined treatment disparity by gender and age among patients newly diagnosed with depressive disorder based on the claims database of health insurance societies between 2008 and 2011 in Japan. **METHODS:** Retrospective cohort database (N=600,000) was followed up for four years to identify patients (18 ≤ age ≤ 65) with newly diagnosed depressive disorder. The patients were followed up for one year after the index date (the first date of diagnosis). Psychotropic drugs used to treat depressive disorder included first- and/or second-generation antidepressant, benzodiazepine, sulpiride, and antipsychotics. The treatment duration and time to treatment by gender and age were evaluated by Cox regression model. **RESULTS:** A total of 5,464 patients (men: 3,483, mean age: 36.1±9.9) with depressive disorder was identified. Median treatment duration was 123 days (men: 150 days, women 92 days). 90.1% of patients was prescribed at least one psychotropic drug within 30 days from the first date of diagnosis (84.5% in women and 93.1% in men). The proportion of patients who were prescribed at least one psychotropic drug for the first time after 6 months from the index date was 5.6% (men: 3.8%, women: 9.1%). The result showed that older patients were more likely to be treated longer period. In addition, men tend to be prescribed at least one psychotropic drug in a shorter period of time from the index date compared to that in women. **CONCLUSIONS:** This study suggested the trend of treatment disparity between men and women as well as age in working population with regard to treatment duration and time to prescription. Further study is needed for generalizability.

PMH13

THE BURDEN OF TREATMENT CHANGE IN MAJOR DEPRESSIVE DISORDER: COMPARISON OF SWITCH VERSUS NON-SWITCH PATIENTS IN THE PERFORM STUDY

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OBJECTIVES: PERFORM (Prospective Epidemiological Research on Functioning Outcomes Related to Major depressive disorder) is a 2-year prospective observational cohort study conducted in Europe (France, Germany, Spain, Sweden and UK). Objectives are to describe the functioning of patients with major depressive disorder (MDD) and factors associated with functional impairment. Here we compare characteristics and outcomes of patients switching antidepressant treatment (ADT) with those initiating ADT at baseline, on an interim 1000-patient dataset. **METHODS:** Outpatients were recruited from primary or secondary care. Inclusion criteria were: DSM-IV-TR diagnosis of MDD, age 18-65 years, initiation or first switch to an ADT, in monotherapy. In addition to socio-demographics and disease history, data collection included clinician assessments (MADRS and CGI-S) and patient-rated scales evaluating depression (PHQ-9), functioning (SDS), work productivity (WPAI-SHP) and quality of life (QoL - EQ-5D). **RESULTS:** Of 947 analysable patients at inclusion, 213 (23%) patients were switching (76% for lack of efficacy), *versus* 716 (77%) initiating ADT. Switchers were slightly older (mean age 46 *versus* 43 years) and more often female (77% *vs.* 72% women). Switching patients had more severe symptom profiles: more had previous depressive episodes (34% *vs.* 24%) and previous suicide attempts (16% *vs.* 12%). Severity of current episode was greater for switchers (46% *vs.* 36% with a CGI-S score above "markedly ill"; 48% *versus* 38% with a PHQ-9 score above the severe depression threshold). MADRS scores were similar: 18.1 *versus* 17.6. QoL was poorer for switchers (EQ-5D: 0.449 *vs.* 0.567), as was overall patient functioning (47% *vs.* 36% with an SDS total score in the highest quartile), while no difference was found for absenteeism (35% *vs.* 34%) and presenteeism (49% vs. 50%) (WPAI-SHP). **CONCLUSIONS:** Patients switching ADT had more severe symptom profiles, lower quality of life and higher functional impairment, compared to non-switching patients.

PMH14

PATIENT-REPORTED COGNITIVE DYSFUNCTION NEGATIVELY IMPACTS FUNCTIONING IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER – PRELIMINARY FINDINGS FROM THE PERFORM STUDY

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OBJECTIVES: PERFORM (Prospective Epidemiological Research on Functioning Outcomes Related to Major depressive disorder) is a 2-year prospective observational cohort study conducted in Europe to describe the functioning of patients with major depressive disorder (MDD) and factors associated with functional impairment. Here we report the impact of patient-reported cognitive dysfunction (PRCD) on quality of life (QoL), work and overall functioning at baseline, on a preliminary 1000-patient dataset. **METHODS:** Outpatients were recruited from primary or secondary care. Inclusion criteria were: DSM-IV-TR diagnosis of MDD, 18-65 years old, initiation or first switch to an antidepressant, in monotherapy. Functioning was assessed by the SDS (Sheehan Disability Scale), work productivity by the WPAI-SHP (Work Productivity and Activity Impairment Questionnaire) and QoL by the EQ-5D (EuroQol-5 Dimensions) and SF-12 (12-Item Short-Form Health Survey). PRCD was assessed by the Perceived Deficit Questionnaire 5-item (PDQ-5). Descriptive analyses stratified on PDQ-5 quartiles were complemented with ANCOVA adjusted for severity of depression. **RESULTS:** At inclusion, over 947 analysable patients, mean PDQ-5 score (ranging from 0 to 20) was 11.5 (SD=4.4). PRCD was associated with impairment of overall functioning, QoL and productivity. SDS total scores were 14.4, 18.5, 20.2, and 23.6 (first to fourth PDQ-5 quartiles, respectively) (p<0.001). Similar patterns were observed for WPAI-SHP presenteeism scores (impairment while working: from 36.9% in first quartile to 64.4% in fourth quartile, p<0.001; overall work impairment: from 41.5% to 71.3%, p<0.001). These associations remained statistically significant after adjustment for baseline depression severity in multivariate analyses. A negative impact of PRCD was also observed on sick-leave length and on QoL. **CONCLUSIONS:** At inclusion, subjective cognitive dysfunction in depressed patients was associated with poorer functioning, work productivity and QoL. This is in addition to any negative impact of the

severity of depression on these outcomes. These preliminary results need to be confirmed on the full dataset.

PMH15

FACTORS ASSOCIATED WITH EARLY RESPONSE TO OLANZAPINE AND CLINICAL AND FUNCTIONAL OUTCOMES OF EARLY RESPONDERS TREATED FOR SCHIZOPHRENIA IN CHINA

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OBJECTIVES: To identify factors associated with early response at 4 weeks of treatment with olanzapine and to assess whether early response is associated with better longer-term outcomes for patients with schizophrenia in China. **METHODS:** A post-hoc analysis was conducted using data from the Chinese schizophrenia subgroup (n=330) of a multicountry, 6-month, prospective, observational study of outpatients with schizophrenia/bipolar mania who were initiated or switched to oral olanzapine. Stepwise logistic regression controlling for baseline clinical characteristics, participation in weight education program at baseline, and compliance with antipsychotics over first 4 weeks of olanzapine treatment was used to identify factors associated with early response. Mixed Models Repeated Measures with baseline covariates were used to compare outcomes over time between early responders and early non-responders to olanzapine. **RESULTS:** A total of 130 patients (40%) achieved early response. The models revealed that significant factors associated with a higher likelihood of achieving early response were higher CGI-Sevirity score (OR=1.51, 95% CI: 1.15-1.97), fewer years since first diagnosis (OR=0.94, 95% CI: 0.90-0.98), a greater number of social interactions (OR=1.22, 95% CI: 1.05-1.40), participation in a weight education program (OR=1.81, 95% CI: 1.04-3.15) at study entry, and high medication compliance with antipsychotics during the first 4 weeks of treatment (OR=2.98, 95% CI: 1.59-5.58). When compared to early non-responders, early responders achieved a significantly higher endpoint response and significantly greater symptom improvement at end point (CGI-Severity) and a greater improvement in level of functional outcomes (all $p<0.05$). **CONCLUSIONS:** High levels of compliance to prescribed antipsychotic and participation in a weight education program were associated with early response in schizophrenia patients in China. Early response was associated with greater improvement in symptomatic, functional and quality-of-life outcomes at 6 months compared to early non-response. Current findings are consistent with previous research outside of China.

PMH16

FACTORS ASSOCIATED WITH PAIN PERSISTENCE IN PATIENT WITH DEPRESSION DURING A 3 –MONTH FOLLOW-UP PERIOD

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OBJECTIVES: Patients with major depressive disorder (MDD) frequently suffer from concomitant pain symptoms, which are associated with higher depression severity and worse quality of life. We describe the baseline factors associated with pain persistence in patients with MDD during a 3-month follow-up period. **METHODS:** Patients from Asia (n=909) presenting with a new or first episode of MDD were enrolled in a 3-month prospective observational study. This report analyzes the 709 (78%) patients assessed at baseline and 3 months. Demographics, depressive symptoms (Hamilton Depression Scale), overall severity (Clinical Global Impression Severity score), somatic symptoms (Somatic Symptom Inventory) and quality of life (Euro QOL -5D) were assessed. Logistic regression models were fitted to assess the relationship between baseline factors and pain persistence during follow-up. **RESULTS:** Of the 709 patients analyzed , 349 (49%) had pain at baseline. Forty three per cent of the patients (151) having pain at baseline still presented with pain at 3-months. Patients with persistent pain had more frequently suffered from previous MDD episodes (54% vs 39%) , were less likely to be older than 60 (11 vs. 21%), and had a higher number of medical comorbid conditions (14% vs 5% with two or more co-morbidities). The logistic model adjusting for other baseline covariates confirmed these results. **CONCLUSIONS:** A high proportion of patients with depression who presented with pain at baseline still suffered from pain symptoms at 3 months. A history of depression and the presence of other medical conditions were risk factors for pain persistence at 3-months.

PMH17

BAYESIAN ANALYSIS OF MALFORMATION OUTCOME IN SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI) USE DURING PREGNANCY: AN INDIRECT COMPARISON OF CITALOPRAM, FLUOXETINE, PAROXETINE, AND SERTRALINE

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OBJECTIVES: Assessing the safety of selective serotonin reuptake inhibitor (SSRI) use during pregnancy is complicated, especially given the array of treatment option. The objective of this study was to evaluate the risks of fetal malformation of SSRI use during pregnancy. **METHODS:** A search for prospective studies evaluating fetal malformation with maternal use of citalopram, fluoxetine, paroxetine, or sertraline was conducted using the databases of MEDLINE, PsycINFO and EMBASE for the period of 1974 to March 21, 2013. The key terms used were: 'serotonin reuptake inhibitors', 'pregnancy', 'prospective studies'. The inclusion criteria in addition to prospective studies included: 1) malformation outcome; 2) citalopram, fluoxetine, paroxetine, and/or sertraline; 3) drug exposure in first trimester; and 4) compared to control group of either 'no SSRI exposure' or 'nonteratogenic agents'. The exclusion criteria included: 1) evaluation of SSRI as a drug class, and 2) venlafaxine or bupropion. A Bayesian random-effects indirect treatment comparison model was used to perform the analysis. **RESULTS:** The search resulted in 64 articles. Eight articles met inclusion/exclusion criteria. The combined odds ratio was 1.72 (95% CI: 1.432 to 2.070), indicating the odds of fetal malformation is higher among women taking antidepressants than those not receiving SSRIs. In the pairwise analysis, 2 of the 14 pairwise comparisons were statistically significant: fluoxetine compared to control (OR 1.774, 95% CI 1.008 to 2.925); paroxetine compared to control (OR 1.752, 95% CI 1.057 to 2.953). The resulting pairwise odds ratios suggested a lowest odds of malformation to highest odds was citalopram, sertraline, paroxetine, fluoxetine. **CONCLUSIONS:** The risk of malformation is an important consideration when treating pregnant women. This study suggests that there is an increase in the odds of fetal malformation when exposed to SSRIs in utero during the period of organogenesis. The risk appears to be highest with fluoxetine and paroxetine, and lower for citalopram.

MENTAL HEALTH – Cost Studies

PMH18

BUDGET IMPACT OF PALIPERIDONE PALMITATE IN AUSTRIA

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OBJECTIVES: The costs of schizophrenia in Austria are high and new long acting injectable (LAI) antipsychotics might be able to reduce costs due to a reduction of hospital stays. We aim to estimate budget effects of the introduction of a new LAI (Paliperidone Palmitate) in Austria. **METHODS:** A budget impact analysis was conducted that took direct costs of illness into account (i.e. costs for inpatient and outpatient services and drug costs). We used official Austrian remuneration prices as input parameters. The robustness of the model was checked by means of deterministic sensitivity analyses with regard to switch rates to Paliperidone Palmitate and rehospitalisation rates. **RESULTS:** According to our calculations, direct total costs of schizophrenia in Austria reach € 254.36 million a year. The drug costs are € 26.14 million and the costs for inpatient and outpatient services are € 228.22 million. Within the next five years, drug costs will slightly decrease to € 25.77 million due to a bigger market share of generic Quetiapine which offsets the higher drug costs of Paliperidon palmitate. The use of Quetiapine is associated with a higher rate of rehospitalisation. Therefore, costs for inpatient and outpatient services will increase to € 228.65 million, which results in an overall effect of € 60,000 additional costs compared to the situation without paliperidone palmitate. **CONCLUSIONS:** The introduction of a new treatment of schizophrenia in Austria is budget neutral.

PMH19

ASSOCIATION BETWEEN COGNITIVE FUNCTION AND 3 MONTH HEALTH CARE COSTS AMONG PATIENTS INITIATING AN ANTIDEPRESSANT FOR DEPRESSIVE DISORDER IN AN AMBULATORY CARE SETTING

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OBJECTIVES: Depression is associated with reduced cognitive function and significant health care costs; however, the extent to which these two are related remains unclear. This study compared follow-up health care costs for major depressive disorder patients with and without cognitive dysfunction after antidepressant (AD) initiation. **METHODS:** A large US health plan affiliated with OptumInsight was used to identify depressed patients with a newly prescribed AD who could be surveyed to assess cognitive function. Patients with neurological diseases associated with cognitive dysfunction were excluded. Patients were mailed a survey invitation and consent form. Patients maintained eligibility by confirming a depressive diagnosis and no excluding diagnoses. Consenting, eligible patients were interviewed by telephone and completed 4 cognitive function tests. Patients were classified as "cognitive normal (CN)" or "cognitive dysfunction (CD)" based on test scores relative to normative data. All-cause health care costs in the 3 months post-AD initiation were calculated from pharmacy and medical claims. T-tests compared 3-month costs of CN versus CD. Gamma models with log link compared health care costs between CD and CN patients, adjusting for race, sex, age, education, employment, depression severity, and comorbidities. **RESULTS:** A total of 13,537 patients were invited to participate in the study and 564 patients maintained eligibility and completed the study. Patients were mostly female (80%), mean age was 41 years, 98% had a high school degree or higher, and 84% were employed. A total of 45% (n=255) met criteria for CD. Mean health care costs were $4,996 for all patients. Costs were $6,457 for the CD group compared to $3,787 for the CN ($p = 0.038$). In the gamma models with costs as the outcome, CD patients had costs 1.43 times higher than CN patients (95% CI: 1.13, 1.81). **CONCLUSIONS:** In this study population, health care costs were significantly higher in patients with cognitive dysfunction compared to those without cognitive dysfunction.

PMH20

ASSESSING THE ECONOMIC BURDEN AND HEALTH CARE UTILIZATIONS OF VETERAN PATIENTS DIAGNOSED WITH POST-TRAUMATIC STRESS DISORDER IN THE UNITED STATES

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OBJECTIVES: To assess the economic burden and health care utilizations of patients diagnosed with post-traumatic stress disorder (PTSD) in the U.S. veteran population. **METHODS:** Patients diagnosed with PTSD were identified (International Classification of Disease 9th Revision Clinical Modification [ICD-9-CM] diagnosis code 309.81) from the Veterans Health Administration (VHA) dataset from October 01, 2009 through September 30, 2011. The first diagnosis date was designated as the index date. A comparator group was created by identifying patients without PTSD but with the same age, region, gender and index year, and who were matched by baseline Charlson Comorbidity Index. A randomly chosen index date served to

minimize selection bias. Patients in both groups were required to be at least 18 years old, and have continuous medical and pharmacy benefits 1 year pre- and 1 year post-index date. One-to-one propensity score matching was applied to compare follow-up health care costs and utilizations between patients with and without PTSD. **RESULTS:** A total of 938,138 patients were identified for the PTSD and comparison cohorts. After 1:1 matching, a total of 333,303 of patients were matched from each group, and baseline characteristics were balanced. Patients diagnosed with PTSD used more health care resources for inpatient (8.57% vs. 2.58%, p<0.01), emergency room (13.45% vs. 7.15%, p<0.01), physician office (99.59% vs. 55.67%, p<0.01), outpatient (99.64% vs. 56.46%, p<0.01), and pharmacy visits (89.97% vs. 56.47%, p<0.01) than patients in the comparator cohort. The PTSD cohort also incurred higher health care costs for inpatient ($2,587 vs. $719, p<0.01), emergency room ($133 vs. $66, p<0.01), physician office ($3,404 vs. $1,254, p<0.01), outpatient ($3,735 vs. $1,430) and pharmacy visits ($629 vs. $362, p<0.01). **CONCLUSIONS:** Study results suggest that the economic burden and health care utilizations were significantly higher for patients with PTSD versus those without.

PMH21

COMPARING THE HEALTH CARE COSTS AND UTILIZATIONS BETWEEN PATIENTS WITH ANXIETY VERSUS THOSE WITHOUT

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OBJECTIVES: To compare health care costs and utilizations between patients with anxiety versus those without in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration (VHA) Medical SAS datasets (01OCT2008-30SEP2012). Patients diagnosed with anxiety were identified (ICD-9-CM: 300.xx) from October 01, 2009 through September 30, 2011. The first diagnosis date was designated as the index date for the anxiety group. A group of non-anxiety patients of the same age, region, gender and index year were identified and matched by baseline Charlson Comorbidity Index (CCI) as the comparison group. The index date for the comparator group was randomly chosen to reduce the selection bias. Patients in both groups were required to be at least 18 years old, and have continuous medical and pharmacy benefits 1 year before and 1 year after the index date. One-to-one propensity score matching was applied to compare the health care costs and utilizations during the follow-up period between the anxiety and comparison groups, adjusted for baseline demographic and clinical characteristics. **RESULTS:** A total of 928,724 patients were identified for the anxiety and comparison cohorts. After 1:1 matching, 338,373 of patients were matched from each group and the baseline characteristics were well-balanced. Patients with anxiety had higher percentages of inpatient (11.03% vs. 2.74%, p<0.01), emergency room (18.64% vs. 7.50%, p<0.01), physician office (99.53% vs. 59.16%, p<0.01), outpatient (99.68% vs. 59.91, p<0.01) and pharmacy visits (91.42% vs. 59.13%, p<0.01). The anxiety group had higher expenditures in inpatient ($3,347 vs. $782, p<0.01), emergency room ($204 vs. $68, p<0.01), physician office ($3,527 vs. $1,435, p<0.01), outpatient ($3,948 vs. $1,621) and pharmacy visits ($745 vs. $429, p<0.01) than the comparison group. **CONCLUSIONS:** Results suggest that patients diagnosed with anxiety used significantly more health care resources and incurred significantly higher health care costs compared to patients without.

PMH22

METHODOLOGICAL CHALLENGES OF COST-OF-ILLNESS STUDIES ON DEMENTIA: AN INTERNATIONAL SYSTEMATIC REVIEW

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OBJECTIVES: Increasing prevalence of dementia highlights the need for a better understanding of the cost burden for health policy makers. By descriptive analysis of specific cost impacts, cost-of-illness (COI) studies are an essential instrument for decision making and planning of health care services. Therefore the purpose of this study was to review COI studies of dementia in order to analyze cost components and underlying methods in an international context. **METHODS:** A systematic review according to the PRISMA-guidelines was conducted from 2002-2012 in order to identify COI studies related to dementia, searching the PubMed, Cochrane, EMBASE and NHS Economics Evaluations databases. Annual outcomes per patients were analyzed for total, direct, indirect and informal costs. **RESULTS:** In total 25 studies were evaluated. Total costs showed an annual range from USD 3.512 to USD 59.526 in 14 health care systems. This is due to the fact, that the composition of cost components and corresponding methods indicated a large heterogeneity in terms of both – study characteristics (e.g. diagnosis, care setting, disease stratification) and composition of cost components. The majority of studies (92%, n=23) included direct costs, however different cost components and underlying measurements were applied. Almost two thirds (60%, n=15) of the studies included informal costs, whereas 9 used the replacement cost approach and 6 studies the opportunity cost approach. **CONCLUSIONS:** Outcomes of COI studies in dementia indicate a large range, due to differences in health care systems, but also because of methodological approaches and cost components included. Dementia as a long-lasting and progressive disease affects multiple cost dimensions and thereby poses a complex challenge for policy makers. In addition, international guidelines on cost analysis of dementia are lacking. Standards regarding the methodology of COI studies in dementia by the scientific community would be useful. Funded by the European Commission, ICT-FP7, project-ID-287509.

PMH23

DIFFERENTIAL RESOURCE USE AND COSTS AMONG INPATIENTS AND OUTPATIENTS WITH SCHIZOPHRENIA IN TIANJIN, CHINA

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OBJECTIVES: To estimate the direct total and component medical costs for inpatient and outpatient care for patients with schizophrenia in Tianjin, China. **METHODS:** Data were extracted from the Tianjin Urban Employee Basic Medical Insurance database. Patients (N=2125) who were aged ≥18 years, at least 1 diagnosis of schizophrenia and 12-month continuous enrollment after their first observed schizophrenia diagnosis between 2008 and 2010 were included. Psychiatric-related inpatient and outpatient direct medical costs were estimated. **RESULTS:** During the study period, 60.8% of patients had at least one inpatient admission and 39.2% used only outpatient services. The mean (± SD) total annual cost for inpatients was $2771.9±2175.6, with 88.9% ($2465.4±2022.5) due to non-drug medical costs and 11.1% ($306.6±461.7) for medications. Total annual costs for the outpatient only group were $230.6±487.3 with 4.4% ($10.1±40.8) for non-drug medical costs and 95.6% ($220.5±470.3) for medications. Antipsychotics accounted for 50.4% of the total annual medication costs in the inpatient group and 60.0% in outpatient only group. On average, inpatients had 2.2 psychiatric hospitalizations and 2.2 outpatient visits. Outpatient only group had 5.9 outpatient visits. The highest costs per psychiatric-related inpatient admission were general care and non-drug treatment (49.8%), followed by examinations (21.6%), bed fee (14.6%), and medications (7.8%). The majority of costs for outpatient visits were due to medications (96.2%). **CONCLUSIONS:** Patients who were hospitalized for schizophrenia incurred considerably more costs than those who were only treated at outpatient setting in Tianjin China, primarily driven by non-drug medical care. This suggests that the use of more effective treatments to minimize the risk of hospitalization could lead to reduced total health care costs.

PMH24

HEALTH CARE RESOURCE UTILIZATION AND DIRECT MEDICAL COSTS AMONG PATIENTS WITH SCHIZOPHRENIA IN TIANJIN, CHINA

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OBJECTIVES: To estimate the health care resource utilization and direct medical costs of patients with schizophrenia in Tianjin, China. **METHODS:** Data were obtained from the Tianjin Urban Employee Basic Medical Insurance database. Adult patients with ≥ 1 diagnosis of schizophrenia and 12-month continuous enrollment after the first observed schizophrenia diagnosis between 2008 and 2010 were included. Both all-cause and psychiatric-related resource utilization and direct medical costs were estimated. Two-sample t-test was used to assess cost difference. A multiple linear regression model was applied to identify factors associated with total cost. **RESULTS:** A total of 2125 patients were included, with mean age of 52.3 years, 49.3% male and 55.7% retired. 60.8% of the patients experienced ≥1 psychiatric-related hospitalizations during the study period. Median (min-max) length of stay was 88 (1-365) days per admission and 91 (1-365) days per patient-year. 58.9% of the patients experienced ≥1 psychiatric related outpatient visits. Median number of outpatient visits was 4 (1-82). Mean (±SD) total all-cause and psychiatric-related direct medical costs were $2863.5±2638.4 and $1774.5±2123.3 per patient-year respectively, with significant difference between hospitalized and non-hospitalized patients ($3953.0 vs. $1176.9, p<0.001; $2771.9 vs. $230.6, p<0.001). The regression model revealed that patients with more hospitalizations/outpatient visits and non-retired patients were more likely to incur higher psychiatric-related annual costs. **CONCLUSIONS:** Costs related to treatment with schizophrenia was considerable in Tianjin China, driven mainly by psychiatric hospitalizations. Patients with psychiatric-related hospitalizations used more medical resources and had higher direct medical cost than patients who were not hospitalized.

PMH25

SOCIO-ECONOMIC IMPACT OF ALZHEIMER'S DISEASE IN GREECE: PILOT STUDY

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OBJECTIVES: The economic burden of Alzheimer disease goes beyond the direct health cost as the disease has significant economic and social impact on both patients themselves and their families (carers). Despite the fact that Greece is plagued by the economic crisis, with major cuts in health expenditure, very little is known about the cost of chronic diseases and the most cost-effective ways to manage them. The study's' aim is to estimate, for the first time in Greece, the cost of Alzheimer's disease, per each severity stage, evaluating apart from the direct costs of disease, the cost of carers. **METHODS:** The pilot sample was 46 patients from two Alzheimer centers. A cost analysis was conducted from the socio-economic perspective. Data regarding the carers' time were collected via a questionnaire developed by the researchers of this study and was partly based on the research tool CATS (Caregiver Activities Time Survey) as it was adopted by Jacobsen et al. (2011). **RESULTS:** The total annual cost of the disease was estimated at €12,140 (SD: 6,555.9) for the mild stage (MMSE* 30-21), at €13,735 (SD: 7,858.7) for the moderate stage (MMSE 20-11), and €22,666 (SD: 8,467.2) for the severe stage (MMSE 10-0) (for outpatient cases), 87% higher compared to the mild stage of disease. On average, from the total cost of disease, 77% was the cost of the primary and the secondary caregiver, 8.7% is the cost of medication and 5% is the hospitalization cost. Productivity loss of the primary caregiver exceeds 5% of the total cost per patient in mild stage. **CONCLUSIONS:** As the patient gets worse and goes from mild to more severe stages, the total health care cost increase. It is important, when possible, to prolong the stay of patients in the early stages of the disease.

PMH26

SCHIZOPHRENIA AND NEGATIVE SYMPTOMS – BURDEN OF THE DISEASE IN SEVEN CENTRAL AND EASTERN EUROPEAN (CEE) COUNTRIES: THE RESULTS OF THE LITERATURE REVIEW

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OBJECTIVES: To gather data concerning burden of schizophrenia in seven Central and Eastern European (CEE) countries (Croatia, Estonia, Hungary, Poland, Serbia, Slovakia, Slovenia) taking into account: epidemiology, clinical guidelines and recommendations, current standards of care, costs of illness, resource utilisation, health-related quality of life (HRQoL), stigmatisation and discrimination related to schizophrenia. The project focused on negative symptoms (NS). **METHODS:** A targeted search was performed focused on publications issued from 1995 onwards and indexed in the following databases: PubMed, Cochrane Library, and Centre for Review and Dissemination. Moreover, searches for literature in local languages from each country of interest were conducted. **RESULTS:** Fourteen reviews related to schizophrenia epidemiology were identified and revealed that the mean incidence of schizophrenia varied greatly from 0.04 to 0.58 per 1,000 population and lifetime prevalence from 0.4% to 1.4%. At least one negative symptom was found to be present in 57.6% of schizophrenia patients and in 50–90% of individuals experiencing their first schizophrenia episode. Primary NS were observed in 10–30% of patients. Mortality of schizophrenia patients was greater than in the general population (Standardised Mortality Ratio varies between 2.58 and 4.3), potentially due to increased suicide risk, effect of illness on lifestyle and environment, and side effects of disease treatment. Identified guidelines indicate a role for second-generation antipsychotics in NS treatment, nevertheless the development of novel therapeutic approaches should be pursued actively. Thirty-seven primary publications identified from the seven CEE countries which relate to HRQoL of patients and caregivers revealed that the disease greatly affects HRQoL of hospitalised patients and has a significant negative impact on caregivers' QoL. **CONCLUSIONS:** The literature review confirmed that schizophrenia is one of the most common and burdensome mental illnesses, with NS present in a relatively large percentage of patients.

PMH27

NEW ESTIMATES OF THE DIRECT MEDICAL COST OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN GERMANY

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OBJECTIVES: To assess the excess direct medical costs associated with a diagnosis of attention-deficit/hyperactivity disorder (ADHD) in Germany. **METHODS:** Nordbaden is a region in Southwestern Germany with a population of 2.74 million. Regional sociodemographics and health care provider density are well understood and reflect, with few exceptions, respective national averages. The Nordbaden database covers the total regional population insured by SHI (2.24 million lives), integrating administrative data from the organization of physicians registered with statutory health insurance (SHI) and SHI, allowing patient-centered evaluation of health care utilization and direct medical cost for years 2003 to 2009. Patients with a diagnosis of ADHD were compared to a control group matched by age, gender, and type of health insurance within SHI. Here we report on years 2006-2009, as nonpharmacological therapy-related cost data were not fully available for earlier years. **RESULTS:** Average annual total cost per ADHD patient increased from €897 in 2006 to €1,006 in 2009 (controls, €261 in 2006 and €337 in 2009). Cost per patient correlated positively with age, and female patients were generally more costly than males (total as well as excess costs). Increasing severity and comorbidity were also associated with higher costs per patient. Physician services constituted the major cost component (on average, overall, €653 per case in 2009), followed by pharmacological therapy (€330 in 2009). **CONCLUSIONS:** The average excess cost (from the perspective of German SHI) per ADHD patient (over all age groups and irrespective of gender, compared to matched controls) was €669 per year in 2009. Extrapolation from the regional to the national level suggests annual outpatient treatment costs attributable to ADHD in the magnitude of €500 million (2009), from the payer's perspective of SHI. This estimate compares to total annual expenditures for health services by German SHI of €160 billion in 2009.

PMH28

A SYSTEMATIC REVIEW OF COST-OF-ILLNESS STUDIES AND COST-EFFECTIVENESS ANALYSES IN BORDERLINE PERSONALITY DISORDER

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OBJECTIVES: The borderline personality disorder (BPD) is a common mental disorder. It is frequently associated with various mental co-morbidities and causes a fundamental loss of functioning. Furthermore, economically relevant consequences such as high utilization of inpatient and emergency room treatment or reduced productivity at work have been reported. The aim of this study is to present the existing health economic evidence regarding BPD and to point out implications for further research. **METHODS:** We performed a systematic literature search in MEDLINE, EMBASE, PsycInfo and NHSEED to identify cost-of-illness studies (COI), cost-effectiveness analyses (CEA) and other cost studies (OCS) regarding BPD. Cost data were inflated to the year 2010 and converted into US-$ using purchasing power parities (PPP). Quality assessment of the studies was performed by means of a standardised quality checklist. **RESULTS:** We identified three COI, eight CEA and six OCS. The methodical quality was moderate. Depending on study perspective and considered cost categories cost per patient and year ranged from 18,306 US-$ PPP to 69,231 US-$ PPP. A co-morbid conduct disorder was reported to be the most influential factor for increased health care costs. All CEA analysed psychotherapy interventions. While CEA reporting cost per avoided parasuicide event indicated favourable incremental cost effectiveness ratios, CEA reporting cost per quality-adjusted life years (QALY) indicated just weak cost-effectiveness. **CONCLUSIONS:** BPD is associated with high costs. Available COI provide a first insight into the structure of cost and its predictors. There are no CEA regarding medication for BPD. Evidence regarding the cost-effectiveness of psychotherapy interventions is ambiguous. Future research should promote the understanding of the economic aspects of BPD and determine the societal value of its treatment. In this context high methodical standards are particularly important.

PMH29

HEALTH INSURANCE COST OF EPILEPSY IN HUNGARY: A COST OF ILLNESS STUDY

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OBJECTIVES: To calculate the annual health insurance treatment cost of epilepsy disease in Hungary. **METHODS:** The data derive from the financial database of the Hungarian National Health Insurance Fund Administration (NHIFA), the only health care financing agency in Hungary. We analyzed the health insurance treatment cost and the number of patients for the year 2010. The following cost categories were included into the study: out-patient care, in-patient care, CT-MRI, PET, home care, transportation, general practitioner, drugs and medical devices. **RESULTS:** The Hungarian National Health Insurance Fund Administration spent 6.341 billion Hungarian Forint (HUF) (23.026 million EUR) for the treatment of epilepsy patients. The annual average expenditure per patient was 41900 HUF (152.1 EUR) while the average expenditure per one inhabitant was 633 HUF (2.3 EUR). Major cost drivers were pharmaceuticals (6.3 % of total health insurance costs), general practitioners (13.1 %) and acute inpatient care (11.4 %). The number of patients with epilepsy was 151 per 100000 populations. We found the highest patient number in pharmaceutical budget (151357 patients), out-patient care (131280 patients) and general practitioners (86704 patients). **CONCLUSIONS:** Epilepsy disease represents a significant burden for the health insurance system. Pharmaceutical treatment is the major cost driver for epilepsy disease in Hungary.

PMH30

HEALTH CARE RESOURCE UTILIZATION AND COSTS ASSOCIATED WITH ATYPICAL ANTIPSYCHOTICS USE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN QUEBEC, CANADA

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OBJECTIVES: To compare health care resource utilization (HRU) and costs among children/adolescents with attention deficit/hyperactivity disorder (ADHD) in Quebec, Canada, who received an atypical antipsychotic (AAP) as either augmentation or alternative therapy to stimulant, before vs. after initiating the AAP. **METHODS:** Patients (6–17 years) with ≥2 documented ADHD diagnoses (ICD-9 codes: 314.0–314.9), who used stimulants for ≥30 days and either switched to an AAP or augmented stimulants with an AAP, were identified in Quebec's health care database, the Régie de l'assurance maladie du Québec between 03/2007 and 02/2012. Patients with a documented diagnosis for which AAPs are indicated were excluded. All-cause and ADHD-related HRU and costs (from a public payer's perspective in 2012 Canadian dollars) were compared between the 6-month period before (pre-index) and after (post-index) patients' first AAP prescription claim. **RESULTS:** A total of 453 children/adolescents met the inclusion criteria (54.5% switched from stimulants to AAPs and 45.5% augmented stimulants with AAPs). The mean age was 10.4 years (SD=2.5) and 25.4% were female. The most prevalent documented mental comorbidities in the pre-index period were adjustment reaction (7.1%), anxiety disorder (5.1%), and learning disability (4.4%). Risperidone (81.7%) and quetiapine (16.3%) were the most common AAPs initiated. Compared to the pre-index period, patients incurred, on average, more all-cause outpatient visits and costs (3.2 vs. 4.6; $207 vs. $303), prescription fills and costs (13.3 vs. 22.2; $710 vs. $889), total medical costs ($644 vs. $1,096), and total health care costs ($1,354 vs. $1,985) (all $p<0.05$) during the post-index period. Similarly, ADHD-related total health care costs ($835 vs. $1,269; $p<0.05$) were higher during the post-index period; all-cause and ADHD-related total health care costs increased by 46.6% and 52.0%, respectively. **CONCLUSIONS:** Children/adolescents with ADHD, who received an AAP as either augmentation or alternative therapy to stimulant, incurred higher HRU and costs after AAP initiation, mostly through ADHD-related HRU.

PMH31

REGISTER BASED ANALYSIS OF TREATMENT COSTS OF SECOND GENERATION ANTIPSYCHOTICS IN SCHIZOPHRENIA

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OBJECTIVES: The goal of our research was to assess and calculate the costs of antipsychotic treatment of schizophrenia patients in Hungary, using the database of the National Health Insurance Fund (NHIF). Based on the results of a recently published study using real world data (Bitter et al. 2013.) we focused especially on the costs linked to the early medication discontinuation and poor adherence of schizophrenia patients. **METHODS:** In Hungary all medicines which are purchased with reimbursement are documented in the centralized register of the NHIF since 1998. We analyzed the Payer's database taking into account the time to treatment discontinuation results of the Bitter et al. study. We calculated the yearly average costs of schizophrenia treatment both per patient, and both per substance

between 2006 and 2012. **RESULTS:** Our findings indicate that in the assessed time period an average yearly amount of approximately €5,5 million (calculation based on yearly average EUR/HUF exchange rates) is spent on second generation antipsychotics, which are prescribed and purchased with reimbursement but finally not used by the patients due to early medication discontinuation. Based on our calculations, the average yearly treatment costs of antipsychotics increased from €612 (2006) to €974 (2012) per patient in the assessed time period. The analysis of the NHIF database resulted, that the average yearly expenditure on different antipsychotics, varied between €173 and €2420 per patient. **CONCLUSIONS:** All-cause medication discontinuation is a major concern in the treatment of schizophrenia both from a clinical and both from a health economic perspective. In order to ensure resources are spent cost-effectively, it is crucial to identify methods which can improve treatment continuation and adherence of schizophrenia patients in the future.

PMH32

ADJUNCTIVE THERAPY WITH PREGABALIN IN GENERALIZED ANXIETY DISORDER PATIENTS WITH PARTIAL RESPONSE TO SSRI TREATMENT: A COST-CONSEQUENCES ANALYSIS IN MEDICAL PRACTICE IN SPAIN

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OBJECTIVES: To compare the effect of adjunctive therapy with pregabalin versus usual care (UC) on health care costs and clinical and patients consequences in Generalized Anxiety Disorder (GAD) subjects with partial response (PR) to previous SSRI course in medical practice in Spain. **METHODS:** Post-hoc analysis of patients with PR to SSRI monotherapy enrolled in a prospective 6-month naturalistic study. PR was defined as a Clinical-Global-Impression scale score >3 and insufficient response with persistence of anxiety symptoms >16 in the Hamilton-Anxiety scale. Two groups (based on psychiatrist judgment) were analyzed 1) adjunctive therapy (AT) with pregabalin (150-600 mg/day) to existing therapy; or 2) usual care (switching to a different SSRI or adding another anxiolytic different than pregabalin). Costs estimation used year-2009 prices for GAD related health care resources utilization. Consequences were a health profile based on the combination of psychiatrist-based-measurements [HAM-A, CGI and Montgomery-Asberg-Depression-Rating (MADRS) scales], and patient-reported-outcomes [sleep (MOS-sleep), disability (WHO-DAAS II) and quality-of-life/quality-adjusted-life-year gain (EQ-5D)]. Changes in both health care costs and scale scores were compared separately at end-of-trial visit by a general-linear-model with covariates. **RESULTS:** Four-hundred-eighty-six newly prescribed pregabalin and 239 UC GAD patients [mean (SD) HAM-A 26.7 (6.9) and CGI 4.1 (0.5)] were analyzed. Adding pregabalin was associated with significantly higher mean (95% CI) score reductions vs. UC in HAM-A [-14.9(-15.6;-14.2) vs. -11.2(-12.2;-10.2), p<0.001] and MADRS [-11.6(-12.2;-10.9) vs. -7.8(-8.7;-6.8), p<0.001]. Changes in all patient-reported-outcomes favored significantly patients receiving pregabalin, including QALY gain; 0.13(0.12;0.14) vs. 0.09(0.07;0.10), p<0.001. Health care costs were significantly reduced in both cohorts yielding similar 6-month costs; €1543 (1375;1711) UC and €1497 (1380;1614) pregabalin, p=0.661. The effect of sex on costs and consequences were negligible. **CONCLUSIONS:** In medical practice, GAD patients with PR to SSRI experienced greater consequences improvements with adjunctive therapy with pregabalin versus UC, without increasing health care cost. The effect of pregabalin was independent of patient gender.

PMH33

COST-EFFECTIVENESS OF ANTIDEPRESSANT AFTER 24 MONTHS OF TREATMENT BASED ON DISCRETE EVENT SIMULATION MODELING (DESM): AGOMELATINE VERSUS MATRIX COMPARATOR OF ESCITALOPRAM, SERTRALINE AND VENLAFAXINE IN A THAI SETTING

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OBJECTIVES: To compare cost-effectiveness of agomelatine versus an escitalopram-sertraline-venlafaxine matrix comparator. **METHODS:** A DESM describes course of depressive disorders with acute , continuation, and maintenance treatment of depression in Thai setting for 24 months. A sample of 250,000 patients with 100 simulations were assumed with Exigo® model. Antidepressants were analyzed for treatment of episodes(12-24 weeks),continuation phase(6-9 months), maintenance phase over 2 years follow-up. Data inputs included Thai data on disease parameters; Cost included antidepressants, drugs for insomnia, sexual side-effects, cognitive behavioral therapy(CBT), electroconvulsive therapy(ECT) and mean cost of psychiatric visits. Impact measures were derived from a systemic review. Results were presented as cost(Thai-Baht currency-THB) per Life-Year-Remission(LYR) averted and Quality-Adjusted Life Year(QALY) compared with branded antidepressants in the matrix comparator (46%escitalopram, 33%sertraline, 21%venlafaxine). Model simulation initiated with either agomelatine 25mg or comparators(escitalopram10mg,sertraline100mg,venlafaxine 150mg by random selection). Relapse cases required dose increase fro each antidepressant, addition of CBT and ECT. Data on impact of treatment on quality of life in patients free from relapse, sexual side effects, insomnia were taken from cochrane database. **RESULTS:** During 24 months, patients treated with agomelatine cost 15,814.2THB and 20,232.0THB per LYR and QALY gains, whereas with comparator cost 17,999.6THB and 23,431.7THB per LYR and QALY gains. As a result, the incremental cost-effectiveness ratio(ICER) shows that agomelatine is the most cost-effective antidepressant for episodic treatment with/without continuation or maintenance phase, its cost being lower than comparator by 153,283 and 83,645 THB per LYR and QALY. These results were robust, probability sensitivity analysis suggested that agomelatine was effective for a willingness-to-pay of 300,000THB,95%CI of -146,120.4 to -179,651.0THB per QALY, with probability of >0.90. **CONCLUSIONS:** Based on the model, agomelatine is the most cost-effective treatment option as compared with escitalopram,sertraline, and venlafaxine in a matrix comparator, with regard to side effects especially sexual dysfunction, agomelatine should be considered as the most cost-effective option for treatment of depression.

PMH34

COST-EFFECTIVENESS OF PALIPERIDONE PALMITATE FOR THE TREATMENT OF SCHIZOPHRENIA IN GERMANY

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OBJECTIVES: Treatment with antipsychotic medication is an important element of relapse prevention in the management of schizophrenia and can reduce inpatient stays. Recently, the long-acting atypical antipsychotic paliperidone long-acting injectable (PLAI), a once-monthly LAI antipsychotic, was approved for treatment of schizophrenia in Germany. The study aims at estimating, based on a previously published model, the cost-effectiveness of paliperidone long-acting injections compared to other common antipsychotic treatment strategies in patients diagnosed with schizophrenia in Germany. **METHODS:** A Markov decision analytic model was adapted to the German health care system. The model considers the cost-effectiveness for PLAI as a maintenance treatment for patients with schizophrenia from the payer perspective. The patients transition between eight health states on a monthly basis over a 5-year time horizon. As therapeutic strategies PLAI, quetiapine, risperidone long-acting injections (RLAI), oral olanzapine, oral risperidone, zuclopenthixol decanoate, olanzapine long-acting injections (OLAI), oral typical and oral atypical were compared. Probability of relapse, level of adherence, side effects and treatment discontinuation were derived from the Swedish original model. Input factors regarding resource use and costs were estimated and adjusted for the German health care system. A probabilistic sensitivity analyses using cost-effectiveness scatter plots was performed to visualize the robustness of the results. **RESULTS:** In base case scenario PLAI is superior to RLAI in gained quality adjusted life years (QALYs) and avoided relapses. Relative to all other treatment strategies PLAI is more effective with regard to gained QALYs and avoided relapses but results in higher treatment costs over a 5-year horizon in base case scenario. The results were tested in probabilistic sensitivity analyses **CONCLUSIONS:** PLAI dominates RLAI and compared to the other treatment strategies PLAI has shown to be more effective but results in higher costs in base case scenario.

PMH35

COST EFFECTIVENESS ANALYSIS FOR THE USE OF EXTENDED RELEASE QUETIAPINE AS ADJUNCTIVE THERAPY IN MEXICAN ADULT PATIENTS WITH MAJOR DEPRESSIVE DISORDER NON-RESPONDERS TO ANTIDEPRESSANT TREATMENT

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Depression is present in 10% of patients attending primary care services and is generally not identified. In Mexico it is estimated a prevalence of 12% to 20% among adults between 18-65 years old. Up to 75% of patients treated with a selective inhibitor of serotonin reuptake (SSRIs) are not responding adequately. Atypical antipsychotics are an effective alternative for these patients. **OBJECTIVES:** To evaluate the cost-effectiveness (CE) of extended release (XR) quetiapine as adjunctive therapy (AT) in patients with major depressive disorder (MDD) that doesn't respond to antidepressant treatment (AD), compared with other antipsychotics listed in the Mexican Formulary (aripiprazole and olanzapine). **METHODS:** A Markov model was developed to perform and incremental analysis with weekly cycles during eight weeks time horizon, based on the meta-analysis developed by Komossa et.al in 2010. Health states: remission, relapse and discontinuation of treatment. The model estimates the remission time gained (RG) by each AT alternative. The analysis was done from society perspective, considered direct costs, and reported in 2013 US dollars. **RESULTS:** Patients with AT with quetiapine XR had 1.83 weeks of RG, while patients under aripiprazole and olanzapine obtained 1.5 and 1.72 weeks of RG, respectively. Quetiapine XR compared to olanzapine generated an additional cost per patient of $94.70, with additional RG of 0.11 weeks and ICER of $881.73. Quetiapine XR dominated extendedly to aripiprazole. Robustness of results were confirmed by additional deterministic and probabilistic sensitivity analysis. **CONCLUSIONS:** The use of quetiapine XR as adjuvant treatment for non-responders patients is a cost-effective compared to aripiprazole and olanzapine, and could be considered as an option in an institutional setting.

PMH36

HOW SHOULD AN ANTIDEPRESSANT WITH REDUCED RISK OF SEXUAL DYSFUNCTION BE POSITIONED IN TREATMENT STRATEGIES FOR PATIENTS WITH MAJOR DEPRESSIVE DISORDER?

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OBJECTIVES: Sexual dysfunctions (SD) is a common adverse event of antidepressants. It has a lasting impact on quality of life and is associated with an increased risk of early treatment discontinuation. Using an open-source Discrete Event Simulation model (https://open-model-mdd.org/), we performed a cost-effectiveness analysis comparing alternative sequences of treatments, to determine whether an antidepressant with moderate efficacy and reduced risk of SD should be positioned before or after a treatment with high efficacy and average risk of SD. **METHODS:** The model used was designed to simulate costs and QALYs in cohorts of patients with major depressive disorder (MDD), under alternative treatment strategies over 5 years. Each strategy consisted of up to 4 lines of treatment, with possibility to switch to different drugs when a patient experienced adverse events or lack of efficacy. We

compared two strategies based on hypothetical treatments: under strategy A, an antidepressant with high response rate/high SD rate was prescribed in first-line and an antidepressant with moderate response rate/low SD rate available in second-line; under strategy B, the positions of these two drugs were reversed. Efficacy and safety parameters were obtained from a meta-analysis and other parameters, from the literature. Costs were estimated for the UK, from payer perspective. **RESULTS:** The numbers of QALYs were estimated at 3.660 QALYs (SE=0.013) and 3.649 (SE=0.012) under strategies A and B respectively. Costs were estimated at £3,894 (SE=60) and £3,918 (SE=61). **CONCLUSIONS:** Positioning an antidepressant with moderate efficacy and reduced risk of SD before or after a treatment with high efficacy and average risk of SD had no significant impact in terms of average costs and QALYs. Thus, differences in efficacy and tolerability can offset each other. In practice, the choice of first-line treatment should take account of patient preferences.

PMH37

COST-EFFECTIVENESS OF INJECTABLE ATYPICAL LONG-ACTING ANTIPSYCHOTICS FOR CHRONIC SCHIZOPHRENIA IN POLAND

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OBJECTIVES: To determine the cost-effectiveness of paliperidone palmitate (PP-LAI; paliperidone long-acting injectable), a new once-monthly long-acting antipsychotic therapy, compared with risperidone long-acting injectable (RLAI) administered biweekly for treating chronic schizophrenia in Poland from the National Health Fund (NHF) perspective. **METHODS:** We adapted a 1-year decision tree model to the Polish health care system with literature-derived data (e.g., length of stay in hospital, treatment patterns, resource utilization) and clinical expert inputs. Costs in 2012 euros were obtained from published sources or in case of non-reimbursed drug price, directly from producer. Drugs compared were PP-LAI, a new treatment option, and RLAI, the established treatment for Polish patients. Clinical rates were derived from published trials. Model outputs included expected cost/patient as well as rates of hospitalization, emergency room visits, days free of symptoms, and quality-adjusted life-years (QALYs). One-way sensitivity analyses were applied to major inputs. As well, all inputs were varied simultaneously in probabilistic sensitivity analyses using 10,000 iterations. **RESULTS:** Despite its higher acquisition cost, PP-LAI had a lower expected cost per patient treated when the benefits are included in the estimation model. PP-LAI was associated with 0.824 QALYS, 323 days with stable disease and 44.6% hospitalization. RIS-LAI had 0.817 QALY, 317 stable days and 51.3% hospitalizations. PP-LAI dominated RIS-LAI in the base case and in 55.0% of 10,000 simulations, and was cost-effective in 76.6%. However, cost-effectiveness was sensitive; it was lost with modest increases for PP-LAI or decreases for comparison drugs with respect to drug prices, relapse rates and adherence rates. Because it is injected monthly as opposed to biweekly, it saves caregiver time. **CONCLUSIONS:** From the viewpoint of the National Health Fund of Poland, as compared with RLAI, PP-LAI is a cost-effective drug that has the potential to reduce health care costs.

PMH38

MOOD STABILIZERS AND ATYPICAL ANTIPSYCHOTICS IN MAINTENANCE THERAPY FOR BIPOLAR DISORDER: A COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: To evaluate the cost-effectiveness of using a combination of atypical antipsychotic agents and mood stabilizers in maintenance treatment of bipolar disorder in Brazil **METHODS:** Analyzing cost-effectiveness, taking direct costs, from the perspective of Brazil's Ministry of Health and its public health system (local acronym SUS), using a Markov model with transitions between possible states: euthymia, mania, depression, discontinuation and death. Efficacy data to populate the model were extracted from clinical trials and prospective cohort studies while direct cost data came from the public health system's databases (current values of 2012, exchange rate: US$ 1 = R$ 2.21). For a hypothetical cohort of 2000 euthymic individuals aged 40, maintenance therapy costs and outcomes were simulated over quarterly cycles through a timeframe that reached an effectiveness of <1 day in remission, for up to 30 years. Discount rates and half-cycle correction were applied, also, sensitivity analyses were run. **RESULTS:** The available efficacy data enabled the analysis to include only a combination with quetiapine. After twelve years (48 cycles) tracking the hypothetical cohort, there were 512 acute episodes (285 depression and 227 mania) for monotherapy against 306 (166 depression and 139 mania) for the quetiapine combination. The incremental cost-effectiveness ratio (ICER) for the quetiapine combination therapy was US$ 565.64 per additional month in remission. The sensitivity analysis with all variables demonstrated the model's robustness, while dosage and quetiapine-price variations had most impact, showing an ICER ranging from US$ 381.88 to US$ 811.24 per additional month in remission. **CONCLUSIONS:** Maintaining the euthymia in bipolar disorder has a clinical relevance, especially, because of its impact on functional capacity in this population. In this context, in specific populations, the ICER shown may justify the use of the therapeutic strategy presented here. This reimbursement by public systems should also consider its budget impact.

PMH39

PATIENT-LEVEL MARKOV MODEL TO ASSESS ECONOMIC IMPACT OF NEW ANTIPSYCHOTICS INTRODUCTION IN SCHIZOPHRENIA

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OBJECTIVES: Antipsychotic treatments can cause several side effects, such as weight gain, metabolic syndrome, which could lead to cardiovascular complications (CVC). A number of models are available for the evaluation of the economic impact of antipsychotics in schizophrenia, but few of them properly consider metabolic syndrome and associated complications. The objective of this study was to build a new model to reflect the real patient therapeutic management of patients with schizophrenia. **METHODS:** An expert meeting was set up to validate the design of the model, and to list all outcomes that should be included in the model structure. The model was programmed in Excel 2010, with VBA coding. **RESULTS:** The expert meeting validated the premise that the aim of the treatment is to prevent relapses, affecting patients' quality of life and generating substantial costs. A patient-level Markov model structure was used, to simulate a cohort of patients with schizophrenia over lifetime, with 6-month cycles. Five lines of treatments are considered in the model. With up to 3 comparators in the first cycle, it models patients' treatment adjustment, and provides the flexibility to specify at any line of treatment a specific distribution of antipsychotics. The model considers treatment response, associated side effects (weight gain, sexual dysfunction, EPS and sedation), diabetes diagnosis and CVC (coronary heart disease and stroke). Non-response and compliance (based on side effects) drive relapse and hospitalization. Each relapse is assumed to require a treatment switch. Patients are also allowed to escape from the health care system, or to die, due to natural death, suicide or CVC-related death. Finally, extensive deterministic and probabilistic sensitivity analyses are also implemented. **CONCLUSIONS:** This new economic model allows taking into account all key features of schizophrenia, in a transparent way.

PMH40

COST-EFFECTIVENESS OF ASENAPINE VERSUS ATYPICAL ANTIPSYCHOTICS USED IN TURKEY IN THE TREATMENT OF SCHIZOPHRENIA

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OBJECTIVES: Asenapine is a new atypical antipsychotic approved in Turkey for the treatment of schizophrenia and bipolar I disorder. Asenapine has demonstrated comparable efficacy over olanzapine in controlling both positive and negative symptoms of schizophrenia in the long-term. However, unlike olanzapine, asenapine is associated with a favorable metabolic profile as well as with a minimal weight gain. Post-hoc analyses of a clinical study vs. olanzapine illustrated higher incidence of developing metabolic syndrome (MetS) with olanzapine than with asenapine after 52 weeks of treatment. The aim of this study is to assess the cost-effectiveness of asenapine in schizophrenia compared with the most widely used atypical antipsychotics in Turkey with a focus on the long-term consequences of MetS which increases the risk of diabetes and cardiovascular diseases (CVD). **METHODS:** Perspective of National Pharmaceutical Reimbursement Authority was applied and life expectancy horizon was adopted. Annual risks of metabolic syndrome were derived from randomized clinical studies of asenapine and indirect comparison of other atypical antipsychotics vs. olanzapine. Risks of developing diabetes and CVD were based on published risk models. Treatment costs associated with metabolic consequences as well as cost of atypical antipsychotics were derived from local sources. Number of diabetes and CVD avoided is used as effectiveness measure in the model. **RESULTS:** Asenapine dominates (more effective and less expensive) all atypical antipsychotics in the treatment of schizophrenia. Compared to olanzapine, quetiapine, aripiprazole, risperidone and paliperidone (all genericized except paliperidone), asenapine was associated with incremental total costs of 1908 TL, 1298 TL, 314 TL, 841 TL and 1958 TL; and associated with incremental total number of diabetes & CVD avoided of 0.046, 0.029, 0.001, 0.028 and 0.028 respectively. **CONCLUSIONS:** The lower incidence of developing MetS associated with asenapine compared to olanzapine and other atypicals is associated with lower treatment costs and lower incidence of diabetes and CVD in Turkey.

PMH41

COST-EFFECTIVENESS OF ASENAPINE VERSUS ATYPICAL ANTIPSYCHOTICS USED IN TURKEY IN THE TREATMENT OF BIPOLAR I DISORDER

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OBJECTIVES: Asenapine is a new atypical antipsychotic approved in Turkey for the treatment of bipolar I disorder (BD-I) and schizophrenia. Asenapine has demonstrated comparable antimanic efficacy over olanzapine in a head-to-head study. However, unlike olanzapine, asenapine is associated with a favorable metabolic profile as well as with a minimal weight gain. Post-hoc analyses of a clinical study vs. olanzapine illustrated higher incidence of developing metabolic syndrome (MetS) with olanzapine than with asenapine after 52 weeks of treatment. The aim of this study is to assess the cost-effectiveness of asenapine in the treatment of BD-I compared with the most widely used atypical antipsychotics with a focus on the long-term consequences of MetS which increases the risk of diabetes and cardiovascular diseases (CVD). **METHODS:** Perspective of National Pharmaceutical Reimbursement Authority was applied and life expectancy horizon was adopted. Risks of metabolic syndrome after 52 weeks of treatment were derived from randomized clinical studies of asenapine and indirect comparison of other atypical antipsychotics vs olanzapine. Risks of developing diabetes and CVD were based on published risk models. Treatment costs associated with metabolic consequences as well as cost of atypical antipsychotics were derived from local sources. Number of diabetes and CVD avoided is used as effectiveness measure in the model. **RESULTS:** Asenapine dominates (more effective and less expensive) all atypical antipsychotics in the treatment of BD-I. Compared to olanzapine, quetiapine, aripiprazole, risperidone and paliperidone (all genericized), asenapine was associated with incremental total costs of 2418 TL, 1786 TL, 804 TL and 877 TL; and associated with incremental total number of diabetes & CVD avoided of 0.054, 0.038, 0.010 and 0.037 respectively. **CONCLUSIONS:** The lower incidence of developing MetS associated with asenapine compared to olanzapine and other atypicals is associated with lower treatment costs and lower incidence of diabetes and CVD in Turkey.

PMH42

COST-UTILITY ANALYSIS OF LISDEXAMFETAMINE IN THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN THE UNITED KINGDOM

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OBJECTIVES: An economic analysis was conducted from the United Kingdom's (UK's) National Health Service (NHS) perspective to evaluate the cost-effectiveness of lisdexamfetamine (LDX) versus atomoxetine (ATX) in treating children and adolescents with attention-deficit/hyperactivity disorder (ADHD) who have had an inadequate response to methylphenidate (MPH). **METHODS:** A 1-year probabilistic decision-analytic model with a Markov structure of nested decision trees was constructed. Health states included "response", "non-response", and "unable to tolerate". Key model assumptions were adapted from a technology assessment for ADHD products by the National Institute for Health and Care Excellence. The analysis used clinical data from a head-to-head randomized controlled trial in inadequate responders to MPH. Response to treatment was defined as a score of 1 (much improved) or 2 (improved) on the Clinical Global Impression-Improvement scale. Tolerability was assessed by rates of discontinuation due to adverse events. Utility weights were identified via a systematic literature review. Health care resource use estimates for responders and non-responders were obtained via a survey of UK specialists. Unit costs from national sources were applied to estimate the corresponding health-state costs. Daily drug costs were based on mean doses reported in the trial. One-way and probabilistic sensitivity analyses were performed. **RESULTS:** The comparison of LDX and ATX, using head-to-head data, resulted in an incremental cost-effectiveness ratio (ICER) of £1,802 per quality-adjusted life year (QALY). At a willingness to pay of £20,000 per QALY, LDX had an 86% probability of being cost-effective compared with ATX. In 38% of sensitivity analysis runs, LDX was a dominant strategy over ATX. The model was slightly sensitive to changes in assumptions about drug costing and to lengthening the titration period for ATX. **CONCLUSIONS:** From the perspective of the UK NHS, LDX provides a cost-effective treatment option for children and adolescents with ADHD who are inadequate responders to MPH.

PMH43

COST-EFFECTIVENESS OF ASENAPINE IN THE TREATMENT OF BIPOLAR DISORDER I PATIENTS WITH MIXED EPISODES

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OBJECTIVES: The cost-effectiveness of second-generation antipsychotic drugs is well established in the treatment of patients experiencing a manic episode associated with bipolar I disorder. However, no studies demonstrating the value of these drugs in patients with mixed episodes according to DSM-IV have so far been undertaken. The aim of this study was to assess the cost-effectiveness of asenapine versus olanzapine in the treatment of this costly subgroup of patients. **METHODS:** A 9-week acute phase model was developed, during which patients receive up to three lines of treatment: asenapine or olanzapine alone, then adjunctive valproate, and finally a switch to adjunctive lithium. Patients can respond during any 3-week period and non-responders move to the next treatment in the sequence. Efficacy of asenapine (46.3%) and olanzapine (37.5%) was informed by a post-hoc analysis of two short-term clinical trials, where response was measured as a composite YMRS and MADRS endpoint. Following initial treatment, patients entered a 5-year maintenance Markov model during which they faced probabilities of treatment discontinuation, recurrent manic, mixed and depressive symptoms and death. Direct costs (year 2012-13 values), including drug, monitoring costs and resource use related to bipolar disorder and selected adverse events, were assessed from a UK NHS perspective. Benefits were measured as quality-adjusted life years (QALYs). **RESULTS:** For patients with a mixed episode, asenapine was a more effective and less costly treatment strategy compared with olanzapine over a 5-year period. Greater health benefits and cost savings were driven by earlier response to asenapine treatment during the acute phase and were well maintained during longer-term follow-up. These results were robust to changes in key parameters including short and longer-term efficacy, unit cost and utility values. **CONCLUSIONS:** Compared with olanzapine, results of this analysis suggest that asenapine generates greater health benefits at lower cost in the treatment of patients experiencing mixed episodes associated with bipolar I disorder.

PMH44

C-QUALITY: A COST AND QUALITY OF LIFE PHARMACOECONOMIC ANALYSIS OF ANTIDEPRESSANTS IN MAJOR DEPRESSIVE DISORDER IN ITALY

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OBJECTIVES: To assess the cost-effectiveness (€ per quality-adjusted life year [QALY]) of all Selective serotonin reuptake inhibitors (SSRIs) and all Serotonin-norepinephrine reuptake inhibitors (SNRIs) for the treatment of Major Depressive Disorder (MDD) in Italy. **METHODS:** A decision analytic model was adapted from the Swedish Dental and Pharmaceutical Benefits agency model to reflect current clinical practice in the treatment of MDD in the largest Italian regions. This adaptation was possible thanks to the collaboration of an expert panel of Italian psychiatrists and health economists. The model evaluated patients with a first diagnosis of MDD and initiating an SSRI or an SNRI for the first time. The time horizon was 12 months. Efficacy and utility data for the model were retrieved from the literature and validated by the expert panel. Local data were considered for resource utilization and for treatment costs based on each regional health service perspective. Population-weighted regional data were used to define a national model. Scenario simulations, one-way sensitivity analyses, and Monte Carlo simulations were performed to test the robustness of the model. **RESULTS:** The base case analysis showed that escitalopram was associated with a lower total cost (€1,562) and a larger health gain (QALYs) at one year (0.732) per patient, and dominated the other treatment strategies since more QALYs were achieved at a lower total cost. Sensitivity analyses support the robustness of the model. **CONCLUSIONS:** The results indicate that escitalopram is the most cost-effective pharmacological treatment strategy for the Italian health service compared with other SSRIs and all SNRIs used in the first-line treatment of MDD.

PMH45

COST EFFECTIVENESS OF PALIPERIDONE PALMITATE IN NATIONAL HEALTH SERVICE (NHS) WALES: A COST UTILITY ANALYSIS BASED ON THE NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE) CORE MODEL FOR THE MANAGEMENT OF SCHIZOPHRENIA

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OBJECTIVES: Paliperidone palmitate has demonstrated non-inferior efficacy to risperidone long acting injectable (LAI) for the treatment of schizophrenia in previous studies. The objective of this analysis was to assess the cost effectiveness of paliperidone palmitate relative to risperidone LAI, based on the cost-utility analysis described in the current NICE Guidelines for the Management of Schizophrenia. The analysis was undertaken from the perspective of NHS Wales and was submitted to the All Wales Medicines Strategy Group for evaluation. **METHODS:** A decision-analytic Markov model was developed to estimate the cost-utility of paliperidone palmitate relative to risperidone LAI. The model adopted an annual cycle length. Patients who entered the model initiated either paliperidone palmitate or risperidone LAI and could subsequently transition between five health states during each annual cycle. AEs associated with each intervention were derived from literature. Utility values were derived from a community-based study, using trade-off technique to elicit HRQoL for schizophrenia according to frequency of injections. Resource use data was sourced from the NICE core model/guidelines, Welsh clinical experts, and a UK Delphi panel. Unit costs were derived from the British National Formulary, NHS reference costs, and the Personal Social Services Research Unit reports. Costs and outcomes were evaluated over a 10-year horizon, and discounted at 3.5%. Results were presented as incremental costs/QALY. Uncertainty was addressed via deterministic and probabilistic sensitivity analyses. **RESULTS:** The base case analyses demonstrated that paliperidone palmitate would incur lower costs (-£3,773) and generate more quality adjusted life years (QALYs) (+0.13) than risperidone LAI. This indicated that paliperidone palmitate 'dominated' risperidone LAI. Extensive scenario/sensitivity analyses confirmed the robustness of the results **CONCLUSIONS:** Compared with risperidone LAI, paliperidone palmitate is a cost-effective therapy for the treatment of schizophrenia in adult patients in NHS Wales.

PMH46

COST-UTILITY ANALYSES OF COGNITIVE-BEHAVIORAL THERAPY FOR MAJOR DEPRESSIVE DISORDER – A SYSTEMATIC REVIEW

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OBJECTIVES: Major depressive disorder (MDD) causes a massive health and economic burden for societies worldwide. Cognitive behavioural therapy (CBT) is an inherent part of the treatment of MDD and is recommended for children, adolescents and adults. Cost-Utility-Analysis (CUA) is an important instrument to support decision-making on resource allocation and health policy as it permits the comparison of interventions for different diseases. The objective of our study was to systematically review CUAs related to CBT in the treatment of patients suffering from MDD. **METHODS:** We conducted a systematic literature search in MEDLINE, EMBASE, PsycINFO and NHSEED. We included all original studies reporting CUA of CBT for patients suffering from MDD. Cost data were inflated to the year 2011 and converted into US-$ using purchasing power parities (US-$ PPP) to ensure comparability of the data. Quality assessment of the studies was performed by means of a standardised quality checklist. **RESULTS:** We identified 22 CUAs. The methodological quality was fair. Two studies considered a lifetime horizon. The mean time horizon of the remaining studies was 19.2 months (SD = 12.6). In most instances individual and group CBT as well as CBT for maintenance showed acceptable cost-utility ratios (ICER < 50.000 US-$-PPP / QALY). The results of CUAs of CBT provided for children and adolescents or by computer were inconsistent. In comparison to medication CBT tends to be more cost effective as stand-alone therapy and in combination with medication. **CONCLUSIONS:** Individual and group CBT is a cost effective treatment for MDD. Further research to determine the cost effectiveness of computerized CBT and of CBT for specific populations like children, adolescents or the elderly is required. Furthermore there is a need for long term evidence of cost effectiveness of CBT.

PMH47

COMPARISON OF HEALTH CARE RESOURCE UTILIZATION AND COSTS AMONG CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER IN GERMANY WHO INITIATED TREATMENT WITH ATOMOXETINE OR LONG-ACTING METHYLPHENIDATE

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OBJECTIVES: This study compared health care resource utilization (HRU) and costs among children/adolescents with attention deficit/hyperactivity disorder (ADHD) in Germany who initiated treatment with atomoxetine (ATX) or long-acting methylphenidate (LA-MPH). **METHODS:** A retrospective propensity score matched cohort analysis was conducted using the IMS electronic medical record database comprising >15 million patient records from ~3,000 German physicians. Included patients were aged 6-17 years, with a first (index) ATX or LA-MPH prescription in 2006-2010; ≥1 ADHD diagnoses 12-month before (pre-index) and after (post-index) index; and ≥1 index medication prescription post-index. Patients in the ATX and LA-MPH

cohorts were matched 1:1 using "nearest neighbor" greedy match propensity score method. HRU (inpatient, outpatient, and medications) and costs were compared between the two cohorts. Unit costs were identified from German Diagnosis-related Group for inpatient, Einheitlicher Bewertungsmassstab doctor fee scale for outpatient, and Rote Liste®for medication costs. Direct medical costs over the post-index period were reported in 2011 Euros. Chi-square for categorical variables and t-test or Wilcoxon-Mann-Whitney for continuous variables were used to test for differences between cohorts (alpha=0.05). Generalized linear models with negative binomial (for HRU) and gamma (for cost) distributions were used to address residual differences between matched cohorts. **RESULTS:** Of 4705 eligible patients, 737 with ATX (mean age=10.9 years, 20.8% female) were identified and matched 1:1 with LA-MPH patients (mean age=11.2 years, 18.6% female). Patients initiating ATX had higher HRU and spending per-patient than patients initiating LA-MPH over the post-index: 20.9 (SD=11.5) vs. 15.7 (SD=9.0) outpatient prescriptions, 10.1 (SD=6.3) vs. 8.3 (SD=5.3) outpatient visits, €1029 (SD=574) vs. €496 (SD=334) in retail pharmacy costs, and €1,258 (SD=739) vs. €684 (SD=515) in total all-cause costs (all $p=<.0001$). **CONCLUSIONS:** Among children/adolescents with ADHD in Germany, ATX initiators consumed significantly more health care resources and were associated with significantly higher direct medical costs compared with LA-MPH initiators.

MENTAL HEALTH – Patient-Reported Outcomes & Patient Preference Studies

PMH48

FACTORS ASSOCIATED WITH POOR ADHERENCE IN PATIENTS INITIATING MEDICATION FOR MAJOR DEPRESSIVE DISORDER: INTERIM RESULTS FROM A PROSPECTIVE, LONGITUDINAL STUDY

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OBJECTIVES: To examine factors associated with low adherence in Major Depressive Disorder (MDD) patients initiating antidepressant medication (ADM) over a 12-week period. **METHODS:** MDD patients initiating an ADM (with no ADM claim in the 6 months prior) were identified from a large pharmacy benefits manager database. Patients completed paper or online assessments including demographics at baseline and patient-reported assessments at baseline, Week 4 and Week 12. Participants were classified as having low, medium, or high adherence based on the modified Morisky Adherence Scale, with the medium and high adherence groups combined for analysis. Logistic regression analyses were run to evaluate the association between adherence and age, gender, and patient-reported assessments of depression and sexual dysfunction (SD), weight gain, sleep problems, nausea, and anxiety. **RESULTS:** Of 2412 patients screened, 591 enrolled and completed baseline assessments. Mean age was 40.4 years (standard deviation=12.1), 82.4% were women, and 87.6% were white. There were 483 who completed Week 4 and 425 who completed Week 12 assessments. At Week 12, 39.6% were high adherers, 20.6% were medium adherers, and 39.8% were low adherers. Thirty-eight percent of low adherers had actually discontinued ADM. Among discontinuers, 40.6% discontinued due to ADM side effects. In logistic regression models, low adherence at Week 4 was significantly associated with weight change ≥5 pounds (OR=2.10, 95% CI: 1.32–3.35), anxiety (OR=1.73, 95% CI: 1.06-2.8) and nausea (OR=2.31, 95% CI: 1.06–5.02). Age, gender, depression severity, sexual dysfunction, and insomnia were not significant in the logistic model. No factors were significantly associated with adherence at Week 12. **CONCLUSIONS:** In this real-world study of patients with MDD, nearly 40% of patients were low adherers. Weight change, anxiety, and nausea were associated with low adherence at Week 4, but not at Week 12.

PMH49

ADHERENCE, SWITCHING, AND DISCONTINUATION DURING THE 12 WEEKS FOLLOWING ANTIDEPRESSANT INITIATION IN PATIENTS WITH DEPRESSIVE DISORDER: RESULTS OF A PROSPECTIVE, LONGITUDINAL STUDY

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OBJECTIVES: This study examined patterns of adherence, switching, and discontinuation, in major depressive disorder (MDD) patients initiating antidepressant medication (ADM) therapy. **METHODS:** Depressed patients recently initiating an ADM were identified from a large pharmacy benefits manager database. Eligible patients were invited to participate by phone or mail and enrolled patients completed. **RESULTS:** Of 2,412 patients screened, 591 were enrolled. Average age was 40.4 years (standard deviation=12.1), 82.4% of participants were women, and 87.6% were white. At Week 4 (n=483), 39.4% were classified as low adherers with 31 (6.4%) patients having discontinued ADM for reasons including side effects (n=14, 45.2%), feeling better (n=5, 16.1%), cost (n=5, 16.1%), and lack of efficacy (n=4, 12.9%). There were 27 (5.6%) patients who switched by Week 4. Of these, 12 (44.4%) switched due to side effects, 11 (40.7%) due to lack of efficacy, and 3 (11%) due to cost. By week 12 (n=425), 33 additional patients had discontinued ADM citing similar reasons as those at Week 4. Of 43 patients who reported switching at Week 4 or Week 12, 15 (34.9%) cited side effects, 16 (37.2%) cited lack of efficacy, and 4 (9.3%) cited cost. **CONCLUSIONS:** In this real-world, 12-week study of MDD patients initiating ADM, adherence to ADM was low. Switching and discontinuing ADM were common within the 12-weeks period and were primarily attributed to side effects and lack of efficacy.

PMH50

FUNCTIONAL OUTCOMES WITH ARIPIPRAZOLE ONCE-MONTHLY IN TWO DOUBLE-BLIND, PLACEBO- AND ACTIVE-CONTROLLED STUDIES (ASPIRE US 246 AND ASPIRE EU 247) FOR THE TREATMENT OF SCHIZOPHRENIA

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OBJECTIVES: To evaluate functional outcomes of aripiprazole once-monthly (ARI-OM) 400 mg (ARI-OM-400) versus a sub-therapeutic dose of ARI-OM (50 mg; ARI-OM-50), oral aripiprazole (ARI), and placebo, in two trials of stable patients with schizophrenia. **METHODS:** Detailed study designs have been reported previously. Results are reported for the double-blind, randomized phase of each study. ARI-OM is an extended-release injectable suspension given at 400 mg in the gluteal muscle. Functional outcome was measured using the Personal and Social Performance scale (PSP) and statistically analyzed using analysis of covariance with last observation carried forward. **RESULTS:** A total of 403 patients were randomized to ARI-OM-400 (n=269) or placebo (n=134) in the first (246) trial. PSP scores at endpoint significantly worsened with placebo (-6.2) versus ARI-OM-400 (-1.7; p=0.0002). In the second study (247), 662 patients were randomized to: ARI-OM-400 (n=265); ARI (n=266); or ARI-OM-50 (n=131). PSP scores with sub-therapeutic ARI-OM-50 significantly worsened (-2.39) versus ARI-OM-400 (+0.45; p=0.03). Similar functional stability was observed with ARI (+0.08). **CONCLUSIONS:** Patient functioning, as assessed by PSP, was maintained with ARI-OM in both studies but deteriorated in patients randomized to either sub-therapeutic doses or placebo, confirming the benefits of adequately dosed antipsychotic therapy in preserving functional stability in long-term management of schizophrenia.

PMH51

THE DEVELOPMENT AND VALIDATION OF A QUALITY OF LIFE MEASURE FOR PEOPLE WITH MILD COGNITIVE IMPAIRMENT (THE MCQ)

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OBJECTIVES: Mild cognitive impairment (MCI) is a state that lies between normal cognition and dementia, and the number of cases with the condition is rising as the population ages. However, to date, no validated patient reported outcome measure (PRO) exists specifically in MCI. We report on a study to develop a PRO for use in MCI. **METHODS:** Semi-structured in-depth interviews were carried out with people with MCI in order to determine the questionnaire items. These interviews were audio-recorded, transcribed and content analysed. The draft questionnaire was refined following feedback from a focus group of patients with a diagnosis of MCI. Questionnaires were posted to subjects recruited from memory clinics and research databases, the completed questionnaires were analysed using factor analytic techniques to produce the final measure; construct validity was assessed by correlation with a generic patient reported outcome measure, the SF-12. **RESULTS:** Interviews were carried out with 23 people with MCI. 280 questionnaires were sent to subjects, with a response rate of 56% i.e.146 were included in the analysis. Factor analysis produced a 13 item measure tapping two domains of patient reported quality of life ('Emotional Effects' and 'Practical Concerns'). Internal consistency reliability was high for both domains (alpha was 0.91 and 0.85 respectively). Both dimensions were found to be highly and significantly correlated with the Mental Component Summary score of the SF-12. **CONCLUSIONS:** The Mild Cognitive Impairment Questionnaire (MCQ) is a short 13 item measure developed specifically to measure patient reported outcomes in people with MCI. It was created on the basis of patient report, and has been shown to have good psychometric properties. It is likely to prove valuable in the evaluation of treatment regimes in this important and growing patient group.

PMH52

SCORING THE CENTER FOR EPIDEMIOLOGIC STUDIES – DEPRESSION SCALE: WHICH ITEMS GO WHERE?

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OBJECTIVES: To guide researchers on the best way to score the Center for Epidemiologic Studies – Depression scale (CES-D) by comparing competing models in the literature. **METHODS:** Radloff (19777), the original CES-D author, first provided scoring for four uncorrelated factors of depression: negative affect (NA), positive affect (PA), interpersonal (I), and somatic (S). Sheehan et al. (1995) validated four correlated factors in the CES-D. However, Radloff and Sheehan results may have differed because Radloff ascribed items of *failure* and *fearful*to NA whereas Sheehan assigned a value of I. Following Sheehan's scoring, Cole et al. (2004) presumed a hierarchical factor of depressed mood that included all four previously identified factors and posited a 10-item short-form of the CES-D. These four models were compared using structural equation modeling for parametric models with Bollen-Stine bootstraps to control for multivariate nonnormality in 225 community-residing subjects, structural validity of the models were compared. **RESULTS:** Fit statistics for the four models were: Radloff comparative fit index (CFI) = .790 & root mean square error of approximation (RMEA) = .011; Sheehan CFI = .926 & RMSEA = .053, Cole hierarchical CFI = .927 & RMSEA = .052; Cole 10-item CFI = .979 & RMSEA = .041 **CONCLUSIONS:** The uncorrelated Radloff model was the poorest fit the day. Both Sheehan and Cole 20-item models were decently fit to the data and nearly identical to each other in fit. Finally, the 10-item Cole short-form of the CES-D was the best fit model to the data. Given the brevity of this form and strong fit with the theoretical structure postulated by Radloff, researchers may want to consider this form of the CES-D for research on depressed mood.

PMH53

PREVALENCE AND RISK FACTORS OF DEPRESSION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN INDIA

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OBJECTIVES: Although depression is a significant co-morbid condition in chronic illness, little is known about the prevalence or risk factors for depressive symp-

toms in chronic obstructive pulmonary disease (COPD) in India. A study was undertaken to investigate the prevalence and risk factors of depression in the Indian COPD patients. **METHODS:** COPD was classified according to GOLD stages based on forced expiratory volume in one second (FEV_1) in 126 stable patients. Depression was examined by administering the nine-item Hindi version of Patient Health Questionnaire-9 (PHQ-9). Linear regression model was used to examine association between predictor variables and risk of depression with adjustment of age and sex. Cronbach alpha was calculated to assess internal consistency of PHQ-9. **RESULTS:** Patients with stable COPD (n=126) were evaluated (73.8% male and 26.2% female). In the study population as whole, 33.3% patients showed moderate to severe depressive symptoms whereas 20.6% patients had major depressive disorder on PHQ-9 Scale. Educational and occupational status, body mass index, FEV_1, respiratory symptoms, physical impairment and dyspnea were found to be potential predictors of depression in COPD patients. **CONCLUSIONS:** One-fifth of the patients with COPD had severe symptoms of related to depression, which was especially higher with severity of COPD. Hence, the patients with COPD should focus on management of these two conditions. Further, future studies should be conducted to assess the role of depression management and timely treatment of it in the patients with COPD.

PMH54

PATIENT FUNCTIONING IN GENERALIZED ANXIETY DISORDER SUBJECTS WITH PARTIAL RESPONSE TO PRIOR SSRI TREATMENT: THE EFFECT OF ADJUNCTIVE THERAPY WITH PREGABALIN IN DAILY MEDICAL PRACTICE

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OBJECTIVES: To analyze the effect of adding pregabalin or usual care (UC) on patient functioning in GAD subjects with partial response (PR) to previous SSRI course in daily medical practice. **METHODS:** Post-hoc analysis of patients with PR to SSRI monotherapy enrolled in a prospective 6-month naturalistic study. PR was defined as a Clinical Global Impression scale score >3 and persistence of anxiety symptoms >16 in the Hamilton-Anxiety scale. Two groups (based on psychiatrist judgment) were analyzed: adjunctive therapy (AT) with pregabalin (150-600 mg/day) to existing therapy; or usual care (switching to a different SSRI or adding another anxiolytic different than pregabalin). Patient functioning was assessed by mean of the disability WHO-DAS-II scale [range 0 (no disability) to 100 (completely unable)]. Changes in domains scale scores were compared at end-of-trial visit by a general linear model with covariates. **RESULTS:** Four-hundred-eighty-six newly prescribed pregabalin and 239 UC patients [mean (SD) HAM-A 26.7 (6.9) and CGI 4.1 (0.5)] were analyzed. AT with pregabalin was associated with significantly higher mean (95% CI) reductions vs. UC in all the domains of the WHO-DAS-II scale. Differences between groups were statistically significant (effect sizes were moderate): understanding and communication [-6.9(-9.8;-4.0), p<0.001], getting around [-5.2(-8.0;-2.8), p<0.001], self-care [-3.6(-5.5;-1.8), p<0.001], getting along with others [-5.0(-8.6;-1.3), p=0.007], household [-5.3(-9.6;-1.0), p=0.015], work activities [-6.5(-11.2;-1.8), p=0.007], and participation in society [-6.3(-9.7;-2.9), p<0.001]. The overall disability score was significantly more reduced in pregabalin group vs. UC: -21.7(-23.3;-20.1) vs. -15.3(-17.5;-13.1), p<0.001. Gender effect was negligible (no interaction) in all the dimensions analyzed except household functioning (higher reduction in women). **CONCLUSIONS:** In medical practice, GAD patients with partial response to prior course of a SSRI experienced greater and meaningful functioning improvements with adjunctive therapy with pregabalin in comparison with usual care. The effect of pregabalin was independent of patient gender except for household functioning.

PMH55

WORK IMPAIRMENT BURDEN OF ANXIETY AND DEPRESSION IN GERMANY

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OBJECTIVES: The effect of mental disorders on absenteeism in Germany has steadily increased. They are now the third-most common reason for sick leave after musculoskeletal and respiratory conditions. The aim of this study was to provide current estimates of the effect of anxiety and depression on both absenteeism and presenteeism in Germany. **METHODS:** Data from the German respondents (N=15,001) of the 2011 National Health and Wellness Survey were used in the analysis. Outcome measures included the Short Form-12v2 (mental and physical component summary [MCS and PCS] and health utility scores) and the Work Productivity and Activity Impairment questionnaire. Respondents who reported a diagnosis of anxiety and, separately, a diagnosis of depression were compared with respective matched controls (matched on demographic and health history variables using propensity score matching). **RESULTS:** A total of 904 (6.0%) respondents reported a diagnosis of anxiety (62.6% female, mean age=44.6 years) and 1574 (10.5%) respondents reported a diagnosis of depression (60.2% female; mean age=44.9 years). Compared with matched controls, respondents with anxiety reported significantly greater absenteeism (17.9% vs. 8.1%) and presenteeism (36.3% vs. 19.4%) (all p<.05). Similar findings were observed for depression (absenteeism: 17%.3 vs. 7.6%; presenteeism: 36.1% vs. 17.1%; all p<.05). These findings translated to an incremental 60.7 and 61.1 days lost per year due to absenteeism alone for anxiety and depression, respectively. Respondents with anxiety and depression also reported significantly lower levels of health status compared with matched controls (anxiety: 33.0 vs. 45.7 and 43.5 vs. 46.6 for MCS and PCS, respectively, all p<.05; depression: 33.3 vs. 46.6 and 43.8 vs. 47.1 for MCS and PCS, respectively, all p<.05). **CONCLUSIONS:** Anxiety and depression were associated with significant work impairment along with reduced mental and physical health status in Germany. These results suggest greater awareness and early treatment could reduce the social and economic burden of these conditions.

PMH56

HEALTH-RELATED QUALITY OF LIFE OF PATIENTS ON OPIATE REPLACEMENT THERAPY

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OBJECTIVES: To evaluate health-related quality of life (HRQOL) and contributing factors in individuals receiving opiate replacement therapy. **METHODS:** This was a cross-sectional study of patients attending for methadone therapy in an inner city drug treatment centre. EQ-5D, SF-36, SF-6D, Hospital Anxiety Depression Scale (HADs) were assessed, along with substance abuse via the Treatment Outcomes Profile (TOPs). Mean values, ranges and standard deviations were calculated and utility scores were derived. Analysis was performed using Spearman's correlation and t-test to determine any significant correlations. **RESULTS:** A total of 115 patients were included, 72% were male and the mean age was 35 years. 63% were HCV-PCR positive and 49% admitted to using drugs in the past month. 57% of patients had high levels of anxiety with the mean score being 11.14 (anxious). 35% were depressed with the mean score being 8.40 (borderline depressed). The mean EQ-5D utility score was 0.56 with 7% having a utility score that was worse than death. The mean SF-36 utility score was 0.55. The mean SF-36 physical component score was 44.25 and the mean mental component score was 33.18. **CONCLUSIONS:** HRQOL was reduced in this opiate replacement therapy cohort. HCV, gender and injecting drug use did not affect HRQOL but anxiety, depression and use of crack cocaine had a significant impact.

MENTAL HEALTH – Health Care Use & Policy Studies

PMH57

NATURALISTIC DISEASE MANAGEMENT STUDY OF PATIENTS WITH ALCOHOL DEPENDENCE IN THE PRIMARY CARE SETTING IN THE UNITED KINGDOM (STREAM)

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OBJECTIVES: Describe the management of alcohol dependence at general practitioner (GP) level. **METHODS:** STREAM is a non-interventional, 6-month prospective study of adult patients undergoing targeted alcohol screening during routine consultation by GPs throughout England and Scotland, for whom alcohol problems were either known or suspected on the basis of clinical signs or patient's report. Inclusion criteria were an AUDIT score >=8 and consent. At baseline, diagnosis of dependence was made using the DSM-IV criteria and data were collected on socio-demographic characteristics, co-morbidities, alcohol consumption with the timeline follow-back method, previous and current alcohol treatment, treatment goal (abstinence or reduction of alcohol consumption). The data were analyzed descriptively. **RESULTS:** A total of 218 patients screened positive and were included in 26 sites. A total of 79% of patients fulfilled the DSM-IV criteria for alcohol dependence; 74% were men, the mean age was 50 years and only 29% were working full or part-time. 40% of patients had a history of alcohol treatment (almost always counseling), 20% had a history of detoxification and 9% a history of pharmacological treatment. At inclusion, the proportion of patients with ongoing treatment for alcohol addiction was 28% and these patients were drinking in average 63 g/day compared to 89 g/d in untreated patients. Of those patients on treatment or about to initiate it, alcohol reduction was more frequently the treatment goal than abstinence (51% vs. 45%). **CONCLUSIONS:** Targeted screening is an effective way for GPs to identify patients with alcohol dependence opportunistically. Many such patients have a history of counseling but few have received pharmacological interventions. Only a minority of those with alcohol dependence have ever received any form of treatment. For the majority of those in treatment, alcohol reduction is the treatment goal of choice. Consumption levels in patients with dependence tend to be high, irrespective of treatment status.

PMH58

ARE PUBLIC SUBSIDIES EFFECTIVE TO REDUCE HOSPITALIZATIONS

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OBJECTIVES: Elderly people facing dependence are exposed to the financial risk of long lasting care expenditures. This risk is high for people facing cognitive, functional and behavioral problems. In the short-term, dependent elderly people face increased non-medical care expenditures. In the long-term, they face increase medical care expenditures, driven by extended hospital stays. In France, providing public financial assistance has been showed to improve dependent people's access to non-medical care services. However, the long-term impact of public financial assistance on care trajectories has not been explored yet. Our study aims at determining whether financial assistance on non-medical care provision decreases hospital stays rates. **METHODS:** We run Fixed Effects Poisson regression models using longitudinal data of 574 French patients diagnosed with Alzheimer's disease. We use instrumental variables to reduce the presence of a potential endogeneity bias. **RESULTS:** We find that beneficiaries of home care subsidies have a 34% lower rate of hospitalization than non-beneficiaries. **CONCLUSIONS:** Providing public financial assistance is effective to reduce hospitalizations in Alzheimer's disease.

PMH59

DEVELOPING AN INDIVIDUALIZED E-HEALTH DECISION SUPPORT SYSTEM FOR DEMENTIA TREATMENT AND CARE: THE FP7 EU-PROJECT E-HEALTH MONITOR (EHM)

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OBJECTIVES: The increasing prevalence of dementia worldwide highlights the need for effective and individualized support systems for dementia treatment and care. Facing the reality of increasing internet usage as well as the large availability of digitalized information, there is a high potential for ehealth interventions. Therefore one purpose of this project is to provide a 'Personal eHealth Knowledge Space' (PeKS)

for dementia patients, caregivers and medical professionals on the basis of a web-based platform. **METHODS:** Within the PeKS, involved endusers will be provided disease- as well as situation-specific information from existing, evidence-based digital information (links, PDFs, videos) but also from local and regional information sources. The overall aim is to enable increased knowledge and competence by providing situation-specific and on time information. On the other hand, the PeKS includes an interactive monitoring tool, thus enhancing (shared) medical decision support by connecting patients/caregivers and medical professionals. After the technical integration of the concept, a running prototype will be available. **RESULTS:** The developed prototype of the 'Personal eHealth Knowledge Space' is realized by integrating service-oriented architecture, knowledge engineering, multiagent systems, and wearable/portable device technologies. An interactive monitoring tool, based on information provided by caregivers will be realized by integrating the 'Nurses' Observation Scale for Geriatric Patients (NOSGER)'. Individualized information is going to be provided through push- and pull mechanisms. **CONCLUSIONS:** Health support systems addressing individual dementia patients/caregiver needs have a large potential, however they are scarce. eHealthMonitor's overall objective is to significantly increase the individualization of personal eHealth services and thereby the quality and patients' acceptance of electronic health care services for prevention, treatment and care. The research is funded by the European Commission, ICT FP7, project ID 287509.

PMH60

PSYCHOACTIVE DRUG USE, POLYPHARMACY AND CO-MORBIDITIES IN NEWLY DIAGNOSED PATIENTS WITH PERVASIVE DEVELOPMENT DISORDER IN THE PROVINCE OF QUEBEC

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OBJECTIVES: A number of medication surveys conducted in the U.S. have demonstrated a high level of psychotropic drug use in patients diagnosed with pervasive development disorder (PDD). Medication use is of interest as not many products are approved for treatment in autism. Describe drug use in subjects newly diagnosed with PDD in Quebec province. **METHODS:** A cohort study was built by using Quebec RAMQ and Med-Echo databases for subjects having a new PDD diagnosis (ICD-9 codes: 299.0-299.9) between January 1998 and December 2010. Cohort entry date was the date of a first diagnosis confirmed by the absence of PDD diagnosis in previous 2 years, and aged less than 26 years. Descriptive analyses of patient characteristics were done at cohort entry and drug use profiles were done the year prior to, and within the 3 years following diagnosis. **RESULTS:** A cohort of 4684 subjects was identified; 78% of patients were male and the age ranges were as follows: 41.9% (1-5 years), 31.2% (6-12 years), 12.3% (13-17 years), 14.7% (18-25 years). Prior to being diagnosed with PDD, 35% received at least 1 psychoactive drug. Methylphenidate was most common in 6-12 year olds (36%) whereas antipsychotics were most common in the 13-17 group (28.6%) and in the adult population (51.7%). Antipsychotic use was also present in younger children: 5.7% in 1-5 year olds and 23% in 6-12 year olds, 1 year after diagnosis. Antipsychotic, antidepressant and anticonvulsant usage increased in the 3 years following diagnosis, and also with age. **CONCLUSIONS:** Prior to PDD diagnosis, more than a third of the patients were on psychotropic medications, a practice that continued and increased after diagnosis. Psychoactive drug utilization is high and could be of concern if used to compensate for limited access to other treatment modalities such as educational and allied health therapies.

PMH61

IS ADJUNCTIVE GUANFACINE-EXTENDED RELEASE ASSOCIATED WITH CHANGES IN STIMULANT ADHERENCE AMONG CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN A MANAGED CARE SETTING?

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OBJECTIVES: To assess stimulant adherence among pediatric patients with attention-deficit/hyperactivity disorder (ADHD) after adding guanfacine extended-release (GXR) as adjunctive therapy to stimulants in a US managed care setting. **METHODS:** Data from the MarketScan Commercial Claims and Encounters insurance claims database (2009-2011) were used. Patient inclusion criteria were: 6-17 years old; ≥1 ADHD diagnosis (ICD-9-CM code 314.00 or 314.01); ≥1 long-acting (LA) and/or short-acting (SA) stimulant prescription; continued stimulant therapy for ≥30 days and ≥6 months of continuous insurance coverage pre- and post-GXR initiation; and nonadherent to stimulant treatment pre-GXR. Adherence was assessed using the medication possession ratio [MPR] (range=0.0-1.0), with MPR <0.80 considered nonadherent. Change in stimulant adherence pre- to post-GXR initiation was assessed using an OLS multivariable model, adjusting for patient age, sex, and geographic region; GXR dose (last observed), adherence, dose stabilization, and year of initiation; number of non-ADHD prescriptions pre-GXR; stimulant MPR pre-GXR; and stimulant received (LA, SA, SA+LA). **RESULTS:** A total of 238 patients nonadherent to stimulants prior to initiating GXR were analyzed; 38% were female, mean (SD) age was 10.3 (3.3) years, unadjusted pre- and post-GXR stimulant MPR was 0.51 (0.16) and 0.82 (0.25), respectively, and the change in MPR was 0.31 (0.28). Among LA patients (n=162), mean unadjusted pre-GXR stimulant MPR was 0.50, and 0.80 post-GXR; among SA and SA+LA patients (n=76), this was 0.53 (pre-GXR) and 0.88 (post-GXR). The mean adjusted (i.e., post-model estimation) change in MPR was 0.29 (95% CI: 0.27-0.32) for LA patients versus 0.34 (95% CI: 0.31-0.38) for combined SA and SA+LA patients (difference=0.05; P=0.013). **CONCLUSIONS:** Among patients nonadherent to stimulant treatment, prior to initiating adjunctive GXR, adding GXR was associated with positive changes in stimulant adherence, with statistically significant differences in the change in MPR observed for patients initiating GXR while on LA stimulants alone versus those on SA or SA+LA stimulants.

PMH62

PATIENTS' CHARACTERISTICS AND PATTERNS OF USE OF DEPOT ANTIPSYCHOTICS IN GERMAN PATIENTS WITH SCHIZOPHRENIA

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OBJECTIVES: To describe patients' characteristics and patterns of use of depot antipsychotics in patients with a diagnosis of schizophrenia in Germany. **METHODS:** Claims data were analysed from German patients covered by Elsevier Health Risk Research Database between 2009-2011 (approx 7.6 million insured persons). The study sample consisted of adult patients who initiated a given depot antipsychotic for schizophrenia (F20) or schizoaffective disorder (F25) in 2010. Baseline clinical characteristics of patients were searched over the year prior to depot initiation. Persistence (treatment duration) with depot treatment was assessed using a Kaplan-Meier survival analysis until discontinuation or end of the study period (31 December 2011). **RESULTS:** A total of 2,240 patients with a diagnosis of schizophrenia or schizoaffective disorder (mean age 50.7 years, 48.8% male) were included. At baseline, the main psychiatric comorbidities were major depressive disorder (38% of patients), substance use disorders (29%) and anxiety disorders (13%). Main somatic conditions were cardiovascular diseases (37%), neurological disorders (33%) and hyperlipidemia (27%). Depot antipsychotics prescribed were mainly risperidone long acting (32%), flupentixol (31%) and haloperidol decanoate (17%). Prescribers were psychiatrists/neurologists (58%), GPs (16%), other/unknown (26%). Median persistence to depot antipsychotic treatment was 156 days. **CONCLUSIONS:** To our knowledge, this is the first large database study conducted in Germany aiming at describing the patients' characteristics and treatment patterns of schizophrenic patients treated with depot antipsychotics. It is notable that the current sub-population of schizophrenic patients treated with depot showed substantial psychiatric and cardiovascular co-morbidities.

PMH63

VARIATION IN TREATMENT PATTERNS AND OUTCOMES IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ACROSS EUROPEAN COUNTRIES

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OBJECTIVES: To visualize heterogeneity in treatment pathways and outcomes among children and adolescents with ADHD in Europe. **METHODS:** Retrospective chart review of 779 ADHD patients (aged 6–17 years) diagnosed by 340 clinicians between 2004 and 2007 in six European countries. Receipt of ADHD medication and/or behavioural therapy (BT) was evaluated across the study period. Patient characteristics, treatment patterns, physician-reported satisfaction and symptom control were analysed in the total population and among patients with at least one switch in ADHD therapy during follow-up (switchers). Optimal treatment success (OTS) was defined as high satisfaction and complete symptom control at chart review. **RESULTS:** Most patients treated with ADHD medication (89.5%) received methylphenidate. Among 386 patients (49.6%) who remained on their initial treatment throughout the chart review period, the majority (86.3%) were treated with ADHD medication alone or in combination with BT. Switchers (n=393; 50.4%) did not differ significantly at baseline from non-switchers. Few patients (n=98; 12.6%) switched more than once. The most common types of switch (first and last treatments considered) were from one monotherapy to another (n=91; 23.2%) or change of medication co-administered with BT (n=54; 13.7%). The most common reasons for last switch were suboptimal response (40.2%), duration of action (18.1%) or both (14.5%). At review, among those who switched, 11.7% discontinued all ADHD treatment and 5.1% received only BT. Overall, OTS was 27.4% with no significant difference between switchers and non-switchers (29.1% vs 25.5%; p=0.281). **CONCLUSIONS:** About half the patients switched from their initial treatment during chart review, mostly due to suboptimal response, with many (16.8%) discontinuing ADHD medications. Furthermore, OTS remained low regardless of whether a patient switched ADHD therapies. Together, these observations suggest currently available ADHD treatments are inadequate for achieving OTS among children and adolescents in Europe.

PMH64

PATIENTS' CHARACTERISTICS AND PATTERNS OF USE OF DEPOT ANTIPSYCHOTICS IN SWEDISH PATIENTS WITH SCHIZOPHRENIA

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OBJECTIVES: To describe patients' characteristics and patterns of use of depot antipsychotics in patients with a diagnosis of schizophrenia in Sweden. **METHODS:** A retrospective analysis was conducted based on longitudinal and population-based data in the Swedish national health registries. The study sample consisted of adult patients who initiated a treatment with any depot antipsychotic for schizophrenia (F20) or schizoaffective disorder (F25) in 2009-2010. Baseline clinical characteristics of patients were searched over the year prior to depot initiation. Persistence (treatment duration) with depot treatment was assessed using a Kaplan-Meier survival analysis until discontinuation or end of the study period (31 December 2011). **RESULTS:** A total of 2,879 patients with a diagnosis of schizophrenia or schizoaffective disorder were included. Mean age was 50.0 years and 54.4% of the patients were male. At baseline, the main psychiatric comorbidities were other psychotic disorders (17% of patients), substance use disorders (11%) and major depressive disorders (3%). Somatic conditions were

infrequent (4% diabetes and 3% neurological disorders). The most common depot antipsychotics prescribed were zuclopentixol (32%), perphenazine (28%) and risperidone LAI (19%). These were prescribed primarily by psychiatrists (85%). Median persistence to depot treatment was 195 days. **CONCLUSIONS:** To our knowledge, this is the first large database study conducted in Sweden aiming at describing the patients' characteristics and treatment patterns of schizophrenic patients treated with depot antipsychotics. It is notable that the current sub-population of schizophrenic patients treated with depot does not show substantial psychiatric and somatic co-morbidities, possibly due to under-diagnosing of co-morbidities, especially somatic diseases, by psychiatrists.

PMH65

ASSESSING THE ECONOMIC BURDEN AND HEALTH CARE UTILIZATIONS OF THE UNITED STATES VETERAN PATIENTS DIAGNOSED WITH SCHIZOPHRENIA

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OBJECTIVES: To examine the economic burden and health care utilizations of schizophrenia in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration (VHA) Medical SAS datasets from October 1, 2008 to September 30, 2012. Patients diagnosed with schizophrenia were identified using International Classification of Disease 9thRevision Clinical Modification (ICD-9-CM) diagnosis codes 295.xx, and the first diagnosis date was designated as the index date. A group of patients without schizophrenia of the same age, region, gender and index year were identified and matched by baseline Charlson Comorbidity Index (CCI) as the comparison group. Patients in both groups were required to be at least 18 years old and have continuous medical and pharmacy benefits 1 year pre- and 1 year post-index date. One-to-one propensity score matching was used to compare health care costs and utilizations during the follow-up period between the schizophrenia and comparison group patients, adjusted for baseline demographic and clinical characteristics. **RESULTS:** A total of 171,086 eligible patients were identified for the schizophrenia and control cohorts. After 1:1 matching, a total of 70,045 patients were matched from each cohort with well-balanced baseline characteristics. Patients diagnosed with schizophrenia had significantly higher health care utilization in inpatient (18.12% vs. 2.30%, p<0.01), emergency room (19.67% vs. 6.46%, p<0.01), office (98.32% vs. 53.26%, p<0.01), and outpatient visits (98.53% vs. 54.16%, p<0.01). Higher health care utilizations translated into higher costs for schizophrenic patients including inpatient ($7,228 vs. $613, p<0.01), pharmacy ($1,012 vs. $343, p<0.01), outpatient ($3,998 vs. $1,302, p<0.01), and total costs ($12,238 vs. $2,260, p<0.01) relative to patients in the comparison group. **CONCLUSIONS:** Schizophrenic patients were associated with a substantial economic burden compared to their matched controls.

PMH66

DIFFERENCES IN HEALTH CARE RESOURCE UTILIZATION AND EXPENDITURES AMONG SCHIZOPHRENIC PATIENTS IN THE UNITED STATES BY HEALTH INSURANCE STATUS, 2007-2008

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OBJECTIVES: To compare health care resource utilization (HRU) among schizophrenic patients in the United States by the type of health insurance and estimate the annual expenditures. **METHODS:** The 2007 National Health and Interview Survey (NHIS) data were used for this study (150 schizophrenia cases). Multivariate regression was conducted to compare HRU (hospitalizations, physician visits, ER visits) by type of health of insurance (any private, public only, and none). Additionally, 2008 Medical Expenditure Panel Survey (MEPS) data were linked with the NHIS data (29 of the NHIS cases). Means, SE and 95% confidence intervals of prescription and total health care annual expenditures were calculated for schizophrenic patients by insurance type. **RESULTS:** Multivariate analysis indicated a significant association between the number of hospitalizations, physician visits and ER visits over 12 months and any private insurance (β=-2.06, SE=0.84, p=0.01; -19.69, 8.92, 0.03; -22.35, 9.55, 0.02, respectively) compared to no insurance (referent). These same associations were not significant for the public only insurance (-0.30, 0.44, 0.16; -5.89, 3.91, 0.13; -7.72, 4.09, 0.06, respectively). Mean, SE [95% confidence interval] prescription expenditures for schizophrenic patients are similar between private insurance holders ($737, 215.3 [312.3-1161.6]) and those without insurance ($718, 237.0 [249.7-1186.3]), but were higher for public insurance holders ($3781, 897.2 [2008.1-5553.0]). Mean total health care expenditures for schizophrenic patients are similar between private insurance holders ($4000, 1382.4 [1273.9-6726.7]) and those without insurance ($4318, 2215.4 [0-8696.6]), but were higher for public insurance holders ($12,584, 2452.2 [7739.6-17,428.8]). **CONCLUSIONS:** Private insurance HRU for schizophrenic patients is lower than public only insurance holders, followed by those without insurance. Seemingly contradictory, a higher expenditure among public insurance holders was observed. This observation could be the result of the more severe schizophrenic cases having only public insurance. Caution should be employed in the use of the expenditure calculations due to the small numbers of patients.

PMH67

EXPLORING DEPENDENCE ON OTHERS IN ALZHEIMER'S DISEASE

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OBJECTIVES: The increasing economic importance of dependence on others in the elderly population is a major problem in Europe. This problem is very concerning for patients with Alzheimer's disease, who heavily rely on informal caregivers' assistance. Exploring the relationship between patients' dependence on others and care expenditures is very important when planning future resources for the elderly and for predicting the economic consequences of interventions which may delay dependence. Few studies have explored such a relationship in Continental Europe. **METHODS:** We use data from the DEP-FR study. We ran ordered logisitic and heckman regressions. **RESULTS:** We provide evidence: that there is a positive and significant correlation between cognitive, functional and behavioral declines and dependence on others, that an increase in dependence on others is associated with a decrease in informal care providers' satisfaction, that there is a linear relationship between dependence on others and informal and formal care use. **CONCLUSIONS:** Our results provide two main dependence policies perspectives. First, public interventions should try to reduce dependence through its three main dimensions of dependence on others (cognitive, behavioral and functional), and not only focus on the functional dimension of dependence. Second, specific measures should be implemented to the release of informal caregivers' burden, which increases with dependence on others.

PMH68

HOW WELL DO WE UNDERSTAND THE ECONOMIC BURDEN ASSOCIATED WITH DEMENTIA? A FOCUS ON TRENDS IN CARE HOME COSTS AND FUTURE PERSPECTIVES IN THE UNITED KINGDOM

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OBJECTIVES: The prevalence and economic burden of dementia is increasing, and in 2007 the UK government declared dementia a national priority. This research aims to evaluate trends in care home costs for dementia patients following this announcement, and to discuss the implications for the future economic burden of dementia. **METHODS:** PubMed was searched for terms related to 'cost', 'care homes' and 'dementia'. Horizon scanning was additionally performed for costs of care home data in the context of the wider economic burden of dementia. Only UK studies published after 2007 were considered, and information from a range of sources was assimilated to understand future implications for the economic burden of dementia. **RESULTS:** Four relevant PubMed articles and an additional twelve publications from horizon scanning were identified. It was reported that two-thirds of care home patients have dementia and that accommodation costs represent the major contributor to the cost of dementia (41%). The average annual cost of a care room had risen from £25,953 in 2011 to £27,404 in 2012 and this was accompanied by a 3.9% deficit in local authority payment increases for care home residents from 2010 to 2012. It is estimated that by 2043, more than double the current number of care home places will be required to match the increase in dementia prevalence, and the economic dependency ratio is expected to increase from 24% to 30% over the next 15 years. **CONCLUSIONS:** A considerable proportion of dementia patients are treated in care homes and, considering the disparity between the rising costs of care homes and funding increases, the burden borne by patients and their families is increasing. There is therefore an imminent need to develop cost-effective service provision for dementia patients; the new remit of NICE in social care may represent an important step towards this.

PMH69

EXAMINING THE EFFECTS OF A FUNCTIONAL RESTORATION AND PAIN MANAGEMENT PROGRAM AMONG CHRONIC PAIN PATIENTS IN THE TEXAS WORKERS COMPENSATION SYSTEM: PILOT STUDY – PART I

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OBJECTIVES: Management of chronic nonmalignant pain (CNMP) is important in both primary care and rehabilitative medicine however, the relationships between CNMP and the diverse types of addiction and chemical dependency are often complex and clinically relevant. The objective of this pilot study was to examine the impact of the Functional Restoration and Pain Management (FRPM) Program on pain severity outcomes and controlled medication use among CNMP patients enrolled in the Texas Workers Compensation (TWC) benefit program. **METHODS:** A retrospective cohort analysis of administrative claims and medical records data was conducted among TWC chronic pain patients enrolled in the FRPM Program receiving buprenorphine therapy. Prescription utilization patterns and pain severity outcomes during a 12-month observation period were examined. Eligible patients were ≥18 years of age, continuously enrolled as TWC beneficiaries, had a history of utilization of chronic pain medications at enrollment, placed on buprenorphine therapy, and received services through the FRPM program within the observation period defined as date from patient entry into the program to 12 months post-enrollment. **RESULTS:** The mean age of eligible participants (N=18) enrolled in the pilot study was 49.6 years ±9.5. A majority of patients were male (61%), white (61%), had a chronic pain lumbar diagnosis (45%), depression comorbidity (78%), and a substance abuse disorder (39%). Overall, patients showed a significant reduction in pain scores (p=0.032) at month 12 compared to baseline. For controlled medication utilization, there was a significant difference in narcotic pain medication use reduction in Hispanics/Latinos (p=0.033) compared to other racial/ethnic groups (i.e., Whites and African-Americans) at month 12 compared to baseline. **CONCLUSIONS:** Though a pilot study, the results suggest that the FRPM program has the potential of improving health outcomes of patients with chronic pain, while reducing their use of controlled medications. A larger follow-up study is needed to validate and expand on these preliminary findings.

PMH70

IMPACT OF AUTISM SPECTRUM DISORDERS ON THE FAMILY – A NATIONAL PERSPECTIVE

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OBJECTIVES: To examine caregiver reported impact of ASD on family as compared to impact of other developmental disabilities (DD) and mental health conditions (MHC) on family. **METHODS:** A cross-sectional study using 2009-2010 National Survey of Children with Special Health Care Needs on caregivers of children aged 3-17 years with either ASD, DD, MHC, or both DD and MHC diagnosis (N = 18,136)

was conducted. Family impact was assessed as: Financial burden, Employment Burden, and Time-related burden. Binary and multinomial logistic regressions were conducted to compare likelihood of adverse family impact across ASD, DD without ASD, MHC without ASD, and DD and MHC without ASD, after adjusting for socio-demographics, number of special children in the household, child's functional ability, and presence of a physical condition. **RESULTS:** Majority of the sample were older children (6-17 years), Whites, caregivers with ≥200% FPL income and greater than high school education. Sixteen percent (n=2,801) of the caregivers had a child with an ASD diagnosis. Caregivers of children with ASD were more likely to have financial burden than caregivers of children with DD (AOR=1.45, 95% CI=1.10-1.91) and MHC (AOR=1.59, 95% CI=1.33-1.91). There were no significant differences in financial burden reports between caregivers of children with ASD and those with both DD and MHC. Caregivers of children with ASD were also more likely to leave a job (employment), as compared to caregivers of children with DD (AOR=1.57, 95% CI=1.23-2.00), MHC (AOR=3.06, 95% CI=2.51-3.74), or both (AOR=1.73, 95% CI=1.36-2.20). Caregivers of children with ASD were more likely to report time-related burden as compared to caregivers of children with MHC (AOR=2.87, 95% CI=2.18-3.78) and DD and MHC (AOR=1.80, 95% CI=1.32-2.44). **CONCLUSIONS:** Caregivers of children with ASD are more likely to report an adverse family impact as compared to caregivers of children with DD, MHC, or both.

PMH71

DEVELOPING A POPULATION-BASED DEMENTIA REGISTRY FOCUSING ON PATIENTS AND CARER NEEDS: METHODOLOGICAL CHALLENGES

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OBJECTIVES: With increasing prevalence of dementia worldwide the interest in the dementia burden and impact on the health care system is rising. Yet comprehensive information about long-term needs and patterns of care of dementia patients and informal caregivers is scarce. Dementia specific registries provide an opportunity to investigate these aspects by long-term-data analysis. However, so far no international standards exist for developing a dementia registry. **METHODS:** An interdisciplinary team (psychiatry, public health, psychology, medical sociology, health economics and gerontology) established a registry structure in 2012. In the conception phase, existing registries, studies of dementia and best practice scenarios were identified. Features were combined in our concept and inclusion criteria, time for follow-up, fields of particular relevance and instruments were determined. A questionnaire was built and tested in exemplar sites. **RESULTS:** The pilot study started with prospective interviews in January 2013 to evaluate the concept. The inclusion criterion is a dementia diagnosis according to ICD-10. Patients are recruited from the regional memory clinic during the process of diagnosis. Patient drop outs occur after initial inclusion because of other ensured diagnosis such as depression. Both patients and caregivers are interviewed separately with internationally approved valid instruments. The follow-up will take place after 6, 12 months and annually until death or loss to follow-up. **CONCLUSIONS:** Existing dementia registries are very rare and heterogeneous in their structure, with currently no standards on quality indicators and processes. However, the complexity of dementia requires a sophisticated organizational structure for covering all aspects of dementia. Despite the challenges, our dementia registry structure provides essential, comprehensive and long-term information about the dementia care setting. The research is funded by the European Commission, ICT FP7, project ID 287509.

PMH72

EFFECT OF NURSE-LED MEDICATION REVIEWS IN PSYCHIATRIC PATIENTS – AN INTERVENTIONAL STUDY

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OBJECTIVES: There is an increasing demand for medication reviews to improve the quality of prescribing for patients with chronic illness such as psychiatric patients. Traditionally, this has been undertaken by physicians. Pharmacists have also proven to be a resource in this field but registered nurses are the health professionals spending most time directly with the patient and very few studies investigate nurses' role and potential in improving the appropriateness of medication. Therefore, the objective of this study is to investigate the effect of educating nurses in general pharmacology and conducting systematic medication reviews using computer based screening. The effect is evaluated in a controlled interventional study. **METHODS:** An interventional study including 2 acute psychiatric wards. In one ward nurses' will receive pharmacological training and the other ward will function as a control. The nurses will perform approximately 250 medication reviews followed by medication reviews performed by pharmacologists. Primary outcomes are the respective frequencies, types and severity of potential inappropriate prescriptions identified by the nurses and pharmacologists and an estimation of the interratervariability between the two professions. **RESULTS:** The hypothesis is that nurse-led medication reviews will reduce potential inappropriate prescribing and that training will increase nurses' ability to identify and report potential inappropriate prescribing. It is assumed that this intervention, in addition to a more appropriate prescribing, will lead to a reduction in length of hospitalization for psychiatric patients. **CONCLUSIONS:** The perspective for this study is to add knowledge about frequency, types and potential severity of potential inappropriate prescribing for psychiatric patients. The study will contribute with information regarding the effect of pharmacological training of nurses and possibly improve medication safety for psychiatric patients. Results from this study could serve as evidence, when hospital management makes decisions on how to accede the need for medication reviews as part of an ongoing accreditation process.

PMH73

MEDICATION USE PATTERNS AND ADHERENCE AFTER INITIATING ANTIPSYCHOTICS TREATMENT FOR PATIENTS WITH SCHIZOPHRENIA IN TIANJIN, CHINA

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OBJECTIVES: To describe medication use patterns and adherence rates for schizophrenia patients after initiating antipsychotic treatment in Tianjin, China. **METHODS:** Data were extracted from the Tianjin Urban Employee Basic Medical Insurance database (2008-2010). Adult patients with a schizophrenia diagnosis, newly initiating or restarting antipsychotics (no antipsychotics during previous 90 days) with 12-month continuous enrollment after their first observed antipsychotic prescription were included. Patients' medication prescribing patterns and antipsychotic adherence are described. **RESULTS:** A total of 1216 patients were identified, with a mean (SD) age of 51.43 (12.48) years, 54.11% female. 83.14% of patients initiated with one antipsychotic and 16.86% with ≥ 2 antipsychotics. 37.99% of patients were initiated on typical antipsychotics, 52.06% on atypicals, and 9.95% on both. A higher portion of typical initiators were co-prescribed antianxiety and anticholinergic medications than atypical starters (both p<0.001). During the following 12 months, the majority of patients remained on medications from their initial antipsychotic class (80.74% of typical initiators vs. 86.41% of atypical initiators) or the same medication (66.45% of typical initiators vs. 70.93% of atypical initiators). More typical initiators switched to, or augmented with, atypical antipsychotics than atypical initiators to/with typical antipsychotics (19.26% vs. 13.59%, P=0.011). During the following 3, 6 and 12 months, antipsychotic continuation rates (≤ 30 days gap) were 50.33%, 23.60%, and 8.88%, respectively. Medication Possession Ratios were low, with means (SD) of 0.58 (0.32), 0.44 (0.30), and 0.34 (0.27) for the 3, 6 and 12 months, respectively. **CONCLUSIONS:** More individuals with schizophrenia were treated with atypicals rather than typical antipsychotics. The majority of patients tended to stay with one antipsychotic drug class or the same medication. Patients' adherence to prescribed antipsychotics was low. This study highlights the importance of selecting an effective medication when starting antipsychotic therapy in China. However much could be done to improve treatment adherence.

MUSCULAR-SKELETAL DISORDERS – Clinical Outcomes Studies

PMS1

THE IMPACT OF COMORBIDITIES ON UTILITY CHANGES IN LOWER-LIMB OSTEOARTHRITIS : KHOALA STUDY

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OBJECTIVES: 1) To determine the minimal important change (MID) of indirect utility score for patients with osteoarthritis (OA) over 3-year follow up, and 2)Estimate the impact of comorbidity for patients reaching the MID. **METHODS:** A total of 878 patients with symptomatic knee or/and hip OA of KHOALA cohort were included. Comorbidity were assessed by Functional Comorbidity Index (FCI). Utility score was assessed using SF-6D, and limitation in activities by WOMAC function score (0-100,0 is better), at baseline and 3-year. The MID of utility was assessed using standard error of measurement (SEM). According to MID, patients were classified as negative/positive change or unchanged. Two separate multinomial logistic models were fitted to determine predictors of positive or negative change over the MID threshold. Both models included sociodemographic characteristics and the mean difference of WOMAC score between baseline and 3-year. **RESULTS:** A total of 650 OA patients completed the questionnaire at both times. The mean (SD) utility was 0.664 (±0.110) at baseline and 0.667 (±0.110) at 3-year. Patients have on average 2.5 (±1.94) comorbidities and a signifcant (p<.0001) decrease of the WOMAC function score at 3-year. The MID of SF-6D utility score was 0.067: 147 patients classified with negative and 156 with a positive change. In the first model including the number of comorbidities, patients with a decrease of the WOMAC function score had an increased utility (OR=0.95; p<.0001). In the second model, patients with pneumologic (OR=1.88; p=0.03) or neurologic (OR=2.73;p=0.047) disease were likely to have improved utility, while patients having a psychiatric disease were less likely to have an improvement (OR=0.54;p=0.029). **CONCLUSIONS:** According to MID, about half of patients had a positive or negative change in their utility score. Compared to functional severity of OA, comorbidities have a relatively marginal impact on indirect utility score. This suggests that clinically, considering the functional severity of OA remains a first priority.

PMS2

THE IMPACT OF COMMODITIES AND EXTRA-ARTICULAR MANIFESTATIONS IN RHEUMATOID ARTHRITIS PATIENTS

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OBJECTIVES: Rheumatoid arthritis (RA) is a chronic, systemic disease associated with comorbidities and extra-articular manifestations (EAM) . The main objective of the study was to estimate the frequency and impact of comorbidities and EAM in well-defined RA patients. **METHODS:** A prospective study was conducted at a tertiary care hospital between the years 2009 & 2012. Patients (age ≥ 18 years) with RA, fulfilling the revised criteria of the American college of rheumatology (1987 & 2010), were enrolled in the study. Standard clinical, laboratory and radiological measures of RA and details of comorbidities and EAM were recorded using patient hospital records. **RESULTS:** Of 602 RA patients, 481 (79.9%) females and 121 (20.1%) males were present. Mean age of 47.57±12.78 years, mean disease duration of 4.52±4.75

years and mean days of hospitalization 6.44±4.47 were observed. Disease duration of more than 2 years was observed in 336 (55.8%) patients. RA alone, RA with 1 comorbidity, RA with 2 comorbidities, RA with 3 comorbidities, RA with 4 comorbidities, RA with 5 comorbidities, were present in 227 (37.7%), 171 (28.4%), 118 (19.6%), 58 (9.6%), 19 (3.2%), 9 (1.5%) patients respectively. The most common comorbidities were diabetes mellitus 114 (18.94%), hypertension 104 (17.28%) and EAM was anemia 351 (58.30%). **CONCLUSIONS:** Comorbidities and EAM were present in substantial proportion of RA patients. Diabetes mellitus, hypertension and anemia were found to be most common in our setting. Early diagnosis and management are necessary to reduce their impact on therapeutic outcomes in RA.

PMS3

IMPACT OF COMORBIDITY BURDEN ON REAL-WORLD HEALTH CARE COSTS OF RHEUMATOID ARTHRITIS PATIENTS IN TURKEY

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OBJECTIVES: To determine the impact of comorbidity burden on real-world health care costs of rheumatoid arthritis (RA) patients in Turkey, using nationwide real-world data. **METHODS:** Study data was obtained from MEDULA (2009-2011). Using International Classification of Disease Tenth Revision Clinical Modification (ICD-10-CM) codes, adult RA patients (ages 18-99) were identified for the identification period (June 1, 2010 - December 31, 2010). Patients were required to have two RA diagnoses at least 60 days apart, and were grouped as prevalent and incident cases. The date of the first RA claim was identified for each patient and designated as the index date. Total health care costs were examined over the 12-month period following the index date. To control for clinical characteristics, a comorbidity index score for each patient during the baseline period was calculated using the Elixhauser method. This index is the sum of a comprehensive set of 30 present comorbid conditions, and is widely-used in the outcomes research field to determine patient health status. Individual comorbidities, such as diabetes, respiratory diseases, allergy and cardiovascular diseases, were identified using ICD-10 codes. **RESULTS:** A total of 2,613 patients met all inclusion criteria (693 incident; 1,920 prevalent patients). Prevalent patients had higher comorbidity index scores relative to incident patients. Nearly 35% of incident and 40% of prevalent patients had at least one cardiovascular, diabetic, respiratory, or allergy comorbid condition prior to the diagnosis. The mean Elixhauser Comorbidity Index score was calculated as 5.31 for incident and 5.7 for prevalent patients. Prevalent patients with respiratory and cardiovascular comorbid conditions incurred additional health care costs of €302 and €283 respectively. For incident patients, respiratory comorbid conditions increased the health care costs with €916. **CONCLUSIONS:** Respiratory comorbid conditions were associated with health care costs for both prevalent and incident RA patients in Turkey.

PMS4

EFFECTS OF CLAIMS-BASED RHEUMATOID ARTHRITIS SEVERITY ON BIOLOGIC THERAPY USE AND HEALTH CARE COSTS IN TURKEY

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OBJECTIVES: To apply a previously validated claims-based severity index for rheumatoid arthritis (SIFRA) to prevalent rheumatoid arthritis (RA) groups in Turkey and assess the effect of claims-based RA severity on health care costs and biologic use. **METHODS:** The Turkish national health insurance database MEDULA (01JUN2009-31DEC2011) was used for the study. Prevalent RA patients were required to be age 18-99 with two RA diagnoses ≥60 days apart and continuous enrollment 1 year pre- (baseline period) and post-index date (follow-up), which was the first RA claim during the identification period (01JUN2010-31DEC2010). SIFRA was calculated for the baseline period. For the follow-up period, total health care costs and biologic use were examined. To determine health care costs, generalized linear models were applied, and multivariate logistic regression determined the effect of SIFRA on outcome measures for biologic use. **RESULTS:** A total of 1,920 RA patients were identified. The mean SIFRA score was 14.21. There was a significant variation in scores across cities. Study results confirmed increased biologic use in more severe patients. After adjusting for differences in age, gender, region and comorbidity index, patients in the high SIFRA tercile were 5.16 times more likely to be prescribed biologics (p<0.001, confidence interval [CI]: 3.46-7.69), and incurred more annual health care costs in the amount of €2,091 (p<0.001, CI: €1,557-€2,625) than those in the low SIFRA tercile. **CONCLUSIONS:** This study showed that RA severity is a significant determinant of health care costs and biologic therapy use. Biologic use was positively correlated with the severity score. According to severity scores, the total medical costs of RA patients in Turkey ranged from €1,435 to €3,275. Since statistically omitting a variable from population models provides biased and inconsistent estimates, any comparative effectiveness studies on RA treatment should include severity scores in the analysis.

PMS5

THE IMPACT OF PERSISTENCE AND COMPLIANCE WITH ORAL BISPHOSPHONATES ON FRACTURE RATES ASSESSED USING THE CLINICAL PRACTICE RESEARCH DATALINK (CPRD) IN THE UNITED KINGDOM

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OBJECTIVES: To assess the impact of persistence and compliance on fracture rates and health care resource use (HRU) in women treated with oral bisphosphonates (oBPs). **METHODS:** This analysis of the UK CPRD included women with first oBP prescription (index event) between January 2004–December 2007, ≥50 years of age, with no history of cancer and a minimum of 12 months' data before and 6 months' after the index event. Follow-up for any osteoporotic fracture was until December 2008. Persistence was defined as duration of continuous oBP use with no gaps >3 months; compliance was assessed using the medication possession ratio (MPR; proportion of time with treatment available). HRU was evaluated using total primary care contact (including prescriptions), and all specialist referrals and hospitalisations. Analyses were stratified by persistence and compliance. **RESULTS:** A total of 21,717 patients were included (mean age, 73.5 years). Between 2004–2007, fracture rates per patient–year were: 0.14 (95% CI: 0.12, 0.16; group with MPR <80%) and 0.11 (0.10, 0.12; MPR ≥80%) for patients with 12–24 months' persistence *vs* 0.09 (0.08, 0.10) and 0.07 (0.06, 0.08), respectively, for patients with ≥36 months' persistence. Hospitalisation rates were 0.38 (0.34, 0.42; MPR <80%) and 0.30 (0.29, 0.32; MPR ≥80%) for patients with 12–24 months' persistence *vs* 0.55 (0.52, 0.59) and 0.18 (0.17, 0.19), respectively, for patients with ≥36 months' persistence. Among patients who discontinued oBPs and had <12 months' persistence and MPR ≥80% before discontinuation, fracture rates were 0.02 (0.01, 0.03) and 0.09 (0.07, 0.12) in the first and second 6 months following discontinuation, respectively, and hospitalisation rates were 0.09 (0.07, 0.11) and 0.48 (0.42, 0.55), respectively. **CONCLUSIONS:** Outcomes associated with oBPs were improved with longer persistence and higher compliance. However, in patients with <12 months' persistence, protection against fractures and hospitalisation diminished 6 months after discontinuation of oBPs.

PMS6

INDIRECT COMPARISON OF JOINT DAMAGE PREVENTION WITH ADALIMUMAB V. ABATACEPT, EACH IN COMBINATION WITH METHOTREXATE, IN EARLY RHEUMATOID ARTHRITIS

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OBJECTIVES: The AMPLE trial concluded comparable efficacy of adalimumab (ADA) and abatacept (ABA) after one-year methotrexate (MTX) combination treatment for rheumatoid arthritis (RA). This study compared effects of adalimumab v. abatacept, each in MTX combination, on progressive RA joint damage, adjusting for study population characteristics. **METHODS:** Two placebo-controlled trials in early RA, PREMIER (ADA+MTX v. MTX) and AGREE (ABA+MTX v. MTX) were selected based on design and comparability of enrollment criteria. Patient-level data from PREMIER were adjusted, using propensity score weighting, to match average baseline characteristics from AGREE, including RA duration and clinical measures. Radiographic progression (RP) was a change in total Sharp score (TSS) > 0 (modified TSS in PREMIER and Genant-modified TSS in AGREE). Joint space narrowing (JSN) and joint erosion (JE) scores in PREMIER were scaled to proportion with AGREE measures. After re-weighting, one-year incremental effects were compared for ADA+MTX vs. ABA+MTX, including RP rates, mean JSN and JE score changes from baseline, disease activity score (DAS28) remission rates, and American College of Rheumatology 50% improvement (ACR50). **RESULTS:** Compared to AGREE patients, PREMIER patients were slightly older, more likely to be Caucasian, had longer RA duration, higher C-reactive protein levels, more severe joint damage, and lower functional impairment at baseline. After re-weighting, more ADA+MTX patients had no RP after one year compared to ABA+MTX patients (27.0% v. 8.3%; p=0.02). Mean improvements in JSN (-1.41 v. -0.04) and JE (-1.54 v. -0.39) scores from baseline were numerically greater with ADA+MTX; statistical significance could not be assessed as standard errors were not published for AGREE. No statistically significant differences were observed in DAS28 remission rates (p=0.47) and ACR50 responses (p=0.72). **CONCLUSIONS:** Although both combination therapies yielded similar disease activity measures at one year in early RA patients, ADA+MTX offered greater protection against radiographically-confirmed joint damage than ABA+MTX.

PMS7

META-ANALYSIS OF EFFICACY OF ETANERCEPT FOR TREATMENT OF PSORIATIC ARTHRITIS

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OBJECTIVES: Psoriatic arthritis (PA) is an inflammatory disease affecting joints and connective tissues. The anti-tumor necrosis factor (TNF) biologics are increasingly being used in patients who have failed traditional disease-modifying antirheumatic drugs. Etanercept has shown efficacy in treatment of PA. The objective of this study was to conduct meta-analysis and present total evidence for etanercept in treatment of PA. **METHODS:** For this meta-analysis we included randomized controlled trials (RCTs)evaluating etanercept for the treatment of PS. RCTs studying adult populations with active and progressive PA with an inadequate response to previous DMARD therapy were eligible. Trials conducted among PA populations with prior experience with anti-TNF agents, including an inadequate response, were excluded. A systematic literature search for Etanercept trials was undertaken for the databases Pubmed, Embase, Biosis, Google Scholar, and Cochrane. Data was collected for the study size, interventions, year, and the three outcomes HAQ, PASI and PsARC. For meta-analysis, random effects and fixed effects models were used to obtain cumulative statistics. **RESULTS:** Two RCTs with a total of 131 patients were identified. The pooled response rates for Etanercept for PsARC were 75% (95% CI 60%-90%), for HAQ were 59% (95% CI 46%-72%), and for PASI were 24% (95% CI 13%-34%). The pooled response rates for placebo for PsARC were 30% (95% CI 26%-35%), for HAQ were 5% (95% CI 1%-9%), and for PASI were 3% (95% CI 0%-7%). For PsARC the cumulative relative risk with Etanercept versus placebo was 0.40 (95% CI 33%-48%). For HAQ, the cumulative relative risk with placebo versus Etanercept was 0.08 (95% CI 5%-12%). For PASI, the cumulative relative risk with placebo versus Etanercept was 0.14 (95% CI 8%-20%). **CONCLUSIONS:** Meta-analysis shows Etanercept offers patients with psoriatic arthritis an effective therapeutic option for control of their disease.

PMS8

EQ-5D UTILITY WEIGHTS ASSOCIATED WITH RESPONSE TO TREATMENT WITH MATRIX APPLIED AUTOLOGOUS CULTURED CHONDROCYTES (MACI) IMPLANT AND MICROFRACTURE FOR CARTILAGE DEFECTS OF THE KNEE

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OBJECTIVES: SUMMIT, a 2-year, multicenter, randomised trial, demonstrated significant improvements in pain and function with matrix applied autologous cultured chondrocytes (MACI) implant versus microfracture in patients with symptomatic knee cartilage defects (NCT00719576). We present post-hoc results of the impact of treatment response on EQ-5D utility scores, and the overall incremental impact of treatment with MACI compared with microfracture over 2 years. **METHODS:** Patients (aged 18-55) with Outerbridge Grade III/IV focal cartilage defect ≥3.0cm^{2}were randomised to receive MACI implant (n=72) or microfracture (n=72). Response to treatment was defined as ≥10-point improvement from baseline in both the Knee Injury and Osteoarthritis Outcome (KOOS) pain and function scores at year 2. EQ-5D was evaluated at baseline, and years 1 and 2. Patients' EQ-5D responses were scored using UK-tariffs. Utility values associated with responders and non-responders were estimated based on results from both treatment arms combined. Incremental quality-adjusted life year (QALY) gains were derived by multiplying the difference in response rates between the treatments with the difference in utility between responders and non-responders. **RESULTS:** The mean utility score for all patients (n=142) at baseline was 0.481±0.296. Responders (n=111) had an improvement in mean utility score from baseline of 0.352 (0.833-0.481) compared with 0.033 for non-responders (n=29; 0.514-0.481) at year 2. Significantly more patients treated with MACI responded to treatment than with microfracture (87.5% vs. 68.1%, respectively; p=0.016), resulting in an incremental QALY gain of 0.11 for MACI compared with microfracture over 2 years. **CONCLUSIONS:** At baseline, patients with chondral defects experienced a substantially reduced HRQoL. Significantly more patients responded to treatment with MACI versus microfracture, and this response was associated with substantial improvements in HRQoL. In this population, the higher response rate for MACI resulted in an incremental QALY gain of 0.11 compared with microfracture over 2 years.

PMS9

EARLY RESPONSE TO CERTOLIZUMAB PEGOL IN RHEUMATOID ARTHRITIS PREDICTS OUTCOME AT ONE YEAR

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OBJECTIVES: Treat-to-target strategies for the treatment of rheumatoid arthritis (RA), as recommended in current treatment guidelines, require the use of reliable early markers of treatment response in order to adapt therapy in a timely way in patients with insufficient response. The objective of this study was to evaluate and compare the performance of different clinical indicators in predicting clinical response at one year. **METHODS:** This was a *post-hoc*analysis of data from the RAPID1 randomised, placebo-controlled Phase III study. A total of 382 severe RA patients treated with certolizumab pegol 200mg and no prior TNF inhibitor were assessed by Week 12 (bW12) and at Week 52 (W52). "Insufficient response" was defined using the ACR response criteria, compared to baseline, DAS28 score (Δ<1.2), HAQ score (Δ<0.22) and CDAI (score<22). The ability of insufficient response to these markers bW12 to predict failure to achieve ACR50 at W52, was compared in terms of positive predictive value (PPV), specificity and sensitivity. **RESULTS:** At W52, 149 (38.1%) patients met the ACR50 response criterion. For all bW12 outcome indicators, the specificity and the PPV was >80%. The higher PPVs were observed for bW12 ACR20 non response (1.00 [95%CI: 0.93-1.00]), bW12 reduction in DAS28 (0.95 [95%CI: 0.82-0.99]) and bW12 CDAI score (0.93 [95%CI: 0.85-0.97]). For bW12 ACR20 non response, bW12 reduction in DAS28 and bW12 CDAI score, specificities were respectively 1.00 (95%CI: 0.97-1.00), 0.99 (95%CI: 0.94-1.00) and 0.95 (95%CI: 0.90-0.98). The highest sensitivity was observed for the bW12 ACR50 (0.70 [95%CI: 0.63-0.76]). **CONCLUSIONS:** All these early response markers have high PPV and high specificity but low-to-moderate sensitivity: 80% to 100% of patients identified as "insufficient-responders" by W12 would fail to fulfil the ACR50 response at W52. Such predictability data for certolizumab pegol should help physicians to make early decisions about the potential discontinuation of the treatment.

PMS10

THE 3D O-ARM SURGICAL IMAGING SYSTEM WITH NAVIGATION EFFECTIVELY AND ECONOMICALLY ADDRESSES THE CHALLENGES OF SPINAL STABILIZATION PROCEDURES

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BACKGROUND: Inaccurate pedicle screw placement and neurological or vascular injury during spinal instrumentation procedures is both costly and preventable. **OBJECTIVES:** To determine the comparative efficacy or effectiveness and value for money of the 3D O-arm Surgical Imaging System with Navigation during spinal stabilization surgery compared with standard practice. **METHODS:** A search of Medical and Health Economic electronic databases (Embase, PubMed, HEED, NHS EED, Cochrane) and conference abstracts up to Nov. 2012 was conducted to identify studies evaluating the effectiveness, efficacy and economics of 3D surgical imaging with navigation. No time or language restrictions were applied. **RESULTS:** Compared with current practice options, the 3D O-arm surgical imaging with navigation was shown to significantly increase the accuracy of instrument placement, reduce surgeons' and patients' exposure to radiation, and offer the opportunity for intraoperative revision for malplaced screws during the index procedure. Results of 10 case series and a European registry show rates of pedicle screw placement accuracy (0 mm to ≤2 mm) between 95% and 100% with 3D O-arm surgical imaging with navigation compared to 84% - 95% reported for various current practice options from multiple meta-analyses. In addition, accuracy rates of between 72% and 92% have been reported for 2D C-arm without navigation. Economic studies demonstrated 3D O-arm surgical imaging with navigation has the potential to reduce the cost of fusion procedures in Europe and the USA by negating the need for pre-operative and post-operative imaging associated with current standard-of-care, reducing the need for reoperations for screw revision, shortening length of procedures and OR time. It has been estimated that it could reduce the cost of hospitalization for spinal surgery by at least 3.8%. **CONCLUSIONS:** Current evidence shows 3D O-arm surgical imaging with navigation substantially reduces the human and financial burden of patients during spinal stabilization surgery compared with standard practice.

PMS11

EVALUATING THE EFFICACY OF BIOSIMILAR INFLIXIMAB WITH THE ACR50 RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS; A META-ANALYSIS IN BAYESIAN FRAMEWORK

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OBJECTIVES: To identify all relevant literature on clinical efficacy and safety evidence for biosimilar infliximab (CT-P13) and comparator biological medications in rheumatoid arthritis and to conduct an up-to-date meta-analysis. **METHODS:** The following comparators were considered for this analysis: abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab. A MEDLINE search was conducted until March 2013. The Cochrane Highly Sensitive Search Strategy was applied to identify randomized controlled publications and was combined with 'arthritis, rheumatoid' MeSH terms and drug names. Randomized, controlled, clinical trials with adults with moderate-to-severe RA and reporting endpoints for 6 months where the full paper can be obtained were included. Direct and indirect evidences were combined in a mixed treatment comparisons in a Bayesian framework. Efficacy measured by ACR50 endpoint and frequency of serious adverse events at 24-30 weeks were analysed. **RESULTS:** Altogether 41 trials were included into current meta-analysis. The relative odds ratios (and 95% credible intervals) for ACR50 of biosimilar infliximab treatments compared to abatacept, adalimumab, certolizumab, etanercept, golimumab, rituximab, tocilizumab and infliximab were 1.0 (0.3-3.8), 0.9 (0.2-3.4), 0.3 (0.1-1.4), 1.0 (0.2-4.2), 1.2 (0.3-5.1), 0.9 (0.2-3.6), 0.5 (0.1-2.2), 1.0 (0.3-3.2), respectively. Similarly, relative odds ratios for serious adverse events were 1.9 (0.8-4.8), 2.0 (0.6-5.8), 0.7 (0.2-2.1), 2.0 (0.8-5.7), 1.5 (0.5-4.2), 1.1 (0.7-2.0), 1.3 (0.8-2.2), 1.3 (0.8-2.1), respectively. **CONCLUSIONS:** The results showed that efficacy and safety of biosimilar infliximab is not significantly different from innovator infliximab and from other biologics.

PMS12

SYSTEMATIC REVIEW COMPARING THE EFFICACY AND SAFETY OF COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX®) INJECTION WITH SURGICAL FASCIECTOMY FOR THE TREATMENT OF DUPUYTREN'S CONTRACTURE

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OBJECTIVES: To compare the efficacy and safety of collagenase clostridium histolyticum (CCH, Xiaflex®) injection with surgical fasciectomy for the treatment of Dupuytren's contracture (DC). **METHODS:** Systematic review and qualitative synthesis of comparative and non-comparative studies reporting efficacy (clinical success, recurrence of contracture) and safety (complication) outcomes for patients undergoing fasciectomy for DC. Informal non-statistical comparison with outcomes from 3 pivotal placebo controlled trials and a long term follow-up study of DC patients treated with CCH. **RESULTS:** Sixty-eight studies of fasciectomy were identified for inclusion in the review: 61 case series (52 retrospective; 9 prospective); 3 randomised controlled trials (RCTs), none of which permitted either a direct comparison with CCH or an indirect comparison via a common comparator; 1 RCT follow-up study; 2 prospective uncontrolled studies; 1 postal survey. Studies varied in terms of fasciectomy technique employed. Follow-up ranged from only immediately post-operatively up to 35 years post-operatively. Definitions of surgical success and recurrence varied, and were frequently ill-defined or less stringent than the robust definitions used in the CCH trials. In studies of fasciectomy where definitions were judged as reasonably comparable to those used in the CCH trials (clinical success: 14 studies; recurrence: 40 studies), clinical success and recurrence rates for CCH and fasciectomy were comparable (clinical success: 63% vs 69% respectively, recurrence: 28% vs 21% at 4 years, respectively). Complication rates were greater for fasciectomy than for CCH. These included digital nerve or artery injury (3.3% vs 0%), complex regional pain syndrome (3.6% vs 0.04%), joint stiffening (8.9% vs 0%), wound infection (6.2% vs 0%), and paraesthesia (4.3% vs 0%). Tendon ruptures were reported with CCH, but were infrequent (0.07%). **CONCLUSIONS:** CCH and surgical fasciectomy can be reasonably considered as comparable in terms of efficacy for the treatment of DC and superior in terms of safety.

PMS13

COMPARATIVE EFFECTIVENESS OF ACTIVE VERSUS SHAM ACUPUNCTURE VERSUS USUAL CARE IN THE MANAGEMENT OF CHRONIC, NON-CANCER PAIN IN PRIMARY CARE

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OBJECTIVES: To examine the effectiveness of acupuncture net of sham effect and usual care, measured using EQ-5D, in the management of chronic, non-cancer pain in primary care. Systematic reviews of acupuncture for the conditions osteoarthritis

of the knee, musculoskeletal pain and headache have been published however no reviews have incorporated the latest trial evidence from the recent large scale high quality RCTs to generate EQ-5D scores. **METHODS:** An individual patient level data (IPD) based Mixed Treatment Comparison (MTC) was undertaken using a database of 28 recent, high quality RCTs containing observations for over 18,000 patients. The analysis evaluated the effectiveness of acupuncture in terms of continuous outcomes, for each of the three conditions over a three month time horizon, mapping generic and disease-specific measures to generate EQ-5D scores and using published mapping algorithms unless none were available. **RESULTS:** Acupuncture, net of sham, is more effective in that it generates greater EQ-5D scores compared to usual care in the management of chronic, non-cancer pain in primary care. Using a random effects IPD MTC, the change in EQ-5D scores from baseline to 3 months was mean 0.0419 (95% credibility interval 0.0066 to 0.0765) for acupuncture net of sham and 0.0573 (95% credibility interval 0.0139 to 0.1006) for acupuncture vs usual care. **CONCLUSIONS:** Based on EQ-5D scores, this analysis suggests that acupuncture, is the most effective option. The analyses synthesise effectiveness evidence using MTC of IPD whilst controlling for sham effect. This analysis is an intermediate step to inform a full cost-effectiveness analysis to support decision-making in the UK.

PMS14

APPLICATION OF A DATA VISUALIZATION TOOL: TREATMENT PATTERNS OF VETERAN PATIENTS WITH ANKYLOSING SPONDYLITIS

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OBJECTIVES: As outcomes research methodologies advance, they should increasingly allow access by different disciplines as clinicians, epidemiologists, economists, and statisticians interact frequently. A data visualization tool can present complex patterns effectively to a diverse audience. The objective of this study was to present treatment patterns among Veterans Health Administration (VHA) patients diagnosed with ankylosing spondylitis (AS) using advanced data visualization techniques. **METHODS:** Using the VHA Medical SAS® dataset, adult patients with at least one AS diagnosis (ICD-9-CM: 720.0) were selected. Prescriptions for anti-tumor necrosis factor (anti-TNF) and non-TNF agents were identified. For 2 years after the date of the first prescription (initiation date), drug switches and discontinuation were examined. Using a processing language, a data visualization tool was developed to demonstrate changes in treatment patterns after the first and second treatment switches. **RESULTS:** A total of 1,021 AS patients initiated therapy with TNF, of which 13.52% switched to another TNF, 0.20% switched to a non-TNF, 49.56% discontinued therapy and 36.73% continued their initial therapy. Among patients who switched to another TNF, 60.87% remained on the switched therapy, while 31.16% discontinued therapy, 7.97% switched to another TNF, and no patients switched to a non-TNF. 81.82% of patients who made a second switch to a TNF medication remained on this TNF, while 9.09% discontinued treatment. A total of 84 AS patients initiated therapy with a non-TNF. 4.76% of these patients switched to a TNF, 1.19% switched to another non-TNF, 93.61% discontinued therapy and no patients continued treatment. Of those patients whose first switch was to a TNF, 50% continued therapy while the remaining 50% discontinued. There were no second switches. **CONCLUSIONS:** When analyzing several years of data including treatment (dis)continuation and switches, treatment patterns can be difficult to capture. Data visualization tools help present complicated flows effectively for a diverse research audience.

PMS15

IMPROVEMENT IN DISEASE ACTIVITY SCORES ASSOCIATED WITH EARLY VERSUS LATE INITIATION OF BIOLOGIC THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A EUROPEAN CHART REVIEW STUDY

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OBJECTIVES: Recent research has suggested that patients may have a "window of opportunity" to reverse immune dysregulation associated with RA onset through aggressive early treatment. This study aimed to evaluate the outcomes associated with early versus late biologic treatment in RA. **METHODS:** Adults (≥18 years) with confirmed RA diagnosis between January 2008 and December 2010, who received biologic therapy for ≥3 months and had ≥12 months follow-up were included in this retrospective, observational medical chart review study in Spain, Germany, and United Kingdom. Physicians abstracted outcomes including 28-joint disease activity scores (DAS28) alongside treatment received. Patients were classified as receiving early biologic treatment if started within 1 year of RA diagnosis. Outcomes included DAS28 reduction of ≥1.2 from scores at biologic start and remission (DAS28<2.6). Time to reaching these outcomes was evaluated using Kaplan-Meier survival curves and log rank tests. **RESULTS:** Of 328 patients included, 310 (178 early; 132 late) had DAS28 measurements and were demographically similar between early vs. late treatment (overall: mean age 47.9 at diagnosis, 71.0% female, 96.1% white). Overall, 73.5% of patients had a DAS28 decrease ≥1.2 points and 44.5% achieved remission. More early versus late biologic treated patients had a DAS28 decrease ≥1.2 (79.2% vs 65.9%, p=0.009) but there was no significant difference in the time to this decrease. More early vs. late biologic treated patients achieved remission (51.1% vs. 35.6%, p=0.009), with a significant difference in survival curves when indexing on time since RA diagnosis (p<0.001) and biologic start (p=0.024). There were no significant differences outcomes across countries. **CONCLUSIONS:** This chart review contributes to the growing literature surrounding outcomes associated with early biologic treatment. Within this study, RA patients who were treated early were more likely to achieve clinically significant improvement and to reach remission earlier in their RA disease trajectory than those treated later.

PMS16

UPTAKE OF DENOSUMAB IN THE TREATMENT OF OSTEOPOROSIS IN THE CZECH REPUBLIC

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OBJECTIVES: The objective was to analyze current trends in consumption as well as prescription practice pattern of the new anti-RANKL monoclonal antibody denosumab in the treatment of osteoporosis since its introduction onto the market in the Czech Republic in 2011. **METHODS:** The prescription-based database of the General Health Insurance Company (VZP) of the CR that covers approximately 62% of the Czech population was used as the data source. An insured person with a recorded prescription for denosumab in the period of interest was defined as a patient. The obtained epidemiological and costing data were also confronted with the prediction in the budget impact analysis in the public reimbursement dossier accessible in the State Institute for Drug Control files. **RESULTS:** A total of 3119 (158) patients (men) treated with denosumab were identified in the first year, i.e. between August 2011 and July 2012. The median age of patients was 73 years. Of the patients prescribed denosumab in the first half-year, 84% received the second dose within the observed period of one year, of which 85% within the authorized period of 6 months (+-1 month). This new drug was most often prescribed by physicians trained in internal medicine (47%) and rheumatology (30%). The cumulative costs for VZP of the drug were CZK 27.3 mil (EUR 1.1. mil) in the first year. **CONCLUSIONS:** The uptake of denosumab has been rapid and agrees with the predictions presented by the manufacturer before the launch of the drug. This preliminary data also suggest that both the prescribing doctors and the patients filling the prescriptions follow the dosing schedule.

PMS17

THE USE OF BIOLOGIC DRUGS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN ITALY

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OBJECTIVES: To describe the clinical profile of patients with rheumatoid arthritis (RA) treated with biologic agents within the former Italian centers "Antares" where autoimmune diseases are treated. **METHODS:** This study analyzed data from patient diaries (PDS), which involved 70 rheumatologists that are regular prescribers of biological treatments for rheumatoid arthritis and were recruited by telephone. The patient diaries were completed via web. **RESULTS:** Study population consisted of 206 (45.9%) patients with RA, 160 (35.6%) with psoriatic arthritis, 61 (13.6%) with ankylosing spondylitis, 14 (3.1%) with Juvenile idiopathic arthritis and 8 (1.8%) with early RA. Female gender prevailed, while the most numerous age group was the one that ranged from 50 to 60 years. The disease was mostly diagnosed before 50 years old and, despite in the group of patients treated with biologic drugs for more than 3 months the percentage of subjects with a value of HAQ less than 1 is higher when compared with those of patients whose treatment has begun more recently, the proportion of patients with a value of HAQ between 2 and 3 is still 40.0%. The same, half of the subjects treated for more than 3 months still have a moderate or high disease activity (DAS28 ≥3.2). **CONCLUSIONS:** The study sample was in line with the literature concluding that it is representative of the Italian context. The fact that there is a proportion of patients treated with biological therapy for more than three months, as well as an important number of patients who have been treated with more than one biologic drugs, and that have a perception of quality of life rather low and / or a disease activity state rather active, leads to conclude that there is still a type of patient for which new therapeutic options should be evaluated.

PMS18

ESTIMATED OSTEOPOROTIC POPULATION AND THE RELATED MEDICATION CONSUMPTION IN MUNICIPALITY LEVEL – DISCREPANCIES OBSERVED THROUGH DATA VISUALIZATION APPROACH

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OBJECTIVES: Osteoporosis is a common health problem among elderly population. Patients with osteoporosis are exposed to low-energy fractures. The prevalence of the disease varies significantly throughout the country due to the strong correlation with demographic factors. National guidelines recommend secondary prevention for all osteoporosis patients suffering from low-energy fractures. The aim of treatment is to prevent further fractures. In order to effectively allocate the resources needed for osteoporosis treatment, it is essential to know the number of patients and treatment practices in local level. **METHODS:** Local registry data was used to estimate the total population with low-energy fractures, as well as to recognize the differences in treatment of osteoporosis in each hospital district (n=21) and municipality (n=320). Data on hip fractures from year 2009 was extrapolated to year 2012 using demographic data. The overall prevalence of low-energy fractures was estimated trough a distribution of different fracture types available from literature. A map-based application was built (Tableau 8) to visualize the differences in the prevalence and treatment of osteoporosis across Finland. The model enables comparison between municipalities or hospital districts. **RESULTS:** The estimated number of osteoporotic fractures was 1733, in a hospital district with 250,000 inhabitants (Northern-Savo). The estimated prevalence rates in different municipalities within the hospital district varied between 0.52–1.7/100 inhabitants. Simultaneously, basic reimbursement for medical treatment (ATC:M05B) was paid for 1.2/100 inhabitants - the range among elderly population (>65y) was 3.21–6.56/100 inhabitants. **CONCLUSIONS:** There are significant local differences in the prevalence of osteoporosis as well as in its treatment. The population demographics do not explain the observed differences in the consumption of osteoporosis medication between different municipalities. The developed map-based application gives multiple possibilities to analyze these issues through data visualization. With this approach the interventions may be targeted to areas needing it the most.

PMS19
COMPARISONS OF THE RISK FOR VENOUS THROMBOEMBOLISM BETWEEN HIP AND KNEE ARTHROPLASTY USING KOREA NATIONAL HEALTH INSURANCE CLAIMS DATABASE
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OBJECTIVES: Venous thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) occurs most often in patients undergoing major joint arthroplasty and major surgical procedures (such as hip arthroplasty, HA or knee arthroplasty, KA). The prevalence of clinically relevant VTE, DVT and PE after hip and knee arthroplasty in nationwide database of Korea were 1.7%, 1.1% and 0.5%, respectively. The aim of this study was to compare the risk for VTE (including DVT and PE) between hip and knee arthroplasty in the Korean population. **METHODS:** A retrospective cohort study was conducted using nationwide claim registry obtained from the Korean Health Insurance Review and Assessment Service (HIRA), which includes medical claims records for 97.0% of South Koreans. We retrospectively identified patients who underwent HA or KA between January 1 and December 31 in 2010. VTE after arthroplasty were identified by diagnostic code (ICD-10: PE - I26, I26.99, DVT - I80, I82, I82.2) within 90days after surgery. Patients' characteristics including sex, age and preoperative comobidities were defined using the HIRA database from 2007 to 2010. We compare the risk for VTE between hip and knee arthroplasty using logistic regression model in patients without VTE history and VTE chemoprophylaxis use . **RESULTS:** A total of 38,024 patients had HA or KA arthroplasty in Korea in 2010 (HA 11,908 patients, KA 26,116 patients). KA was associated with an increased risk of DVT [aOR=1.3; 95% CI=(1-1.7), p-value=0.048], but KA was associated with a decreased risk of PE compared with HA [aOR=0.5; 95% CI=(0.3-0.7), p-value<0.001]. **CONCLUSIONS:** This study suggest that the risk of PE was high in HA rather than KA, but the risk of DVT was high in KA rather than HA. These results were due to differences in pathogenesis of DVT or PE.

PMS20
CORRELATION BETWEEN PROGNOSTIC FACTORS AND NON PROSTHETIC FURTHER FRACTURE RELATED TREATMENT AFTER FEMORAL NECK FRACTURE UNDERWENT INTERNAL FIXATION IN ELDERLY
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OBJECTIVES: To investigate the correlation between prognostic factors and non prosthetic fracture related treatments following internal fixation of femoral neck fractures in elderly patients. **METHODS:** This retrospective observational cohort study data were collected from the Hungarian National Health Insurance Fund Administration and from the health care provider institutes based on S7200 ICD-10 codes. The patients with femoral neck fractures following internal fixation aged 60 years or older were provided in 2000. The secondary non prosthetic fracture related treatments during the 8 year follow-up period were registered. Of the prognostic factors, age, gender, type of fracture and surgical intervention, season and day of the primary surgery, surgical delay and the accompanying diseases were evaluated. Statistical analyses were performed using multivariate Cox regression models and Kaplan Meier survival methods. **RESULTS:** A total of 3306 patients met the criteria. The mean of age was 78.04 years (SD:8.59). The non-prosthetic fracture related treatment was performed in 307 patients (9.3%). With Cox regression analysis, significant correlation was revealed between the incidence of non prosthetic treatment and younger age (year, HR=0.978), surgical delay (12-24h vs 0-6h, HR=1.730; 24h+ vs 0-6h, HR=1.578), season of primary osteosynthesis (winter vs summer, HR=0.707; fall vs summer, HR=0.638), type of primary surgical intervention (screw vs DHS fixation, HR=2.096; femoral neck nailing vs DHS fixation, HR=3.223; Ender nailing vs DHS fixation, HR=4.515) and type of femoral neck fracture (intracapsular displaced vs intracapsular undisplaced, HR=1.360; extracapsular vs intracapsular undisplaced, HR=1.634). There was no significant effect of the day of primary surgery, the gender and the presence of comorbidities on the incidence of further surgical interventions. **CONCLUSIONS:** We have demonstrated that summertime primary surgical intervention, delay of surgery longer than 12 hours, type of femoral neck fracture and method of fixation are independent predictors of non prosthetic further treatment of femoral neck fractures.

MUSCULAR-SKELETAL DISORDERS – Cost Studies

PMS21
BUDGET IMPACT ANALYSIS OF BIOSIMILAR INFLIXIMAB TREATMENT FOR RHEUMATOID ARTHRITIS IN SIX CENTRAL EUROPEAN COUNTRIES
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OBJECTIVES: To analyse the budget impact of introducing biosimilar infliximab for the treatment of rheumatoid arthritis in six central European countries' – Bulgaria, Czech Republic, Hungary, Poland, Romania and Slovakia - health care systems. **METHODS:** This budget impact model estimates the potential impact of the biosimilar infliximab on the health care budget over a three year time frame. The model considers third-party payer perspective. A spreadsheet-based country specific dynamic population model was developed. The model functioned in quarter year time units according to the three months long evaluation period. The model tracked the movement of the RA population between main states: 1) on synthetic DMARD; 2) on infliximab; 3) on biosimilar infliximab; 4) TNF inhibitors other than infliximab; and 5) biologics other than TNF inhibitor. Switching between biologics and biosimilar infliximab was taken into consideration too. Scenario analyses were conducted, different rate of interchanging and switching were considered. A -25% percentage price difference was assumed for biosimilar infliximab compared to originator infliximab. The budget impact was calculated as the difference in the total cost of the scenarios with and without biosimilar infliximab in each year of the model. **RESULTS:** Over the entire 3-year period with gradually interchanging 80% of infliximab patients to biosimilar infliximab is expected to leading to a net benefit of 29,810,000 euros compared to the scenario in which biosimilar infliximab would not be available. In the scenario in which interchangeabilty was disallowed the budget savings was 18,765,000 euros. If budget savings were spent on reimbursement of additional biosimilar treatments, approximately 1,615 or 1,025 more patients could be treated in the six countries, respectively. **CONCLUSIONS:** This budget impact analysis indicates that introducing biosimilar infliximab might result significant budget savings or increasing of the number of patient access to biological therapy. Interchanging by prescribing physicians could substantially increase budget savings.

PMS22
INTRODUCTION OF AN INFLIXIMAB BIOSIMILAR (CT-P13): A FIVE-YEAR BUDGET IMPACT ANALYSIS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN IRELAND
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OBJECTIVES: Biosimilars have similar efficacy and safety profiles to the originator biologics such that their introduction into Ireland is expected to increase competition, lower prices and improve the affordability of costly therapies. The objective of this study sought to estimate the budget impact of introducing an infliximab biosimilar (CT-P13) as a treatment option for rheumatoid arthritis (RA) patients in Ireland. **METHODS:** An Excel-based budget impact model was developed over a five-year time horizon. The annual population in Ireland receiving treatment with a biologic was based on national population statistics and published literature including: prevalence and incidence of RA; proportion of patients eligible for treatment with a biologic; and proportion of patients receiving treatment with a biologic. After the first year, an annual population growth rate of 1.1% was assumed. Maximum conversion of all existing and new infliximab patients to the infliximab biosimilar was assumed for years one to five. The total cost/patient was based on published literature and included drug acquisition, administration, and monitoring costs. Outcomes are reported as the annual and cumulative budget impact over five years. **RESULTS:** In year one, 3,776 prevalent and 119 incident patients entered the model. Of these, 13% received the infliximab biosimilar with the total cost/patient calculated as €15,754 in the first year of treatment and €12,789 in subsequent years. The drug acquisition cost for the infliximab biosimilar was assumed to discount infliximab by 20%. Annual budget saving estimations following introduction of the infliximab biosimilar were €579,631, €1,165,400, €1,177,553, €1,189,463 and €1,201,137 for years one to five, with a cumulative budget saving of €5,313,184. **CONCLUSIONS:** Introducing an infliximab biosimilar as a treatment option for RA patients in Ireland represents a cost saving of up to €5,313,184 over five years; equivalent to treating an extra 337 new patients with a biosimilar for one year.

PMS23
DEMINERALISED BONE MATRIX (DBM) VERSUS ILIAC CREST BONE GRAFT (ICBG) FOR LUMBAR SPINAL FUSION PROCEDURES IN THE UNITED KINGDOM; A BUDGET-IMPACT ANALYSIS
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OBJECTIVES: Iliac Crest Bone Graft (ICBG) is a commonly used bone graft material in lumbar spinal fusion procedures. Demineralised Bone Matrix (DBM) added to supplement Local Bone (LB) provides an alternative graft material that does not require a secondary surgery site to harvest iliac crest bone. The objective of this study was to investigate the economic impact associated with the use of DBM in lumbar spinal fusion procedures in the UK. **METHODS:** A decision tree model was developed to evaluate the two-year budget impact associated with adding DBM as an alternative bone graft material in the lumbar spinal fusion surgical procedure. The model structure was based on previously published economic models, identified via a structured literature search, and compares surgical treatment with either ICBG or DBM added to the LB procedure. The model includes the costs of the surgical procedures, for adverse events and for treatment failure (reoperations). Further, the model was validated by UK clinical experts to ensure its adherence to UK clinical practice. The model population included UK-based patients with lumbar degenerative disc disease (LDDD) considered eligible for lumbar spinal fusion with either LB or ICBG. In the model's base-case analysis, ICBG was compared with DBM added to LB. **RESULTS:** The model predicts cost-savings of £44 467 over two years when adding DBM to LB compared with using ICBG alone for the lumbar spinal fusion procedure in a hypothetical population of 100 patients. The cost-savings are realised through reduced surgical time and fewer adverse events associated with surgery. **CONCLUSIONS:** In a defined population of spinal fusion patients in the UK that would otherwise be treated with ICBG, the addition of DBM to LB presents an economically viable and potentially cost-saving clinically appropriate treatment option.

PMS24
POTENTIAL ECONOMIC IMPACT OF USING SUGAMMADEX FOR THE ROUTINE REVERSAL OF NEUROMUSCULAR BLOCKADE IN RUSSIAN HEALTH CARE SETTING
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OBJECTIVES: To evaluate the potential economic impact of sugammadex used for reversal of rocuronium-induced neuromuscular blockade (NMB) in comparison with neostigmine and spontaneous reversion of NMB in Russian health care setting. **METHODS:** We constructed the model to compare two scenarios of general anesthesia with rocuronium-induced NMB: 1) routine practice (70% spontaneous

reversal from NMB, 30% use of neostigmine), and 2) sugammadex used in all cases. We estimated costs associated with NMB and time when operation rooms are occupied. Calculations were made for a typical Russian hospital providing 5000 surgeries per year, 160 of them performed with rocuronium-induced NMB. The model inputs included current practice patterns derived from the survey of experts, data on the recovery time from NMB and rates of residual NMB and its complications were taken from published sources. Costs were estimated on the basis of data on governmental tenders and reimbursement rates for services in the compulsory medical insurance system. **RESULTS:** Introduction of sugammadex can decrease number of residual NMB cases by 93,6% and save 70 hours in operation room due to shorter period till extubation in comparison with base case scenario. The overall spending related to general anesthesia increased by EURO 20,510. In case of rational hospital management saved operating time could be used for providing extra surgeries that will generate additional revenue of EURO 14,395 – 48,041 for a hospital, depending on the type of surgery provided in a saved time. **CONCLUSIONS:** The reduction of recovery time with sugammadex may generate additional revenue for the hospital and improve access to health care for public. Still optimization of workflow processes is necessary.

PMS25

BUDGET IMPACT ANALYSIS OF BIOLOGIC DRUGS FOR TREATMENT OF POLIARTICULAR JUVENILE RHEUMATOID ARTHRITIS IN RUSSIA

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OBJECTIVES: To assess impact on the 3-year health care budget of 3 biologic drugs (BD) – abatacept, adalimumab and etanercept – provided for all eligible children with poliarticular juvenile rheumatoid arthritis (JRA) not responding to the standard therapy **METHODS:** The indirect comparison of the results of randomized controlled trials (RCT) demonstrated that compared BD have approximately the same effect on the rate of disease flares in children with poliarticular JRA. We developed four scenarios assessing direct costs (drugs, medical services and sick leave payments for parents caring for children) bared by the government during 3-years period in base case and in cases of provision of one of compared BD for all children with poliarticular JRA. The hypothesis was that introduction of BD decreases the rate of disease flares and thus reduces related costs. The potential reduction of costs related to disability was not assessed due to the lack of data. The model inputs were derived from Russian cost of illness analysis of JRA and RCTs on the efficacy of BD. The costs estimation was based on the average wholesale price of BD and reimbursement rates in the compulsory medical insurance system. **RESULTS:** The lowest costs are expected in the scenario with abatacept – EURO 63 mln in comparison with EURO 81.62 mln for etanercept and EURO 134.18 mln for adalimumab. Adoption of BD would reduce the costs of hospital treatment and sick leave payments for the caring parents by 14-17%. Overall the increase of budget spending during 3 year period per 1 patient receiving BD varies from EURO 10,328 (abatacept) to EURO 23,255 (adalimumab). **CONCLUSIONS:** Supplying with BD all eligible children with JRA requires high additional spending of the health care budget, the least burden is imposed by the adoption of abatacept in comparison with etanercept and adalimumab.

PMS26

STRATAFIX™ KNOTLESS TISSUE CONTROL DEVICE: A BUDGET IMPACT ANALYSIS FROM ITALIAN HEALTH SERVICE PERSPECTIVE

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OBJECTIVES: STRATAFIX™ Knotless Tissue Control Device is a new medical device. With significantly more points of fixation than traditional sutures, STRATAFIX™ gives surgeons more consistent tension control over every pass, and combine the strength and security of interrupted closure with more efficiency than continuous closure. A Budget impact analysis was developed to estimate the cost saving associated with use of new technology from the Italian Health Service perspective over a 1 year time horizon. **METHODS:** A literature review was conducted to evaluate the time savings in different procedures: hysterectomy and myomectomy (Gynecology), breast reconstruction and abdominoplasty (Plastic Surgery), prostatectomy and nephrectomy (Urology), hip and knee replacement (Orthopedics). Moreover, a survey with clinicians was conducted to estimate the number of sutures used for the different procedures. The means and 95% confidence interval (95%-CI) for the budget impact were estimated using bootstrap methods (10.000 simulations) assuming lognormal distribution for costs and time data, and beta distribution for percentage data. **RESULTS:** Cost savings per procedure with STRATAFIX™ would be 217 € and 227 € for hysterectomy and myomectomy respectively, 274 € and 60 € for breast reconstruction and abdominoplasty, 56 € and 230 € for prostatectomy and nephrectomy, 48 € and 50 € for hip and knee replacement. Considering the evolution of annual procedures performed with the introduction of STRATAFIX™, the cost saving associated will be about 1.340.129 € (95%-CI: 218.530- 3.089.771 €): 30% for myomectomy, 26% for breast reconstruction and 22% for hysterectomy. **CONCLUSIONS:** The additional costs for this new medical device permits to generate appropriateness and to reallocate staff and operation rooms for other activities. STRATAFIX™ technology appears cost-saving for the reduction of procedure time. The results were consistent according to the developed probabilistic sensitivity analysis, STRATAFIX™ leads to cost savings in 99% of the simulation.

PMS27

GLOBAL VARIATIONS IN BIOLOGICS ACCESS AND RHEUMATOID ARTHRITIS TREATMENT COSTS

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OBJECTIVES: Biological therapy is effective at slowing disease progression in Rheumatoid Arthritis (RA), particularly in severe RA. Recent clinical trials also demonstrated efficacy of biologics for moderate RA. However, access to biologics varies substantially by country, in part due to differing eligibility criteria of reimbursement policies. Here we investigated the proportion of patients who receive biologics, and whether eligibility criteria were correlated with total costs per RA patient across a range of countries. **METHODS:** PubMed searches were performed to establish which countries reimburse biologics for RA treatment. Eligibility requirements, percentage of patients who received biologics and cost per patient were extracted from a variety of sources. Simple regression analysis was used to compare total cost of RA treatment per patient and severity of RA (DAS score) required for biologic access. **RESULTS:** Regarding eligibility criteria, 16 out of 21 countries restricted biologics to patients with severe RA (DAS score >5.1) and/or who failed 2 previous DMARDs. Eligibility was linked to reimbursement policy for 14 countries. New Zealand had the most stringent reimbursement criteria, with only 1 biologic reimbursed and limiting eligibility to severe, active erosive RA >6 months, 4 failed DMARDs including MTX, and DAS score >5.1. Taking into account the relative prevalence of RA, 20% of RA patients received biologics in Norway and Belgium, 10% in the UK, 9% in Australia, 5% in Germany and Italy and only 3% in New Zealand and Austria. Out of 14 countries, there was poor correlation between total cost of RA treatment per patient and the severity of RA required for biologics access (R Square: 0.09, p=0.29). **CONCLUSIONS:** Reimbursement policies for biologics in RA vary substantially between countries, as does the proportion of RA patients who receive biologics. No significant correlation was found between cost per patient and DAS score required for biologics treatment.

PMS28

ASSESMENT OF THE COST OF BIOLOGICAL THERAPY IN RHEUMATIC DISEASES: ECONOMIC IMPACT OF DOSAGE MODIFICATION IN CLINICAL PRACTICE

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OBJECTIVES: To evaluate the real annual cost of biological therapies (BT) in rheumatic diseases in a tertiary hospital in 2012 and to compare the real annual spending, in daily clinical practice, with theoretical costs with conventional doses. To analysis the reduction of costs after creating BT outpatient clinic. **METHODS:** Cost minimization analysis based on an observational, cross-sectional study. Patients with different rheumatic diseases in follow-up by Rheumatology service in Hospital Carlos Haya(Spain) who have been treated with BT under conventional and modified doses were included. *Outcome 1º*: Annual average cost (in Euros) of BT in patients with rheumatic diseases in clinical practice compared with theoretical cost.*Secondary Variables*: cost reduction in Euros after implantation of a specialized outpatient clinic of BT. *Dose reduction protocol*: After 6 months with label dose activity disease is assessed, if DAS28<2,6 or BASDAI<4, we reduce the standard dose and we reevaluate every 6 month. We performed a descriptive analysis of the sample. Cost minimization analysis to evaluate annual costs were carried out. **RESULTS:** A total of 478 patients were treated with BT in our service in 2012. Most of them were Reumatoid arthritis(265,55.4%). Theoretical annual cost in 2012, it would be of 5,647,969.35 Euros (11,791.17 Euros patient-year). However, during 2012 32 patients reduced doses of their biological therapy in clinical practice. This represented a saving of 146,129.67 Euros in 2012. From December 2012 until June 2013 in our outpatient clinic of BT, 76 patients went into remission or low disease activity and the biological drug dose was reduced. This dose modification resulted in a reduction of the total cost of 159, 004 Euros in 6 months associated with adequate disease control **CONCLUSIONS:** It is possible to reduce doses and associated costs of BT. The follow-up of patients in a specialized outpatient clinic leads to a better patient management and a cost reduction

PMS29

BURDEN OF INFUSION-RELATED COSTS AND STAFF TIME FOR RHEUMATOID ARTHRITIS IN THE HOSPITAL SETTING

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OBJECTIVES: Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting 0.6% of the population in the US. Current RA infusion therapy incurs substantial cost and time to the hospital and patient. The purpose of this study was to model the infusion and related staff costs within a hospital center to better understand the economic and time burden of RA infusion therapy. **METHODS:** We developed an Excel model to estimate the annual time and cost burden associated with RA infusion services in a hypothetical hospital center. We assumed patients received abatacept, tocilizumab, or rituximab monotherapy. Product package inserts informed the number of annual maintenance infusions (13 infusions for abatacept [30 minutes each] and tocilizumab [60 minutes each]; 4 infusions for rituximab [195 minutes each]) per patient. The model projected annual direct costs and total value of staff time for infusion drug administration, infusion-related services, facility-related services, laboratory tests, and patient/caregiver costs. Costs were derived from the literature and adjusted to 2012 USD; 29.5% allocated overhead was applied to laboratory, facility and infusion service costs. Time estimates were obtained from the literature and survey data, converted to annual wages using BLS data, and adjusted to 2012 USD. **RESULTS:** The baseline model estimated total infusion drug and service-related costs to be $24,645 for abatacept, $27,840 for rituximab, and $31,339 for tocilizumab. Roughly 54%, 62% and 58% of these annual costs are associated with hospital labor, respectively. Patient/caregiver costs, comprising of lost wages and indirect medical costs, were estimated to be $788 for abatacept, $793 for rituximab, and $1,063 for tocilizumab. **CONCLUSIONS:** Our findings show that direct and infusion-related contribute to a substantial economic and time burden to both the hospital and patient. These findings can help decison makers assess the relative benefits and cost implications of administering infusion drugs to RA patients.

PMS30
COST ANALYSIS OF THE USE OF AN OPERATING ROOM WITH FULL-ROTATION 3-D INTRAOPERATIVE IMAGING AND NAVIGATION IN DIFFERENT SPINE SURGERIES
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OBJECTIVES: The use of navigation and intraoperative imaging permits to perform a large number of procedures more accurately and safely. The aim of this study was to estimate the cost savings achieved by an integrated operating room with full rotation 3-D intraoperative imaging and navigation (NT) compared with a standard operating room in three types of surgery: balloon kyphoplasty, lumbar fusion, and fusion cervical. **METHODS:** We developed a cost analysis through a published literature review of full rotation 3-D intraoperative imaging and navigation studies, taking into account a hospital perspective. We identified the studies with data related to hospital resource savings when compared with a standard operating room (imaging test outside the operating room). Subsequently, potential savings per patient were estimated for each surgery and were updated to euros 2013. Cost data were taken from e-Salud database and Spanish regional tariffs. **RESULTS:** The use of full rotation 3-D intraoperative imaging and NT versus a standard operating room increases surgical process efficiency due to: avoid post surgery computer tomographies to confirm the success of the procedure, increase the accuracy of surgical interventions, avoid complications and reduce the need for re-interventions, reduce the operating room time, faster patient recovery and reduce hospital length of stay. Potential savings by type of surgery were € 615, € 3,242, and € 4,458 for balloon kyphoplasty, posterior cervical fusion, lumbar fusion, respectively. **CONCLUSIONS:** The use of full rotation 3-D intraoperative imaging and NT leads to improved clinical outcomes and increased hospital efficiency in surgeries carried out with it. A 3-D intraoperative imaging system is a cost-saving strategy for balloon kyphoplasty, lumbar fusion, and cervical fusion surgeries from a hospital perspective.

PMS31
HEALTH CARE UTILIZATION AND EXPENDITURES OF OSTEOPOROSIS PATIENTS TREATED WITH ORAL BISPHOSPHONATE IN TIANJIN, CHINA
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OBJECTIVES: To estimate the health care utilization and expenditures for osteoporosis patients treated with oral bisphosphonate in Tianjin, China and examine factors associated with health care expenditures. **METHODS:** Data were obtained from Tianjin Urban Employee Basic Medical Insurance database (2008-2010) with 30% random sample of enrollees. The index date was the first pharmacy claim date of oral bisphosphonate in 2009. Patients of 40 years of age or older, continuously enrolled for 12 months prior to and following the index date, were included if osteoporosis was diagnosed and oral bisphosphonate (alendronate and etidronate) was claimed accordingly. All-cause cost, osteoporosis-related cost, drug cost, and related health care utilization were estimated at 2009 dollars. Logistic regression analysis was applied to identify factors associated with expenditures. **RESULTS:** Of 853 patients identified, 64.6% were for women. The mean age was 64.6 (±10.4) years. Of $2039.2 (±2782.6) all-cause cost per person per year, out-of-pocket cost accounted for 2.1%; drug cost accounted for 61.1%; osteoporosis-related cost accounted for 37.9%. Of $1026.5 (±1108.8) all-cause outpatient cost per person per year, drug cost accounted for 82.3%; osteoporosis-related cost accounted for 14.6%. Of $1012.7 (±2586.2) all-cause inpatient cost per person per year, drug cost accounted for 39.6%; osteoporosis-related cost accounted for 61.5%. An average of 7.0 (±3.7) outpatient visits and 0.4 (±0.8) hospitalization admissions were found. Regression results demonstrated that patients with diabetes mellitus and nephropathy had higher all-cause cost; female patients and patients with pre-fracture had higher osteoporosis-related cost. **CONCLUSIONS:** The economic burden of osteoporosis is high for osteoporosis patients and is expected to increase considering the increment of life expectancy and the increasing number of elderly population. Greater emphasis and policy guidance should be given to the impact of osteoporosis prevention and treatment in elderly population.

PMS32
THE COST OF OSTEOPOROTIC FRACTURES IN THE ROMANIAN POSTMENOPAUSAL WOMEN POPULATION
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OBJECTIVES: Little data are available regarding the economic burden of osteoporosis on the Romanian (public payer) health care system. This retrospective chart review estimated the direct costs of osteoporotic fractures in postmenopausal women in Romania. **METHODS:** Women aged >65 years diagnosed with osteoporosis, who sustained an osteoporotic hip, wrist or vertebral fracture between December 1, 2007 and November 1, 2011 (and 1-5 years prior to study enrolment), admitted as inpatients to a sample of Romanian general and specialist hospitals were eligible; patients with multiple fractures or fractures resulting from co-morbidities were excluded. The duration of post-fracture follow-up was one year. The cost perspective included direct costs incurred by the Romanian national health insurance agency and the patients' own budgets. Health care utilization was recorded from hospital and primary care resources, and then multiplied with national tariffs to obtain total costs. Bootstrapping was conducted to generate bias corrected and accelerated confidence intervals. **RESULTS:** Five general hospitals and two specialist hospitals in three Romanian cities participated. A total of 140 patients were included: 60 (42.8%) with hip, 68 (48.6%) with vertebral and 12 (8.6%) with wrist osteoporotic fractures. The mean [95% CI] total cost of osteoporotic fracture management was €1,155 [€1,044 - €1,304] per patient. Medications (mean [95% CI], €544 [€477 - €624]) and hospital care (€447 [€393 - €512]) were the major cost drivers, accounting for 47.1% and 42.8% of the average total cost respectively. Hip fractures were more costly than vertebral and wrist fractures (mean [95% CI]: €1,384 [€1,186 - €1,643]; €991 [€852 - €1,172]; and €934 [€659 - €1,177], respectively). **CONCLUSIONS:** This study provides the first estimates of the direct cost of osteoporotic fractures in the Romanian health care system. The results suggest that osteoporotic fractures pose a significant burden on both drug and hospital budgets. Effective treatment strategy to avoid such fractures may reduce this burden.

PMS33
MEDICAL COSTS OF PATIENTS WITH RHEUMATOID ARTHRITIS AND ASSOCIATION WITH GLOBAL DISEASE ACTIVITY IN TURKEY
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OBJECTIVES: To identify factors associated with the cost of RA care and calculated risk-adjusted costs associated with RA in Turkey. The relationships between costs of RA treatment and disease activity was also examined. **METHODS:** This cross-sectional study was performed in 10 tertiary rheumatology centers. Eligible patients were ≥18 years of age diagnosed as having RA for at least 12 months according to the American College of Rheumatology (ACR) 1987 criteria. Overall costs were categorized as inpatient, outpatient and pharmacy costs. Generalized linear models were used to calculate risk-adjusted direct costs. **RESULTS:** A total of 698 patients were studied. Patients' visual analog scale (VAS), patient's global disease activity (GDA) and routine assessment of patient index data 3 (RAPID-3) scores were on average 44.15, 5.19 and 5.10 respectively. Most patients were prescribed immunosuppressive medications and glucorticoids (87.8% and 61.2%, respectively). After adjusting all variables, total annual medical cost was €2,671. The most significant portion of overall expenditures was due to pharmaceutical costs €1,987, while outpatient costs were €303, inpatient costs were €360 and co-payments were €21. 14% of patients experienced work loss due to RA. On average, annual costs due to workday loss were €480. 5.4% of patients also had other RA-related consultations, which were not covered by insurance, bringing the average annual burden to €1,600 for these patients. 6.5% of RA patients had additional costs related to their condition such as the need for a new car, apartment or special equipment, spending an additional €1,640 in 1 year. 13.7% of patients required caregivers. The average annual out-of-pocket amount paid to caregivers was €624. **CONCLUSIONS:** The annual medical cost of RA in Turkey, although significantly lower compared to European estimates, causes considerable economic burden. Drug costs constitute the major part of annual cost for RA followed by indirect costs.

PMS34
PATIENTS AS A SOURCE FOR COST OF RHEUMATOID ARTHRITIS STUDY
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OBJECTIVES: To perform the cost of rheumatoid arthritis analysis based on inquiry study with patients. **METHODS:** It is a micro costing study which was conducted between August and December 2012. The information was gathered with the support of the Association of patients with rheumatoid arthritis. The questionnaire was made and distributed to patients waiting in front the physicians' offices. Clarification in case of missing data was made by phone. The questions aimed to gather basic information about the characteristics of the patients, their pharmacotherapy, frequency of physicians' visits, hospitalizations, and their health status self- evaluation. The direct health costs were calculated based on patients' answers and insurance fund tariff. **RESULTS:** A total of 119 patients participated in the study, and nineteen were excluded due to insufficient information. Twenty-two patients were male and 78 were female aged 54.78 years on average. Almost half of the patients (42 patients) were employed. Thirty-four of patients had duration of the RA less than 5 years, 19 had duration between 5-7 years, another 14 patients had duration of between 7-10 years and 33 patients had duration more than 10 years. The total cost for the treatment of the patients for one month was 82 523 BGN (per patient, per month on average 825 BGN). To one quarter of the patients a biological treatment was prescribed with a total cost of 74 026 BGN per year. Ninety-two of the patients answered that they are strictly taking their medicines. Our study shows that most of the patients doesn't knows what medicines they are taking or even doesn't knows their dossing regime. **CONCLUSIONS:** The percentage of the patients that are not following the doctor's prescription is very high and their reliability as a source of cost studies is not sufficient that impose the need of patient education.

PMS35
WORK PRODUCTIVITY LOSS DUE TO RHEUMATOID ARTHRITIS IN POLAND. RESULTS OF CROSS-SECTIONAL STUDY OF OUTPATIENTS WITH CHRONIC INFLAMMATORY DISEASES AND COMPARISON WITH SELECTED STUDIES
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OBJECTIVES: To measure productivity loss of RA patients in Poland compared to results of selected studies. **METHODS:** In this study consecutive patients in

productive age (18-60 for women and 18-65 for men) were recruited at regionally stratified sample of rheumatology outpatient centers around the country and were offered a questionnaire including Work Productivity and Activity Impairment (WPAI) instrument (a standardized tool for loss of work productivity estimation). The survey was complemented by disease activity assessment questionnaire filled out by specialists who were also responsible for patients recruitment during the routine visits. Employed patients were estimating i.a. the absenteeism and presenteeism rates (% of work time missed due to health and % of impairment while working). Subsequently, systematic review of Medline database was conducted. Two studies using WPAI questionnaire were found (Bansbrack 2012, Zhang 2010). **RESULTS:** In the study, mean age of RA patients was 49 (mean age at RA onset was about 39), mean DAS28 result 3,77 (moderate disease). 40% of the group had first symptoms for less than 5 years (mean duration since symptoms onset was 90 months). Meanwhile, in Bansbrack 2012 mean age at RA onset was 48 and mean duration since onset of symptoms was 48.6 months. Mean age of patients described in Zhang 2010 was 51, 45.8% had disease duration of less than 5 years. The participants had a low function disability level and moderate arthritis. In the study absenteeism rate was 18%, while presenteeism rate reached 27%. The corresponding values in Bansbrack 2012 were 8.7% and 24%. In Zhang 2010 only presenteeism rate was analyzed and equaled 17.8%. **CONCLUSIONS:** RA reduces work ability and lower work productivity in people in productive age both in Poland and in other countries. Differences in patients characteristics are probably the cause of results variation between studies.

PMS36

HEALTH CARE RESOURCE USAGE, TREATMENT AND COSTS AMONG PATIENTS WITH HIP FRACTURE IN THE UNITED KINGDOM

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OBJECTIVES: Available data on economic impact of hip fractures in the U.K. are mostly derived from clinical trials or published before the year 2000; recent estimates are lacking. This study examined health care resource usage, treatment and costs among patients with hip fracture in the U.K. **METHODS:** The study used data from the Clinical Practice Research Datalink (CPRD) linked to the Hospital Episode Statistics (HES). Adult patients hospitalised for hip fracture (ICD-10: S72 or M84.4; admission date as index date between January 1, 2006—March 31, 2011) and no previous hip fracture 7 days to 1 year pre- index, and computerised data available 1 year pre and 1 year post-index were identified in HES. Hip fracture-related inpatient and outpatient visits and pharmaceutical treatments were estimated for pre- and post-index periods. Associated costs were calculated by multiplying resource units by official publicly available costs from the NHS perspective. **RESULTS:** A total of 8,028 hip fracture patients were identified (mean age 79; 27% age 85+; 75.8% female; mean Charlson comorbidity index score 2.1). The most common comorbidities were osteoarthritis (42%), pulmonary disease (25%), and renal disease (23%). Pre-index, average resource use per patient included 1 inpatient stay (mean 5.7 days), 7.4 General surgery visits, 4.4 blood tests, and 0.76 General Practice phone consults. Average overall costs pre-index were £3122. For the index hospitalisation, mean length-of-stay and costs were 19.5 days and £14223, respectively; 18% were discharged to another hospital; and 39% and 5% had partial or total hip arthroplasty procedures performed. Post-index frequent medications included acetaminophen (56%), opioids (46%), and bisphosphonates (46%); 51% had hospital stays; and 5.7% had subsequent hip fractures. Average post-index overall costs were £7359. **CONCLUSIONS:** Our study provides recent estimates of resource usage, treatment and costs among U.K. hip fracture patients. This information can be useful in burden of illness and economic analyses.

PMS37

RESOURCE UTILISATION AND COSTS OF TOTAL HIP ARTHROPLASTY IN THE UNITED KINGDOM: A DESCRIPTIVE ANALYSIS

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OBJECTIVES: Total hip arthroplasty (THA) is a commonly performed surgical procedure in the elderly, projected to increase substantially due to the aging population. Newer resource use and cost estimates are needed to understand the potential THA burden. The study objective was to estimate health care resource use and costs in THA patients in the U.K. **METHODS:** The Clinical Practice Research Datalink (CPRD) linked to the Hospital Episode Statistics (HES) was used to estimate resource use in THA patients. Inclusion criteria were: first inpatient stay for THA (OPCS procedure code W37-W39, W46-W48, W93-W95) (index event between 1/1/2006--3/31/2011); no THA diagnosis/procedure 7 days to one year pre-index date; 1-year pre and 1-year post-index of computerised data available; age 18+. Inpatient, outpatient and pharmacy THA-related costs were calculated by multiplying resource units by official publicly available costs (British Pound Sterling, 2012) from the NHS perspective. **RESULTS:** THA patients identified (n=15,288) were mostly female (66%), elderly (mean age 72; 45%>75), and 84% had osteoarthritis. Pre-index, the most common medications were opioids (53%), NSAIDs (41%), and acetaminophen (35%); 95% had General surgery visits; 64% had inpatient stays; 36% had x-ray; and overall costs (std. dev) were £4,556 (7850). The index hospital event average length-of-stay (LOS) was 9 days and mean costs were £11,321. Post-index medication usage for opioids, NSAIDs, and acetaminophen was 49%, 29%, and 45%, respectively. The most frequent resources were General surgery visits (94%), hospital stays (39%), and General Practice phone consults (35%). For patients with utilisation, means per patient were 7.4 for General surgery visits, 5.4 days for hospitalisations. Mean (std. dev) overall post-index costs were £3,567 (9612), comprised mostly of inpatient costs (85%). **CONCLUSIONS:** This study described resource utilisation, pain medications usage and associated costs for THA patients. These estimates may offer a better understanding of the economic burden.

PMS38

OUTPATIENT MEDICAL COSTS, INDIRECT COSTS, AND FAMILY BURDEN OF OSTEOPOROSIS FRACTURE IN CHINA

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OBJECTIVES: The prevalence of osteoporosis fractures is anticipated to increase rapidly due to China's aging population. However, representative data on the economic burden of osteoporosis fractures are lacking. The aims of this study were to estimate direct outpatient medical costs, indirect costs and family burden associated with patients with osteoporosis fractures in China. **METHODS:** One hundred and fifty osteoporosis fracture patients and/or care-givers were interviewed within 149 days [median] post-fracture in three tertiary hospitals in Beijing, Wuhan and Chongqing representing eastern, middle and western China. Fracture patients were discharged from hospital between January 2011 and January 2013. The survey collected data on demographics; ambulatory status; outpatient services and costs (emergency room, drugs, other outpatient); indirect medical services and supplies and costs (nursing, transportation, rehabilitation, devices, etc.); and lost work time from caregivers. **RESULTS:** Of the 123 valid respondents (female: 64.2%; mean age: 71.3 years), 62.6% were hip fractures, followed by vertebral fracture (34.1%), non-vertebral/non-hip fracture (2.4%), and multiple fracture (0.8%). All patients received surgical treatment, 8.9% had historical fractures, 80.5% had comorbidities and 82.9% of patients had post-discharge outpatient visits. The most frequent comorbidities were hypertension (61.0%), rheumatoid arthritis (41.5%), high cholesterol (35.0%) and cardiovascular disease (34.2%). Reported disability (walk w/aid or could not walk) increased from 13% pre-fracture to 36% post-fracture. Average post-acute outpatient care costs and indirect medical costs were 2084 RMB and 3526 RMB, respectively. Care-givers reported an average of 33.2 days lost from work. Using median income from the three regions, the estimated average lost income for caregivers was 5910 RMB (weighted by share of responders per region). **CONCLUSIONS:** The study suggests the economic burden of osteoporosis fractures is considerable in terms of outpatient medical costs, indirect medical costs and family burden. Osteoporosis-related fractures may pose a significant burden to China due to the aging population.

PMS39

ANNUAL EXPENDITURE ON ANTI-TNF TREATMENT OF RHEUMATOID ARTHRITIS FOR THE PUBLIC HEALTH SYSTEM IN BRAZIL

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OBJECTIVES: Provide clinically relevant evidence and drug expenditure information for brazilian public health system management. **METHODS:** We performed a systematic review on the use of anti-TNF biological agents, infliximab, adalimumab and etanercept in the treatment of patients with rheumatoid arthritis, using the precepts of evidence-based medicine, ensuring methodological quality of clinical studies, prioritizing clinical outcomes. Clinical evidence was retrieved in PubMed, Central Cochrane, EMBASE and medicine purchase costs in July 2010. **RESULTS:** Twenty-three randomized trials met the eligibility criteria, six on infliximab, nine on adalimumab and eight on etanercept. Adalimumab and etanercept showed no benefits when not associated with methotrexate. The ACR50 response to infliximab (NNT = 6) and adalimumab (NNT = 5) were similar while the results for etanercept were considered heterogeneous. The annual cost of infliximab to treat six patients and get ACR50 response in a single patient was US$ 125,997.00 while for adalimumab to treat five was US$ 186,990.00. The ACR70 response was similar between etanercept (NNT = 9) and adalimumab (NNT = 10), being lower in the recommended dose of infliximab (NNT = 12). The most favorable annual cost of acquisition was observed with adalimumab which US$ 311,651.00 is needed to treat 10 patients and get ACR70 response in a single one, compared to expense of US$ 365,107.00 with etanercept (NNT = 9). The unusual infliximab dose of 10mg/kg showed similar results (NNT = 9), however with the most unfavorable spent of US$ 680,385.00. **CONCLUSIONS:** Adalimumab was the agent who showed the most favorable annual expenditure for medicine purchase from the perspective of the public health system in Brazil, considering the most clinically relevant response.

PMS40

BIOLOGICAL TREATMENT PATTERNS AND ASSOCIATED COSTS FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN TAIWAN

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OBJECTIVES: To examine the pattern of biological treatment and the medical costs for patients with rheumatoid arthritis (RA). **METHODS:** A longitudinal dataset that includes the claims of service used by a cohort of RA patients from the Bureau of National Health Insurance was used for this study. The inclusion criteria for the study cases were patients who: 1) were holding the Catastrophic Illness Card with RA; 2) had the 1st line TNF-α antagonist treatments for at least 6 months; 3) were aged over 17. Treatment patterns were defined based on their TNF-α Antagonist within 12 months after the initial 6-month treatment period. Wilcoxon signed rank tests were performed to compare differences in service costs and service uses between the pre- and post-biological treatment periods. **RESULTS:** In total, 2425 patients were eligible for analysis. In the first year after TNF-α initial 6-month treatment, 94% remained using the same TNF-α antagonist, 3% had switched from one to another TNF-α antagonist, and 3% discontinued use of TNF-α antagonist. RA patients treated with TNF-α antagonist were significantly associated with reductions in emergency room visits ($p < 0.001$), hospital days ($p < 0.01$) and total medication costs (excluding biologics) ($p < 0.01$). However, total RA-related outpatient visits and overall medication costs went up significantly ($p < 0.001$). Reduction in services use was not

significantly observed among patients who switched during their TNF-α antagonist treatment. **CONCLUSIONS:** RA with biological treatment was associated with reductions of service uses; however, overall service costs were compromised by costs incurred from increased utilization of outpatient service and TNF-α antagonist medication costs under the context of health care in Taiwan.

PMS41

REDUCTION IN NSAIDS CONSUMPTION AFTER VISCOSUPPLEMENTATION WITH HA: IS IT COSTS SAVING?

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OBJECTIVES: Multicentric, open, retrospective study to determine whether NSAID consumption may be reduced by the use of US-guided Intra-articular injection (USGIAI) of hyaluronic acid (HA), in hip joint in patients affected by symptomatic hip OA. **METHODS:** Patients affected by mono or bilateral hip OA entered the study and were administered with a single HA (HyalOne-Hyalubrix 60) injection every six months. As primary endpoint, consumption of NSAIDs was evaluated by recording the number of days a month the patient used NSAID during the month previous to the visit, reported at each visit during the 24 months follow-up period, while secondary endpoints was represented by the percentage of patients assuming NSAIDs at baseline and at each control visit. **RESULTS:** A total of 755 patients entered the study from 2008 to 2013. Consumption of NSAIDs was reduced from a consumption rate mean of 21,3 to a mean of 5,08 at the third month; this reduction further improved at 12th and 24th month with a reduction respectively to 4,14 and 3,79. Percentage of patients not taking NSAIDs at baseline was 45%; this percentage raised to 57% at 12 months and remained stable (58%) at 24 months. We performed an evaluation of costs of therapies for hip OA for two hypothetic populations of 1000 patients each, the first one undergoing to HA USGIAI every six months for a total of 4 injections in 2 years, and the second one of 1000 patients undergoing to chronic daily NSAIDs therapy, both for two years. Our results confirmed in the USGIAI population a cost savings in comparison with the NSAIDs population. **CONCLUSIONS:** HA USGIAI, administered every 6 months, reduce the assumption of NSAIDs in patients affected by hip OA, reflecting its efficacy on pain relief and cost saving.

PMS42

PHARMACOTHERAPEUTIC MONITORING OF PATIENTS USING IMMUNOBIOLOGICAL IN A HEALTH INSURANCE COMPANY IN BRAZIL: TO KNOW TO BETTER MANAGE

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OBJECTIVES: To determine the clinical and pharmacoeconomic indicators from pharmacotherapeutic monitoring of patients using immunobiological (IMB) in a Health Insurance Company in Fortaleza - Brazil. **METHODS:** Cross-sectional study in two hospitals accredited Insurance, from March/2012 to May 2013 (n = 96 patients). Data were recorded by medical (rheumatologist) in computerized management system (Sabius ®) performed after the query. Later, these were entered into Microsoft Excell 2007 and analyzed by clinical pharmacists auditors. The cost was calculated from the unit value in the book Brasíndice 765, using the Consumer Price Maximum and average weight of 70 kg in standard doses. **RESULTS:** Most patients were women (66, 68.75%), averaging 67 kg, aged between 30-59 years (62.50%) and higher incidence of rheumatoid arthritis among the diseases treated (45; 46.88%). The higher costs per capita were checked with Infliximab (R$ 62,459.40) and abatacept (R$ 41,989.55), while Adalimumab (R$ 16,614.60) and golimumab (R$ 10,385.05) represented the lowest cost per capita. There was a significant difference between the average cost per capita of IMB intravenous (91, R$ 48,975.27) and subcutaneous (11, R$ 10,695.49). The average cost for treatment / dose first line was R$ 6,068.91 and the second line was R $ 9,590.06, resulting in an incremental cost / dose of R $ 3,521.16 (36.72%). **CONCLUSIONS:** The pharmacotherapeutic monitoring becomes important for planning strategies aimed at streamlining and optimization of these drugs and pharmacoeconomic clinical management.

PMS43

DELAY OF TOTAL HIP REPLACEMENT (THR) USING HA VISCOSUPPLEMENTATION: IS COST EFFECTIVE?

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OBJECTIVES: Retrospective study to determine whether THR may be delayed by the use of US-guided Intra-articular injection (USGIAI) of hyaluronic acid (HA), in hip joint in patients affected by hip OA. **METHODS:** We evaluate the delaying in the THR considering 176 patients suffering from hip OA and treated with HA USGIAI, candidates for THR according to the judgment of six orthopaedics. Then, we imaging two hypothetic populations of 1000 patients each candidates to THR, the first undergoing to 1 injection of HA (HyalOne-Hyalubrix 60) USGIAI and the second one undergoing to THR for a follow-up period of one year and four years. We performed the cost evaluation on hip surgery, eventual revision of the prosthesis, post-operative complications and mortality, rehabilitation, lost working days. **RESULTS:** At 24 months, 159 out of 76 (90 %) patients did not undergo to THR. At 48 months, 82 % (N = 144) of the study population treated with HA USGIAI avoided THR. In the group of 93 patients candidates for THR (that is, in which 4, 5, or 6 orthopaedic surgeons agreed that the patient was a suitable candidate for THR), only 17 had undergone THR, with survival results of 82 % at 24 months. At 48 months, this percentage reduced to 66 % in this group. Results show that the treatment with HA USGIAI is the most favorable option, from a clinical and economic perspective, and also considering the social impact (higher value of quality-adjusted life-years (QALYs)). Analyzing hospital perspective, there are even higher benefits, estimated to be between approximately 940,000 euros in one year and 580,000 euros after 4 years. **CONCLUSIONS:** Data simulation comparing HA USGIAI vs THR in patients eligible for surgery, shows that HA viscosupplementation has the most favorable outcome, both from a clinical and economic point of view.

PMS44

COST-EFFECTIVENESS MODELLING OF A 3-MONTH TIGHT CONTROL PATIENT MANAGEMENT OF RHEUMATOID ARTHRITIS WITH CERTOLIZUMAB PEGOL IN FRANCE

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OBJECTIVES: European registries of Rheumatoid Arthritis (RA) patients treated by biological agents suggest that 70-80% are maintained in first line at 1 year despite potential insufficient efficacy. Post hoc analyses of certolizumab pegol (CZP) studies indicate that a 3 month clinical response had a high predictive value of the 1 year outcome. The objective was to examine the efficiency of a strategy consisting of early switching from CZP to a second line TNF inhibitor in case of insufficient clinical response at 3 months (3M) in the French setting versus current clinical practices. **METHODS:** A decision-tree model was built to estimate the clinical outcomes (ACR50 cumulated time) and the direct costs of different cohorts of RA patients over a 2 year period. ACR50 was considered as an RA satisfying clinical outcome. The "3M tight control" strategy consisted of stopping CZP at 3 months in patients not achieving the ACR50 criterion and switching them to other biologics. Three reference cohorts treated with first line CZP, etanercept or adalimumab, respectively, according to current clinical practices were considered as comparators (reference). All TNF inhibitors were assumed to have equal efficacy in first line. Costs were estimated at 2013 French public prices. **RESULTS:** The proportion of patients achieving ACR50 after a 2 year follow-up was 58% in all reference cohorts and 75% in the "3M tight control" CZP strategy cohort. The costs per patient-year in ACR50 were €19,326 with the "3M tight control" strategy cohort and €23,588, €26,774 and €30,285 for the CZP, etanercept and adalimumab reference cohorts, respectively. The strategy "3M tight control" had an incremental cost-effectiveness ratio of €5,605/patient-year in ACR50 versus CZP reference, and was dominant versus etanercept or adalimumab reference. **CONCLUSIONS:** A 3-month tight control management of RA patients with CZP as first line treatment is cost-effective compared to alternatives.

PMS45

COST-PER-RESPONDER ANALYSIS OF BIOLOGICAL AGENTS FOR THE TREATMENT OF ACTIVE ANKYLOSING SPONDYLITIS IN GERMANY

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OBJECTIVES: To conduct a cost-per-responder analysis of biologic treatments (adalimumab, etanercept, golimumab, and infliximab) for the treatment of active ankylosing spondylitis (AS) from the German Statutory Health Insurants (SHI) perspective. **METHODS:** A systematic literature review was conducted to identify randomized clinical trials for biologic treatments for active AS. The clinical efficacy of biologic therapies and standard of care was evaluated using Assessment of SpondyloArthritis international Society (ASAS) 20 response, which is defined as at least 20% improvement from baseline using ASAS criteria. The relative probability of achieving ASAS 20 at Week 12 with each biologic therapy was estimated via network meta-analysis. Evaluation was conducted in terms of cost-per-incremental ASAS 20 responder. Twelve-week costs were assessed in terms of 2012 euros, and included drug acquisition, administration, laboratory tests, and clinic visits based on German treatment guidelines. Weight-based dosing for infliximab assumed an average weight of 78.6 kg. **RESULTS:** Thirteen randomized controlled trials of active AS with a minimal duration of 12 weeks were identified; 10 reported ASAS 20 at Week 12. The estimated rates of ASAS 20 response at Week 12 were not statistically different between infliximab (70.8%), adalimumab (62.9%), golimumab (61.2%), and etanercept (60.5%). However, all 4 biologic therapies were significantly better than the standard of care (27.1%). In the base case, adalimumab had the lowest cost-per-incremental ASAS 20 responder compared with standard of care (€13,282 per incremental ASAS 20 responder), followed by golimumab (€13,947), etanercept (€14,221), and infliximab (€22,838). These rankings were unchanged in sensitivity analyses based on ASAS 40 response rates (estimated from 6 trials). **CONCLUSIONS:** All 4 biologic treatments were more efficacious in terms of ASAS 20 response than the standard of care. Among biologics, adalimumab showed the lowest cost per incremental ASAS 20 responder at Week 12 for active AS from the German SHI perspective.

PMS46

COST-EFFECTIVENESS ANALYSIS OF BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN THE TREATMENT OF RUSSIAN PATIENTS WITH RHEUMATOID ARTHRITIS WHO FAILED PREVIOUS ANTI-TNF-ALFA THERAPY

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OBJECTIVES: To assess the cost-effectiveness of rituximab and anti-TNF-alfa agents in the treatment of Russian patients with rheumatoid arthritis (RA) who failed previous anti-TNF-alfa therapy. **METHODS:** The pharmacoeconomic model was developed based on the data from multicentre prospective 3-year observational MIRAR-study (J. Gomez-Reino et al., 2012). A one-year time horizon was adopted in the model. The cost analysis included costs of medicines and expenses for the day care services. The efficacy of therapies was defined as a reduction of disease activity score in 28 joints (DAS28) and proportion of patients achieved EULAR good or moderate response after 6, 9 and 12 months since biological therapy was started. To assess the robustness of the results, one-way sensitivity analysis (SA) was carried out. **RESULTS:** Treatment with rituximab was associated

with the lowest total costs (437,620.24 RUB per one patient). The costs further increased in the row: etanercept (554,912.15 RUB), adalimumab (977,470.00 RUB), and infliximab (1,039,363.68 RUB). It should be noted that in the infliximab group the bulk of the costs (more than 60% of total) incurred within first six month of therapy. This may potentially increase the financial losses associated with inadequate response to infliximab. The estimated cost-effectiveness ratios (CERs) were 241,779.14 RUB, 334,284.43 RUB, 630,625.81 RUB, and 670,557.21 RUB per unit of DAS28-reduction in the rituximab, etanercept, adalimumab and infliximab groups, respectively. The similar results were observed for the CERs estimated per one patient with EULAR good or moderate response (533,683.22 RUB, 730,147.57 RUB, 1,286,144.74 RUB, and 1,367,583.79, respectively). SA demonstrated that results are robust. **CONCLUSIONS:** The present study has demonstrated that administration of rituximab is economically effective strategy in the treatment of Russian patients with rheumatoid arthritis who failed previous anti-TNF-alfa therapy. Furthermore, treatment with rituximab is associated with considerably lower costs as compared to etanercept, adalimumab and infliximab.

PMS47

COST-EFFECTIVENESS ANALYSIS OF TOCILIZUMAB IN RHEUMATOID ARTHRITIS, IN COLOMBIA

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OBJECTIVES: Assess the cost-effectiveness of first-line tocilizumab biological treatment as monotherapy or in combination with methotrexate, in patients with rheumatoid arthritis (RA) refractory to treatment with non-biological DMARDs. **METHODS:** A markov model was used of the natural history of RA to assess: tocilizumab, tocilizumab+methotrexate, adalimumab, adalimimab+methotrexate, etanercept, etanercept + methotrexate and infliximab+methotrexate. The systematic review of literature don't show results for infliximab in monotherapy. The strategies were evaluated in combination with methotrexate in the first or second line, for a total of 11 strategies evaluated. Outcomes were measured as quality adjusted life years (QALYs). Analysis from the payer perspective, only direct costs were considered, COP 2012. Ratios were calculated cost-effectiveness and incremental cost-effectiveness, and sensitivity analyzes deterministic and probabilistic were conducted. For the RA chronicity, was used time horizon until life expectancy used discount rate of 3% for both costs and health outcomes. **RESULTS:** Tocilizumab was one of the least expensive strategy in first and second-line treatment. For life expectancy horizon monotherapy with tocilizumab followed by infliximab in second line are efficient frontier with an ICER per QALY gained of COP $165,918,610.58. The ICER is sensible to price of medicaments, with a inferiority limit, the results change to COP $106.160.64. The probabilistic analysis indicates that a threshold to willingness to pay of COP $ 150 million higher than monotherapy with tocilizumab, be cost-effective in Colombia. **CONCLUSIONS:** The use of tocilizumab in first and second line like monotherapy and in combination strategy remains lower costs per benefit gained; in that sense, can be considered as an efficient therapy in the Colombian context.

PMS48

A MODEL TO EVALUATE THE IMMUNOGENICITY COSTS OF TUMOUR NECROSIS FACTOR-ALPHA INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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OBJECTIVES: The prognosis of rheumatoid arthritis (RA) has improved dramatically with the development of tumour necrosis factor-alpha (TNFα) inhibitors. However, some patients develop immunogenicity to TNFα inhibitors that can result in treatment failure and higher costs. In addition, immunogenicity to one TNFα inhibitor may create cross-resistance to others. Previous studies have shown the TNFα inhibitor etanercept (ETN) is less immunogenic than adalimumab (ADA) and infliximab (INF). The objective of this study was to determine the costs incurred due to the immunogenicity of ETN, ADA, and INF. **METHODS:** A Markov model was created using data from previously published studies (i.e. the proportions of patients developing antibodies against ADA and INF; the size of increase of dose or drug administration frequency in patients receiving ADA and INF if treatment failed; and the rate of effective dose escalation in patients with and without immunogenicity) and from expert opinion (i.e. physician visit intervals). It was assumed that patients receiving ETN did not develop immunogenicity. Patients initially started ETN, ADA, or INF were allowed to switch treatment to a second or third TNFα inhibitor if treatment failed. Costs due to immunogenicity were calculated from: drug usage after treatment failure, dose or frequency increase after treatment failures, and additional visits due to lack of response. **RESULTS:** Initiating treatment with ETN resulted in the highest proportion of patients still receiving first-line therapy after 5 years, compared with ADA or INF. Assuming 15,000 patients (1% prevalence of RA in The Netherlands) treated for 5 years, the immunogenicity costs incurred with different sequential treatment strategies were: ETN-ADA-INF €4,937,176, ETN-INF-ADA €5,409,593, ADA-ETN-INF €10,140,206, INF-ETN-ADA €11,160,699, ADA-INF-ETN €14,735,996, and INF-ADA-ETN €15,980,783. **CONCLUSIONS:** The 5-year results of our model showed initiating treatment with ETN rather than ADA or INF resulted in higher adherence to first-line therapy and lower immunogenicity costs.

PMS49

COST-EFFECTIVENESS ANALYSIS OF DIAGNOSTIC TESTS IN THE WORK-UP OF PATIENTS WITH INTERMEDIATE RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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OBJECTIVES: Several technologies are currently being developed for better stratifying individuals at risk of developing Rheumatoid Arthritis (RA) to patient-tailored treatment. We assessed the potential cost-effectiveness of four technologies (MRI, il6-serum test, RNA B-cell signature, genetic assay) applied to patients with intermediate risk for RA (3-5 points on ACR/EULAR) using an one-year horizon. **METHODS:** The cost-effectiveness was simulated with a decision model using data from the Rotterdam Early Arthritis Cohort (prevalence of RA: 55%). The comparator was 2010 ACR/EULAR classification criteria. Test properties (sensitivity (se), specificity (sp) and costs) were based on literature and expert opinion. Patients were classified true positive (TP) if they score >=6 points on the criteria or were test positive and used MTX at 12 months. True negative (TN) patients were those who that scored <6 points or were test negative and did not use MTX at 12 months. Utility changes within one year were assigned to TP (+0.1), TN (+0.1), false positive (+0.05), and false negative (-0.05). **RESULTS:** RNA B-cell signature (se: 0.60; sp: 0.90; costs: €150) has the largest net benefit (ΔTP-ΔFP) (45%) and is most cost-effective with an incremental cost effectiveness ratio (ICER) of €13,939. The il-6 serum test (se 0.70; sp: 0.53; costs: €100) has an ICER of €17,343. The MRI and genetic assay have ICERs of €38,541 and €70,347 due to the higher incremental costs of these strategies. To stay below a willingness to pay (WTP) threshold of €20,000/QALY gained (given current utility assumptions), the extra test costs of the new test strategy can maximally be €230. **CONCLUSIONS:** The RNA B-cell signature or il6-serum tests have most potential to be cost-effective in patients with intermediate risk of developing RA.

PMS50

INVESTIGATING THE VALUE OF ABATACEPT IV IN THE TREATMENT OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW OF COST-EFFECTIVENESS STUDIES

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OBJECTIVES: Rheumatoid arthritis is a progressive inflammatory disease that affects greatly patients' quality of life and demands for aggressive management early on during the course of the disease. The emergence of biologics has equipped rheumatologists with evolutionary treatment tools but it has also influenced the costs of the disease, thus highlighting the necessity of cost-effectiveness data. In this light, the purpose of this study was to conduct a systematic review of cost-effectiveness data for abatacept i.v. in the treatment of moderate to severe rheumatoid arthritis. **METHODS:** Pubmed, the International Society for Pharmacoeconomics and Outcomes Research Outcomes Research Digest, the National Health System Economic Evaluation Database, and the Database of Abstracts of Reviews of Effects were searched for papers published in the last decade (2002-2012). An initial search using the keywords "abatacept, cost effectiveness, and rheumatoid arthritis" was followed by a search of related citations. The quality of independent economic evaluation studies was evaluated in accordance to the Centre for Reviews and Dissemination set of guidelines. **RESULTS:** In total 301 studies were identified and 42 met the inclusion criteria. The majority of rejected studies were due to lack of cost data, failure to include abatacept as a comparator to other biologic agents, and failure to include RA as a treatment indication. Half of the selected studies evaluated abatacept in the treatment of rheumatoid arthritis, after failure of or intolerance to tumor necrosis factor alpha inhibitors. Of those, 82% were in favor of abatacept as a cost-effective or dominant strategy versus varying alternatives, whereas 18% favored other treatments. **CONCLUSIONS:** The majority of evidence from the published literature supports that abatacept IV can be a cost-effective alternative in the treatment of moderate to severe rheumatoid arthritis.

PMS51

PHARMACOECONOMIC ASPECTS OF THE FIRST-LINE BIOLOGIC THERAPIES IN RUSSIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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OBJECTIVES: To assess the cost-effectiveness of tocilizumab and TNF-alfa inhibitors in the treatment of Russian patients with rheumatoid arthritis (RA) and intolerance or inadequate response to disease-modifying antirheumatic drugs (DMARDs) or for whom continuation of DMARDs was deemed inappropriate. **METHODS:** Based on the data from ADACTA-trial and the results of indirect comparison of tocilizumab and anti-TNF-alfa agents (G. Bergman et al., 2010) two pharmacoeconomic models were developed. A six-month time horizon was adopted in the models. Cost-effectiveness of tocilizumab and adalimumab was estimated in the first model. In the second model, cost-effectiveness of tocilizumab was compared to the cost-effectiveness of antirheumatic therapy in the mixed treatment group, which included patients who received infliximab, etanercept and adalimumab in proportion 1:1:1. The cost analysis included costs of medicines and expenses for the day care services. The efficacy of the treatment was defined as a DAS28-reduction, proportion of patients achieved a low or moderate DAS28, EULAR good or moderate response (was considered only in the first model) and ACR20, ACR50, ACR70 responses. Sensitivity analysis (SA) was performed by changing costs of medicines and relative proportions of patients received infliximab, etanercept and adalimumab in the mixed treatment group. **RESULTS:** Despite the higher cost of treatment with tocilizumab (591,112.92 RUB as compared to 488,735.00 RUB for adalimumab), it had the better cost-effectiveness ratios (CERs): 179,125.04 RUB vs 271,519.44 RUB per unit of DAS28-reduction, respectively. The similar results were observed for the CERs estimated per one patient with clinical response. Compared to the mixed treatment group, tocilizumab also had better CERs. SA confirmed the robustness of the model. **CONCLUSIONS:** The study has demonstrated that tocilizumab is an economically effective strategy in the treatment of Russian patients with RA and intolerance or inadequate response to DMARDs or for whom continuation of DMARDs was deemed inappropriate.

PMS52
ASSESSMENT OF THE ECONOMIC IMPACT OF BELIMUMAB FOR THE TREATMENT OF SYSTEMIC LUPUS ERITHEMATOSUS IN THE ITALIAN SETTING: A COST-EFFECTIVENESS ANALYSIS
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OBJECTIVES: Systemic Lupus Erythematosus (SLE) is a chronic non-organ specific autoimmune disease and is characterized by a dysregulation of the immune system that involves many organs and systems. It affects about 28,500 people in Italy, especially women of childbearing age (female-male ratio 9:1) that may have a compromised functional state and a decreased quality of life. The purpose of this analysis is to determine the cost-effectiveness of belimumab, a new biological treatment specifically developed for the treatment of SLE, in the Italian setting. **METHODS:** A cost-effectiveness micro simulation model with a lifetime horizon was adapted to the Italian setting. The analysis compares the standard of care (SoC) alone vs belimumab plus SoC from the perspective of the National Healthcare System. Clinical-economic consequences of the therapy and of the development of organ damage were calculated. When available, Italian data were used, otherwise UK costs were transformed into euros using the purchasing-power parity approach. The utility values were based on the EQ-5D of belimumab clinical trials (BLISS 52 and 76). The results were discounted by 3% for both costs and effects. It was considered a duration of treatment with belimumab of 6 years and it was assumed that the drug is used with wastage. **RESULTS:** The results of the cost-effective analysis in terms of cost per life year gained (ICER) and cost per QALY (ICUR) were € 22,990 and € 32,859 respectively. These values drop to € 20,119 and € 28,754 respectively when indirect costs are included. **CONCLUSIONS:** In this analysis, the results of ICER and ICUR show that belimumab is cost-effective in the Italian setting, according to the guidelines of the Italian Association of Health Economics (€ 25-40,000/QALY).

PMS53
TOCILIZUMAB IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS – A COST-UTILITY MODEL FOR THE UNITED KINGDOM
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OBJECTIVES: To evaluate the cost-effectiveness of tocilizumab (TCZ) in the treatment of polyarticular juvenile idiopathic arthritis (pJIA) in the United Kingdom (UK). **METHODS:** An individual sampling model was developed to reflect the health care system and treatment pathway in the UK. Benefits were measured in terms of Quality Adjusted Life years (QALYs) and were derived from HUI3 data collected by the Dutch Arthritis and Biologicals in Children (ABC) Register [Prince et al., 2011]. Costs were calculated from a National Health Service and Personal Social Services perspective. The analysis calculated incremental costs and benefits associated with the addition of first line TCZ to the standard care pathway involving etanercept (ETN), adalimumab (ADA), and abatacept (ABA). The economic model used efficacy inputs derived from an indirect comparison of TCZ and ADA [Sawyer et al., 2013]. Due to fundamental differences in the clinical trial populations and trial design, it was not possible to compare the response rates of TCZ with ETN and ABA. Therefore in the absence comparative data, the economic analysis assumed response rates for ETN and ABA were similar to ADA. Longer-term treatment discontinuation was linked to level of response and assumed to be independent of treatment. **RESULTS:** Base case results estimated incremental costs of approximately £1,750 and incremental QALYs of 0.1011. The incremental cost-effectiveness ratio (ICER) was £17,000 per QALY gained. **CONCLUSIONS:** The results of this analysis suggest that TCZ represents an efficacious and cost-effective addition to the current standard of care for treating pJIA patients in the UK.

PMS54
COST-MINIMIZATION ANALYSIS OF SUBCUTANEOUS ABATACEPT IN THE TREATMENT OF RHEUMATOID ARTHRITIS IN SPAIN
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OBJECTIVES: To compare the cost of using subcutaneous abatacept (SC ABA) versus other first-line biological disease-modifying antirheumatic drugs (DMARDs) available in Spain, in the treatment of patients with rheumatoid arthritis (RA) who have failed an initial treatment with methotrexate (MTX). **METHODS:** With regards to efficacy and safety outcomes, SC ABA was considered non-inferior vs intravenous ABA (IV ABA), adalimumab (ADA), certolizumab pegol (CZP), etanercept (ETN), golimumab (GLM), infliximab (IFX) and tocilizumab (TCZ), based on results of an indirect comparison using mixed treatment analysis. Therefore a cost- minimization analysis for a 3 year time horizon was developed. The perspective was that of the Spanish National Health System (NHS). Pharmaceutical and administration costs (€, 2013) of all biological DMARDs which are available in Spain as first-line treatment after MTX were considered. Drug costs were included in terms of ex-factory price with mandatory rebate. Administration costs were obtained from local published data. The analysis was developed for an average patient weight of 70 kg. A 3% annual discount rate was applied. Deterministic and probabilistic sensitivity analyses were performed. **RESULTS:** SC ABA treatment was associated with a yearly cost of €11,521.36 per patient during the first year of treatment and €11,002.23 in subsequent years. The total 3-year cost of SC ABA was €32,138.43 per patient, proving to be cost saving versus most of the other biological DMARDs. In all cases, pharmaceutical costs lead to more than 85% of total disease management costs. Sensitivity analyses proved the model to be robust. **CONCLUSIONS:** According to these results, SC ABA would lead to cost-savings versus IV ABA, ADA, CZP, ETN, GLM and TZC in the management of RA patients initiating treatment with biological DMARDs.

PMS55
THREE TNF-A-INHIBITORS FOR TREATMENT OF RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS
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OBJECTIVES: To perform pharmacoeconomic analysis of golimumab (GOL) vs adalimumab (ADA) and infiliximab (INF) for rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PA) in Russia **METHODS:** Indirect comparison demonstrated that compared drugs have similar efficacy and safety. Cost-minimization analysis was performed to compare the cost for 1-year treatment with GOL, ADA and INF in doses according to the approved recommendations. Expected cost for treating all eligible patients with RA, AS and PA with TNF-α-inhibitors in Russia were calculated in a model, assuming that INF is used in the 1st line therapy during one year and ADA or GOL in the 2d line therapy during the 2d year. Number of patients to be treated with TNF-α-inhibitors was calculated based on state statistical data and data on the percentage of patients who do not respond to therapy with synthetic disease-modifying antirheumatic drugs (DMARDs) and first-line biologic DMARDs from clinical trials. **RESULTS:** INF dosing regimen is different for RA and other rheumatic diseases, 1 year treatment with INF costs €16,212 for RA and €24,319 for AS and PA. GOL and ADA have the same dosing regimen for all rheumatic diseases and costs €16,544 and €24,243 per year correspondingly. If all eligible patients with rheumatic diseases in Russia receive biologic DMARDs when necessary, treatment with GOL in the 2d line is less expensive than ADA, difference in costs is €89,062,427 (for all eligible patients per year). It allows treating additional 4959 patients RA, 278 AS patients and 147 PA patients per year. **CONCLUSIONS:** GOL is cost-saving vs ADA for the 2d line therapy of rheumatic diseases in Russia. 1-year treatment with GOL is less expensive that INF for AS and PA and may be considered as the 1st line option.

PMS56
PHARMACOECONOMIC ANALYSIS OF ABATACEPT FOR TREATMENT OF ADULTS WITH RHEUMATOID ARTHRITIS IN RUSSIA
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OBJECTIVES: to conduct a pharmacoeconomic analysis of abatacept vs etanercept, tocilizumab and adalimumab for rheumatoid arthritis (RA) in adult patients, resistant to methotrexate therapy, in Russia. **METHODS:** Indirect comparison of clinical efficacy of abatacept, etanercept, tocilizumab and adalimumab was performed. Data on safety from clinical studies and meta-analysis was analyzed. The differences in the direct medical costs for compared biological drugs (BD) in adult patients with RA were calculated using the cost-minimisation analysis. The cost of abatacept vs etanercept and tocilizumab were calculated on the basis of the registered manufacture's prices for vital and essential drugs (VED) in 2012. The costs of abatacept vs adalimumab were calculated based on the price of tender purchases in 2011 (adalimumab is not included into the VED List, and its price is not registered). The costs of day care for patients during the BD administration were calculated based on the cost norms per volume of medical care approved by the Program of State Guarantees for the provision of free medical care to Russian citizens in 2012. The calculations were performed over the BD application period for 2 years. **RESULTS:** Indirect comparison showed no statistically significant differences in the efficacy of compared BD. There was no data about clinically meaningful differences in safety. The use of abatacept is less costly than etanercept and tocilizumab when registered manufacture's prices are used for cost estimation. The difference in costs (in favor of abatacept) amounted to 1431.34 EUR and 16058.34 EUR per patient per 2 years respectively. Abatacept is less costly than adalimumab (the costs are calculated based on prices of tender purchases in 2011): the difference in costs amounted to 1502.07 EUR per patient per 2 years in favor of abatacept. **CONCLUSIONS:** Abatacept is a cost-saving option compared with etanercept, tocilizumab and adalimumab.

PMS57
CURRENT AND FUTURE STRATEGY FOR OSTEOPOROSIS SCREENING AND DIAGNOSTICS: COST-EFFECTIVENESS OF FRAX WITH OR WITHOUT PULSE-ECHO ULTRASOUND MEASUREMENT OF BONE MINERAL DENSITY AND DXA ON DEMAND
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OBJECTIVES: Over 75% of osteoporotic patients are not diagnosed with osteoporosis and do not receive treatment because effective on-site diagnostics is lacking in primary care facilities. We compare the cost-effectiveness of two pathways of osteoporosis diagnosis: 1) Fracture Risk Assessment Tool (FRAX) followed by pocket size pulse-echo ultrasound device (Bindex®) followed by Dual-energy X-ray absorptiometry (DXA) when needed ("proposed"), and 2) FRAX followed by DXA when needed ("guideline"). **METHODS:** A new Markov model of preventive osteoporosis treatment (assumptions: generic alendronate treatment; efficacy based on published meta-analysis and modified by compliance/persistence; wrist, vertebral, hip and other fractures included; Finnish health care payer perspective with 10-year timeframe and 3% discounting per annum) was extended to include the proposed pathway and osteoporosis screening/diagnosis in terms of sensitivity/specificity. FRAX with body mass index and age dependent National Osteoporosis Guideline Group thresholds was the initial screening tool common to both pathways. Bindex® was calibrated to 90% sensitivity and specificity thresholds (International Society for Clinical Densitometry). In the proposed pathway, only the patients with Bindex result between these calibration

thresholds (32,6% of the patients) required a DXA measurement to verify the diagnosis of osteoporosis. Cost-effectiveness was assessed in five patient cohorts: women (BMI 24 kg/m^2) aged 65 years with previous fracture and 75 or 85 years with and without previous fracture. **RESULTS:** Among the cohorts modeled, the average screening cost saved with Bindex® including proposed pathway in comparison to current guideline pathway were around €230/patient. At a cost of €50/screen, the probability that the pathway including Bindex® was cost-effective compared to the current pathway was 100% in all patient cohorts. Bindex® including pathway appeared to be cost-effective at prices as high as €100/screen. **CONCLUSIONS:** Bindex® including pathway appears to be cost-saving strategy compared to the current and recommended Finnish osteoporosis diagnosis and care pathway.

PMS58

A MODEL OF THE COST EFFECTIVENESS OF INFLIXIMAB FOR THE TREATMENT OF SEVERELY ACTIVE ULCERATIVE COLITIS, IN CHILDREN AND ADOLESCENTS AGED 6 TO 17 YEARS, WHO HAVE HAD AN INADEQUATE RESPONSE TO CONVENTIONAL THERAPY

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OBJECTIVES: To evaluate the cost-effectiveness of Infliximab (IFX) treatment in severe, active paediatric ulcerative colitis (pUC). **METHODS:** A Markov model was constructed based upon the literature, to model the progression of a cohort of pUC patients treated with IFX and ciclosporin (CIC) used off-label in the rescue therapy setting. The transition probabilities were estimated from the IFX phase III trials (T72, ACT1 and ACT2). The comparative efficacy was incorporated by using the odds ratio for IFX *vs.* CIC from a head to head trial in adults (Laharie *et al*). Utility weights from observational studies (SOLUTION and Arseneau *et al*) were assigned to the health states within the Markov process. Incremental cost-effectiveness ratios (ICERs) were estimated with a one year time horizon. Uncertainty around key variables was explored through deterministic sensitivity analysis. **RESULTS:** Compared to CIC in the rescue therapy setting, IFX was a dominant treatment option (produced more QALYs at a lower cost). The results were sensitive to the number of days patients were hospitalised for each treatment, the comparative rates of adverse events and altering the odds ratio for comparative effectiveness. **CONCLUSIONS:** IFX is a highly effective and well-tolerated therapy for the treatment of paediatric patients with severely active ulcerative colitis. IFX is the only biologic treatment licensed for this population, and is cost-effective when compared to the commonly used off-licence treatment CIC.

PMS59

COST-UTILITY OF RHEUMATOID ARTHRITIS MONOTHERAPY WITH TOCILIZUMAB IN SPAIN

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OBJECTIVES: Analyze Tocilizumab (TCZ) monotherapy cost-utility for moderate/severe rheumatoid arthritis in patients who are intolerant/contraindicated to MTX, compared with two standard treatment sequences: comparison 1: Etanercept-Adalimumab-Certolizumab-Support treatment vs. Tocilizumab-Etanercept-Adalimumab-Support treatment, and comparison 2: Adalimumab-Etanercept-Certolizumab- Support treatment vs. Tocilizumab-Adalimumab-Etanercept-Support treatment. **METHODS:** A life time micro-simulation model with 6 months cycles was performed in order to calculate the incremental cost-effectiveness ratio of the TCZ treatment sequences vs. standards sequences, which were determined by an expert panel of Spanish rheumatologists. Demographic data on age, HAQ score and sex were obtained from the ADACTA trial, while body weight data was obtained from the PRAXIS study. The efficacy data (ACR clinical response) were obtained from the pivotal clinical trial of each drug. Utilities were calculated from the relationship between ACR response, HAQ score and EQ5D instrument, according to the VACAR study, conducted in the Spanish population. The analysis was done from National Health System (NHS) perspective. Unit costs (€; 2012) were obtained from Spanish sources. Annual discount rate was 3.5% for costs and outcomes. Probabilistic sensitivity analyses were performed. **RESULTS:** TCZ sequences generated more costs per patient than the standard sequence (€ 7,107 in comparison 1; € 6,087 in comparison 2). However, the TCZ sequence generated more QALYs than the standard sequence (0.330 in comparison 1 and 0.297 in comparison 2). The cost of gaining a QALY with TCZ sequences versus the standard sequence was € 21,529 (comparison 1) and € 20,496 (comparison 2). According to probabilistic sensitivity analyses, the probability that the TCZ sequences are cost effective is 86.8% for the comparison 1 and 86.1% for the comparison 2. **CONCLUSIONS:** In both comparisons, the analysis results indicate that the inclusion of TCZ monotherapy as first-line represents an effective and cost-effective alternative in Spain versus the current sequences used for the treatment of patients with rheumatoid arthritis and MTX intolerance/contraindication.

PMS60

COST-UTILITY ANALYSIS OF TOCILIZUMAB MONOTHERAPY VERSUS STANDARD OF CARE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN GREECE

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OBJECTIVES: Rheumatoid Arthritis (RA) is a chronic, inflammatory disease affecting 0.68% of the adult population in Greece. RA is associated with a lowered quality of life and a serious economic burden. This study aims to evaluate the cost-effectiveness of adding tocilizumab to a treatment sequence for patients with active RA, who had an inadequate response to one or more traditional disease-modifying antirheumatic drugs (tDMARDs) and are intolerant or contraindicated to methotrexate (MTX). **METHODS:** A patient-level simulation model was applied to project lifetime costs and outcomes for 10.000 patients from a payer's perspective. The analysis compared a standard treatment pathway (STP) (adalimumab, etanercept and palliative care) with a similar pathway initialized with tocilizumab (TCZ). Disease severity was reflected by Health Assessment Questionnaire (HAQ) scores. As primary efficacy outcomes, American College of Rheumatology (ACR) response rates were used. Patient characteristics (age, gender and baseline HAQ score) and TCZ efficacy data were derived from the ADACTA trial, whereas efficacy data for the remaining DMARDs were derived from a network meta-analysis of each medication's trial outcomes. A mapping model transformed HAQ scores into QALYs. Clinical practice standards were defined by an expert panel of Greek Rheumatologists. Costs for pharmaceuticals and resource unit costs were obtained from official (Social Insurance) price lists. A discount rate of 3% was used for both costs and QALYs. **RESULTS:** Results indicate that a treatment sequence starting with TCZ yields 1.17 more QALYs (9.38 vs. 8.21) for an additional cost of €33,145 (€125,409 vs. €92,264) compared to the STP. The Incremental Cost – Effectiveness Ratio (ICER) was 28,325.5€/QALY gained. Sensitivity Analysis confirms robustness of findings below a threshold of €45.000. **CONCLUSIONS:** The results of the analysis suggest that TCZ as a first-line biologic drug can be a cost-effective treatment option for the management of active RA in patients intolerant or contraindicated to MTX.

PMS61

HEALTH ECONOMIC MODELLING OF SEQUENTIAL THERAPIES FOR RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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OBJECTIVES: A systematic review was conducted to: 1) Identify economic evaluations of therapies for rheumatoid arthritis (RA), and 2) assess and critique how sequential therapies were modelled and evaluated. **METHODS:** Systematic searches of ten databases were undertaken to identify published economic evaluations of disease modifying therapies for RA. Searches were undertaken in February 2013, with no date restriction. Studies were included if they reported a full comparative economic evaluation. Identified studies were appraised using the Drummond economic evaluation checklist. Data extracted included economic evaluation data, along with data relating to sequential treatments. Data on the modelling methods used were also extracted, to identify how data sources were synthesised. The systematic review was conducted to the PRISMA standards. **RESULTS:** Fifty-seven studies were identified. 43 (75%) were cost-utility analyses. 11 (19%) had a UK perspective, and 11 (19%) had a US perspective. The remainder were mainly undertaken within Europe (26 (46%) studies). There was a distinction between studies in recent-onset RA (14 (25%)), and those in established RA (42 (74%)). One study (1%) was unclear. The review identified approximately 30 RA treatments. Using individual level modelling was associated with improved quality of the evaluation and the ability to evaluate sequences. Reporting about the impact of future treatments on costs and health benefits was poor. When downstream treatments were modelled, the evidence used was often poorly reported. No study considered identifying the optimal sequence of treatments given a set of alternative treatments. Where models have been developed that consider a lifelong time horizon and downstream treatment sequences, evidence gaps were identified. **CONCLUSIONS:** The review has identified that methods have not been consistently applied, which has led to varied estimates of cost-effectiveness. Sequences of treatments have not been appropriately considered and modelled, potentially biasing estimates of cost-effectiveness.

PMS62

COST-UTILITY ANALYSIS OF TOCILIZUMAB IN COMBINATION WITH METHOTREXATE VERSUS STANDARD OF CARE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN GREECE

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OBJECTIVES: Rheumatoid Arthritis (RA) is a chronic, inflammatory disease affecting 0.68% of the adult population in Greece. RA is associated with a lowered quality of life and a serious economic burden. This study aims to evaluate the cost-effectiveness of adding tocilizumab to a treatment sequence on a background of methotrexate (MTX) for patients with active RA, who had an inadequate response to one or more traditional disease-modifying antirheumatic drugs (tDMARDs). **METHODS:** A patient-level simulation model was applied to project lifetime costs and outcomes for 10.000 patients from a payer's perspective. The analysis compared a standard treatment pathway (STP) (Adalimumab, Etanercept, Abatacept and Palliative care along with MTX) with a similar pathway initialized with Tocilizumab (TCZ). Disease severity was reflected by Health Assessment Questionnaire (HAQ) scores. As primary efficacy outcomes American College of Rheumatology (ACR) response rates were used . Patient characteristics (age, gender and baseline HAQ score) and drug efficacy for TCZ were obtained by an analysis of pooled data from three phase-III clinical trials. Efficacy data for comparators were derived from indirect comparisons. A mapping model transformed HAQ scores into QALYs. Standards regarding clinical practice were defined by an expert panel of Greek Rheumatologists. Costs for pharmaceuticals and resource unit costs were derived from official (Social Insurance) price lists. A discount rate of 3% was used for costs and QALYs. **RESULTS:** Results indicate that a treatment sequence starting with TCZ yields 0.79 more QALYs (11.68 vs. 10.89) for an additional cost of €21,174 (€168,963 vs. €147,788) compared to STP. The Incremental Cost – Effectiveness Ratio was 26,686€/QALY gained. Sensitivity Analysis confirms robustness of findings below a threshold of €45.000. **CONCLUSIONS:** The results of the analysis suggest that TCZ, combined with MTX, as a first-line biologic drug can be a cost-effective treatment option for the management of active RA compared to STP.

PMS63
COST-UTILITY OF FIRST-LINE ADALIMUMAB AND TOCILIZUMAB MONOTHERAPIES IN RHEUMATOID ARTHRITIS BASED ON HEAD-TO-HEAD DATA
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OBJECTIVES: Until recently, large-scale head-to-head randomized clinical trials (RCT) involving biologic drugs in the treatment of rheumatoid arthritis (RA) have been lacking. In addition, most evidence of biologic RA treatments has relied on combination treatment with methotrexate. The RCT ADACTA compared adalimumab vs. tocilizumab monotherapies as the 1st biologic treatments for severe RA, and demonstrated tozilizumab's clinical superiority over adalimumab. Based on this evidence, we assess the cost-utility of adalimumab and tocilizumab monotherapy in RA after the failure of traditional disease modifying antirheumatic drug(s) (tDMARD). **METHODS:** Two sequences, namely adalimumab or tocilizumab followed by etanercept followed by best supportive care (BSC) including tDMARDs, were implemented in a probabilistic, individual sampling (microsimulation model) setting in order to compare the results among 1,230 Finnish RA patients in a lifetime scenario (based on the Finnish social insurance institution reimbursement data, 1,230 [42.6%] of anti-TNF users purchased anti-TNF without tDMARD in 2012). Clinical outcomes (no ACR20, ACR20, ACR50 and ACR70 responses, and their impact on Health Assessment Questionnaire, HAQ) were obtained from ADACTA and drug survivals from literature. HAQ-scores were linked non-linearly to EQ-5D scores based on the tocilizumab trials, and to hospitalizations and lost production days through literature data. All resources were valued with Finnish unit costs (drugs 4/2013, other costs 2012 real value). Analyses were performed from the Finnish payer perspective (excluding productivity loss) and societal perspective including 3% annual discount rate. **RESULTS:** A QALY gained with the tocilizumab sequence costs €14,294 (€9,111) compared with the adalimumab sequence from the payer (societal) perspective. The respective expected value of perfect information (EVPI) for the payer was €996/patient. Population EVPI was €121,770 with €20,000/QALY gained. According to cost-effectiveness acceptability frontier, the tocilizumab sequence had 89% probability for cost-effectiveness at €20,000/QALY gained. **CONCLUSIONS:** After tDMARD(s) failure, tocilizumab monotherapy was cost-effective in comparison to adalimumab monotherapy.

PMS64
LONG TERM COSTS AND OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS NOT RESPONDING TO CONVENTIONAL THERAPY TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS: THE EXTENSION OF PSORIATIC ARTHRITIS COST EVALUATION (PACE) STUDY
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OBJECTIVES: Poor information on long term outcomes and costs on Tumor Necrosis Factor-α (TNF-α) inhibitors in Psoriatic Arthritis (PsA) are available. Our aim was to evaluate long-term costs, benefits and cost-effectiveness of TNF-α inhibitors in PsA patients with inadequate response to conventional treatment with traditional disease-modifying antirheumatic drugs (DMARDs). **METHODS:** A total of 55 of the 107 enrolled patients included in the study at one year, completed the 5 years follow up period (2005-2010). Patients aged older than 18 years, with different forms of PsA and failure or intolerance to DMARDs therapy were treated with anti-TNF agents. Information on resource use, quality of life, disease activity, function and laboratory values were collected at baseline and through the 5 years of therapy. Costs (expressed in Euro 2011) and utility (measured by EQ-5D instrument) before and after TNF-α inhibitorstherapy were compared in order to estimate the incremental cost per quality adjusted life year (QALY) gained. The cost-effectiveness acceptability-curve was also calculated. **RESULTS:** Thirty-four patients were males (61.8%), aged mean(SD)= 48.94(11.09) years. The majority of patients (83.6%) had a predominant or exclusive peripheral arthritis. At the end of the 5 years, there was a significant increase in direct costs due to an increase of drug cost caused by TNF-αinhibitors that was partially offset by the decrease in indirect costs. The incremental cost estimated and the utility gained of 0.22 gave an incremental cost-effectiveness ratio of 39,678.6 € per QALY gained for the society. The acceptability curve showed there would be a 90% likelihood that anti-TNF therapy would be considered cost-effective at willingness-to-pay threshold of €60,000 per QALY gained. **CONCLUSIONS:** Cost-effectiveness ratios are within the commonly accepted Italian willingness-to-pay threshold. These results show how TNF-α inhibitors could be long-term cost-effectiveness treatment. Our results need to be confirmed in larger samples of patients.

PMS65
HIGH ECONOMIC BURDEN OF MODERATE TO SEVERE PSORIATIC ARTHRITIS ON PAID WORK AND HOUSEHOLD PRODUCTIVITY: BASELINE RESULTS FROM THE RAPID-PSA STUDY
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OBJECTIVES: To estimate the economic burden of moderate to severe psoriatic arthritis (PsA) on workplace and household productivity using data from RAPID-PsA. **METHODS:** The ongoing Phase 3 RAPID-PsA trial (NCT01087788) recruited patients (pts) with active PsA. Impact of PsA on workplace and household productivity and daily activities was assessed at study baseline, using the validated arthritis-specific Work Productivity Survey (WPS). **RESULTS:** At baseline, pts had a mean age of 48 years and 55% were female; 61.6% had psoriasis skin involvement ≥3% body surface area. 59.5% of pts were employed, 14.0% work disabled due to PsA, and 13.5% retired. Overall, a high burden of PsA on workplace and household productivity and on social activities was reported, with on average >1 week (wk) of paid work affected and >2 wks of household duties or social activities affected per month. Household productivity losses were on average, up to 2 to 3 times higher in non-employed or disease work disabled pts vs employed pts: on average household duties were affected 18 days or 26 days vs 10 days/month, respectively. Employed pts with manual jobs reported higher productivity losses at work and within the home vs those with non-manual jobs. Overall, 41.8% of pts required regular assistance from relatives, friends or paid caregivers in their usual activities because of PsA. These pts reported on average 2 to 3 times higher workplace and household productivity losses vs pts who did not require help. **CONCLUSIONS:** PsA is associated with a high burden of disease on workplace and household productivity that could lead to large financial burden for pts and society. Effective PsA treatments are needed to prevent disability and work losses, and reduce economic burden of the disease.

PMS66
ECONOMIC BURDEN OF AXIAL SPONDYLOARTHRITIS RELATED TO PAID WORK AND HOUSEHOLD PRODUCTIVITY AT BASELINE IN THE RAPID-AXSPA STUDY: DIFFERENCES AND SIMILARITIES BETWEEN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS
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OBJECTIVES: To estimate the economic burden of axial spondyloarthritis (axSpA) and directly compare ankylosing spondylitis (AS) and axSpA with no definitive sacroiliitis on X-ray (non-radiographic axSpA, nr-axSpA) in terms of workplace and household productivity losses. **METHODS:** The ongoing Phase 3 RAPID-axSpA trial (NCT01087762) recruited patients (pts) with adult-onset active axSpA according to ASAS criteria, and included AS and nr-axSpA pts. The impact of axSpA on workplace and household productivity was assessed at study baseline (BL), using the arthritis-specific Work Productivity Survey (WPS). **RESULTS:** At BL, 69.2% of axSpA, 67.4% AS and 71.4% nr-axSpA pts were employed outside the home. A high burden of axSpA on workplace and household productivity and on social activities was reported, with slightly higher burden in nr-axSpA vs AS pts. More AS vs nr-axSpA pts were unable to work (15.7% vs 8.2%). On average, axSpA pts reported >1 wk of paid work and >2 wks of household duties or social activities affected/month. Household productivity losses were up to 2–3 times higher in non-employed and disease work disabled vs employed pts. Employed pts with manual jobs reported higher losses at paid work and within household vs pts with non-manual jobs. 39.1% of axSpA pts required regular assistance in their usual activities (42.1% in AS vs. 35.4% in nr-axSpA) and reported higher workplace and household productivity losses vs those who did not require help. Similar patterns were observed in AS and nr-axSpA. **CONCLUSIONS:** A similarly high burden of disease on workplace and household productivity was seen in AS and nr-axSpA pts that could lead to large financial burden for pts and society. Effective axSpA treatments are needed to prevent disability and work losses and to reduce the economic burden of axSpA.

PMS67
LOSS OF PRODUCTIVITY IN POLISH PATIENTS WITH RHEUMATOID ARTHRITIS
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OBJECTIVES: To assess loss of paid productivity in Polish rheumatoid arthritis (RA) patients according to disease activity and disability. **METHODS:** We conducted a prospective one-center observational study with 6-month time horizon. The sample consisted of 109 RA patients of working age (women:<60 years; men:< 65 years), stratified according to Disease Activity Score (DAS28-CRP) and disability index of the Health Assessment Questionnaire (HAQ-DI). Productivity loss was expressed by absenteeism and employment status changes: reduced work hours (part-time), unemployed and/or early retirement due to RA. Spearman rang correlation coefficient test was used to investigate the relationship of productivity loss with disease activity and disability. **RESULTS:** Patients were on average 48.5 years of age, had a mean disease duration of 8.5 years, and 85% were female. DAS28-CRP was ≤5.1 in 52 patients (group A) and >5.1 in 57 patients (group B). HAQ-DI was >2 in 22 patients (group I), >1 and ≤2 in 54 patients (group II), ≤1 in 33 patients (group III). Number of patients who lost productivity was 94 (86%) (79% in A vs. 93% in B, 100%, 94% and 63.6% in I, II and III, respectively). Of them 63 (58%) patients received disability pension due to RA (48% in A vs. 67% in B, 77%, 76% and 15% in I, II and III, respectively). Mean number of working days lost was 120.7 (97.2 in A vs. 142.9 in B; 157.3, 143.1 and 59.8 in I, II and III, respectively). Proportion of patients with productivity loss and number of working days lost were correlated with disease activity ($p<0.01$ and $p<0.001$, respectively) and disability index (both $p<0.001$). **CONCLUSIONS:** This study indicates high impact of disease activity and disability on productivity loss in RA patients. Treatment aiming at reducing disease activity decreases disability progress and may enhance productivity in Polish patients with RA.

PMS68
RESOURCE USE DUE TO DISABILITY IN POLISH RHEUMATOID ARTHRITIS PATIENTS: SIGNIFICANT INCREASE OF TRANSPORTATION NEEDS AND HOME VISITS
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OBJECTIVES: To assess transportation needs and number of home visits in relation to disease activity (DAS-28CRP) and disability index of the Health Assessment Questionnaire (HAQ-DI) in Polish patients with rheumatoid arthritis (RA) **METHODS:**

Prospective data on distance covered due to RA (paid and non-paid, self and caregiver's transport) and about number of medical home visits were gathered during 6 months observation after discharge of non-selected RA patients from one tertiary academic hospital. Patients were stratified according to their DAS28-CRP and HAQ-DI. Spearman rang correlation coefficient test was used for statistical analysis. **RESULTS:** A total of 205 consecutive RA patients included into the study were stratified in 5 groups: A: DAS-28CRP ≤5.1 (89 patients), B: DAS28-CRP >5.1 (116 patients), I: HAQ-DI ≤1 (51 patients), II: HAQ-DI ≤2 and >1 (88 patients) and III: HAQ-DI > 2 (66 patients). In the whole study group 157 (77%) patients used transport for a mean distance of 461 kilometers in 6 months. Corresponding values for group A, B, I, II and III were as follows: 67% for 329 km, 84% for 563 km in B, 55% for 159 km in I, 81% for 528 km in II and 88% for 605 km in III. 7 patients used home visits (3% for a mean number of 0.1 visits - 2% for 0.2, 4% for 0.2, 0% for 0, 1% for 0.3 and 9% for 0.3 in A, B, I, II and III, respectively). There was significant positive correlation between disability and both proportion of patients using transport and distance covered (both p<0.0001), between disability and home visits and between disease activity and transport (both p<0.01). **CONCLUSIONS:** Problems with moving around and need for travelling due to the disease result in significant resource use in RA patients. Comprehensive services meeting these needs may diminish the burden of disease in Poland.

PMS69

BURDEN OF INFORMAL CARE IN RELATION TO DISEASE ACTIVITY AND DISABILITY IN POLISH PATIENTS WITH RHEUMATOID ARTHRITIS

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OBJECTIVES: To assess informal care use in relation to disease activity (DAS-28CRP) and disability index of the Health Assessment Questionnaire (HAQ-DI) in Polish patients with rheumatoid arthritis (RA). **METHODS:** Data on amount of time consumed for informal care (unpaid assistance of family member or other caregiver) was collected during a prospective one center cohort observational study of non-selected RA patients discharged from tertiary academic hospital. At enrollment patients were divided according to DAS28-CRP and HAQ-DI. Observational period was 6 months. Spearman rang correlation coefficient test was used to investigate the relationship between informal care and disability. **RESULTS:** A total of 205 patients were included in the analysis: 89 with DAS-28CRP ≤5.1 (group A), 116 with DAS28-CRP >5.1 (group B), 51 with HAQ-DI ≤1 (group I), 88 - with HAQ-DI ≤2 and >1 (group II) and 66 patients with HAQ-DI > 2 (group III). 164 (80%) patients have been looked after by informal caregivers (64% and 92% in A and B, respectively, and 47%, 89% and 94% in I, II and III, respectively). Mean number of hours of informal care per patient during 6 months was 467 (336, 567, 153, 412 and 783 hours in A, B, I, II and III, respectively). There were significant (p<0.0001) positive correlations between both disease activity and disability index and both number of patients being looked after by informal caregivers and number of hours of informal care. **CONCLUSIONS:** Informal care involves substantial time inputs depending on disease activity and functional status of the care receiving RA patients. On one side, improving access to formal caregiving might be a good solution to improve quality of life and enhance productivity of present informal caregivers in Poland. On the other side slowing down the disease process might reduce the need of informal care for RA patients.

PMS70

THE USE OF DEXA SCANS IN POSTMENOPAUSAL OSTEOPOROSIS IS ASSOCIATED WITH REDUCED LONG TERM FRACTURE RISK

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OBJECTIVES: Postmenopausal osteoporosis (PMO) leads to an increased risk of fractures, which in turn is associated with high resource utilisation. DEXA scans measure the patient's bone mineral density and are an important tool in assessing fracture risk. We aim to determine if the monitoring of PMO patients using DEXA scans is associated with lower incidence of fracture. **METHODS:** Analysis was undertaken using data from the 2012 Adelphi Osteoporosis Disease Specific Programme (DSP), a cross-sectional survey of patients with osteoporosis across the EU5 and the US. Physicians completed a detailed patient record form (PRF) for the next 10 consulting osteoporosis patients. The PRF captured patient information which included age, BMI and physician-perceived severity of the patient's osteoporosis as well information on fracture history, DEXA scans received and date of diagnosis. Bootstrapped survival time regression using an exponential distribution on time to fracture was used to determine the hazard ratio (relative fracture risk) for those that had received a DEXA scan, compared with those that had not. Other covariates in the model were age, BMI, severity, and the possibility that the likelihood of a DEXA scan increases with duration of time since diagnosis. **RESULTS:** Of the 2508 PMO patients with complete information required for the analysis, 1107 had received a DEXA scan (and had associated treatment intervention) and 1401 had received no DEXA scan. Patients who had received a DEXA scan had 59% (0.594, p=0.006) of the fracture risk of those who had received no DEXA scan, adjusted by possible confounders (ceteris paribus). **CONCLUSIONS:** Patients tested with DEXA scans were associated with a significantly lower risk of fracture than those patients who were not. Over time increased use of DEXA testing could lead to a reduction in fractures and subsequently lower resource use and disease burden.

MUSCULAR-SKELETAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PMS71

COMPLIANCE PROTECTS AGAINST FRACTURE IN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS IN HUNGARY

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OBJECTIVES: Compliance to osteoporosis drugs is frequently very low, leading to an increased fracture risk. We investigated the factors associated with fracture risk in women with postmenopausal osteoporosis (PMO) in Hungary, with a focus on compliance. **METHODS:** This retrospective analysis of data from the National Health Insurance Fund Administration included women aged ≥50 years with a diagnosis of osteoporosis (ICD-10 codes, M80 or 81), who started an osteoporosis drug prescription between Jan 2004–Dec 2012 (index event) and had a 13-month non-treatment period prior to this prescription. The relationship between all factors (covariates) and fracture risk was assessed using a dynamic Cox regression model and Andersen-Gill analysis, estimating 95% confidence intervals. Compliance was measured using the medication possession ratio (MPR); MPR≥80% at 1 year was considered compliant. **RESULTS:** A total of 181,239 patients matched the inclusion criteria; 40.4% of patients were > 70 years old and 12.2% had prior fractures in the 36-month period before each index date. Compliant patients had a 35% (RR=0.65, CI=0.59-0.72) fracture risk reduction versus non-compliant patients. Patients aged 70-79 years, and > 80 years, had an increased fracture risk of 71% (RR=1.71, CI=1.54-1.90) and 118% (RR=2.18, CI=1.94-2.46), respectively, compared to patients aged 50-60 years. Prior fractures were associated with a 32% increased risk of one new fracture (RR=1.32, CI=1.18-1.49), and with a 90% increased fracture risk (RR=1.90, CI=1.64-2.19) in patients with 2+ prior fractures, respectively, compared to patients with no prior fractures. There was also a relationship between any co-medication and fracture risk, with a 12% (RR=1.12, CI=1.03-1.22) increase with one co-medication and an 11% (RR=1.11, CI=1.01-1.21) increase with 2+ co-medications compared to none. **CONCLUSIONS:** Compliance was associated with protection against fracture (reduction of relative fracture risk). However, age, any co-medication and prior fractures were associated with an increased relative risk of fracture.

PMS72

TREATMENT PERSISTENCE IN SWEDISH WOMEN INITIATING DENOSUMAB TREATMENT FOR POSTMENOPAUSAL OSTEOPOROSIS

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OBJECTIVES: Persistence to orally and/or frequently administered osteoporosis treatments is poor. Indeed, previous retrospective research has shown that approximately 50% of patients discontinue oral treatments within one year. Denosumab is administrated as a treatment for postmenopausal osteoporosis (PMO) via a subcutaneous injection once every 6 months, and better persistence with denosumab has been shown in randomized trials. The current study estimated treatment persistence among women initiating denosumab for PMO in Sweden. **METHODS:** The study included post-menopausal women who initiated denosumab between May 2010 and July 2012 in the Swedish National Prescription Register. One injection of denosumab was defined as 6 months of persistence. Patients were considered persistent for an additional 6 months if they filled their next denosumab prescription within 6 months + 56 days (permissible gap). Subgroup analyses included comparisons of pre-treated vs. treatment-naïve patients to other osteoporosis treatments, and of patients initiating denosumab treatment in 2010/2011 vs. 2012. **RESULTS:** The study identified 2,315 incident users of denosumab. Mean (SD) age was 73.7 (9.0) years and 60.7% were pre-treated. 83% (CI_{95}:81-84) of patients were persistent at 12 months, 69% (CI_{95}:67-71) at 18 months and 62% (CI_{95}:60-65) at 24 months. Increasing the permissible gap to 90 or 180 days resulted in 12-month-persistence of 85% and 91%, respectively. Pre-treated patients were more persistent than treatment-naïve patients after 18 (71% vs. 67%) and 24 months (65% vs. 58%), but not at 12 months. No difference was observed between patients starting their treatment during 2010/2011 and 2012. **CONCLUSIONS:** Among Swedish women with PMO, persistence to denosumab treatment is high, and pre-treated patients are more persistent than treatment-naïve patients. Given the poor persistence to oral osteoporosis treatments, denosumab treatment could, in these patients, be considered a relevant alternative to increases persistence and hence optimizes outcomes in PMO.

PMS73

PERSISTENCE & COMPLIANCE TO TREATMENT FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN IN HUNGARY: A RETROSPECTIVE COHORT STUDY

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OBJECTIVES: Persistence and compliance with prescribed medication are important factors in treatment success. This study calculated persistence and compliance to treatment among postmenopausal women with osteoporosis in Hungary. **METHODS:** This retrospective analysis of data from the National Health Insurance Fund Administration included women aged ≥50 years with a diagnosis of osteoporosis (ICD-10 codes, M80 or 81), who started an osteoporosis prescription (including bisphosphonates, strontium ranelate, hormone replacement therapy, parathormone and denosumab) between January 2004 to December 2012. We estimated 12- and 24-month persistence per active substance and administration type, with an 8-week grace period; and measured compliance using the medication possession ratio (MPR; MPR≥80% at 12-months considered compliant). **RESULTS:** A total of 288,194 patients matched the inclusion criteria;43.8% were aged >70 years and 6.6% had prior fractures at first index date; 84.4% and 3.1% were receiving oral and intravenous bisphosphonates, respectively, and 12.5% other osteoporosis therapies. 12-month persistence to oral and injectable drugs was 31% and 76%, respectively. 12-month persistence was lowest for daily (23%) and monthly (27%) versus quarterly (58%) and half-yearly (84%) administration (100% persistence and compliance assumed for yearly administration), declining at 24 months to 10%, 10%, 36% and 44% for daily, monthly, quarterly and yearly drugs, respectively (24-month persistence to half-yearly drugs not available). Only 46% of patients were compliant with treatment, with compliance higher for injectable (daily, quarterly,

half-yearly or yearly) (78%) versus oral (daily, weekly, or monthly) drugs (35%). The lowest compliance was observed with daily (24%) and monthly (34%) drugs. Less frequently administered drugs (except yearly) had the highest compliance with quarterly drugs having 63% and half-yearly drugs 70%. **CONCLUSIONS:** This analysis shows that persistence and compliance to osteoporosis treatment is very low in postmenopausal women in Hungary. However, higher persistence and better compliance was observed for injectable, less frequently administered drugs, which may lead to better outcomes.

PMS74

VALIDATION OF THE FRENCH TRANSLATED VERSION OF THE OSTEOPOROSIS SPECIFIC MORISKY MEDICATION ADHERENCE SCALE (OS-MMAS) IN FRANCE

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OBJECTIVES: The OS-MMAS is a disease-specific 8 item self-reported measure of adherence for osteoporosis patients. This study evaluated the measurement properties of its French translated version. **METHODS:** A cohort of women aged 55 or older, with post-menopausal osteoporosis (PMO) residing in France and treated with daily or weekly oral bisphosphonates (OBPs) were selected based on their historical data from the French Longitudinal Patient Database; following their visit to one of the participating practices. Eligible patients were given an OS-MMAS questionnaire for completion at home. Internal consistency was evaluated using the Cronbach's coefficient and construct validity using confirmatory one factor analysis (CFA). Convergence validity was assessed using agreement between patients' medication procession ratio (MPR) and their total score from OS-MMAS. To assess reproducibility, a subset of respondents received a second questionnaire approximately 3 months later. Reproducibility was tested using the intra-class correlation (ICC). **RESULTS:** From a network of 1200 French general practices, 117 participated; 687 eligible women visited these practices during the period 20-Jul-2012 to 31-Dec-2012. Of these women, 218 (mean 73.2 years; SD= 8.1) completed ≥1 OS-MMAS. The 6 and 12 month MPR was less than 80% for 25.7% patients and 59.1% patients, respectively. Cronbach's alpha coefficient was 0.76 and varied between 0.71 and 0.79 with the deletion of one item. The Chi-Square test of association between MPR (<80%, >80%) and OS-MMAS scores (<6; 6-8; 8+) was statistically significant at 6 months (p= 0.025), but not at 12 months (p-value= 0.059). CFA reported a standardized root mean square residual of 0.06. The ICC on 70 patients was 0.24 with 95% confidence interval [0.01-0.45]. **CONCLUSIONS:** This study demonstrated acceptable agreement between classification of patient's adherence to OBPs assessed using French translated OS-MMAS and that using historical 6 months MPR; but also indicated that the construct of the OS-MMAS could be improved.

PMS75

CHANGE OF BURDEN OF DISEASE IN GERMAN RHEUMATOID ARTHRITIS PATIENTS SINCE THE UPTAKE OF TNF-INHIBITORS: A LITERATURE REVIEW OF GERMAN REAL LIFE DATA

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OBJECTIVES: To obtain a comprehensive overview of the impact of TNF-inhibitors on the components of the burden of Rheumatoid Arthritis (RA) in Germany. **METHODS:** A systematic literature research in EMBASE, Medline, grey literature including rheumatology congress abstracts (ACR, EULAR, DGRh), German RA registry homepages, and the Information System of the Federal Health Monitoring (2002-2012) was performed. Published data on the effect of TNF-inhibitors on mortality, morbidity, and health care resource utilization (HCRU) was included. **RESULTS:** Overall, 15 partially overlapping full-text articles (0 mortality, 12 morbidity, 5 HCRU), 6 additional unique abstracts excluding encore publications (1 mortality, 4 morbidity, 1 HCRU) and two other sources (1 morbidity, 1 HCRU) were included in the final review. Reviewed literature reported an association of TNF-inhibitor use with a 35% lower mortality rate (HR=0.65; p=0.0004) compared to synthetic disease modifying antirheumatic drugs (DMARDs). Disease severity based on symptoms decreased over time in Germany: the chances of reaching DAS28 remission (OR=1.97; 95%-CI: [1.20-3.21]) and functional remission (OR=2.21; 95%-CI: [1.06-4.63]) were doubled, the odds of functional independence were quadrupled (OR=4.09; 95%-CI: [1.80-9.29]) with TNF-inhibitor treatment. All SF-36 domains and fatigue scores increased significantly after treatment initiation. TNF-inhibitor treatment is associated with fewer limitations in daily activities (OR=0.77; 95%-CI: [0.65-0.90] and less perseverant limitations (OR=0.82; 95%-CI: [0.68-0.98]. Standardized disability pension ratios in patients with biologics use decreased over time from 12.5 (2001–2003) to 3.4 (2010-2011). Frequency and average duration of hospitalization have fallen from 2001 (19% of patients hospitalized with average duration of 19 days) to 2011 (12%, 12 days). No HRCU data was available for the outpatient sector or surgery. **CONCLUSIONS:** Based on available German data, treatment with TNF-inhibitors is associated with lower mortality, increasing likelihood to reach clinical remission, better symptom control, functional status, work ability and quality of life.

PMS76

PREDICTING EQ-5D UTILITY SCORES FROM SF-36 SCORES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN JAPAN

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OBJECTIVES: To develop a mapping model for estimating EuroQol 5D (EQ-5D) utility values from Short Form 36 (SF-36) scores in Japanese patients with rheumatoid arthritis (RA), with or without clinical characteristics. **METHODS:** Linear regression models were applied to a cross-sectional data set of 112 patients with RA collected from a regional hospital in Niigata prefecture, Japan. Four model specifications were estimated, where EQ-5D was regressed on 1) eight SF-36 scores; 2) as per 1) plus squared and pair-wise interaction terms, 3) as per 1) plus clinical characteristics; and 4) as per 3) plus squared and pair-wise interaction terms, respectively. Model 2 and 4 were developed by using stepwise regression analyses. Model goodness of fit was examined by using Akaike information criterion (AIC), R2, and adjusted R2. Predictive performance was evaluated by using root mean square error (RMSE). **RESULTS:** Model 1 with eight SF-36 scores explained more than 59% of the variation in EQ-5D utility values. The best-performing model based on goodness of fit and predictive performance was model 4 (AIC=□-200.4, R^2=0.767, adjusted R^2=0.709, RMSE=0.090). The model included four SF-36 scores (GH, MH, PF, and RP), five squared terms, twelve pair-wise interaction terms, and log transformed simplified disease activity index (SDAI). Also model 2, which included no clinical characteristics, had similar predictive ability (AIC=□-195.0, R^2=0.764, adjusted R^2=0.699, RMSE=0.093). **CONCLUSIONS:** EQ-5D utility values can be predicted from SF-36 scores and SDAI with Japanese patients with RA. The mapping model can be applied to SF-36 datasets to produce utility scores for economic evaluation of RA treatments from the perspective of Japan health care system.

PMS77

HEALTH-STATE UTILITIES IN MEASURING HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN TAIWAN

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OBJECTIVES: Rheumatoid arthritis is (RA) associated with numerous comorbidities that have major impacts on patients' quality of life. The purpose of this study is of twofold, first, to measure the health related utilities on patients with RA using time trade-off (TTO) and EQ-5D and to examine how these different measures were related to a disease specific measure, Health Assessment Questionnaire (HAQ) and disability level of RA. Second, to investigate absenteeism and presenteeism using Work Productivity and Activity Impairment Questionnaire for Patients with RA (WPAI-RA). **METHODS:** Face-to-face patient interviews on patients with mild RA (DAS <3.2), moderate RA (3.2<=DAS<5.1) and severe RA (DAS>=5.1) have been carried out since June 2013 at rheumatology outpatient clinics at four hospitals located in northern, central and southern Taiwan, and will be continued until the desired sample size of 120 is attained. Health state utilities were elicited using time trade-off (TTO), visual analogue scale (VAS) and EQ-5D. Productivity losses and activity limitation were measured by WPAI-RA. The mean value of the total HAQ score is the mean of the scores for the eight categories: dressing, rising, eating, walking, hygiene, reach, grip and usual activities. **RESULTS:** Based upon the preliminary sample collected, the mean age was 54.5 years, mean history of disease was 8.16 years, and 77% were female in the study patients. The mean health utility was 0.87 (EQ-5D), 0.72 (VAS) and 0.75 (TTO). The mean value of the total HAQ score is 0.83. Employed patients reported 10% reduced work productivity in the previous week, as well as 21.0% reduced productivity in daily activities (all patients). **CONCLUSIONS:** EQ-5D and VAS are consistent measures for HAQ and have high potentials for use in assessing the well-being of the patients with RA in Taiwan. Productivity losses associated with absenteeism and presenteeism are substantial.

PMS78

PATIENT PREFERENCE FOR ORAL VERSUS INJECTABLE AND INTRAVENOUS METHODS OF TREATMENT FOR RHEUMATOID ARTHRITIS

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OBJECTIVES: For patients with rheumatoid arthritis (RA), convenience, frequency of dosing, and invasiveness vary greatly across different administration routes and may influence their everyday lives. The objective of this study was to investigate the impact of administration method on patients' quality of life, understand their resulting unmet needs, and establish an overall preference for method of administration for RA treatment. **METHODS:** Patients from France, UK, Germany, Italy, Spain, Belgium, Sweden, and The Netherlands diagnosed with RA by a physician and taking prescription medication – disease-modifying anti-rheumatic drug (DMARD) monotherapy, biologic monotherapy, or DMARD and biologic combination therapy – completed a 20-minute online survey. Patients were asked about: 1) benefits and drawbacks of their current treatment administration method; 2) their preference for twice-daily oral therapy versus injection or intravenous (IV) infusion therapy if it met their safety and efficacy expectations; 3) if told by their doctor that they needed to change their current RA therapy, would they switch to twice-daily oral tablets, injections, or IV infusion if efficacy and safety requirements were met. **RESULTS:** 1400 patients were included: n=250 patients in each of France, UK, Germany, Italy, and Spain and n=50 in each of Sweden, Belgium, and The Netherlands. Oral DMARDs were seen as having more benefits and fewer drawbacks than DMARD injections, biologic injections, and IV therapy. The majority of patients (79%) would prefer a twice-daily oral tablet than an injection or IV infusion (21%) if it met efficacy and safety expectations. If told by their doctor that they needed to change their current RA therapy, 83% of all patients would prefer switching to twice-daily oral tablets over injection (13%) or IV infusion (4%). **CONCLUSIONS:** Oral therapy can meet some of the key practical and emotional unmet needs RA patients face with injectable or IV infusion therapy, providing efficacy and safety requirements are met.

PMS79

ARE PATIENTS' PREFERENCES FOR OSTEOPOROSIS DRUG TREATMENT TRANSFERABLE BETWEEN COUNTRIES? RESULTS FROM A DISCRETE-CHOICE EXPERIMENT CONDUCTED IN TWO EUROPEAN COUNTRIES

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OBJECTIVES: To evaluate the preferences of osteoporotic patients for medication attributes in Belgium and Ireland, and to assess whether preferences are transferable across these jurisdictions. **METHODS:** A discrete-choice experiment was designed in which patients were asked to choose between two unlabelled drug alternatives (and an opt-out option), which vary in five attributes: efficacy in reducing the risk of fracture, type of potential common side-effects, mode and frequency of administration and out-of-pocket costs. An efficient experimental design was used to construct the sets of treatment options and a mixed logit panel data model was employed to estimate patients' preferences. To assess the significance of the differences between countries, a joint model was estimated using interaction terms. **RESULTS:** A total of 257 Belgian and 200 Irish osteoporotic patients completed the experiment. In both countries, patients preferred a drug treatment with a higher risk reduction and a lower cost. They disliked more being at risk of gastro-intestinal disorders than at risk of skin reactions and flu-like symptoms and preferred 6-month subcutaneous injection compared with weekly oral tablets. In Belgium, patients also preferred oral monthly tablet over weekly tablets, while Irish patients preferred yearly intravenous over weekly tablets. Some differences between countries were significant. Irish patients attached higher value to being at risk for skin reactions or flu-like symptoms, and the parameter of yearly intravenous was higher (and significant) in Ireland. In addition, higher costs are more acceptable for Irish patients. These differences were generally robust in subgroups analyses including patients over 65 years, with prior fracture, high income or high education. **CONCLUSIONS:** In this study, the preferences of osteoporosis patients for drug therapy did not substantially differ between two European countries. Only for levels of some attributes significant differences were observed, which could not only be related to health and socio-demographic factors.

PMS80

LONG-TERM MAINTENANCE OF IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES WITH CERTOLIZUMAB PEGOL IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, INCLUDING ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 48-WEEK RESULTS OF THE RAPID-AXSPA STUDY

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OBJECTIVES: To report the effect of certolizumab pegol (CZP), a PEGylated Fc-free anti-TNF, on patient-reported outcomes (PROs) in axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA), over 48 weeks (wks) in the RAPID-axSpA trial. **METHODS:** The ongoing RAPID-axSpA trial (NCT01087762) is double-blind and placebo (PBO)-controlled to Wk24 and dose-blind to Wk48. Patient (pts) fulfilled ASAS criteria and had active axSpA. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks 0, 2, 4) continued on their assigned dose in dose-blind phase; PBO pts entering dose-blind phase were re-randomized to CZP loading dose followed by CZP 200mg Q2W or 400mg Q4W. We report efficacy data for the full analysis set (FAS) originally randomized to CZP. PRO endpoints included physical function (BASFI), total spinal pain, fatigue (from BASDAI), ASQoL, Sleep Problems Index II domain of MOS Sleep scale, and SF-36. Missing data were imputed by LOCF. **RESULTS:** Of 111 and 107 pts randomized to CZP 200mg Q2W and 400mg Q4W, 105(94.6%) and 98(91.6%) completed the double-blind period, and 98(88.3%) and 93(86.9%) completed the dose-blind period. Rapid improvements from baseline to Wk24 were maintained to Wk48, for both CZP 200mg Q2W and 400mg Q2W, in total spinal pain (Wk24: -3.3 and -3.2; Wk48: -3.6 and -3.5), fatigue (Wk24: -2.6 and -2.8; Wk48: -2.8 and -2.9), BASFI (Wk24: -2.4 and -2.3; Wk48: -2.6 and -2.4), ASQoL (Wk24: -5.1 and -5.1; Wk48: -6.0 and -5.6) and sleep (Wk24: -12.7 and -12.9; Wk48: -14.7 and -14.2). CZP-treated pts also maintained improvements in SF-36 components and domains. Similar outcomes were seen in AS and nr-axSpA populations. **CONCLUSIONS:** Improvements in PROs observed with both CZP dosing regimens were maintained over 48 wks, including those in pain, fatigue, physical function and HRQoL. Maintenance was observed in both AS and nr-axSpA pts.

PMS81

LONG-TERM MAINTENANCE OF IMPROVEMENTS IN MULTIPLE FACETS OF PSORIATIC ARTHRITIS WITH CERTOLIZUMAB PEGOL: 48-WEEK PATIENT-REPORTED OUTCOME RESULTS OF THE RAPID-PSA STUDY

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OBJECTIVES: To report the effect of certolizumab pegol (CZP), a PEGylated Fc-free anti-TNF, on patient-reported outcomes (PROs) in psoriatic arthritis (PsA) over 48 weeks (wks) in the RAPID-PsA trial. **METHODS:** The ongoing RAPID-PsA trial (NCT01087788) is double-blind and placebo-controlled to Wk24 and dose-blind to Wk48. Patients (pts) had active PsA and had failed ≥1 DMARD. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks 0, 2, 4) continued on their assigned dose in dose-blind phase; placebo pts entering dose-blind phase were re-randomized to CZP loading dose followed by CZP 200mg Q2W or 400mg Q4W. We report efficacy data for the randomised set (RS) of pts originally randomized to CZP. Mean changes from baseline in patient assessment of pain (VAS), fatigue assessment scale (NRS), HAQ-DI, SF-36, PsAQoL and Dermatology Life Quality Index (DLQI) were assessed with LOCF imputation. **RESULTS:** Of 138 and 135 pts randomized to CZP 200mg Q2W and 400mg Q4W, 128 (92.8%) and 120 (88.9%) completed the double-blind period, and 123 (89.1%) and 114 (84.4%) completed the dose-blind period, respectively. Rapid improvements from baseline to Wk24 observed in double-blind period were maintained to Wk48 for pain (Wk24: -28.6 and -28.4; Wk48: -31.6 and -29.5), fatigue (Wk24: -2.2 and -1.9; Wk48: -2.4 and -2.0), HAQ-DI (Wk24: -0.52 and -0.43; Wk48: -0.56 and -0.49), SF-36 physical component summary (Wk24: 8.4 and 7.6; Wk48: 8.6 and 8.4) and mental component summary (Wk24: 5.5 and 3.5; Wk48: 4.8 and 3.2), PsAQoL (Wk24: -4.4 and -3.3; Wk48: -4.8 and -3.5), and DLQI (Wk24: -6.3 and -5.2; Wk48: -6.2 and -5.6) for CZP 200mg Q2W and 400mg Q4W patients, respectively. **CONCLUSIONS:** Improvements in generic and disease-specific PROs observed over 24 wks were sustained over 48 wks in CZP-treated PsA pts. Improvements were observed regardless of CZP dose regimen.

PMS82

EXPANDING THE MEASUREMENT OF TREATMENT BENEFIT IN RHEUMATOID ARTHRITIS: THE ROLE OF THE PATIENT-REPORTED OUTCOME CONSORTIUM'S RA WORKING GROUP

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OBJECTIVES: To develop a patient-reported outcome (PRO) instrument that can be qualified by the Food and Drug Administration (FDA) for use in rheumatoid arthritis (RA) randomized controlled trials (RCTs) to support treatment benefit claims. **METHODS:** On August 28, 2012, a consensus development workshop was held by the RA Working Group (WG) within the Critical Path Institute's PRO Consortium to identify RA-related PRO concepts to determine their potential role in the documentation of treatment benefit in RA RCTs. Key stakeholders participated in this one-day meeting, including RA patients, representatives from the FDA (Division of Pulmonary, Allergy, and Rheumatology Products [DPARP] and Study Endpoints and Labeling Development [SEALD]), experts from the American College of Rheumatology (ACR), European League Against Rheumatism (EULAR), Outcome Measures in Rheumatology (OMERACT), National Institutes of Health (NIH, NIAMS) and the pharmaceutical industry (RA WG members). **RESULTS:** Over the course of the workshop, a consensus emerged that there are several outcomes important to RA patients not explicitly assessed by the ACR response criteria (i.e., fatigue, stiffness, and social participation). Finally, consensus amongst the various stakeholders was reached that any new measure needs to provide information over and above what is currently captured by the traditional primary composite endpoints and the priority would be to focus on FDA qualification of a PRO measure evaluating RA-related fatigue. **CONCLUSIONS:** The RA WG is initiating a collaboration with clinical experts through OMERACT to provide an operational definition of fatigue and to develop a conceptual framework to support its measurement in clinical trials. Following this preliminary step, qualitative and quantitative steps will be launched to develop the fatigue measure.

PMS83

SHORT RUN DYNAMICS OF INADEQUATE PAIN RELIEF (IPR): EVIDENCE FROM A EUROPEAN MULTINATIONAL SURVEY OF REAL WORLD THERAPIES (SORT)

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Osteoarthritis (OA) is the most prevalent musculoskeletal disorder and has been associated with poorer quality of life for patients who experience heightened pain and decreased functionality. Despite the importance of OA management in clinical practice settings, there has been limited evidence confirming the adequacy of pain relief in patients with knee OA who take analgesics to manage their symptoms. **OBJECTIVES:** To assess changes in pain relief states in the short run (30 days) and evaluate associated changes in outcome measures: SF-12, Brief Pain Inventory (BPI) and WOMAC in participants with knee OA. **METHODS:** The Survey of Real World Therapies (SORT), a 12-month prospective study across 6 EU countries (N=1,254), enrolled participants > 50 years old with knee OA who were prescribed analgesics. Patient-reported outcomes measures were collected at baseline and one month post baseline: BPI, SF-12 and WOMAC. Inadequate pain relief (IPR) was defined as BPI pain score of "moderate or greater pain" (>4). **RESULTS:** A total of 1153 participants were included: 67.3% women; mean age 68 years (SD=9.4); mean OA duration 5.9 years (SD=6.2). 54% of participants reported experiencing IPR. After 30 days, 28% of participants reported changes in pain relief, which was equally distributed (14% each) between the two baseline pain-relief states. Changes in IPR states were significantly associated with changes in SF-12 composite summary scores and WOMAC subscales. Patients who reported improvements in pain scores showed statistically significant improvements in average pain (2.7 points) and both QOL composite measures ($p<0.01$): WOMAC subscales improvement ranged from 8-11 points and the Physical and Mental Component Summaries scores decreased 1.83 and 1.79 points, respectively. Those who experienced worsening pain had an increase in average pain of 2.7 points on the BPI. These participants showed statistically significant decreases in QOL - WOMAC scores decreased between 4-9 points and PCS and MCS scores increased 2.10 and 2.27 points, respectively. **CONCLUSIONS:** Changes in pain states were significantly associated with overall quality of life and physical function.

PMS84

HEALTH OUTCOMES AND ECONOMIC BURDEN OF POST-KNEE REPLACEMENT SURGERY IN OSTEOARTHRITIS PATIENTS: COMPARISON WITH MATCHED CONTROLS

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OBJECTIVES: Osteoarthritis (OA), a degenerative condition of the articular cartilage, primarily affects the knee joint and surgery is often required for late-stage patients. The number of total knee arthroplasties (TKAs) is expected to grow to 3.48 million procedures by 2030 in the US alone. However, the devices lack an ideal safety profile. The objective of this study was to examine real-world outcomes among OA patients post-knee replacement. **METHODS:** Data from the 2012 U.S. National Health and

Wellness Survey, an Internet health survey administered to a representative sample of adults, were used. Respondents who reported experiencing OA, with the knee being the only joint affected, and who reported having had joint surgery in the past year were considered to have had a knee replacement. A matched control group was identified as a comparator to the knee replacement group by using a propensity score matching method (matching variables include demographics and health history). Knee replacement respondents and matched controls were compared with respect to the Short Form-36v2, activity impairment (from the Work Productivity and Activity Impairment questionnaire), and health care resource utilization using ANOVA tests. **RESULTS:** A total of 102 respondents were identified as part of the knee replacement group (52.0% male, 57.9 years). Compared with matched controls (n=102), those in the knee replacement group reported significantly worse physical health status (42.5 vs. 47.6, p<.05) though equivalent mental health status (49.7 vs. 49.0, p=.67). Levels of activity impairment (38.0% vs. 27.0% impairment, p<.05) and health care resource utilization (physician visits: 7.3 vs. 4.5, p<.05; emergency room visits: 0.6 vs. 0.2, p<.05; and hospitalizations: 0.6 vs. 0.2, p<.05) were all significantly higher among the knee replacement group relative to matched controls. **CONCLUSIONS:** These results suggest a significant burden among knee replacement respondents across both health status and economic outcomes. Improved management of these patients may have significant societal benefits.

PMS85

COMPARING HEALTH-RELATED QUALITY OF LIFE ACROSS RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: ANALYSES FROM CERTOLIZUMAB PEGOL CLINICAL TRIAL BASELINE DATA

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OBJECTIVES: Inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) are associated with significant burden on patients' (pts) health-related quality of life (HRQoL). The objective was to compare HRQoL across RA, PsA and axSpA populations. **METHODS:** Baseline data used from: RA pooled RAPID1 (NCT00152386) and RAPID2 (NCT00160602), RAPID-PsA (NCT01087788) and RAPID-axSpA (NCT01087762). Differences between SF-36 HRQoL scores and US general population age/gender-matched population norms were calculated and descriptively compared between the overall RA, PsA and axSpA populations, PsA subpopulations with skin involvement (≥3% body surface area) and without, and axSpA subpopulations of ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA). Physical function was assessed using HAQ-DI in RA and PsA, and was also compared between PsA subpopulations. **RESULTS:** Comparison of SF-36 score decrement vs population norms (mean±SD) revealed axSpA pts (N=317) experienced a higher burden on overall physical HRQoL (-19.3±7.5) compared to RA (N=1535; -17.4±7.0) and PsA (N=403; -16.6±8.0) pts, while RA pts reported a higher psychological burden (-11.3±11.2) compared to axSpA (-9.3±12.3) and PsA (-8.6±12.2) pts. Comparison of HAQ-DI scores revealed RA pts experienced greater difficulties in all physical function aspects assessed, compared to PsA pts. For axSpA pts, the burden of disease (SF-36 scores) was similar between AS and nr-axSpA subgroups. For PsA pts, comparison of HRQoL scores confirmed that skin involvement does not significantly add to the physical health burden of disease but adds to some of the psycho-social aspects (eg. social function). **CONCLUSIONS:** Trends suggested axSpA had the highest burden on overall physical HRQoL followed by RA and PsA, while the burden on overall mental HRQoL was highest in RA followed by axSpA and PsA. HRQoL burden in axSpA did not appear different between subpopulations, however the presence of skin involvement in PsA was associated with a higher burden on social function.

PMS86

LONG-TERM BENEFITS OVER MORE THAN 4 YEARS OF CERTOLIZUMAB PEGOL COMBINATION THERAPY ON WORKPLACE AND HOUSEHOLD PRODUCTIVITY, AND PARTICIPATION IN SOCIAL ACTIVITIES IN RHEUMATOID ARTHRITIS: RESULTS FROM THE OPEN-LABEL EXTENSION STUDY OF RAPID1

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OBJECTIVES: In the RAPID1 randomized controlled trial (RCT; NCT00152386), certolizumab pegol (CZP) every 2 weeks (Q2W) plus MTX provided rapid improvements in clinical measures, and workplace and household productivity over 52 weeks (wks) in patients (pts) with active rheumatoid arthritis (RA). We report the long-term effect of CZP+MTX Q2W on workplace and household productivity and social participation in RA pts from the RAPID1 open-label extension (OLE; NCT00175877). **METHODS:** RAPID1 52-wk Completers and Wk16 Withdrawers were eligible for treatment in OLE with CZP 400mg Q2W +MTX, reduced per study protocol to 200mg Q2W +MTX after ≥6 months in OLE. Workplace and household productivity were assessed through the validated RA-specific Work Productivity Survey (WPS-RA). WPS-RA responses (observed cases) are summarized for CZP RCT Completers who enrolled in OLE and completed WPS-RA at OLE completion/withdrawal visit (C/W). **RESULTS:** Of CZP Completers who enrolled in OLE (N=508), 388 remained at Wk208 (4yrs) and a subset of 290 completed WPS-RA at OLE C/W (after minimum 4.3 and maximum 6.2 years CZP treatment from RCT baseline [BL]). Of these pts at RCT BL (N=267), 49% were employed outside the home, 21% were RA work-disabled, 14% were homemakers and 13% were retired. Employed pts reported long-term reductions in absenteeism [mean BL:3.7 (N=131), C/W:0.1 (N=129)], number of days with decreased productivity (presenteeism) (mean BL:7.8, C/W:0.4) and level of RA interference with work productivity (mean BL:5.0, C/W:1.3, on 0–10 scale) per month. Similar decreases were reported in the number of household work days missed (mean BL:8.1, C/W:1.0), days with ≥50% decreased household productivity (mean BL:10.5, C/W:1.2), RA interference with household productivity (mean BL:6.2, C/W:2.0) and days missed per month of family/social/leisure activity (mean BL:5.8, C/W:0.7). **CONCLUSIONS:** In the RAPID1 OLE, CZP Q2W plus MTX maintained improvements in workplace and household productivity and increased social activity participation over >4yrs.

PMS87

CONTINUED IMPROVEMENTS IN WORKPLACE AND HOUSEHOLD PRODUCTIVITY WITH CERTOLIZUMAB PEGOL TREATMENT IN AXIAL SPONDYLOARTHRITIS, INCLUDING ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: 48-WEEK RESULTS FROM THE RAPID-AXSPA STUDY

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OBJECTIVES: Investigate certolizumab pegol (CZP) effect on workplace and household productivity up to 48 weeks (wks) in patients (pts) with axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS, meeting modified New York criteria) and non-radiographic axSpA (nr-axSpA). **METHODS:** The ongoing RAPID-axSpA trial (NCT01087762) is double-blind and placebo-controlled to Wk24 and dose-blind to Wk48. Pts had active axSpA, according to ASAS criteria, including AS and nr-axSpA. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks 0, 2, 4) continued on their assigned dose in dose-blind phase; placebo pts entering dose-blind phase were re-randomized to CZP loading dose, followed by CZP 200mg Q2W or 400mg Q4W. The validated arthritis-specific Work Productivity Survey (WPS; administered Q4W) assessed the impact of axSpA on workplace and household productivity. WPS responses (LOCF imputation) in pts originally randomized to CZP in the full analysis set (FAS) are summarized descriptively over 48 wks. **RESULTS:** A total of 325 pts were randomized, of which 218 were assigned to CZP 200mg Q2W or CZP 400mg Q4W. 69.4% and 74.9% of pts were employed at baseline (BL) in the CZP 200mg Q2W and CZP 400mg Q4W groups, respectively. By Wk48, employed CZP pts reported reduced workplace absenteeism (Wk48: mean 0.4 and 0.1 days missed/month for CZP 200 mg Q2W and 400 mg Q4W, respectively vs BL: mean 2.3 and 1.4 days/month) and presenteeism (Wk48: mean 1.0 and 1.6 days with reduced productivity/month vs BL: mean 5.8 and 4.7 days/month). Continued improvements in both CZP groups to Wk48 were also observed in household productivity and participation in social/leisure activities. Similar improvements were seen in AS and nr-axSpA populations. **CONCLUSIONS:** The initial improvements with CZP in workplace and household productivity and increased participation in social/leisure activities observed over 24 wks were continued to Wk48 in axSpA, AS and nr-axSpA pts.

PMS88

SUSTAINED IMPROVEMENTS IN PRODUCTIVITY AT PAID WORK AND WITHIN HOUSEHOLD, AND INCREASED PARTICIPATION IN DAILY ACTIVITIES OVER TIME WITH CERTOLIZUMAB PEGOL IN PATIENTS WITH PSORIATIC ARTHRITIS: 48-WEEK RESULTS FROM THE RAPID-PSA STUDY

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OBJECTIVES: To examine the effect of certolizumab pegol (CZP) on workplace and household productivity up to 48 weeks (wks), in patients (pts) with active psoriatic arthritis (PsA). **METHODS:** The ongoing RAPID-PsA trial (NCT01087788) is double-blind and placebo-controlled to Wk24 and dose-blind to Wk48. Pts had active PsA and had failed ≥1 DMARD. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks 0, 2, 4) continued on their assigned dose in dose-blind phase; placebo pts entering dose-blind phase were re-randomized to CZP loading dose, followed by CZP 200mg Q2W or CZP 400mg Q4W. This publication reports data for pts in the randomised set (RS) originally randomized to CZP. The validated arthritis-specific Work Productivity Survey (WPS), administered Q4W from baseline (BL), assessed the impact of PsA on workplace and household productivity. WPS responses (LOCF imputation) in both CZP groups are summarized descriptively over 48 wks. **RESULTS:** 409 pts were randomized, of which 273 were assigned to CZP 200mg Q2W or CZP 400mg Q4W. 87% of patients randomized to CZP completed to Wk48. 60.1% and 61.5% were employed at BL in the CZP 200mg Q2W and CZP 400mg Q4W groups, respectively. By Wk48, employed CZP pts reported reduced workplace absenteeism (Wk48: mean 0.1 and 0.6 days missed/month for CZP 200mg Q2W and 400mg Q4W, respectively vs BL: mean 2.0 and 1.6 days/month) and presenteeism (Wk48: mean 0.8 and 1.9 days with reduced productivity/month vs BL: mean 5.2 and 5.1 days/month). CZP groups also reported improvements in household productivity and increased participation in social/leisure activities up to Wk48. **CONCLUSIONS:** The initial improvements with CZP in workplace and household productivity, and participation in social/leisure activities observed over 24 wks were maintained over 48 wks in PsA pts.

PMS89

FACTORS ASSOCIATED WITH ABSENTEEISM IN RHEUMATOID ARTHRITIS PATIENTS IN EMPLOYMENT: RESULTS OF A SURVEY AMONG FRENCH PATIENTS

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OBJECTIVES: To investigate the contribution of different socio-economic and clinical factors to absenteeism in the workplace in a population of Rheumatoid Arthritis (RA) patients currently in employment. **METHODS:** A national retrospective survey was conducted in French RA patients (age <60, either employed or unemployed) recruited by rheumatologists or who were members of a patients' association (ANDAR). Patient-reported outcomes, socio-economic characteristics and various measures of productivity loss were collected using structured telephone interviews. Multivariate

regression analyses were performed to identify the contributing factors to absenteeism. **RESULTS:** A sample of 503 patients agreed to participate, of which 488 were evaluable. 364 patients (74.6%) were in employment, 31 (6.4%) were unemployed and 93 (19.1%) were out of the labor market. Among the 364 patients currently in employment, 102 (28.0%), 138 (37.9%) and 124 (34.1%) were in ACR functional class of I, II and III/IV, respectively. The mean HAQ scores were 0.6, 1.4 and 1.5 (p<0.0001), and 2.9%, 16.7% and 29.0% (p<0.0001), respectively, had an occupational disability status. An overall proportion of 48.3% patients declared an RA associated work absence over the last year. This proportion increased from 28.4% in ACR I to 62% in ACR III/IV group, and from 7.8% to 31.4% (p<0.0001), respectively, for absence >1 month. Despite a high uptake of biologic agents (60.4%) among these patients, RA was active for a significant period of time; mean 2.2 (±3.2) months in ACR I group and 4.8 (±4.2) months in ACR III/IV group. Regression analyses suggested that ACR functional class and frequencies and duration of flares were the major factors contributing to absenteeism, far ahead of any other socio-economic characteristics. **CONCLUSIONS:** Loss of productivity due to RA could be further reduced through better control of disease activity.

MUSCULAR-SKELETAL DISORDERS – Health Care Use & Policy Studies

PMS90
A REVIEW OF COST-EFFECTIVENESS EVALUATIONS AS PART OF NATIONAL HTA ASSESSMENTS OF BIOLOGIC DMARDS IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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OBJECTIVES: Rheumatoid arthritis is an autoimmune chronic disease which is associated with an increasing disability of patients and high socioeconomic burden. Given the large number of economic evaluations considered by national HTAs, this review attempts to clarify whether biologic DMARDs cost-effectiveness and cost-utility results form the basis for official recommendation by national HTA agencies. **METHODS:** Both older biologic anti-TNFα drugs (etanercept, infliximab and adalimumab) and novel bDMARDs (abatacept, tocilizumab, certolizumab, golimumab and rituximab) were considered. All main HTA agencies were searched for published economic evaluations up to 2012. Documents were selected if they included cost-effectiveness or cost-utility as outcome, if they referred to at least one of the drugs of interest, if they were published in English and if they were not superseded by other analysis. PICO statements were used to define exclusion criteria. **RESULTS:** Of the 65 documents initially identified through the search strategy, 20 documents were selected. The associated HTA agencies were PBAC (Australia), CADTH (Canada), SMC (Scotland) and NICE (England). In relation to older anti-TNFα, documents published by NICE were found to be the only explicitly recommending the drugs on the basis of obtained cost-utility results. Economic evaluations of novel bDMARDs published by SMC and NICE appeared to inform HTA decisions not to recommend abatacept and to list all other drugs conditional on price facilitation and following failure of rituximab. By contrast, cost-utility analysis published by PBAC and CADTH did not appear to influence official recommendations on novel biologic DMARDs. **CONCLUSIONS:** Cost-effectiveness and cost-utility evidence was not equally perceived by decison makers and did not have equal weight in defining the official listing of biologic DMARDs for the treatment of RA. Further research should therefore address methods for a greater integration between health economic analysis and final decisions taken by National HTA agencies.

PMS91
COST-EFFECTIVENESS ANALYSIS OF ALENDRONATE THERAPY FOR SECONDARY PREVENTION OF OSTEOPOROTIC FRACTURES

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OBJECTIVES: Although osteoporotic fractures impose a heavy financial burden on society as a whole, only 20% of patients with osteoporosis and in risk of fracture are being treated. The purpose of this study was to estimate the cost-effectiveness of alendronate therapy for secondary prevention of osteoporotic fractures in Japan. **METHODS:** A patient-level simulation model with nine health states was developed to predict lifetime costs and quality-adjusted life years (QALYs) of five years of alendronate therapy versus no preventive treatment for Japanese women with osteoporosis, who have a history of hip fracture. Fracture risk associated with age and bone mineral density (BMD) was derived from epidemiologic studies in Japan. We ran the model with different combinations of age (50, 60, and 70), BMD (T-score of −2.5 and −2.0), and BMD-independent fracture risk factors. **RESULTS:** For patients with T-score of -2.0 having no additional risk factors, the incremental cost-effectiveness ratio (ICER) of alendronate was $3,023 and $7,389 per QALY gained for those aged 60 and 70 years, respectively. In all other situations, alendronate was dominant over no preventive treatment, with lifetime cost savings ranging from $30,849 to $1,498,961. These results were fairly robust to variations in model parameters. **CONCLUSIONS:** Alendronate therapy for secondary fracture prevention in Japanese women with osteoporosis provided good value for money.

PMS92
COMPARISON OF CLINICAL CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING THEIR FIRST BIOLOGIC AND BIOLOGIC-NAÏVE PATIENTS CONSIDERED BIOLOGIC-SUITABLE IN THE UNITED STATES

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OBJECTIVES: To assess clinical characteristics of RA patients considered suitable for biologic therapy (by their physicians) in comparison to those currently treated with 1st line biologics in the US. **METHODS:** A medical chart-review study of RA patients was conducted among physicians (primarily rheumatologists) in hospitals/private practices to collect de-identified data on patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status. Physicians from the US were screened for duration of practice and patient volume and recruited from a large panel to be geographically representative. Eligible patient charts (>6 biologic patients, > 2 biologic-suitable (and yet biologic-naïve) patients per physician judgment) were randomly selected from a sample of prospective patients visiting each center/practice during the screening period. **RESULTS:** Ninety-seven physicians abstracted 726 eligible RA patient charts; 378(52%) patients were on their first biologic and 175(24%) patients have never experienced biologic but were considered suitable for one. Mean age was: 1st line-52.8yrs, biologic-suitable-51.5yrs; Female: 1st line-73%, biologic-suitable-76%. Disease severity at diagnosis and current disease severity (both per physician judgment) (mild:moderate:severe) were: 1st line – 6%:74%:14% and 67%:29%:3%, biologic-suitable – 11%,74%, 10% and 25%:66%:9% respectively. Current drug class usage differed between the two groups (1st line/biologic-suitable): non-biological-DMARD (57%/88%), steroids (19%/36%), NSAIDs-COX2-inhibitors (6%/10%), NSAIDs- non-COX2-inhibitors (14%/22%), and analgesics (11%/12%). Key lab measures were (1st line/biologic-suitable): ESR(24.2/40.0 mm/h) and CRP(2.5mg/5.6 dl). Current ACR-scores were (1st line/biologic-suitable): no response(2%/19%), ACR20(12%/36%), ACR50(18%/15%), ACR70(20%/5%), ACR90(26%/1%). Among patients with available data, current HAQ (1st line-0.7, biological-suitable-1.1), DAS28 (1st line-2.5, biological-suitable-4.1), 100mmVAS (1st line-2.3, biological-suitable-4.6), Swollen Joint Count (1st line-2.0, biological-suitable-5.9) and Tender Joint Count (1st line-2.8, biological-suitable-7.0) differed between the patient groups. **CONCLUSIONS:** Compared to the patients currently treated with 1st line biologic, RA biologic-naïve but suitable patients (per physician judgment) had relatively higher disease burden. Reasons for non-initiation of biologic treatment among 'biologic-suitable' patients warrant further investigation to alleviate disease burden.

PMS93
COMPARISON OF DISEASE STATUS, TREATMENTS AND OUTCOMES OF PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING THEIR FIRST BIOLOGIC IN THE EUROPEAN UNION AND UNITED STATES

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OBJECTIVES: To compare the disease status and outcomes of patients with PsA receiving their first biologic in UK, Germany, France, Italy and Spain (5EU) with the US. **METHODS:** A multi-country multi-center medical chart-review study of PsA patients was conducted among physicians (majority: rheumatologists) in hospitals/private practices to collect de-identified data on patients who were recently treated with a biologic as part of usual care. Physicians were screened for duration of practice and patient volume and recruited from a large panel to be geographically representative in each country. Eligible PsA patient charts (>3) were randomly selected from a sample of prospective patients visiting each center/practice during the screening period. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status/outcomes. **RESULTS:** In 4Q2012, 434 physicians (5EU:337, US:97) abstracted 790 eligible PsA patient charts (5EU:606, US:184); 674 (85%) (5EU:527, US:147) patients were on their first biologic (mean-age: 5EU:47.4yrs, US:47.6yrs; female: 5EU:48.6%, US:44.9%). Time-to-1st biologic from diagnosis (5EU:41.0months, US:27.2months) and time-on-current biologic (5EU:23.2months, US:36.7months) differed between regions. Top-2 biologic treatments observed were adalimumab (5EU:47%, US:47%) and etanercept (5EU:36%, US:32%). Among the top-4 reasons for biologic treatment initiation, 'mechanism of action', 'improve signs/symptoms', 'positive personal experience' and 'prevention of structural damage' were observed in both the 5EU and US. Key lab measures documented were: ESR (5EU:20.6mm/h, US:23.7mm/h) and CRP (5EU:9.4mg/dl, US:2.8mg/dl). Current disease severity per physician-judgment (mild:moderate:severe) was: 5EU-61%:33%:5%, US-73%:26%:1%. Among patients with available data, current HAQ (5EU:1.3, US:0.6), VAS provider score (5EU:3.1, US:2.6), VAS patient score (5EU:3.4, US:2.7) and Swollen Joint Count (5EU:2.0, US:1.7) differed across regions. **CONCLUSIONS:** Among PsA patients receiving their first biologic, disease severity and outcomes differed between 5EU and US, with patients in 5EU with relatively higher burden and poorer outcomes.

PMS94
PATTERNS OF DISEASE REMISSION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING THEIR FIRST BIOLOGIC IN EUROPEAN UNION

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OBJECTIVES: To assess the patterns of disease remission among RA patients receiving their first biologic in 5-EU countries, namely, UK, Germany(DE), France(FR), Italy(IT) & Spain(SP). **METHODS:** A multi-country multi-center medical chart-review study of RA patients was conducted among physicians (majority: rheumatologists) in hospitals/private practices to collect de-identified data on patients who were recently treated with a biologic as part of usual care. Physicians were screened for practice-duration and patient-volume and recruited from a large panel to be geographically representative in each country. Patient charts (>=5) were randomly selected within each center/practice. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status (incl. assessment of 'disease remission', per physician clinical judgment). **RESULTS:** In 4Q2011, 370 physicians abstracted 2208 eligible RA patient charts (UK:410, FR:499, DE:404, IT:415, SP:480); patient mean-age:51yrs, female:71%; 75% and 20% were on 1st line and 2nd line biologic respectively. Overall, 53% of patients were in remission (UK:54%, FR:56%, DE:61%, IT:41%, SP:53%). Remission-rates differed by biologic lines: 1st-line:53%, 2nd-line:53%, 3rd-line:46%, 4th-line:42%, 5th-line:38%. Among those with lab measures, results differed between those in remission vs. those who were not: mean ESR(mm/h): 17.0vs.32.1, mean CRP(mg/dl): 7.0vs.15.6, mean MMP3(ng/ml): 2.8-vs-4.7, Rheumatoid Factor (% positive): 83%-vs-86% and Anti-CCP (% positive): 75%-vs-79%. Among those with data, recent (mean) disease severity scores

differed between those in remission vs. those who were not: Tender Joint Count: 2.3-vs-6.1, Swollen Joint Count: 1.2-vs-4.2, 100mm VAS score: 18.6-vs-42.8, HAQ: 0.7-vs-1.6 and DAS28: 2.6-vs-4.4. **CONCLUSIONS:** More than half of the patients were not in remission in this diverse cohort of RA patients in 5-EU and they experienced disproportionate level of disease burden. As the line of treatment increased, proportion of individuals achieving remission decreased. These observed patterns warrant further scrutiny to determine the best practices and improve remission rates, thereby alleviating patient burden.

PMS95

COMPARISON OF CLINICAL CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING THEIR FIRST BIOLOGIC IN EUROPE UNION AND THE UNITED STATES

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OBJECTIVES: To assess the clinical characteristics of patients with RA receiving their first biologic in EU and the US. **METHODS:** A multi-country medical chart-review study of RA patients was conducted among physicians (majority: rheumatologists) in hospitals and private practices to collect de-identified data on patients who were recently treated with a biologic as part of usual care. Physicians from UK, Germany, France, Italy and Spain (5EU) and the US were screened for duration of practice and patient volume and recruited from a large panel to be geographically representative in each country. Eligible RA patient charts (>5) were randomly selected from a sample of prospective patients visiting each center/practice during the screening period. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status. **RESULTS:** In 4Q2012, 434 physicians (5EU:337; US:97) abstracted 2085 (5EU:1534; US:551) eligible RA patient charts; current biologic patterns (5EU/US) were: 1st line (78%/69%), 2nd line (16%/21%) & 3rd+ line (6%/11%). 1577 (5EU:1199; US: 378) patients were on their first biologic. Mean age – 5EU:50.8yrs, US:52.8yrs; female – 5EU:73%; US:73%. Mean time-to-1st biologic (5EU/US) from diagnosis was 40/28 months; mean time on current 1st biologic (5EU/US) was 24/34 months. Top-3 biologic treatments observed were – etanercept (5EU/US:37%/42%), adalimumab (5EU/US:34%/32%), and infliximab (5EU/US:8%/10%). The top-5 reasons for biologic treatment initiation were the same across 5EU/US ('mechanism of action', 'improve signs/symptoms', 'prevent structural damage', 'positive personal experience', 'inhibits disease progression'). Key lab measures documented were (5EU/US): ESR (22.7/24.2mm/h) and CRP (10.9/2.5mg/dl). Current disease severity per physician judgment (mild:moderate:severe) were: 5EU-57%:37%:6%, US-67%:29%:3%. Among patients with available data, current HAQ (5EU:1.2/US:0.7), DAS28 (5EU:3.4/US:2.5), 100mmVAS (5EU:3.5/US:2.3), Swollen Joint Count (SWC) (5EU:2.6/US:2.0) and Tender Joint Count (TJC) (5EU:3.9/US:2.8) differed within between 5EU and US. **CONCLUSIONS:** Among RA patients receiving their first biologic, disease severity differed between 5EU and US, with patients in 5EU with relatively higher burden.

PMS96

PATIENT ELIGIBILITY AND USE OF BIOLOGICS IN RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS IN THE UNITED STATES

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OBJECTIVES: To evaluate physician assessment of patient eligibility and eventual use of biologics in RA, AS, and PsA in the US. **METHODS:** A multi-country cross-sectional survey of physicians (primarily rheumatologists) was conducted in the US. Physicians were screened for biologic patient volume (>2RA biologic patients/week, >5AS biologic patients/month, >5PsA biologic patients/month) and recruited from a large physician-panel to be geographically representative. Practice characteristics, patient-volume, physician perceptions and practice patterns were assessed; physicians' target patient population was grouped into 2 categories, based on physician input: Group1 – patients perceived to be eligible for biologics, Group2 – patients who ended up receiving biologics within Group1. Summary statistics across the US are reported. **RESULTS:** In 4Q2012, 97 physicians participated in the study. Mean age: 47.6yrs; female: 30%. Main practice: private office (non-hospital):46%. Patient volume per physician was: total-1904, RA-419, AS-82, PsA-145. Average frequency of patient encounters were (RA/AS/PsA; weeks): 11/12/11. Physician judgment of patient disease severity were (average across their patients): RA – mild:28%/moderate:47%/severe:25%, AS – mild:31%/moderate:43%/severe:26% and PsA – mild:30%/moderate:44%/severe:27%. Physician assessment of patient eligibility and use of biologics were: within RA-mild-patients – Group1:21%/Group2:14%, within RA-moderate-patients – Group1:63%/Group2:51%, within RA-severe-patients – Group1:81%/Group2:70%; within AS-mild-patients – Group1:32%/Group2:24%, within AS-moderate-patients – Group1:66%/Group2:55%, within AS-severe-patients – Group1:79%/Group2:69%; within PsA-mild-patients – Group1:30%/Group2:23%, within PsA-moderate-patients – Group1:66%/Group2:55%, within PsA-severe-patients – Group1:81%/Group2:71%. Among the top-3 biologic treatments used, etanercept, adalimumab, and infliximab were observed throughout RA, AS and PsA. **CONCLUSIONS:** Across the markets, between 30-45% of biologic eligible patients (per physician perception) within moderate/severe disease severity groups did not end up receiving a biologic therapy across RA/AS/PsA cohorts. Reasons behind these patterns and the impact on subsequent patient outcomes warrant further scrutiny.

PMS97

DISEASE BURDEN AMONG PATIENTS WITH PSORIATIC ARTHRITIS WHO HAVE EXPERIENCED FIRST LINE TUMOR NECROSIS FACTOR INHIBITOR REGIMEN FAILURE IN THE EUROPEAN UNION

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OBJECTIVES: To assess treatment patterns and disease burden among PsA patients on 2nd-line biologics after 1st-line anti-TNF failure. **METHODS:** A multi-country chart-review study of PsA patients was conducted among physicians in hospitals/private practices to collect de-identified data on patients recently treated with a biologic as part of usual care. Physicians from UK/Germany/France/Italy/Spain (5EU) were screened for practice-duration and patient-volume and recruited from a large panel to be geographically representative in each country. Eligible patient charts (>2) were randomly selected from a sample of prospective patients visiting each center/practice during the screening period. Physicians abstracted patient diagnosis, treatment patterns/dynamics and patient symptomatology/disease status. **RESULTS:** Between Jan2011-Dec2012, 454 PsA patients (mean age:48.8yrs;female:49.6%) on 2nd-line biologic after 1st-line anti-TNF failure were identified. Mean time-to-1st-line anti-TNF from diagnosis was 51.6months; mean time on 1st-line anti-TNF was 18.3months (patients <6/7-12/13-24/>24months:33%/21%/19%/27%). Top-3 1st line anti-TNFs observed were: etanercept(38%), adalimumab(32%), and infliximab(27%). The top-5 reasons for 1st-line anti-TNF discontinuation were 'long-term efficacy failure', 'disease worsened', 'side-effects not tolerated', 'insufficient-improvement', and 'initial failure of efficacy'. Mean time on current 2nd-line biologic was 18.5months (patients <6/7-12/13-24/>24months:28%/21%/25%/27%). Current 2nd-line biologics (top-5) included: adalimumab(39%)/etanercept(31%)/infliximab(14%)/golimumab(11%)/abatacept(2%). Top-5 reasons for choice of 2nd-line biologic were 'mechanism of action', 'prevention of structural damage', 'improve signs/symptoms', 'disease worsened', 'positive personal experience'. Key lab measures documented were: ESR-21.7mm/h and CRP-8.3mg/dl. Among patients with available data, current HAQ was 1.1, Swollen Joint Count was 1.9 and Tender Joint Count was 3.4. Current disease severity per physician judgment (mild:moderate:severe) were: 48%:47%:5%. Current disease severity (mild:moderate:severe) by time on 1st line anti-TNF biologic (<6/7-12/13-24/>24months) were 47%:48%:5% / 55%:42%:3% / 49%:48%:4% / 44%:49%:7% respectively. **CONCLUSIONS:** Among PsA pts on their 2nd biologic who experienced anti-TNF failure, 54% discontinued their 1st line anti-TNF regimen within 12months of initiation and continue to have considerable disease burden despite current 2nd line biologic.

PMS98

ECONOMIC IMPACT ASSOCIATED WITH A BIOLOGICAL THERAPY PRIORITIZATION PROTOCOL IN RHEUMATOID ARTHRITIS PATIENTS IN THE HOSPITAL OF SAGUNTO

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OBJECTIVES: Until 2010 the cost of biological treatments in Rheumatoid Arthritis (RA) was increased annually by 15% in our hospital. In 1st January 2011, a Hospital Commission and Protocol of Biological Therapies were created to improve the cost-effectiveness usage of biological drugs in RA. To evaluate the economic impact associated with a biological therapy prioritization Protocol for RA patients in the Hospital of Sagunto. **METHODS:** Observational, ambispective study comparing the associated cost of biotreated RA patients pre-protocol (2009-2010) versus post-protocol periods (2011-2012). Inclusion criteria: RA patients treated with Abatacept (ABA) Adalimumab (ADA), Etanercept (ETN) or Infliximab (IFX) for at least 6 months during the study period (2009-2012). ETN was selected as 1st line therapy because our successful experience of ETN 25 mg/weekly in certain RA patients, its subcutaneous administration and lowest theoretical cost per patient in Spain. Cost savings and economic impact were calculated using Spanish official prices. **RESULTS:** In the pre-protocol period (2009-2010), total expenses were increased by 110,000€, up to 1,761,000€ in 2010 (11,362€ pat/year). After protocol implementation, total expenses decreased by 53,676€ on the 2010-2011 period, and 149,200€ on the 2011-2012 period. On the 2010-2011 period the cost of biological therapy per patient-year decreased 355€ (11,007€ pat/year) and additional 653€ (up to 10,354€ pat/year) by 2012, with a cumulative effect of the protocol implementation of 1,008€ per patient-year. In the pre-protocol period, the annual cost/patient was 10.812€ with ETN, 10.942€ with IFX, 12.961€ with ADA and 12.739€ with ABA. By 1st Jan 2013, the annual cost per patient was 9,469€ with ETN, 10,579€ with IFX, 11,117€ with ADA and 13,540€ with ABA. **CONCLUSIONS:** The creation of our Commission of Biological Therapies is key to rational management of RA patients and optimization of resources, allowing us to save 200,000€ after 2-year efficiency protocol implementation.

PMS99

REAL WORLD UTILIZATION OF BIOLOGICAL AGENTS IN RHEUMATOID ARTHRITIS PATIENTS: A FRENCH NATIONAL CLAIMS DATABASE ANALYSIS OVER THE PERIOD 2009-2011

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OBJECTIVES: To describe the current medical management of Rheumatoid Arthritis (RA) patients in routine practice in a national representative sample of patients, focusing on biological agents (BA) uptake. **METHODS:** The EGB database is a 1/97 representative sample of the national claims database covering the whole French population. RA patients were identified as adults (age >18) benefiting from full coverage ("ALD" eligibility criteria) for RA (ICD-10 codes M05-06) on January 1, 2009. Patients treated by BA were defined as RA patients with at least one claim for at least one BA over the period. BA-naïve treated patients were identified by the absence of a BA claim during the first 3 months of the study period, followed by at least one BA claim. **RESULTS:** Over the 3-year period, 236 patients had a BA reimbursed and 5,336 deliveries by pharmacists were observed. The proportion of BA users, either alone or in combination, was 14.0% in 2009, and 70 patients (32.7%) used a BA in combination with methotrexate. Among patients treated by BA, 85.2% used at least one TNF inhibitor during the study period. Etanercept had the highest delivery record (58.1%), followed by adalimumab (28.8%) and infliximab (15.3%). Among the whole group of patients treated by BA, 13.6% were delivered rituximab at least once. Over the period, a proportion of 73.3% of patients had one BA agent only, 19.1% experienced one switch and 7.6% had two or more switches.

At 18 months, drug survival rate of the mix of first-line biologics was 71.8% [95% CI: 60.1% - 80.6%]. **CONCLUSIONS:** Claims database is a useful tool to describe the medical management of RA patients. These observations suggest that BA clinical use in RA disease management in France is similar to other existing European registries data.

PMS100

ETANERCEPT 25 MG ONCE WEEKLY COULD BE A COST-EFFECTIVE OPTION FOR RHEUMATOLOGY PATIENTS IN SUSTAINED CLINICAL REMISSION

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OBJECTIVES: Etanercept 50mg/week (ETN50) has demonstrated efficacy in rheumatoid arthritis (RA), psoriatic arthropathy (PA) and ankylosing spondylitis (AS) patients. In certain patients in sustained clinical remission, a dose reduction to etanercept 25 mg/week (ETN25) could be done. Determine the economic impact of ETN25 in RA, PA and AS patients in sustained clinical remission. **METHODS:** Observational, retrospective cohort of patients treated with ETN50 that achieve and maintain clinical remission (DAS28<2.6 or BASDAI<2) during 1 year and slow worsening of structural changes, enrolled in an off-label program (January 2006-June 2013) to switch ETN50 to ETN25. Economical impact was assessed using Enbrel® Spanish official prices. **RESULTS:** From January 2006 to June 1, 2013, 98 RA, 40 PA, 47 AS patients were treated with ETN50; 39 (24%) patients (18 women; age 53±7 years; 24 RA, 7 PA, 8 AS) received ETN25 for at least 0.5 years (2.6±2.0 years; range 0.5-7.3 years). At June 1, 2013, 29 (74%) patients continued on ETN25. RA patients: 17 continued on ETN25, 5 patients discontinued due to reactivation of RA (4 switched to ETN50 and 1 switched to adalimumab, all regained clinical remission) and 2 patients due to adverse reactions. PA patients: 4 continued on ETN25, 2 patients discontinued due to reactivation of PA (switched to ETN50 regaining clinical remission) and 1 patient due to adverse reaction. All AS patients continued on ETN25. Total associated savings with ETN 25 throughout the 7-year observation period were 622.073€, leading to treat 52 additional patients with ETN50 for a year without increasing ETN total costs. **CONCLUSIONS:** ETN25 produces cost savings when used in patients in clinical remission for at least 1 year with ETN50. At a time when therapy cost is an unavoidable component of health care treatment decisions, ETN25 could be a cost-effective option for selected RA, PA and AS patients.

PMS101

BURDEN OF DOSE ESCALATION WITH BIOLOGICS IN RHEUMATOID ARTHRITIS: A REVIEW OF FREQUENCY AND COSTS

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OBJECTIVES: Switching or dose escalation of TNF inhibitors is an option for rheumatoid arthritis (RA) patients unresponsive or with a partial response to first-line treatment. Drug costs increase with higher dosing but the frequency and impact of dose escalation on other costs is not well known. A literature review of biologic dose escalation in RA was conducted to assess how often it occurs and the economic impact to payers. **METHODS:** A search of PubMed, EMBASE, Cochrane, and Centre of Disseminated Reviews was conducted for TNF inhibitors in inflammatory arthritis diseases. Searches were focused on dose escalation and economic terms in RA. Limits were Human, English and time frame (2003 to 2013). A weighted proportion of dose escalators in RA was calculated for each drug as an alternative to reporting ranges. **RESULTS:** Forty-one publications were identified with 36 reporting values for dose escalation in RA. The proportion of dose escalators varied widely: adalimumab 7.5 to 36%, etanercept 0 to 22%, and infliximab 0 to 80%. Various definitions of dose escalation led to the wide range. The weighted proportion of dose escalators for each drug was adalimumab 14.9%, etanercept 4.9%, and infliximab 41.7%. Six studies reported economic data comparing dose escalators to non-dose escalators. Adalimumab drug costs increased 27 to 43% with total costs increasing 28 to 34%; infliximab drugs costs increased 6 to 75%, RA-related costs increased 25 to 54%, and total costs increased 15% to 35%. Lowest costs were reported with etanercept: drug costs increased 3.2 to 19%, RA-related costs increased 4.5%, and total costs increased 2.2 to 15%. **CONCLUSIONS:** Pooled results demonstrated dose escalation in RA occurred most frequently with infliximab and least frequently with etanercept. Not only were biologic costs increased, but also RA-related and total costs. Etanercept was associated with the lowest cost increases.

PMS102

RATIONALE FOR INITIATING AND SWITCHING BIOLOGIC THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A EUROPEAN CHART REVIEW STUDY

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OBJECTIVES: This study aimed to describe the rationale for selection of initial biologic therapy and changes in biologic therapy among patients with RA in Germany, Spain, and the United Kingdom (UK). **METHODS:** This retrospective, observational medical chart review captured patient data via 118 Spanish, German, and British rheumatologists. Patients(≥18 years) had a confirmed diagnosis of RA between January 2008 and December 2010, and received a biologic therapy for ≥3 months and had ≥12 months of follow-up. Physicians recorded all RA regimens and rationale for drug selection. **RESULTS:** The 656 patients (n=328; Germany: n=111, Spain: n=106, UK: n=111) were 71.3% female, had a mean (standard deviation) age of 48.3 (12.6) years at diagnosis and mean 28-joint Disease Activity Score of 5.1±1.2 at biologic initiation. Patients most frequently initiated biologic therapy with adalimumab (41%) or etanercept (38%). The most common reason for initial biologic treatment was inadequate response from traditional disease-modifying anti-rheumatic drugs (DMARDs) alone (54.9%), followed by symptom control (13.4%). Among the remaining responses, clinical data (e.g., results from clinical trials) was cited most frequently in the UK (17.1%) compared to Germany/Spain (9.0%/4.7%), while personal experience was cited most in Germany (15.3%) vs. UK/Spain (2.7%/0.9%). Inadequate response to DMARDs was most frequently reported for adalimumab (61.5%) vs. etanercept (46.9%) or other biologics (40.2%); inadequate DMARD symptom control was more cited for etanercept (18.8%) vs. adalimumab (11.1%) or other biologics (9.8%). Among the 23 patients who switched to a second biologic agent, 72.7% were switched due to inadequate response to the first biologic agent. **CONCLUSIONS:** Across the three study countries, prescribers most frequently initiated biologic therapy due to inadequate response or lack of symptom control on traditional DMARDs. Other reasons varied by country, however differences across biologic agents prescribed were minimal.

PMS103

BURDEN OF DISEASE OF CERVICAL DYSTONIA IN THE UNITED KINGDOM

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OBJECTIVES: Cervical Dystonia (CD), the most common adult-onset dystonia, is characterised by involuntary contractions of the cervical muscles that result in abnormal, sustained, and painful postures of the head, neck and shoulders. Annual prevalence rate of CD in Europe is approximately 117 per million. To date, very few studies assessed the burden of the disease, and those published focused on costs of specific treatments. The objective of this study was to describe health care resource utilisation of patients with CD during the first year after diagnosis in the UK. **METHODS:** In this retrospective cohort study, adult patients with a first ever diagnosis of primary or secondary CD (Read code: F138200 Spasmodic torticollis) between January 2007 and December 2011 were selected from The Health Improvement Network (THIN), a large UK Primary Care database. Patients were required to have a follow-up time of at least 24 months after diagnosis. Analyses performed described demographic and clinical characteristics at diagnosis and all-cause utilization of CD-related health care resources including treatment during follow up. **RESULTS:** This study included 4,497 patients, 65.40% were female, median age at diagnosis was 41 years old and 8.05% were diagnosed with depression. During that first year, patients had on average 6 visits to the GP (SD: 5.45) and were newly referred most frequently to the orthopaedist (5.09%); less than 2% of patients had an all-cause hospitalisation and less than 1% underwent neurosurgery; 80.23% were managed with pharmacological treatment for CD, and the most commonly prescribed drugs were analgesics (69.85%) and benzodiazepines (41.23%); 14.65% received physical therapy. **CONCLUSIONS:** This study provides first-time estimates of the health care resource utilisation related to management of patients with CD in UK during the first year. To describe the complete burden of CD further research will have to investigate secondary care data and longer time horizon.

PMS104

THE COST SAVING POTENTIAL OF UTILIZING BIOSIMILAR MEDICINES IN BIOLOGIC NAIVE SEVERE RHEUMATOID ARTHRITIS PATIENTS

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OBJECTIVES: To analyze the potential cost savings associated with utilization of a quota for biosimilar RA medicines in a biologic naïve but potentially biologic eligible population (those defined as severe). **METHODS:** High patient numbers in rheumatoid arthritis (RA) and biologic therapy costs place significant pressures on health care budgets. Currently biologic therapies are underutilized in severe RA (DAS Score ≥3.7) patient populations that may be eligible for treatment. Biosimilar treatments are expected to reach the market (for the top 3 molecules adalimumab, etanercept and infliximab) by 2017 and may provide an avenue to reduce treatment costs and increase patient access to these agents. Biologic naïve RA populations were estimated for France, Germany and the UK as severe RA patients are assumed to be eligible for biologic therapy. Total cost of applying biologic treatment to a 50% quota of the estimated eligible patient population was compared to a situation of initiating patients on a biosimilar equivalent with a price point 30% lower than the originator. Reinvestment potential was calculated, defining how many more patients could be treated with yearly savings. **RESULTS:** By 2017, when all 3 biosimilars are expected to be available, the assumed 50% quota resulted in yearly savings of €98 million for the UK, €351 million for Germany and €26 million for France compared to the budget impact of using the originator. If these savings were reinvested potentially 40%, 36% and 39% of the remaining biologic naïve patients could be initiated on biosimilar treatment in the UK, Germany and France respectively. **CONCLUSIONS:** The cost savings from biosimilar adoption in naive severe RA patients presented potentially increase access by removing budgetary pressures from health care systems. Proactive payer encouragement for biosimilar utilization is necessary through the use of guidelines and prescription quotas so that health care systems can realize significant savings.

PMS105

THE RESOURCE USE RELATED TO HIP FRACTURES BASED ON DATA FROM ICUROS

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OBJECTIVES: The International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS) is an ongoing 18 months prospective observational study with the objective of estimating resource use and health related quality of life related to osteoporotic fractures. This study aims to describe the resource utilization for hip fractures (sustained during 2007-2012) pooled from 10 countries: Australia, Austria, Estonia, France, Italy, Lithuania, Mexico, Russia, Spain, and the UK. **METHODS:** Patients studied were ≥ 50 years and lived at home prior to fracture. Data were collected through patient interviews and review of medical records: at baseline and 4, 12, and 18 months after fracture. Only resource use related to the fracture event was collected. **RESULTS:** There were 1,795, 1,435, 1,256 patients available for analysis at 4, 12 and 18 months follow-up, respectively. The mean age (±SD) at fracture was 77±10 years and 79% were women. 96% of patients were hospitalized. Mean hospital length of stay (LoS) (±SD) was 17.2±20.4 days during months 0-4 and 1.2±6.8 during months 5-18. Mean LoS varied from 9.3 days to 26.5 days during months 0-4 across countries. The mean number of physician visits (±SD) was 2.8±3.1 during months 0-4 and 2.5±5.6 between months 5-18. The mean number of nurse visits (±SD) was 2.4±9.6 and 3.8±31.9 during corresponding periods, respectively. During months 0-4, 65% of patients used analgesics, 41% calcium/vitamin D, and 27% pharmacological interventions for osteoporosis. The respective uptakes for months 5-18 were 47%, 46% and 25%. **CONCLUSIONS:** Almost all patients were hospitalized after fracture and the mean number of inpatient days is high, although there is a large variation. The vast majority of health care consumption in relation to fracture occurs during the first 4 months but substantial consumption persists up to 18 months after fracture.

PMS106

METHODOLOGY OF AN OBSERVATIONAL STUDY TO EVALUATE THE CARE MAP OF WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS (PMO) IN SWITZERLAND

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OBJECTIVES: The diagnosis and management of PMO involves multiple specialists and referrals. To better understand patient management, an ongoing observational study will evaluate the care map of women with PMO treated in routine clinical practice in Switzerland, and estimate the 2-year treatment cost of parenterally administered medications (denosumab, ibandronate, zoledronate). Here, we describe the study design and methodology. **METHODS:** Of 52 specialist centers across Switzerland operating a DXA machine, 22 agreed to participate in the study. Women diagnosed with PMO and initiated on parenteral antiresorptive treatment were enrolled in the study between June 18, 2012 and May 31, 2013. To minimize selection bias, treatment initiation must have occurred within 6 months before study initiation visit at the participating center. The planned follow-up period is 24 months. Patients may be followed by the specialist or referred back to the general practitioner. Where available, the following data will be collected: demographics and patient history, co-morbidities and co-medications, DXA T-scores, osteoporosis risk factors, PMO treatment and rationale, bone turnover markers, vitamin D level, and costs related to PMO diagnosis and treatment. These parameters will be recorded at baseline and at any visit in the 24-month observation period as available from routine practice. Continuous outcomes will be summarized by descriptive statistics. For categorical outcomes, the number and percentage of patients in each category will be presented. Baseline covariates (demographic, patient characteristics and site characteristics) will be described overall and by treatment received. **RESULTS:** As of May 31, 2013 at least 280 eligible women were enrolled into the study. Full study results will be reported at a later date. **CONCLUSIONS:** The recruited number of patients confirms the feasibility of the planned methodology. Data from this study will provide valuable information regarding the care map of women with PMO in routine clinical practice in Switzerland.

PMS107

AGE AND GENDER DISTRIBUTION OF OUTPATIENT CARE PHYSIOTHERAPY SERVICES FOR DORSOPATHIA DISEASES IN HUNGARY

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OBJECTIVES: To assess the utilization of out-patient care physiotherapy services related to dorsopathia diseases of the musculoskeletal and connective tissue diseases according to age and gender. **METHODS:** The data come from the financial data base of the National Health Insurance Fund Administration (in Hungarian: OEP) involving the year of 2009. The activity list was provided by the rulebook on the application of the activity code list in out-patient care. The dorsopathia diseases of musculoskeletal and connective tissue diseases (M00-M99) are listed in the International Classification of Diseases (ICD) with code of M40–M54. The number of cases in physiotherapy activities were determined per 10,000 persons by age and gender in outpatient care. **RESULTS:** The total number of the provided 151 different types WHO-classified physiotherapy services was 32.318.413 in the year of 2009; 19.095.614 (59,09%) of them with the musculoskeletal and connective tissue diseases. The prevalence of the dorsopathia diseases were 51,17% in the group of the muskuloskeletal and connective tissue diseases. The average number of cases of physiotherapy activities per 10,000 persons accounted for 12.015 cases in 2009. The average number of cases per 10,000 persons for males and females were 15.589 cases for males and 8.061 cases for females. The number of cases increase from the 20. age groups in the men and women patients. The highest number of physiotherapy treatment is provided for both gender in the age group 50 to 59 followed by age groups of 60 to 74. **CONCLUSIONS:** The physiotherapy services occurred with the highest incidence in cases of the 'diseases of the musculoskeletal system and connective tissue' ICD group. The dorsopathia diseases at the ICD groups show the highest prevalence, indicating the importance of prevention.

PMS108

AGE AND GENDER DISTRIBUTION OF OUTPATIENT CARE PHYSIOTHERAPY SERVICES FOR HIP AND THIGH INJURIES IN HUNGARY IN 2009

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OBJECTIVES: The medical aspects of injuries of the lower extremity is well known, however, limited information is available on physiotherapy treatment of these diseases. The aim of our study is to assess amount and frequency of the physiotherapy services in hip and thigh injuries based on age and gender distribution. **METHODS:** Data were derived from the countrywide database of Hungarian Health Insurance Administration (HHIA), based on official reports of outpatient care institutes in 2009. The total numbers of different physiotherapy services were determined by selecting the reported specific diagnoses codes and counting the number treatments provided for that specific diagnosis code. The different types of treatment codes are listed in the chapter of the Guidelines of HHIA for 'Physiotherapists, massagetherapists, conductors and other physiotherapy practices'. The number of cases in physiotherapy activities related to for hip and thigh injuries (BNO S70-79) were determined per 10,000 persons by age and gender in outpatient care. **RESULTS:** The total number of the 151 different physiotherapy services was 353.260 cases at the hip and thigh injuries in the year of 2009 at the. In 2009 the average number of cases of physiotherapy activities per 10,000 persons accounted for 351.91 cases. The average number of cases per 10,000 persons for males and females were 443.7 cases for males and 249.75 cases for females. The number of cases of the hip and thigh injuries were higher in the 15-49 age group in males, and in the age group of elderly females. **CONCLUSIONS:** In case of the hip and thigh injuries, the highest demand of the outpatient care physiotherapy services occurred older injured patients. The differences in young males vary with the physical activity and the type of recreation activities, and with the condition of osteoporosis in elderly females.

PMS109

BONE EVALUATION STUDY (BEST): PREVALENCE AND TREATMENT RATES OF MALE PATIENTS WITH OSTEOPOROSIS (OP) IN GERMANY

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OBJECTIVES: With an aging population, prevalence of OP and OP-attributable fractures (OAF) is expected to rise dramatically. We evaluated prevalence and treatment rates for male OP (MOP) in Germany. **METHODS:** BEST, a retrospective analysis of de-identified claims data from a German sickness fund, included male and female OP patients, aged ≥50 years and insured ≥ 1 day between 01/2006–12/2009. Two populations were defined. Inclusion criteria for population B were: 1) OP diagnosis (M80.x, M81.x), and/or 2) prescription for OP-related medication (OPM), and 3) exclusion of diagnoses M88.x, E83.5x, and M90.7x (ICD-10). Population A included population B plus patients solely experiencing OAF. **RESULTS:** Population A included 104,938 men. In 2009, prevalence of MOP was 6%. While 67% of men experienced ≥1 OAF during observation period, with the highest rate in those aged 50-54 years (78%), only 15% received OPM. Population B included 47,694 men. In 2009 prevalence of MOP was 4.8%. 27.2% of those diagnosed experienced ≥1 OAF, with the highest rate in men aged ≥ 75 years (2006-2009). Only 41.8% of men with ≥ 1 OAF received OPM during the observation period. **CONCLUSIONS:** While prevalence of MOP is lower than that of postmenopausal OP (6% vs. 24% in 2009), high fracture rates in OP-patients represent a significant burden to the German health care system. The low treatment rates reported may lead to suboptimal outcomes, and must be optimized to reduce risk of follow-up fractures in MOP.

RESEARCH POSTER PRESENTATIONS – SESSION V
RESEARCH ON METHODS STUDIES

RESEARCH ON METHODS – Clinical Outcomes Methods

PRM1

THE BENEFIT-HARM FRONTIER OF DIFFERENT PRIMARY SCREENING STRATEGIES FOR CERVICAL CANCER IN GERMANY

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OBJECTIVES: Using a benefit-harm frontier (BHF) approach, we systematically compared benefits and harms of different HPV- and cytology-based primary cervical cancer screening strategies in Germany. **METHODS:** A previously validated and published Markov modelwas used to analyze the trade-off between benefits and harms of different screening strategies differing by length of screening interval and test algorithms, including cytology alone, HPV testing alone, in combination with cytology or with cytological triage of HPV-positives. We used published German clinical, epidemiological and international test accuracy data from meta-analyses. Predicted outcomes included reduction in cervical cancer incidence and unnecessary treatment (defined as conizations of lesions <CIN3). **RESULTS:** Overall, comparing identical screening

intervals HPV-based screening was more effective than cytology alone, with a relative reduction in cervical cancer incidence of 49%-90% compared to 33%-80% with cytology alone (depending on screening intervals). In HPV- compared to cytology screening the incremental gain in effectiveness was higher with extended screening intervals and the increase in harms lower. Based on the BHF, 12 of 17 screening strategies were dominated, including annual cytology, the current recommended standard in Germany. Biennial HPV-screening was similarly effective as annual cytology and reduced unnecessary treatment. Moving from biennial HPV- with cytological triage to annual HPV-screening alone results in an incremental harm-benefit ratio of 15-533 unnecessary treatments per additional prevented cervical cancer case (depending on screening adherence rate). **CONCLUSIONS:** The benefit-harm frontier is a useful tool to demonstrate the trade-off between expected gains and risks of different screening strategies. Based on our analyses, HPV-based cervical cancer screening is more effective than cytology alone, but has a higher risk of overtreatment when used in annual screening. In the German health care context, depending on screening adherence rates biennial or triennial HPV-screening for women ≥30 years is similarly effective as annual cytology with significantly reduced unnecessary treatments.

PRM2

EVALUATING WHETHER INCONSISTENCIES ARE PRESENT IN A MIXED TREATMENT COMPARISON OF TROUGH FORCED EXPIRATORY VOLUME IN 1 SECOND AT 12 WEEKS

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OBJECTIVES: To evaluate whether there are inconsistencies in the network of randomized controlled trials (RCTs) used for a network meta-analysis (NMA) comparing alternative long-acting bronchodilators among patients with moderate to severe chronic obstructive pulmonary disease (COPD) in terms of trough forced expiratory volume in 1 second (FEV1) at 12 weeks. **METHODS:** The change from baseline (CFB) in FEV as observed with placebo, tiotropium 18µg/5µg once daily (OD), salmeterol 50µg twice daily (BID), formoterol 12µg BID, aclidinium 400µg BID, glycopyrronium 50µg OD, indacaterol 75/150/300µg OD, formoterol 12µg+ tiotroipum 18µg BID/OD, indacaterol 150µg+ tiotropium 18µg OD, and indacaterol 110µg+ glycopyrronium 50µg OD in RCTs identified with a systematic literature review were synthesized with a NMA. Where possible, treatment estimates from fixed effect (FE) and random effects (RE) NMA models (assuming consistency between direct and indirect evidence) and independent means (IM) models (pooled direct evidence) were compared to assess whether any inconsistencies in the network were present. **RESULTS:** Thirty-two RCTs identified through a systematic literature review were included in the analysis. Direct evidence was available for the monotherapies versus placebo, the combination therapies versus tiotropium, for indacaterol+ glycopyrronium versus placebo, and for tiotropium versus salmeterol. The largest differences between the estimated treatment effect estimates from the NMA and the IM models were observed for the comparisons between indacaterol 150µg versus tiotropium (FE difference=0.025 [95% Credible Intervals (95%CrI): 0.002, 0.047]; RE difference=0.027 [95%CrI: -0.007, 0.61]), indacaterol+ glycopyrronium versus placebo (FE difference=-0.022 [95%CrI: -0.053, 0.008]; RE difference=-0.018 [95%CrI: -0.059, 0.022]), and indacaterol+ glycopyrronium versus tiotropium (FE difference=0.011 [95%CrI: -0.014, 0.036]; RE difference=0.015 [95%CrI: -0.024, 0.053]). **CONCLUSIONS:** Based on a comparison of the findings of a NMA and IM models, some minor inconsistencies in treatment effects for trough FEV1 at 12 weeks were identified that will be explored through additional sensitivity analyses.

PRM3

TESTING THE EUNETHTA INTERNAL VALIDITY OF RANDOMIZED CONTROLLED TRIALS GUIDELINE AND TOOL IN HUNGARY

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OBJECTIVES: The reliability of the results of a randomized trial depends on the extent to which potential sources of bias have been avoided. We tested the EUnetHTA Internal Validity guideline so that to harmonize our risk of bias assessments with the European standard and finally to improve the reliability of relative efficacy and cost effectiveness assessments for decision makers in Hungary. **METHODS:** We translated the risk of bias standardized assessment questions of the EUnetHTA Internal Validity (of randomized controlled trials) into Hungarian. We first chose ten studies for internal validity testing from the ones that were submitted for reimbursement at the beginning of 2012, and their results were used for health economy assessment. **RESULTS:** We found adequate randomization sequence generation in seven studies and we marked it unclear in three trials (e.g.: lack of information, age related sequence generation). The allocation concealment was labeled suitable in six studies (e.g.: IVRS, IWRS) and unclear in four trials. All studies could be classified according the the type of blinding. We found selective reporting in one trial where the non-inferiority results in the per-protocol population were not published. We rated the risk of bias low for eight trials and high for two trials due to unclear sequence generation and publication bias. We also evaluated 77 endpoints and we labelled 22 endpoints with high risk of bias. The most common reasons for high risk ratings were the not appropriately implemented ITT principle and selective reporting. **CONCLUSIONS:** The EUnetHTA guideline gives an opportunity to estimate the risk of bias of randomized controlled trials in a structured and harmonized way without leaving out any important considerations. The results of the internal validity evaluation can lead the focus of interest to those endpoints where the sensitivity analysis is requisite in the health economic models.

PRM4

CLINICAL OUTCOMES ASSESSMENTS IN SCHIZOPHRENIA: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: There is a growing interest from health technology assessment agencies in determining the clinical outcomes assessments and endpoint strategies that can establish treatment benefits. We describe a systematic literature review of endpoints and outcomes used in schizophrenia trials to determine treatment benefit. **METHODS:** The therapies selected in the search strategy included pharmacological interventions, cognitive-behavioural therapies, family intervention, and music therapy. These were chosen to reflect the range of interventions in current use, and to allow comparison between outcomes reported for different therapies. The search terms were designed to include all outcomes for each therapy area, and were used to search four electronic databases for published English language studies. Randomised controlled trials (RCTs) were retrieved if they included patients with schizophrenia treated with the chosen therapies, and clinical outcomes from a predefined list (e.g. symptom improvement, functionality, quality of life, remission rates, response rates, and recovery). **RESULTS:** Of 2,221 RCTs identified, 271 progressed to data extraction; 225 assessed pharmacological interventions and 46 non-pharmacological interventions. Approximately 76 outcomes were measured across the trials. The most common scale used in pharmacological trials was the Positive and Negative Syndrome Scale (PANSS) total score (76.9%), and the PANSS positive subscale in non-pharmacological trials (50%). However, even within the common outcomes, the specified level of reduction to define a relevant response varied; among trials reporting PANSS total, five different levels of reduction were defined (≥20%, ≥25%, ≥30%, ≥40%, ≥50%). Common outcomes were also measured differently in terms of improvement from baseline and proportion achieving response/remission, with little consensus on clinical meaningfulness. **CONCLUSIONS:** The RCTs included in this review reported a broad range of outcomes, making comparison of different therapies a complex task. The disparity in outcomes between pharmacological and non-pharmacological outcomes scales highlights the challenges in designing trials to demonstrate clinical benefit.

PRM5

MULTI-DIMENSIONAL CAPTURE OF PATIENT-RELEVANT ENDPOINTS IN REGULATORY TRIALS AND HEALTH TECHNOLOGY ASSESSMENTS IN ONCOLOGY TWO YEARS AFTER INTRODUCTION OF THE GERMAN AMNOG HEALTH CARE REFORM

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OBJECTIVES: With the introduction of AMNOG in January 2011, an early benefit assessment (EBA) was required for new medicines in Germany. EBAs are based on the additional therapeutic benefit of a drug on patient-relevant endpoints (PREs). We compared the acceptance of PREs for oncology in regulatory trials, and in EBAs conducted by German health technology assessment (HTA) bodies. **METHODS:** EBAs on oncology drugs and the respective regulatory trials were reviewed. The Federal Joint Committee (G-BA) website was used to obtain manufacturers' value dossiers, Institute for Quality and Efficiency in Health Care (IQWiG) assessments, and G-BA resolutions. Acceptance of endpoints in the dimensions of mortality, morbidity and quality of life (QoL) by HTA bodies, IQWiG and G-BA, were compared to those accepted for regulatory trials. Data on endpoints used in regulatory trials were obtained from the manufacturers' value dossiers. **RESULTS:** Overall survival (OS) and measures of disease morbidity, such as progression-free survival (PFS), were generally accepted in regulatory trials. OS was accepted by IQWiG and G-BA as a mortality endpoint for evaluating additional benefit. Widely accepted morbidity endpoints such as PFS were not deemed patient-relevant by IQWiG and G-BA. In general, QoL questionnaires used in regulatory trials were accepted by the HTA bodies, although minor variability between questionnaires led to some exclusions from the HTA evaluations and the obtained QoL data revealed a number of missing values. **CONCLUSIONS:** HTA and regulatory bodies largely agree on the acceptance of mortality and QoL endpoints typically evaluated in oncology. Considerable variability was observed in the acceptance of PREs in morbidity. Evaluating additional benefit based only on mortality and QoL endpoints underestimate the potential value of new drugs. Multiple endpoints, which capture all three dimensions, should be evaluated in regulatory trials and accepted by IQWiG and G-BA to confirm patient-relevant additional benefit.

PRM6

THRESHOLD SELECTION IN BIOMARKERS USING COX REGRESSION. AN APPLICATION TO NON-SMALL-CELL LUNG CANCER

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OBJECTIVES: To select thresholds for predictive biomarkers using Cox regression. **METHODS:** We used data from a Cuban trial designed to assess the efficacy of immunotherapy against the epidermal growth factor (EGF) to test our approach. The trial included 122 patients diagnosed with non-small-cell lung cancer (NSCLC) who had basal EGF concentration available. The EGF concentration was analysed as a predictor of immunotherapy success over the range of all possible values of the biomarker (w [a,b]). For each w_i, patients with $w > w_{i0}$ were selected and a Cox model adjusted to assess survival. We then identified the w_{0s} with significant treatment results to find (a) the lowest biomarker threshold where the effect of treatment was significant and also to find (b) the biomarker threshold that reflected the highest difference between treatments. **RESULTS:** For NSCLC we observed that EGF concentration thresholds range from 870 pg/ml to 2000 pg/ml were significant. At the lowest threshold (870 pg/ml) the immunotherapy group showed a 6-month difference for the median survival ($p = 0.022$) whereas at the threshold that showed the maximum difference between treatments (EGF = 1750 pg/ml) the immunotherapy group presented a 10-month difference for the median survival ($p = 0.004$). **CONCLUSIONS:** The evaluation of p-values of the effect of treatment for each w_0 [a,b] allows the selection of the thresholds where the treatment result is significant. Whereas the

lowest threshold where the effect of treatment is significant allows the selection of patients that could be mostly benefited with the treatment, the selection of the threshold with the minimum p-value will reflect the higher difference between treatments.

PRM7

SYSTEMATIC LITERATURE REVIEW AND VALIDITY EVALUATION OF THE EXPANDED DISABILITY STATUS SCALE (EDSS) AND THE MULTIPLE SCLEROSIS FUNCTIONAL COMPOSITE (MSFC) IN PATIENTS WITH MULTIPLE SCLEROSIS

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OBJECTIVES: There are a number of instruments to describe severity and progression of multiple sclerosis, which are increasingly used as endpoints to assess the effectiveness of therapeutic interventions. We examined to what extent the psychometric properties of the two accepted instruments - EDSS and MSFC – meet the methodological standards and what value they have in clinical trials. **METHODS:** We conducted a systematic literature search in relevant databases [MEDLINE (PubMed), ISI Web of Science, EMBASE, PsycINFO & PSYNDEX, CINAHL] yielding 3,860 results. The identification of relevant full-text publications was conducted using abstract and then full-text reviews. **RESULTS:** For evaluation of psychometric properties (validity, reliability, sensitivity of change) of EDSS and MSFC, 120 relevant full-text publications were identified, 54 of them assessed the EDSS, 26 the MSFC and 40 included both instruments. The EDSS has some documented weaknesses in reliability and sensitivity to change. For the MSFC, the main limitations are the learning effects and the z-scores method used to calculate the total score. However, the methodological criterion of validity applies sufficiently for both instruments. For use in clinical studies, we found that the EDSS has been preferred as a primary and secondary outcome measure in recent studies (50 EDSS, 9 MSFC). **CONCLUSIONS:** Recognizing their strengths and weaknesses, both EDSS and MSFC are suitable to detect the effectiveness of clinical interventions and to monitor the disease progress. Almost all publications identify the EDSS as the most widely used tool to measure disease outcomes in clinical trials. Despite some limitations, both instruments are accepted to generate "hard endpoints". In no publication, EDSS or MSFC are discussed as surrogate parameters. A great advantage of the EDSS is the international acceptance (e.g. by EMA) as a primary endpoint in clinical trials and its broad use in trials, enabling cross-study comparisons.

PRM8

IMPACT OF MEDICATION ADHERENCE ON HEALTH CARE COST IN ASTHMA

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OBJECTIVES: To evaluate the impact of medication adherence on health care utilization and costs of the patients with asthma in Hungary. **METHODS:** The authors conducted a retrospective observation of the patients continuously enrolled in medical and prescription benefit plans from July 2007 to June 2012. The study is based on patient attendance data of Hungarian National Health Insurance Fund -NHIFA. The accessible resource uniquely contains the detailed provision data (medicine, out- and inpatient services) about the whole 10 millions Hungarian populations. Inclusion criterion for the patients was at least one diagnosis of asthma in inpatient or outpatient care (ICD code J45) and at least one relevant asthma therapy prescription in a twelve months period, and at least one relevant asthma therapy prescription during the following twelve months period. Disease-related and all-cause related medical costs, drug costs, and hospitalization risk were measured. These measures were modeled at varying levels of medication adherence using regression analysis. Adherence (Sokol, 2005) was defined as the percentage of days during the analysis period that patients had a supply of 1 or more maintenance medications for the condition. The days of supply are calculated based on WHO DDD's. This measurement strategy reduces the risk of overestimating adherence. For prescriptions extending beyond the end of the analysis period, days' supply is truncated at the end of the period. Patients in each study sample are stratified into 5 categories based on their adherence score: 1–19%, 20–39%, 40–59%, 60–79%, or 80–100 %. **RESULTS:** High level of medication adherence was associated with lower hospitalization and exacerbation rates. **CONCLUSIONS:** Increased drug utilization can provide a net economic return when it is driven by improved adherence.

PRM9

IMPACT OF MEDICATION ADHERENCE ON HEALTH CARE COST IN COPD

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OBJECTIVES: To evaluate the impact of medication adherence on health care utilization and costs of the patients with COPD in Hungary. **METHODS:** The authors conducted a retrospective observation of the patients continuously enrolled in medical and prescription benefit plans from July 2007 to June 2012. The study is based on patient attendance data of Hungarian National Health Insurance Fund - NHIFA. The accessible resource uniquely contains the detailed provision data (medicine, out- and inpatient services) about the whole 10 millions Hungarian populations. Inclusion criterion for the patients was at least one diagnosis of COPD in inpatient or outpatient care (ICD code J44) and at least one relevant COPD therapy prescription in a twelve months period, and at least one relevant COPD therapy prescription during the following twelve months period. Disease-related and all-cause related medical costs, drug costs, and hospitalization risk were measured. These measures were modeled at varying levels of medication adherence using regression analysis. Adherence (Sokol, 2005) was defined as the percentage of days during the analysis period that patients had a supply of 1 or more maintenance medications for the condition. The days of supply are calculated based on WHO DDD's. This measurement strategy reduces the risk of overestimating adherence. For prescriptions extending beyond the end of the analysis period, days' supply is truncated at the end of the period. Patients in each study sample are stratified into 5 categories based on their adherence score: 1–19%, 20–39%, 40–59%, 60–79%, or 80–100 %. **RESULTS:** High level of medication adherence was associated with lower hospitalization and exacerbation rates. **CONCLUSIONS:** Increased drug utilization can provide a net economic return when it is driven by improved adherence.

PRM10

USING SATURN PLOTS TO DESCRIBE CO-MORBIDITY PATTERNS WITHIN COHORTS

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OBJECTIVES: It is a common practice in outcomes research studies to examine several co-morbidities over two or more cohorts to develop some intuition about the health status of each group. It is also a common practice in claims data to record the co-morbid condition as a binary variable (i.e., absence or presence of the co-morbidity). If an investigator is interested in studying the absence or presence of 10 co-morbidities, he or she will have to consider 2^{10}= 1024 possible co-morbidity patterns, a seemingly daunting task. The common current practice is to construct summary tables and examine them to understand cohort co-morbidity patterns. Even with this summarization, it is difficult to deduce what the composition is for the cohort over all co-morbidities simultaneously. Once again, this can be a daunting task. The objective of this research is to develop a means of summarizing these rich and somewhat complex data to enhance clinical decision making. **METHODS:** Graphical approaches for the summarization of data enable geometry, scaling, shading, and or color to describe such "high dimensional" data. The author will introduce a novel means of plotting the co-morbid conditions that will afford investigators the ability to study patterns of co-morbidities simultaneously and understand the relative frequencies of their occurrence in one display. **RESULTS:** The use of a novel graphical procedure (a Saturn plot) allows an investigator to examine co-morbidity patterns readily when the number of binary co-morbidities is 10 without having to resort to poring over several tables or one large table partitioned into smaller ones based on co-morbidities. **CONCLUSIONS:** A newly developed graphical data summary called a Saturn plot allows investigators to indentify the relative frequency of various subgroups (as defined by their co-morbidity pattern) within a cohort without the need to study large sets of tables.

PRM11

DESIGN OF A RANDOMIZED CONTROLLED TRIAL (RCT) EVALUATING OUTCOME AND COST-EFFECTIVENESS OF A LOCAL CASE MANAGEMENT INTERVENTION OF PATIENTS SUFFERING FROM CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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OBJECTIVES: In December 2011 the Danish Government issued a new plan of action for chronic disease management in the Danish counties and DKK 100 million were granted to set up new positions as case managers to help vulnerable elderly patients. No precise job description was provided, however, and the Danish counties request evidence for the effect of case management (CM). The aim of this study was to 1) design a job description for a case manager, and 2) design a RCT evaluating consequences and costs of providing local CM to patients with COPD. **METHODS:** By use of the UK Medical Research Councils (MRC) framework for development of complex interventions, the design of the case manager job description and the RCT was determined through a systematic literature review, interviews with key persons and discussions in a specialist-comprised steering group. **RESULTS:** CM was designed to encompass coordination of care, facilitation of relevant health- and social services and promotion of patient self-care through advocacy and education. The RCT was powered to detect the effect of CM on hospital admissions. Secondary measures include mortality, quality of life, self-care and cost-effectiveness of CM versus usual care. 150 COPD patients are randomized into two groups after referral to pulmonary rehabilitation at the local rehabilitation center in Aalborg County, Denmark. The control group will receive usual care, whereas the interventional group will receive CM besides their usual care. Each patient is followed for 12 months. The questionnaires SF-12, EQ-5D, Sct. George-Respiratory-Questionnaire (SG-RQ) and The Patient-Activation-Measure (PAM-13) are completed at baseline and 12 months. Prospectively collected data from national population-based medical registries are used to estimate events and resource usage. **CONCLUSIONS:** The study is expected to provide further insight to the future organization of CM, and if being cost-effective, the intervention could be applied to comparable health care settings.

PRM12

REVIEW OF META-ANALYSIS METHODS FOR MULTINOMIAL DATA

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OBJECTIVES: Indirect comparisons are often based on binary outcomes (e.g. relapse / remission) or continuous outcomes. In these cases logistic or linear models are applied to make the indirect comparisons. However, sometimes datasets contain multinomial outcomes, such as 'complete', 'partial' and 'no' response in oncology, that need to be indirectly compared. With multinomial data, different indirect comparisons methods may be required to answer different research questions. Our goal was to identify and qualitatively compare the different techniques that have been used to model multinomial data in an indirect comparison framework. **METHODS:** A systematic review of the PubMed database was conducted to identify different methods for handling multinomial data in a meta-analysis. Key words included 'meta-analysis', 'ordinal', 'ordered', 'multinomial' and 'proportional odds', in various combinations. Models were qualitatively compared according to their assumptions, flexibility and complexity. **RESULTS:** The systematic review identified three methods: a proportional odds model, an ordered logistic model, and a multinomial model. The proportional

odds model has a natural interpretation of the treatment effect, is flexible in terms of handling data with different numbers of categories, but relies on the proportional odds assumption. The ordered logistic model also has a natural interpretation of the treatment effect, but increases in complexity when handling data with a large number of categories. The multinomial model's interpretation for the treatment effect is difficult, but it can model a large number of categories and can handle unordered competing risks and time dependent data. **CONCLUSIONS:** There are three methods for incorporating multinomial data in a meta-analysis framework with various advantages and disadvantages. Selection of the appropriate model appears to be most dependent on the characteristics of the dataset. We determine that there is sufficient cause for future research focusing on a quantitative comparison of these different methods.

PRM13

EASING DECISION-MAKING BY EXPANDING METHODS OF MULTIPLE TREATMENT COMPARISON META-ANALYSIS – INCORPORATING NON-COMPARATIVE STUDIES VIA INFORMATIVE PRIORS

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OBJECTIVES: While multiple treatment comparisons (MTC) generally provide strong evidence, many are accompanied with uncertainty that makes life challenging for decison makers. Seeking reduction in uncertainty from non-comparative trial can ease decision-making, but the validity of this approach must be tested. Using an example of treatments for cryptococcal meningitis (CM), our objective was to assess the value and validity of incorporating non-comparative trial evidence via prior distributions in the Bayesian MTC framework. **METHODS:** We conducted a Bayesian MTC meta-analysis with and without informative priors and reported odds ratios (OR) with 95% credible intervals (CrI). Non-comparative data were incorporated in a two-stage approach. First meta-analysis for proportions was used to pool all relevant non-comparative outcomes for each treatment. Second, these results were used to construct informative priors for the comparative treatment effect parameters (the log odds ratios) in the Bayesian MTC. Treatments considered were amphotericin (AmB)-based therapy coupled with either flucytosine (5FC) or fluconazole (Azole). **RESULTS:** Twenty-seven studies (N=1,938), 15 head-to-head drug comparison trials and 12 studies evaluating a single drug, described early mortality. Twenty-nine studies, 17 head-to-head and 12 single-arm studies, described late mortality. Incorporating non-comparative trials via informative priors improved the precision of several comparisons. For early mortality for example, the OR for AmB+Azole vs AmB+5FC was 0.26 (95%CrI 0.04-1.26) with a conventional MTC, and 0.24 (0.04-0.98) with informative priors. Use of informative priors reduced the DIC by 38% and the heterogeneity by 28%, indicating a better model fit. Moreover, evidence from the non-comparative studies was coherent with the randomized evidence, adding to the validity of the approach. **CONCLUSIONS:** Incorporating non-comparative studies as informative priors in Bayesian MTCs appears a viable approach for reducing the uncertainty in MTCs, and thus easing decision making.

PRM14

DEVELOPMENT OF THE SCHIZOPHRENIA CAREGIVER QUESTIONNAIRE: MODIFICATION OF THE ZARIT BURDEN INTERVIEW INFORMED BY QUALITATIVE INSIGHTS

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OBJECTIVES: Understanding the impact of caring for a person with schizophrenia on caregivers' lives and emotional and physical well-being is of increasing interest for health care decison makers. The Zarit Burden Interview (ZBI) is an established measure of caregiver impact for Alzheimer's disease. Face and content validity of the ZBI have not yet been established in schizophrenia and were explored in this study based on qualitative insights from caregivers of people with schizophrenia. **METHODS:** A targeted literature review and consideration of best practice guidelines for development of self-report questionnaires informed initial ZBI modifications. Face and content validity of the newly labelled Schizophrenia Caregiver Questionnaire (SCQ) were assessed via comprehensive semi-structured interviews with a diverse range of 19 US caregivers of people with schizophrenia. Interviews were initially open-ended and explored caregivers' experience of caring for a person with schizophrenia (concept elicitation). Cognitive debriefing of the draft SCQ then assessed relevance and understanding. **RESULTS:** Initial review of the ZBI informed changes to item wording, recall period, and response scales to improve face validity. The qualitative literature review and concept elicitation interviews informed ten additional items assessing concepts important to caregivers, not included in the ZBI: tiredness, stress, disturbed sleep, sadness, medication administration issues, worries about future episodes, worsening symptoms, frustration, emotional highs and lows, and impact on work. Following cognitive debriefing interviews, five items were modified to improve relevance and understanding; otherwise, caregiver feedback supported the content validity and comprehensiveness of the resulting SCQ. **CONCLUSIONS:** SCQ demonstrated good face and content validity for the assessment of caregiver impact in schizophrenia and is a promising tool for communication of caregiver outcomes to health care decision makers. Tiredness, disturbed sleep and sadness are included in depression scales hence there may be overlap if depression is assessed). Further work determining final SCQ content/scoring and psychometric properties is ongoing.

PRM15

USING AN EXCEL CALCULATOR TO ESTIMATE ANKYLOSING SPONDYLITIS COSTS IN TURKEY

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OBJECTIVES: To build an Excel calculator, including demographic and clinical characteristics of Ankylosing Spondylitis (AS) patients, and estimate annual health care costs of AS patients in Turkey. **METHODS:** The study data was obtained from the Turkish national health insurance database, MEDULA (2009-2011). Adult AS patients (ages 18-99) were identified for the identification period (June 1, 2010 - December 31, 2010) through the use of International Classification of Disease Tenth Revision Clinical Modification (ICD-10-CM) codes. Patients were required to have two AS diagnoses at least 60 days apart, with at least 1 year of continuous health plan enrollment for the baseline and follow-up years. Patients were grouped as prevalent and incident cases, and generalized linear models (GLMs) were used to estimate risk-adjusted total annual costs for prevalent and incident cases. The expected annual cost value was based on patient demographic and clinical characteristics. Coefficients of patients' demographic and clinical characteristics were built in the Excel calculator. Using the calculation, a marginal effects table was created after GLM estimation. **RESULTS:** A total of 2986 patients met all inclusion criteria (603 incident; 2383 prevalent patients). Demographic and clinical characteristics of the patients were entered into the Excel calculator. Risk-adjusted annual total costs were calculated as €3307 for prevalent cases and €2000 for incident cases. Prior biologic use significantly contributed to total medical costs for both prevalent and incident AS patients ($p<0.001$). For incidence cases, the cost of care was lower for the 18-39 age group when controlling for other factors. For prevalent cases, there were no differences in health care costs in terms of region, gender, age, comorbidities, or prior non-steroidal anti-inflammatory drug (NSAID) or disease-modifying anti-rheumatic drug (DMARD) use. **CONCLUSIONS:** An Excel calculator is an important tool to estimate and compare AS-related health care costs in outcomes research.

PRM16

DERIVATION OF SEVERITY INDEX FOR RHEUMATOID ARTHRITIS

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OBJECTIVES: To derive a claims-based severity index for rheumatoid arthritis (SIFRA) and examine its impact on prevalent rheumatoid arthritis (RA) patients in Turkey. **METHODS:** Using the Turkish national health insurance database MEDULA (01JUN2009-31DEC2011), prevalent RA patients were identified. Patients were required to be age 18-99, have two RA diagnoses $\geq$60 days apart and be continuously enrolled 1 year pre- (baseline period) and post-index date (follow-up), which was the first RA claim during the identification period (01JUN2010-31DEC2010). The SIFRA score was derived for each patient. RA-related indicators were sub-grouped as clinical and functional status, extra-articular manifestations, surgical history and medications. The strength of each relationship was measured from 0=no relationship to 6=perfect relationship, and assessed by six board-certified, clinically active rheumatologists according to the Delphi panel method. The index was previously validated and applied to the U.S. Department of Veteran Affairs, Veterans Health Administration (VHA) data. **RESULTS:** For the total of 1,920 identified RA patients, SIFRA scores ranged between 0 and 69.40, with a mean value of 14.21, and a standard deviation (SD) of 10.26. Mean SIFRA scores were 7.05 (49.57%), which consisted of clinical and functional status variables, followed by 6.32 (44.47%) for medications, 0.48 (3.40%) for radiology and laboratory findings, 0.32 (2.25%) for extra-articular manifestations (pulmonary nodules, subcutaneous nodules, vasculitis ever, Felty's syndrome ever), and 0.04 (0.31%) for surgical history (cervical spine fusion, hand/foot joint replacement, foot joint/ankle/wrist fusion, total hip/knee/elbow/shoulder replacement). **CONCLUSIONS:** SIFRA demonstrated evidence of being a significant determinant for health care costs and biologic therapy use. This study suggests that SIFRA could be an important methodological tool to control for severity in RA-related outcomes research. Any comparative effectiveness studies in RA treatment should include severity scores in the analysis.

PRM17

PHYSICIAN PANELS SUPPORTING CLINICAL TRIALS AND POST-APPROVAL STUDIES IN ONCOLOGY: A WILLINGNESS-TO-PARTICIPATE STUDY

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OBJECTIVES: Clinical oncology research projects require participation of oncologists and/or hematologists to recruit patients and/or assess clinical outcomes. A variety of methods is used to recruit office or hospital based physicans. Specifically for studies with an epidemiological aspect, the study should not rely on the typical clinical expert sites, thus, alternative recruitment pathways are increasingly considered. The objective of our study was thus to assess the benefits of using physician panels for site recruitment. **METHODS:** In 2012, a representative survey among members of a managed physician panel (All Global's managed panel of oncologists and hematologists in US, UK, GER, FR, IT and SP) was conducted. A Sample of oncologists and hematologists was selected. The panel was stratified by country and within the strata physicians were randomly selected. 335 out of 1.303 oncologists and hematologists in the sample (25,7%) reported about their former experience with clinical trials and post-approval studies, their willingness to participate in future studies and their adherence to aspects of GCP rules. **RESULTS:** A total of 284 (84,7%) of the physicians have formerly participated in clinical trials and 276 (67,2%) in post-approval studies. A total of 88,9% of the experienced oncologists and hematologists were willing to participate in future studies. More than 80% of this group was ready to be named as principal investigator to an ethical committee, to report serious adverse events to the sponsor of the study and to ask patients for written informed consent. No substantial difference between countries was detected. **CONCLUSIONS:** Since no special incentive was offered for participation the response rate was satisfactory Managed oncologist panels are a cost-effective,

experienced and high-quality source for post-approval studies. Elaborated management processes in multi-country panels guarantee a constant quality of the panel over geographies.

PRM18

CLASSIFICATION OF COGNITIVE DYSFUNCTION AND COGNITIVE NORMAL USING SCORES FROM FOUR COGNITIVE ASSESSMENTS IN PATIENTS WITH DEPRESSIVE DISORDER

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OBJECTIVES: Cognitive functioning is a multidimensional attribute comprising various domains including attention, memory, executive function, and psychomotor speed. The number of impacted domains and magnitude of deficits that equate to a classification of cognitive dysfunction (CD) are unclear. This analysis examined criteria used for CD classification in an observational study of depressed patients. **METHODS:** A large US health plan was used to identify depressed patients with a newly prescribed antidepressant. Consenting, eligible patients were interviewed by telephone and completed a structured assessment of cognitive function measuring 4 domains: verbal episodic memory (Hopkins Verbal Learning Test-Revised), attention (Digit Span Forward), working memory (Digit Span Backward), and executive function (D-KEFS-Letter Fluency Test). Patients were classified into 2 groups based on test scores relative to normative data. "CD" was defined as patients with ≥2 scores that were ≥1.5 standard deviations (SD) below the normative mean (criterion 1) or patients with ≥3 scores that were ≥1.0 SD below the normative mean (criterion 2). Patients not meeting either of these were classified as "cognitive normal (CN)." T-tests compared differences between the groups across cognitive domains. **RESULTS:** Of 564 eligible patients who completed the study, 45% met criteria for CD. Among these, 63% met both criteria for classification of CD, 19% met only criterion 1, and 18% met only criterion 2. The percentage of patients with scores ≥1.0 SD below the mean and ≥1.5 SD below the mean were significantly higher in the CD group compared to the CN for all 4 tests. Mean scores on all domains were significantly lower ($P < 0.001$) in the CD group compared to the CN group. **CONCLUSIONS:** Among patients with depression, those with cognitive dysfunction had significantly worse functioning across all domains. This suggests that the criteria appropriately identified a subset of patients with impaired cognitive functioning.

RESEARCH ON METHODS – Cost Methods

PRM19

TIME DEPENDENT RESOURCE USE AND COSTS ASSOCIATED WITH DIFFERENT STATES OF DISEASE IN PATIENTS DIAGNOSED WITH HER-2 POSITIVE METASTATIC BREAST CANCER

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OBJECTIVES: Adequate reflection of disease progression and costs over time is essential in cost-effectiveness analyses (CEAs) based on health state transition models. However costing studies normally investigate the burden of metastatic breast cancer (MBC) without explicitly examining impact of specific disease states on health care costs over time. The objective of this study was to assess time-dependent costs of different health states of human epidermal receptor 2 (HER-2) positive MBC and the factors contributing to these costs. **METHODS:** In The Netherlands, HER-2 positive MBC patients were identified in three different hospitals. Resource use was collected during 24 months, which was linked to unit costs and related to time with respect to date of MBC diagnosis, disease progression and death for each individual patient. Subsequently, monthly costs for different health states were calculated. Finally, a nonlinear mixed effect modelling approach was used to provide a quantitative description of the time course of cumulative progression costs. **RESULTS:** Costs during stable disease were constant over time with a mean of €3,236. In contrast, monthly costs for progressive disease demonstrated a change over time with the largest costs in the first two months after diagnosis ($p<0.005$). The developed mixed effect model adequately described cumulative cost time course and associated variability. During the last months of life, costs varied over time, with the last month of life as the most expensive one with a mean of €4,522 per patient per month. **CONCLUSIONS:** To reflect costs of HER-2 positive MBC accurately in Markov models, costs stable disease can be defined time-independent, however, costs of progressive disease should be defined time dependent, and costs related to the final months of life should be modeled as such. The mixed effect model we have developed could now be considered for adequate description of the time-dependent cost of progressive disease.

PRM20

ASSESSING THE FUTURE BURDEN OF RENAL REPLACEMENT THERAPY IN THE UNITED KINGDOM

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OBJECTIVES: The UK has an ageing and growing population and the prevalence of renal replacement therapy (RRT) has grown by 5.0% annually since 2000. RRT accounts for over 2% of the current NHS expenditure. Transplantation increases survival, improves quality of life and maintenance costs are less than dialysis. Despite increasing rates of transplantation, an estimated 7,000 patients remain on the waiting list. The objective of this study was to quantify the relationship between graft survival time, total estimated cost and the number of projected patients on the transplant waiting list. **METHODS:** We utilized a population based simulation model with published disease progression, incidence and prevalence parameters specific to the UK. We evaluated the number of years of functioning graft required for transplantation to remain cost saving compared to dialysis; the number of future transplants or improvement in graft survival required to avoid the transplant waiting list increasing. The study utilises UK costs and future costs and benefits were discounted at 3.5% **RESULTS:** Over a 10-year projected time horizon the total per-patient cost saving associated with remaining on dialysis compared to transplant was £276,330; however, a cost saving was conditional upon achieving at least 3-years of functioning graft. In order to maintain the transplant waiting list at approximately 7,000, the number of annual transplants conducted would need to increase from 2,645 in 2010 to 3,640 by 2022 (a 37.6 % increase). At current activity levels the transplant waiting list is projected to increase by approximately 1,983; improvement in graft survival could potentially reduce this by 941. **CONCLUSIONS:** For kidney transplantation to be cost saving recipients must maintain at least 3 years of functioning graft. As early graft failure also impacts on future transplant waiting time, management strategies that maximize graft survival will reduce costs and improve service delivery targets.

PRM21

COMPARISON OF ALTERNATIVE METHODS OF RESOURCE-USE DATA COLLECTION FOR THE ECONOMIC EVALUATION OF HEALTH CARE INTERVENTIONS: A CASE STUDY IN FRAIL OLDER PEOPLE

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OBJECTIVES: Economic evaluations require patient-level resource-use to estimate patient costs. The National Programme for IT (2002) prompted UK health and social care to record patient-level resource-use using Electronic Administration Records (EAR's). Retrieving EAR's is labour intensive, but may provide better information than self-report methods, such as the Client Service Receipt Inventory (CSRI), particularly in cognitively impaired people. Study objectives are to examine agreement, and associated cost estimates, between resource-use obtained from EAR's or CSRI in frail older (≥70) participants. **METHODS:** Health and social care data for 247 patients (193 cognitively impaired) were sought retrospectively six months post-index hospital admission. Resource-use data were collected using a self/proxy-reported modified CSRI, and EAR systems for primary (PC), secondary (SC), and social (SoC) care. Lin's coefficient (ρc) assessed agreement between methods, where <0.4 = poor agreement. **RESULTS:** Agreement between EAR and CSRI 'per contact' resource-use was: good, primary care ($\rho c = 0.60$); fair, outpatient care ($\rho c = 0.53$). Agreement was incomparable for social care due to different resource-use recording formats; CSRI's inpatient care question was removed due to the preferred detailed information available in EAR's. EAR data provided detailed patient care information, such as diagnosis and procedure type, allowing improved allocation of unit costs. Difference in mean cost per patient between methods varied by service (CSRI/EAR (£): PC = 61/433; SC = 7281/7833; SoC = 252/886); CSRI inpatient costs were simulated assuming perfect agreement with EAR, but using level of information outlined within the CSRI. **CONCLUSIONS:** EAR's provided more complete patient costs. Using EAR's reduces burden upon participants, which is important for frail and cognitively impaired people. Although the CSRI can be modified and simple to administer, poor recall and inadequate detail about patient care contacts prevented accurate patient-level cost estimation. Gaining access to EAR's is labour intensive, but recommended in cognitively impaired participants.

PRM22

CARBON COST-EFFECTIVENESS OF COCOONING IMMUNIZATION AGAINST PERTUSSIS IN ENGLAND AND WALES: AN ECOLOGICAL PERSPECTIVE

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OBJECTIVES: The cost-effectiveness of pertussis vaccination has been demonstrated for various vaccination strategies. However, beyond financial cost expressed in monetary terms vaccines also incur environmental cost expressed in CO_2equivalent (CO_2e) emission. By preventing disease, this cost might be offset by avoided events such as doctors' visits, hospital bed stays, medication, amongst other items. In this exercise we examine the CO_2e savings of a pertussis (dTpa) booster dose for cocooning in England and Wales. We propose a complementary measure to the classical Incremental Cost-Effectiveness Ratio that includes environmental cost instead of monetary cost. **METHODS:** The cradle to gate carbon footprint (from raw material extraction, to manufacturing, to disposal) for a typical dTpa vaccine dose was assessed to estimate the total amount of CO_2e emitted ("carbon cost"). A previously published static epidemiological model was used to account for the reduction in incidence of pertussis. Two scenarios were compared: the current pertussis vaccination schedule and the same schedule with additionally a cocooning strategy. **RESULTS:** For each dose of a dTpa vaccine manufactured, results show approximately 1kg of CO_2e was emitted. The model shows cocooning immunization against pertussis is projected to reduce the reported incidence of pertussis in young infants. Results also show that due to the reduction in emitted CO_2e after the introduction of a cocooning strategy, vaccination is an acceptable alternative to the current strategy to control pertussis infection. **CONCLUSIONS:** The method presented demonstrates how traditional economic models can be utilized to model environment features. Assessment of the cradle to gate carbon footprint of a vaccine provides a preliminary view of both the impact on the environmental in general and on the environment profile of health care in the UK.

PRM23

MODELLING THE COST-EFFECTIVENESS OF FIRST-LINE BIOLOGICS FOR RHEUMATOID ARTHRITIS IN ENGLAND AND WALES

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OBJECTIVES: In 2012, NICE initiated a multiple treatment assessment reviewing all licensed biologics for the treatment of rheumatoid arthritis (RA) previously treated

with conventional DMARDs only. The sequence of treatments used after the failure of first biologic treatment was to be included as part of the cost-effectiveness modelling. We therefore built a model to match the treatment pathway for first-line biologics and beyond. **METHODS:** We researched the treatment pathway and existing cost-effectiveness models in order to create an appropriate model. We rebuilt the model used by the technology assessment group in TA195, which considered second-line biologics and beyond. We adapted this model to reflect the current treatment pathway and consider first line biologics. **RESULTS:** We created a patient simulation model, which generated a cohort of virtual patients and tracked their costs and QALYs over the pathway. Patients began treatment with a biologic, and could discontinue at month 6 due to an adverse event (AE), in which case they switched to a different biologic, with first-line efficacy. Patients who did not have an AE discontinued at month 6 if their DAS 28 improvement was insufficient. After discontinuation at month 6, or later, patients next received rituximab, unless contraindicated. If rituximab was contraindicated, or the patient had an AE by month 6, they moved onto another biologic treatment, after which they received a DMARD treatment sequence (including palliative care). Patients who had insufficient DAS28 response on rituximab at month 6 switched to tocilizumab (unless received previously), after which they received the DMARD sequence. Patients who had sufficient DAS28 improvement with rituximab remained on rituximab long-term, until they received the DMARD treatment sequence. Patients could exit the model at any point if they died. **CONCLUSIONS:** We used robust methodology and clinical rationale to assess the cost-effectiveness of licenced treatments reflected across NICE's recommended treatment pathway for RA.

PRM24

MODELLING THE COST-EFFECTIVENESS OF FIRST LINE BIOLOGICS FOR RHEUMATOID ARTHRITIS IN IRELAND

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OBJECTIVES: In 2013, NCPE assessed the cost-effectiveness of subcutaneous (SC) abatacept as a first line biologic for the treatment of rheumatoid arthritis (RA), compared to existing biologics. It was necessary to consider the treatment pathway beyond first line biologics. We therefore built a model to match the treatment pathway for first line biologics and beyond. **METHODS:** We used our individual patient sampling model for England and Wales as a starting point to create a model which considers biologic cycling, to match the treatment pathway in Ireland. We differentiated between the efficacy of a biologic at first line, and at second line or later. **RESULTS:** We created a model which could be used to calculate the cost-effectiveness of biologics for the treatment of RA in Ireland. Patients first received treatment with SC abatacept, intravenous abatacept, adalimumab, etanercept, infliximab, certolizumab pegol or golimumab. If they experienced an adverse event (AE) on that treatment within 6 months, they switched to another biologic at first line efficacy. If not, their response to treatment was tested using the DAS28: if this improved by 1.2 or more, their time on treatment was sampled from a Weibull distribution, otherwise they discontinued at month 6. The patient then moved onto a randomly sampled second line biologic, which was either one of the first line biologics or rituximab. The time on second line biologic was sampled from a Weibull distribution, and then the patient moved onto a third line biologics (second line biologics and tocilizumab). The patient cycled through the biologics until they died, or had received all 8 treatments. After 8 biologics, remaining patients received leflunomide, cyclosporin, azathioprine and palliative care. **CONCLUSIONS:** We used robust methodology and clinical rationale to model the treatment pathway of biologics for RA in Ireland and facilitated cost-effectiveness comparison between first line biologics.

PRM25

A SYSTEMATIC REVIEW OF ECONOMIC EVIDENCE IN HEPATITIS C: METHODS USED IN RECENT ECONOMIC EVALUATIONS

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OBJECTIVES: To perform a systematic literature review of economic evidence for genotype 1 hepatitis C virus (HCV) treatments and to summarise and assess the methods used in recent economic evaluations. **METHODS:** Multiple databases were searched to identify economic evaluations in patients with genotype 1 HCV. Detailed review methods are presented elsewhere. **RESULTS:** 53 economic analyses and 17 Health Technology Assessment (HTA) documents were identified. Most economic analyses were performed using lifetime horizon Markov models, all for interferon-containing regimens. Most were performed in the United Kingdom (UK) (n = 13), United States (n = 13), or Germany (n = 7). Two recent National Institute for Health and Care Excellence (NICE) submissions were included: telaprevir triple therapy (with peginterferon plus ribavirin) and boceprevir triple therapy, for previously treated and untreated patients. The models used were different; however their structures and some inputs were based on previous NICE appraisals for peginterferon plus ribavirin. There were a number of limitations found in the included economic evaluations, which may have affected the cost-effectiveness outcomes: 1) The models did not adequately capture all health benefits and costs in their quality-adjusted life-year calculations; 2) The models did not account for the possibility of benefits caused by reduced transmission of HCV; 3) The models did not incorporate patient factors that may influence disease progression; 4) Modelling of subgroups may have been insufficient, particularly as the understanding of patient and viral factors that predict treatment response grows; and 5) Some made generalisations for the compensated cirrhosis population that were not comparable with the UK population. **CONCLUSIONS:** Recent economic models have generally adhered to previous iterations of HCV models and have not evolved with our knowledge of the disease. In light of upcoming treatment alternatives, model refinement may be necessary to capture the increasingly complex treatment decisions that will be required.

PRM26

IMPACT OF USING EITHER MULTIPLICATIVE OR ADDITIVE UTILITY DECREMENTS IN DECISION MODELS

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OBJECTIVES: In cost-utility analyses (CUAs) it is common to estimate the utility of patients while on treatment or when experiencing comorbidities by adjusting their baseline utility with the treatment/comorbidity-related utility decrement. This study assessed the impact of adjusting patients' baseline utility with additive versus multiplicative utility decrements on the lifetime quality-adjusted life years (QALYs) in CUAs for two chronic illnesses. **METHODS:** Two Markov models were developed. In the first model, utility during treatment was obtained by adjusting the baseline utility with the treatment-related utility decrement; treatment was given for one year. In the second model, utilities with comorbidities were obtained from external sources and were combined with the health state utilities by considering the lowest value. In both models, the response of the multiplicative, additive and the combined approach was investigated by comparing the number of QALYs gained over a lifetime. **RESULTS:** In the first model, as treatment was only given during the first year, the impact on the number of QALYs gained over a lifetime was minimal. Thus, a similar incremental cost-effectiveness ratio per QALY (ICER/QALY) was obtained with all the approaches. In contrast, for the second model, the number of QALYs gained over a lifetime between the approaches was significantly different. This is because comorbidities were experienced during a longer period of time. Consequently, the difference in ICER/QALY was also substantial. **CONCLUSIONS:** When developing CUA, either a multiplicative or combined, rather than additive, approach should be used to calculate the utility of patients during treatment or with comorbidities, using utility decrements, if considerable uncertainty is present in the baseline utility. However, if QALYs gained with treatment or with comorbidities represent only a small fraction of the overall QALYs gained, the difference between the approaches is not expected to have a significant impact on the results.

PRM27

UNCHARTERED TERRITORY – ANALYSIS OF CROSS-BORDER SERVICE PROVISION WITHIN PUBLIC HEALTH SYSTEMS

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OBJECTIVES: The European Union's (EU) 2011 Directive on cross-border health care establishes the right of EU citizens to receive treatment abroad and be reimbursed in their home country. While the focus has been on patient mobility and access, it may also facilitate international outsourcing of services between countries. This research examines the methodological challenges in evaluating the costs and consequences of cross-border service provision. **METHODS:** Using the example of deep brain stimulation (DBS) treatment in Ireland, we conducted an economic analysis of the provision of cross-border services from the perspective of the public health system. This included an analysis of clinical and cost-effectiveness, ethical and societal implications and the challenges of integrating care between separate health systems. **RESULTS:** Accurate modelling of the provision of a new or expanded service serves as the basis for evaluating costs, impact on patients and potential gaps in continuity of care. Cost minimisation analysis may be appropriate under some circumstances, with due regard to the importance of patient selection and follow up. Cross-border services may have significant implications for equity of access, with potential negative consequences for those most in need of treatment. Results of the economic analysis indicate that a national DBS service in Ireland would cost an additional €20,900 per patient over 10 years. The potential for anomalies within health systems with a mixture of private and public funders is highlighted, with the difference being reduced to €4,100 per patient in a single payer scenario. **CONCLUSIONS:** Health care funding structures can impact significantly on the cost-effectiveness of cross-border services, even when differences in the actual cost of care are minimal. Given the externalities involved, analysis from the payer perspective may be too narrow for the economic evaluation of routine cross-border provision of elective services.

PRM28

EMPIRICAL EVIDENCE FOR THE VALIDITY AND RELIABILITY OF RESOURCE-USE MEASURES BASED ON PATIENT RECALL: A SYSTEMATIC REVIEW

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OBJECTIVES: Accurate measurement of resource use is required for economic evaluations alongside clinical trials. Patient-completed questionnaires are commonly employed as a means of collecting data; however, concerns over data quality persist, and there is little certainty about best practice. This review collates the evidence concerning the validity and reliability of resource-use measures based on patient recall with the aim of aiding health economists in developing better measures. **METHODS:** A search strategy incorporating terms covering health care resources, utilisation, patient-reported measures and validation/reliability concepts was applied to the MEDLINE, EMBASE and PsycINFO bibliographic databases. Studies were included if they reported original research to inform costing studies, and were about patient or proxy self-reports of direct health care-related resource use in which a comparator (to assess validity or reliability) was specified. Studies were excluded if they were not in English or if they assessed general population surveys. Reference and citation lists of included studies were hand searched to identify additional studies. Data on study and population characteristics, type of instrument, recall period and sample size were extracted. Results and conclusions concerning the validity and reliability of reports of types of resource use consumed (*e.g.*medication, inpatient stays) were also extracted. **RESULTS:** A total of 13,367 abstracts were identified as potentially relevant through the database searches. Following abstract and full-text screening, 60 articles were deemed relevant, with a further 9 identified through hand searching. The majority focused on adults (60/69),

and nearly half originated from north America (31/69). Emerging themes suggest that better accuracy is achieved when patients are answering questions about inpatient and specialist care. **CONCLUSIONS:** There is only a limited amount of validity and reliability information available to inform best practice for resource-use measurement in clinical trials. This ongoing review will identify the gaps, giving a clearer view of where research efforts should be concentrated.

PRM30

FUTURE COSTS INCLUSION IN PUBLISHED ECONOMIC EVALUATIONS: WHAT IS THE CURRENT SITUATION?

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OBJECTIVES: Nowadays, there is a general agreement about the need of including future related medical costs in life years gained while no consensus has been achieved about future unrelated medical costs (indirect medical costs) and future non-medical costs. The aim of this study has been to assess the extension of published economic evaluations that incorporated future costs and what types of future cost were included. **METHODS:** Three general health economic journals (*Pharmacoeconomics, Value in Health and European Journal of Health Economics*) were reviewed to identify economic evaluations from 2008 to 2011. Only complete economic evaluations were accepted for this research. From each selected article, future cost inclusion was evaluated along with the type of future costs included. **RESULTS:** A total of 148 articles were founded from the three journals fulfilling the inclusion criteria; 67 of them (45.27 %) incorporated future related medical costs, 9 (6.08 %) included also future unrelated medical costs and none included future non-medical costs. Percentage of articles including future costs increased from 2008 (33 %) to 2011(57 %) and no differences were detected between the three journals in the proportion of economic evaluations incorporating future costs. **CONCLUSIONS:** Despite most of health economic guidelines advice the need of incorporating future costs in l economic evaluations, less than the half of articles reviewed incorporated them. Moreover, the inclusion of future unrelated medical costs and future non-medical costs was much lower. Results of economic evaluations can change dramatically depending on future costs inclusion. It is necessary to change the current practice and systematically include future related medical costs in the base case of economic evaluations and future unrelated medical costs and future non medical costs at least in sensitivity analysis.

PRM31

CHALLENGES OF CONDUCTING ECONOMIC EVALUATIONS USING LINKED ELECTRONIC HEALTH RECORDS - CPRD AND HES IN THE UNITED KINGDOM

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OBJECTIVES: A range of linked electronic health records (LEHR) datasets are becoming available in the NHS in England. Understanding the benefits such large LEHR datasets can offer when performing cost-effectiveness analysis and overcoming the challenges inherent in utilising such datasets using as a case study: the CALIBER (Cardiovascular Disease Research using Linked Bespoke Studies and Electronic Records) dataset to assess the cost-effectiveness of treatment of patients with chronic stable angina. **METHODS:** The CALIBER dataset links primary care data from CPRD with secondary care data from HES, mortality data from ONS and disease-specific data from MINAP. This dataset is used to provide a generalisable baseline for cost-effectiveness models and to provide effectiveness estimates for treatments observed in the dataset. It is also used to explore decisions that, due to ethical concerns, could not be researched through RCTs - for example, optimal durations and combinations of treatments used in current practice. The statistical methods of matching, differences in differences and instrumental variables are used to overcome the selection bias problems associated with inferring treatment effects using observational data. The models are also combined with RCT results for novel treatments to assess their cost-effectiveness in a real world as opposed to trial setting. **RESULTS:** There were significant challenges involved in working with LEHR ranging from correctly linking the data to plausibly imputing missing data and correcting for selection bias in estimates. Having addressed these challenges we were left with a rich dataset, from which to estimate costs, risks of health events and treatment effects in a generalisable real world setting. **CONCLUSIONS:** While the selection biases associated with the use of LEHR within the NHS makes them challenging to work with, the large sample sizes, generalisability of the results and relatively low cost of the research makes them a hugely valuable resource for economic evaluation.

PRM32

DEVELOPMENT OF THE SCHARR HUD (HEALTH UTILITIES DATABASE)

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OBJECTIVES: The retrieval of studies containing evidence of health state utility values (HSUVs) is currently problematic using generic bibliographic databases such as Medline. This is due to a lack of standardised search vocabulary and inadequate and inconsistent indexing. The objective of this project is to develop a bibliographic database providing access to details of research studies containing health state utility values generated using the EQ-5D and other preference-based instruments. **METHODS:** The initial phase of the project has focussed on the EQ-5D. An alpha version of the database was created using Mendeley reference management software. A corpus of potentially relevant studies was identified by searching Medline and by sifting the reference lists of systematic reviews of HSUVs in a range of diseases and conditions. The sifting of retrieved studies is an ongoing process. Studies are included in the database if they contain estimates of HSUVs. The names of instruments used in the studies, including and in addition to the EQ-5D, are extracted and added to the database record to create a searchable index of instruments. A beta version of the database, using bespoke software to improve functionality, is currently undergoing ad hoc testing. **RESULTS:** The alpha version of the database contains over 3,500 potentially relevant studies identified by the search process. Several hundred studies have been data extracted and indexed. The names of over 50 instruments, including quality of life, disease specific and generic preference-based measures have been added to the index. A programme of sifting, data extraction and indexing is ongoing. Public access to the beta version of the database is planned for Autumn 2013. **CONCLUSIONS:** The purpose of the health utilities database is to improve access to HSUV evidence, in the first instance in studies using the EQ-5D with a view to including all major preference-based utility measures.

PRM33

THE REVIEW OF PUBLICATIONS OF PHARMACOECONOMIC RESEARCH IN RUSSIA DURING 2007-2012

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OBJECTIVES: To analyze the publications on methodology and normative regulations of pharmacoeconomic studies, including materials providing results of conducted researches in Russia or translated international publications, as well as to analysis the dynamics of publications and identify the structure of methodological approaches in Russia. **METHODS:** The screening of publications from the data of the Central Medical Scientific Library of the First MSMU was conducted based on the key words - "pharmacoeconomic*" and "pharmacoeconomical*" with corresponding endings. The time horizon of the study was 6 years (from 2007-2012). **RESULTS:** By the beginning of 2013, 280 literature sources were found and analyzed in the timeline from 2007 to 2013. It was found that the most common type of publications for the reporting period have been the inaugural dissertations showing the researches results - they are accounted for about 47% of all studies, followed by further research reports, accounted for 44%, methodical publications - 5%, dissertations devoted to the methodology of the pharmacoeconomics- 3%, regulatory guidance documents and translations of foreign studies - 1%. The most common structure of published researches was monocenter (56%), with a retrospective time-restricted directivity (74%). Russian authors use the methodology of the "cost-effectiveness" analyzing in their works the most frequently (48%). 64% of Russian researchers take into account only direct costs, 32% of researchers analyze their studies based on indirect costs. **CONCLUSIONS:** Based on our review of the published works from 2007 to 2012, we can make a conclusion on the formation and development of high-grade pharmacoeconomics as an independent research area in the Russian Federation.

PRM34

EVALUATING DIFFERENT MODES OF RADIOTHERAPY BASED ON A PATIENT-LEVEL SIMULATION MODEL

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OBJECTIVES: Use of proton instead of photon radiation therapy for head and neck cancer reduces the primary tumor and damage to adjacent organs risk, which results in fewer complications. These complications decrease quality of life (QOL). To support better decision making concerning which patients benefit most from proton therapy, a patient-level simulation model is developed and applied to compare outcomes. **METHODS:** Model estimates, such as patient and tumor characteristics, follow-up time, and survival, were based on patient-level data containing patients treated with radiation therapy as first line therapy for head and neck tumor in The Netherlands between 1980–2010 at the UMC Groningen (n=277) and VU Amsterdam (n=736). In silico radiation treatment planning schemes for both proton and photon therapy allowed to compare a priori expected health benefits and cost consequences for both therapy modes to support a patient tailored choice. **RESULTS:** Patients experienced their first event at a median time of 30 (0-270, SD 34) months' time. Loco-regional recurrency in 29%, distant metastasis in 4.2%, both combined in 1% and dead in 13.3% of patients. Cost per year for photon was estimated €15000, proton €30000, disease free state €190, local regional recurrence €28000, metastases €35000, and both €35000. For the complication sticky saliva costs per year of an average patient were €31, xerostomia €194, dysphagia €57, tube feeding €4262, and hypothyroidism € 117. Proton radiation therapy leads to less complications and improved QOL. **CONCLUSIONS:** Given the high costs of proton therapy, this was found not to be cost-effective compared to best photon therapy in an average patient with head and neck cancer. However, the outcomes vary substantially between patients. Depending on patient and tumor characteristics for selected patients with high complication risks, proton therapy can be a better option.

PRM35

THE ECONOMIC FOOTPRINT OF THE GREEK PHARMACEUTICAL INDUSTRY

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OBJECTIVES: To assess the overall impact of the production and distribution of pharmaceutical products in the Greek economy, in terms of Value Added, GDP, employment and tax revenues. **METHODS:** The overall impact in the Greek economy is estimated as an exogenous change in the economic activity by using the Leontief input-output model. **RESULTS:** The results indicate that the direct effect of the industry on domestic economic activity is €1.5 billion in terms of GDP. The indirect effect, which represents the value created by auxiliary sectors as (main suppliers) of the pharma industry is €2.2 billion. Finally, the induced effect, which is the impact from the final consumption, as a result of the wages and salaries gained by employees across the production chain of the specific industry is €3.8 billion. Hence, the overall effect on GDP is approximately €7.5 billion, which repre-

sents almost 3.4% of the country's GDP (2010). In terms of employment 23.000 are directly employed in the sector, while the total benefit for the Greek economy (both direct and indirect) is estimated to approximately 132.000 jobs. Finally, the industry accounts for nearly €400 million tax revenue, half of which affects the economy directly. **CONCLUSIONS:** Taking these effects in consideration it stems that for every €1 of Value added in the production / distribution of the pharmaceutical sector some €2.6 of Value added is created as an indirect effect and €5.3 as an induced effect. Additionally every job position in the sector in the pharmaceutical (production / distribution) sector supports 2.5 jobs due to indirect effects and almost 6 jobs in the economy. Finally, for every €1 in tax revenue provided by the sector, an additional €1.6 is generated though indirect effect and a total of €2.2 if the induced effect is taken into consideration.

PRM36

AN ASSESSMENT OF THE USE OF UTILITY DATA IN LONG-TERM COST-EFFECTIVENESS MODELS OF LIPID LOWERING THERAPIES

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OBJECTIVES: To determine through a literature review how economic evaluations incorporate utility data into models when estimating long-term cost-effectiveness of lipid lowering therapies in primary and/or secondary cardiovascular disease (CVD) prevention. **METHODS:** We used MEDLINE to identify published articles reporting cost-effectiveness models. Inclusion criteria included: English language articles published from 2000-2013, studies in adults ≥18 years old, studies assessing statins or ezetimibe for primary and/or secondary CVD prevention, and studies in the US, Canada, UK, Spain, Germany, Australia, Sweden, France, and Italy. Two researchers independently identified articles and disagreements were resolved by consensus. **RESULTS:** Sixty-one studies fulfilled the inclusion criteria. Forty-eight studies assessed the long-term cost-effectiveness (≥10 years) of lipid-lowering therapy— 20 studies were in primary CVD prevention, 19 were in secondary prevention, and 9 were in both primary and secondary prevention. 36/48 studies incorporated utility parameters into their models. 23/36 models differentiated short-term versus long-term utility impact of cardiovascular events. Eleven models were able to differentiate between short-term and long-term utilities through model structure, where separate health states were created for events versus post-events (e.g., stroke versus post-stroke), and utility values could be assigned to these health states accordingly. Twelve models were able to differentiate short-term versus long-term utilities by changing the model inputs, where different utility values were applied to a health state according to length of time after the event (e.g., event year versus subsequent years for a health state, or <6 months versus >6 months from time of event). Eleven models accounted for the occurrence of multiple events by applying disutilities or combining utilities multiplicatively for patients experiencing ≥1 event over time. **CONCLUSIONS:** Around two-thirds of the published long-term models differentiated short-term versus long-term utility impacts of cardiovascular events through model structure or utility inputs, which should be incorporated into future models on this topic.

PRM37

AN EXCEL CALCULATOR TO ESTIMATE RHEUMATOID ARTHRITIS COSTS IN TURKEY

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OBJECTIVES: To build an Excel calculator, taking demographic and clinical characteristics of rheumatoid arthritis (RA) patients in Turkey, and estimate the annual health care costs. **METHODS:** 2009-2011 data from MEDULA, the Turkish national health insurance database, was used for the study. RA patients (ages 18-99) were identified for the identification period (June 1, 2010 - December 31, 2010) using International Classification of Disease Tenth Revision Clinical Modification (ICD-10-CM) codes. Patients were grouped as prevalent and incident cases and required to have two RA diagnoses at least 60 days apart. In order to estimate risk-adjusted total annual costs for prevalent and incident cases, generalized linear models (GLMs) were used. Patients' demographic and clinical characteristics were factors to determine the expected annual cost value, with coefficients of the characteristics built in the Excel calculator. A marginal effects table was created after GLM estimation by using such calculation. **RESULTS:** A total of 2,613 patients met all inclusion criteria, of which 693 were incident and 1,920 prevalent cases. Patients' demographic and clinical characteristics were entered into the Excel calculator. Risk-adjusted annual total costs were calculated at €2,021 for prevalent cases and €1,818 for incident cases. The most expensive contributor to annual expenditures was prior biologic use for both groups. Prevalent patients who were prescribed disease-modifying anti-rheumatic drugs (DMARDs) in the baseline period incurred €5,898 more costs than those who were not. For incident cases, male patients incurred lower costs (€1,818 - €708 = €1,110), whereas respiratory comorbid conditions increased the total expected health care cost of incident RA patients by €916 (€1,818 + €916 = €2,734). **CONCLUSIONS:** In outcomes research, an Excel calculator serves as an important tool to estimate and compare RA-related health care costs.

PRM38

UNCOVERING THE GAP BETWEEN MODEL VALIDATION RECOMMENDATIONS AND PRACTICE

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OBJECTIVES: Health technology agencies and payers rely on economic models to evaluate the value of new treatments. It is therefore critical to ensure the scientific credibility of these models through validation, which is also required by NICE since 2012. The aim of this study is to understand which of the validation methods recommended in health economics and financial guidelines are practically used across different disease areas and business fields. **METHODS:** For this study we reviewed guidelines, economic models for diabetes, cardiovascular diseases, and cancers, as well as risk-prediction models. The identified validation methods were collected and categorized into three groups: face validity, internal verification, and cross validity. **RESULTS:** Twenty-two (22) economic models, 8 risk prediction models, 5 financial and 7 health economics guidelines were identified. In the guidelines we found 3, 14 and 5 methods within the face validity, internal verification, and external validity categories respectively. Almost three quarters of the 22 methods identified were also described in the ISPOR guideline on model validation and the other guidelines described 5 to 15 methods. External validation was done for 14 out of the 22 economic models reviewed in which (part of) the model results were compared against other clinical/epidemiology studies (14 models) or other validated models (10 models). Internal verification was mainly done through comparison against the trials that the models were built on (10 models). Out of the remaining 13 internal verification methods only 3 were performed for the economic models. Face validation was only performed for 3 economic models. **CONCLUSIONS:** This study found that there is a substantial gap between the validation steps recommended and those actually performed. Hence a more consistent and pragmatic approach needs to be taken to validate economic models. In addition, the validation methods performed need to be consistently reported.

PRM39

ANALYSIS OF HEALTH CARE COSTS IN ELDERLY PATIENTS WITH MULTIPLE CHRONIC CONDITIONS USING A FINITE MIXTURE OF GENERALIZED LINEAR MODELS

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OBJECTIVES: Multimorbid individuals consume a disproportionally large share of health care resources. Usually standard (1-component) regression techniques are applied to analyse costs in samples of patients with multiple chronic conditions. However, the patient specific number and combination of co-occurring single diseases results in inhomogeneous data leading to biased estimates when using traditional regression techniques. In this study we analyse health care costs in a sample of patients suffering from multimorbidity using a more elaborate approach to address this heterogeneity. **METHODS:** We used a subsample of N=1050 patients from a multicentre prospective cohort study of multimorbid primary care patients aged 65 to 85 years in Germany who completed a questionnaire on health care utilization covering a 6-month-period. We applied a finite mixture of generalized linear models, which belongs to the group of statistical learning algorithms, in order to control for unobserved heterogeneity of patient level health care costs focussing on the identification of multimorbidity patterns. **RESULTS:** We detected four different groups of patients with regard to total costs. The effect of the presence of an additional disease on costs differs between these groups. Two diametrically opposed cost trends were detected with respect to the number of co-occurring diseases. While in one group containing hypertension, joint arthrosis, diabetes, gout, anxiety and lower limb varicosis cost increased with the number of co-occurring diseases, in a second group including severe hearing loss, asthma/COPD, osteoporosis, neuropathies, Parkinson's disease and chronic ischemic heart disease cost decreased. Diversities between groups were also found in the results indicated by diametrically opposed influence of single diseases. **CONCLUSIONS:** Our results indicate existing unobserved heterogeneity in costs among patients suffering from multimorbidity with different combinations of single diseases which would remain unconsidered using standard regression techniques. Especially different costs trends were detected with regard to the number and nature of co-existing diseases.

RESEARCH ON METHODS – Databases & Management Methods

PRM40

USE OF THE CLINICAL PRACTICE RESEARCH DATALINK (CPRD) TO ASSESS 'REAL-WORLD' MANAGEMENT OF TUBEROUS SCLEROSIS COMPLEX (TSC) IN THE UNITED KINGDOM

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OBJECTIVES: TSC is a multi-system genetic disorder associated with benign lesions throughout the body, neurological manifestations, and impaired cognition. As many as 8000 people in the UK may have TSC; many cases likely go undiagnosed. Long-term morbidity and treatment burden associated with TSC are significant, suggesting substantial economic burden. This preliminary study assessed presentation patterns of select TSC manifestations in CPRD. **METHODS:** TSC patients were retrospectively identified in CPRD (Read: PK5.00) and linked Hospital Episodes Statistics (HES; ICD-10: Q85.1) databases. CPRD includes over 5 million active patients from UK primary care practices (~8% coverage). A total of 55% of practices (375) are linked to HES, allowing events in secondary care to be analysed (e.g. hospitalisations, procedures). Patients not linked to HES were excluded. Available history was extracted for each patient; descriptive statistics for select TSC-related diagnoses and procedures are presented. All ages reported below are median values. **RESULTS:** A total of 244 patients (49% male) with a TSC diagnosis were identified; age at diagnosis was 8 years, with 70% under 18 years. Patient data history was 20 years; 3 and 11 years pre/post initial TSC diagnosis. By age 4, 72% had a record of epilepsy; by 16 years, 9% had a record of subependymal giant-cell astrocytoma (SEGA); by 18 years, 1% had obstructive hydrocephalus; by 43 years, 4% had renal angiomyolipoma (AML) [median age at initial recorded diagnosis]. **CONCLUSIONS:** Preliminary analyses affirm the utility of CPRD in a real-world study of TSC, and the many emergent TSC-related manifestations, in a longitudinal fashion. Data are suggestive of evolving diagnostic and treatment patterns (30% adults) and may highlight a need for better coordination of adult care. Relatively low prevalence of AML was unexpected and

warrants further investigation. Robust analyses are planned to comprehensively describe the clinical and economic burden of TSC in the UK.

PRM41

EXPLORING THE IDENTIFICATION OF MULTIPLE SCLEROSIS INCIDENT COHORTS IN CLAIMS DATABASES: METHODOLOGY AND CHALLENGES

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OBJECTIVES: To explore whether multiple sclerosis (MS) incident cohorts can be identified in claims databases. **METHODS:** We used several approaches to try and identify MS incident cohorts in the US Department of Defense (DOD) and MarketScan® databases, based on diagnostic and treatment history. Patients were first identified with 1 year of no MS claims or treatment before their first MS claim. Sensitivity analyses identified patients with 1–4 years of no MS claims or treatment before their first MS claim. **RESULTS:** In patients with a 1-year baseline history with no MS claims or treatment, age and baseline characteristics were similar to all MS patients. The mean age at index date (second MS claim) was ~50 years, in contrast with previous research reporting a mean age at diagnosis of 25–40 years. Patients aged ≤65 years with ≥1 MS claim and 4 years of continuous baseline enrolment were identified in the DOD (n=16 444) and MarketScan® (n=16 352) databases. With increasing years of baseline history, more patients showed evidence of pre-existing MS; the percentage of total patients with no MS claim or treatment before the first MS claim decreased from 53.3% (1 year history) to 42.2% (4 years history) in the DOD database, and from 23.5% to 15.5% in MarketScan®. Despite the decrease in patient numbers, the mean age at index date remained high (44–49 years). **CONCLUSIONS:** Results indicate that >4 years of patient history is needed to define an incident MS cohort in claims databases. However, the 4-year claim and treatment-free cohort may be useful for studying treatment patterns and their impact on outcomes in recently treatment-naïve MS patients. There are substantial challenges in retrospectively identifying incident cohorts of MS patients using claims databases and a need for additional, large, real-world data sources to study newly diagnosed MS patients.

PRM42

SCREENING CHARACTERISTICS AND DIABETES BIOMARKERS IN FRENCH AND UK PATIENT-LEVEL DATABASES

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OBJECTIVES: Describe the patient characteristics and diabetes markers of type 2 diabetes (T2D) patients in the newly launched IMS LifeLink Diabetes Cohort in France. Monitor the data quality through comparison of measures with a French national survey of diabetes patients (ENTRED), the UK National Diabetes Audit (NDA) where possible, and the "gold standard" UK Clinical Practice Research Datalink (CPRD). **METHODS:** The IMS Diabetes cohort in France supplements patient-level data from general practitioners with additional patient data via pop-up technology within electronic medical records to facilitate robust epidemiological studies. This study compares the T2D patients in the Diabetes Cohort with similar populations in terms of gender, age, disease duration, and proportion of patients meeting key disease-specific targets (data presented as summary statistics). **RESULTS:** Patient characteristics and diabetes markers were analyzed for T2D patients in the Diabetes Cohort (n=5,142), ENTRED (n=3,894), UK NDA (n=1,909,494), and UK CPRD (n=268,618). The mean (SD) age in years was 66 (12.58) in the Diabetes Cohort, 66 in ENTRED, and 61 (15.35) in CPRD. The mean (SD) time since T2D diagnosis was 8 (7.7), 11, and 7.7 (6.2) years in the Diabetes Cohort, ENTRED, and CPRD, respectively. Mean (SD) BMI was 30.5 (5.76) in the Diabetes Cohort, 29.5 in ENTRED, and 30.8 (6.51) in CPRD. HbA1c target level of ≤6.5% was met by 32.5%, 34%, 23.5%, and 26% of the patients in the Diabetes Cohort, ENTRED, CPRD, and NDA, respectively. **CONCLUSIONS:** Health care systems and data collection methods vary across EU countries in general. Data monitoring helps assess data quality and robustness. Based on comparison of patient characteristics and diabetes markers, the IMS Diabetes Cohort population does not appear to differ from the ENTRED population. Although some differences between the Diabetes Cohort and CPRD data were noted, this unique French Diabetes Cohort appears appropriate for epidemiological research.

PRM43

MEDICAL AND PHARMACY CLAIMS-BASED ALGORITHMS FOR IDENTIFYING RELAPSES IN PATIENTS WITH MULTIPLE SCLEROSIS

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OBJECTIVES: To develop appropriate algorithms for identifying and classifying relapses among patients with multiple sclerosis in claims databases. **METHODS:** Algorithms for detecting relapses in claims databases were identified by literature searches and refined by neurologists and database experts to identify relapses in inpatient and outpatient settings. Definitions were used in the US Department of Defense (DOD) and MarketScan® databases to determine annualized relapse rates (ARR) occurring after index date (date of second MS medical claim separated by ≥30 days, following ≥12 months of continuous enrollment) during the 12-month and all available follow-up time. **RESULTS:** A relapse was defined as an inpatient visit with a primary ICD-9-CM diagnosis code 340.xx or both an outpatient visit with any 340.xx diagnosis code and oral or intravenous corticosteroid use ≤7 days of the outpatient visit. ARR estimates in the DOD (N=15,447) and MarketScan® (N=35,134) databases were 0.25–0.30 and 0.20–0.27, respectively. For inpatient relapses, estimates were 0.04–0.06 in the DOD database and 0.02–0.03 in the MarketScan® database. The corresponding estimates for outpatient relapses were 0.20–0.23 and 0.18–0.24. Severe relapses required an inpatient visit plus additional evidence of brain or spinal magnetic resonance imaging ≤7 days before or during hospitalization, or an outpatient visit combined with extended treatment (starting 0–30 days after outpatient visit) with ≥1 of the following: a further course of intravenous corticosteroids >7 days after the first course; a course of oral corticosteroids >7 days after the intravenous course; intravenous immunoglobulins or plasma exchange. Algorithms for identifying atypical relapses were also developed. **CONCLUSIONS:** General and outpatient ARRs are consistent between the two distinct claims databases and are similar to those reported in the literature. Differences in inpatient ARRs may indicate differences between clinical practices in the two systems. Further investigation in the real-world setting is required.

PRM44

COMPARISON OF METHODS TO IDENTIFY STAGE IIIB OR IV METASTATIC LUNG CANCER PATIENTS FROM ELECTRONIC MEDICAL RECORDS

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OBJECTIVES: Increased use of electronic medical records (EMR) has necessitated efficient ways to identify patients with certain clinical characteristics. This study compared use of standard fields and standard language recognition of progress notes to identify patients with metastatic lung cancer within an oncology-specific EMR. **METHODS:** Lung cancer patients (ICD-9-CM: 162.2 - 162.9) with second line erlotinib treatment were identified from a proprietary EMR. Method 1 identified metastatic disease using standard data fields for diagnoses (196.x – 198.x) and/or stage (3B/IIIB or 4/IV); Method 2 utilized keyword searches for indications of metastases or stage within progress notes. Chart reviews were used to confirm advanced disease. Positive and negative predictive values (PPV and NPV) were then compared across methods. **RESULTS:** A total of 740 patients were identified with suspected metastatic disease; 60.1% (n=448) using Method 1. Of the remaining 292 patients, 282 (96.5%) were identified by metastases and 117 (40.1%) by stage keywords (Method 2). Overall, 671 (86.6%) were confirmed "metastatic" with chart review and 5 patients excluded for evidence of other cancers. Overall, PPV was 100% and NPV 6.3%. Of those identified as metastatic using the standard fields, the PPV for metastases and stage were 65.5% and 66.3% respectively and 99.3% combined. The PPV and NPV among the 287 patients identified only by keyword searches, was 98.2% and 8.7% respectively for metastases and 49.3% and 89.9% respectively for stage. **CONCLUSIONS:** Utilization of standard EMR fields for diagnosis and disease stage, when used together, resulted in identification of large numbers of confirmed metastatic lung cancer patients. However, for those patients requiring text searches for metastases and stage, neither separately nor in combination, could adequately identify metastatic disease patients. Further standardization of EMRs and consistent entry within oncology practices could reduce the need for labor-intensive, costly human chart review in real-world oncology research.

PRM45

ASSESSMENT OF A CANADIAN PRIMARY CARE ELECTRONIC MEDICAL RECORD DATABASE FOR USE IN OBSERVATIONAL STUDIES

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OBJECTIVES: Observational data derived from clinical practice is becoming increasingly important to answer questions that cannot be addressed by RCTs. Although there are a number of administrative databases in Canada, access to more comprehensive, longitudinal clinical data such as smoking status, body weight and laboratory values in the primary care setting is limited. The objective of this study was to evaluate a Primary Care EMR (Electronic Medical Record) system to determine its feasibility for use in observational studies. **METHODS:** We analyzed de-identified patient data from primary Health Care Professionals (HCPs) including General Practitioners from 2009-2011. Comprehensiveness and completeness of each variable by visit were evaluated. First steps were taken to understand how the patient population compares to data from published sources. **RESULTS:** There were 3,019,954 patient visits observed by 255,274 active patients (≥1 visit). The patient visits were entered by 497 HCPs (152 physicians). Data are available for demographics, vitals, smoking status, laboratory values, prescriptions, medical history, diagnosis (ICD-9), short term absences and referrals. Completeness of each variable by visit ranged from 26% for pulse to 100% for age, sex, lab results and referrals. Initial assessment revealed that 85.6% of written prescriptions and 88% of diagnoses were recorded using structured fields. The median age of patients in the EMR was 37.2 years compared to 39.9 years reported by Statistics Canada (July 2011). Younger age groups were overrepresented, with the largest difference found in those 20-29 years; no difference was observed for sex. **CONCLUSIONS:** The status of electronic primary care health records in Canada is still in its infancy. The research suggests this is a valuable new addition to support observational studies in Canada. Disease specific validation studies will be required prior to further analysis. Further research is being undertaken to review quality measures.

PRM46

EVALUATION OF DISSEMINATION OF BRAZILIAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT (REBRATS)

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OBJECTIVES: The Brazilian Network for Health Technology Assessment (REBRATS) is composed of universities, hospitals and managing institutions who have among their goals the objective to elaborate and disseminate HTA information. The network's website and database are found at the http://www.saude.gov.br/rebrats and are tools to disseminate the policies and methodological guidelines of the network's institutional organization and the studies produced by its members. To evaluate the degree of the network's dissemination on national and international levels by analyzing the level of access and the rate of return from site users. **METHODS:** To analyze the number of visits to the REBRATS site registered through the Google Analytics monitoring and data extraction tool, with the intention of identifying

the user's behavior upon navigating the site. **RESULTS:** Since the site began to get monitored on July 1, 2012 and up until June 25, 2013, 19.738 hits were registered, with a monthly average of 1.661 hits. More than 65 countries accessed the site, the majority coming from the USA, UK and Portugal. Brazil leads with 93%. The rate of return of people who frequently accessed the site was 24,7%. Upon navigating the site, more than 45.000 visualizations of the web page were registered. **CONCLUSIONS:** This monitoring began in 2012 and therefore no previous years exist to serve as a basis for comparison. The results show that a considerable number of users have access to the site and consequently know about REBRATS. From the perspective of the website, the number of hits is still low, however, considering that the HTA field is a recent one in Brazil, its growth has been gradual. On an international level, new dissemination strategies are necessary in order to create greater visibility and promotion of the network.

PRM47

DESCRIPTION OF TREATMENT PATHWAYS IN CHRONIC DISEASES USING LARGE GENERAL PRACTITIONER LONGITUDINAL DATA: THE EXAMPLE OF PHARMACOTHERAPY IN PARKINSON'S DISEASE IN THE UNITED KINGDOM

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OBJECTIVES: Identifying treatment pathways based on administrative data or electronic medical records is generally a complex task, as many incidental events may hide the key trends. The purpose of this study was to propose a transparent methodology for defining treatment pathways using a large longitudinal real life database. The application of two alternative algorithms with different variants in Parkinson's disease (PD) was described. **METHODS:** In the first method, a new treatment line was assumed to start when a pre-specified number of consecutive prescriptions of drugs from the same PD drug class or combination of classes (rasagiline, selegiline, dopa agonists, COMT inhibitors, levodopa and derivatives) occurred. In the second method, start and end dates of continuous treatment periods (i.e. without gaps higher than six months between prescriptions) were determined for each drug class independently of each other. Combinations were assumed to be used when different treatment periods overlapped. Algorithms were tested using medical records of patients with Parkinson's disease (PD) extracted from the UK Clinical Practice Research Datalink (CPRD). The outputs of the different algorithms were described in details for ten patients, randomly selected. The sensitivity of the algorithms to changes in assumptions was tested. **RESULTS:** The first algorithm did not systematically capture the addition of a new drug to the current treatment as combined drugs were not necessarily prescribed or renewed during the same consultations. However, the second method well captured the treatment lines observed but sometimes created undue treatment lines from isolated prescriptions. This issue was overcome by deleting short lines lasting less than three months. **CONCLUSIONS:** The second algorithm developed in this study provided an accurate description of the treatment strategies developed by prescribers in Parkinson's disease in the UK using a limited number of assumptions and may be useful for other chronic diseases.

PRM48

IDENTIFICATION AND QUALITATIVE ASSESSMENT OF REAL WORLD DATA SOURCES: EXAMPLE OF LYMPHOMA AND MULTIPLE MYELOMA IN EUROPE

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OBJECTIVES: To identify and assess real world data sources for observational research on lymphoma and multiple myeloma (myeloma) in Europe. **METHODS:** Structured (EMBASE and MedLine) and grey literature searches were conducted to identify relevant European data sources. Identified data sources were screened based on the following criteria: inclusion of patient-level data and patients with NHL, HL, or MM diagnoses, possession of data dictionaries, and ongoing data accrual. Where regional registries were proven to feed data into national registries, only the national data source was retained for evaluation. Data sources passing initial screening were subjected to further evaluation based on publicly reported information, questionnaires and / or interviews with data source owners, and informed by lymphoma and myeloma treatment pathway analysis. **RESULTS:** One hundred eighty-six data sources from 21 countries were identified; of which cancer registries (R) accounted for 65%. The remaining 35% non-registry (NR) sources included biobanks, clinical audits, data linkage initiatives, drug databases and electronic medical records. Screening removed 101 sources. Of the 85 sources retained after screening, roughly half (52%) were NR sources and a majority (74%) were from six countries: France, Germany, Spain, Sweden, The Netherlands, and The UK. NR data sources generally collected more data attributes than R data sources. These data attributes included symptoms (collected by 52% NR, and 21% R data sources), treatment regimens (81% NR, 40% R), and resource use (49% NR, 8% R). **CONCLUSIONS:** Compared with disease registries, non-registry data sources in Europe typically have more diverse data attributes and are therefore potentially better for lymphoma and myeloma research. This result may guide the selection of data sources for observational research. As scrutiny of real-world outcomes for reimbursement of oncology drugs increases, much work remains to be done to increase the visibility and utility of data sources for health care payers and providers.

PRM49

COVERING THE PASS: DEVELOPMENT OF PROTOCOL TEMPLATE LANGUAGE (PTL) FOR DATA COLLECTION AND DATA MANAGEMENT (DM) IN POST-AUTHORIZATION SAFETY STUDIES (PASS)

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OBJECTIVES: To address non-interventional study (NIS) protocol DM and data collection requirements in PASS observational study designs. These studies may include =>1 cohorts, retrospective or prospective data collection, disease or treatment-based inclusion criteria, various outcomes (safety, prescription pattern or off-label use, comparative effectiveness, quality of life or other patient-reported outcomes[PRO], health economics, or other objectives), site/investigator selection (in-house, commercial, professional organization, or government databases), and country-specific requirements. **METHODS:** Studies that used integrated and non-integrated DM systems were evaluated to identify criteria for use and associated protocol template language (PTL), including required, preferred, or optional text based on various study designs and objectives. **RESULTS:** Multiple DM systems were evaluated and algorithms created with use criteria. For integrated DM systems that combined data capture and trial management, simplified PTL was identified. DM PTL was adjusted to include paper or electronic data capture (EDC) methods, paper/electronic-based PROs, paper/electronic case report forms (CRFs), data (eg. subject/physician entered, site or aggregate, medical or laboratory records) and appropriate subject data protection. For non-integrated systems that required separate DM and trial management, additional PTL was identified for these complex DM systems. The templates denoted minimum required language and suggested extended language for more elaborate designs. To support the numerous NIS study design types, we included decision trees to account for various study goals, associated outcomes, and data collection requirement. Our data collection decision tree summarized the variety of potential study designs with frequently used study goals/outcomes and associated data collection techniques. **CONCLUSIONS:** Integrated DM systems provided the most flexibility and simplicity of protocol template language. All template language was created as adjustable to meet the typical study designs encountered in PASS studies. This additional information was to support the protocol development team in creating the final protocol in a timely manner and in reviewing client-provided templates.

PRM50

BUILDING A REAL WORLD PRACTICE-BASED NETWORK DATA PLATFORM TO LINK RARE DISEASE PATIENTS: CASE STUDY OF MYELOFIBROSIS PATIENTS IN THE UNITED STATES

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OBJECTIVES: Conducting real world evidence (RWE) research on patients with rare diseases is particularly challenging when using only one type of data (e.g. insurance claims). Myelofibrosis (MF) is a rare, hematological cancer with global annual incidence rate of <1 - 2.4 cases per 100,000 patients. MF is characterized by the reduced ability of bone marrow to synthesize blood cells which can result in anemia, thrombocytopenia, and higher risk of infection. Absent adequate, recent data on MF patients, a practice-based network (PBN) data platform was developed to facilitate RWE research on MF patients. **METHODS:** MF patients observed in IMS Health databases between November 2010 to October 2012 were identified. Academic centers of excellence and large community oncology practices treating MF patients were then identified to link additional patients into the platform using a HIPAA-compliant patient de-identification algorithm. Patient demographics and attributes of dispensed prescriptions, private practitioner visits, and electronic medical record data including laboratory information were collected across patients from January 2000 to March 2013. Descriptive analyses of demographic and clinical characteristics were conducted to assess the generalizability of the sample versus literature. **RESULTS:** A total of 6362 U.S. MF patients were identified in the platform. Mean (SD) age was 67 (12.6) and 45% of patients were female. Mean (SD) Charlson Comorbidity Index was 4.36 (2.4). Among the subset of 529 patients with laboratory results, 63% were identified as anemic and 34% had platelet counts 50,000 - 100,000 / microL. All U.S. geographic regions were represented. **CONCLUSIONS:** Demographic and clinical results suggest that this large sample of MF patients is comparable to prior estimates of the broader MF population. This case study of U.S. MF patients suggests it is important to look beyond any one data source and to build PBN platforms with key clinical domains spanning multiple geographic regions when conducting RWE research on patients with rare diseases.

PRM51

FROM CLINICAL TRIAL TO REAL-WORLD EVIDENCE: A SYSTEMATIC APPROACH TO IDENTIFYING DATA SOURCES FOR OBSERVATIONAL RESEARCH

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OBJECTIVES: Observational studies are often planned on an ad hoc basis, with the risk that methods are inconsistent and that aims overlap rather than complement each other. Our objective was to develop a systematic approach for identifying observational data sources for an integrated global programme of real-world evidence gathering, to support an important new indication for an antiplatelet drug. **METHODS:** Systematic literature and Web searches, supplemented with email and telephone contact with data owners, were used to identify and characterize registries and health care databases suitable for use in observational studies of myocardial infarction and acute coronary syndromes. The ability to identify patients across data sources was also assessed. Data were captured and evaluation criteria applied, including compatibility with aspects of an ongoing randomized clinical trial (patient population, treatments, outcomes, and length of follow-up [≥3 years]). Selection criteria included accessibility; availability of inpatient, outpatient, cardiac event, and drug data; and generalizability. **RESULTS:** Over 2700 publications were screened; we identified 216 registries and 380 databases (primarily of administrative claims and electronic medical records). Of these, 12 registries, and 21 databases met the evaluation criteria and were assessed in depth. After application of the selection criteria, 5 registries and 12 databases were recommended. Recommended data sources ranged in size, each capturing data on between 4000 and 11 million

patients, and were geographically diverse, representing populations in Europe, the USA, and Australia. Each recommended data source had unique strengths and limitations for use in real-world evidence studies, and together they had the potential to provide consistent and complementary information. The study output provided a valuable tool for global and local investigators. **CONCLUSIONS:** Observational data sources are diverse. A systematic understanding of real-world evidence can guide the development of a coherent strategy for designing observational studies to support clinical research.

PRM52

FEASIBILITY OF USE OF MEDICAL TRANSCRIPTION DATA FOR REAL WORLD EVIDENCE GENERATION IN THE UNITED STATES: A PILOT STUDY OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS INITIATED ON BELIMUMAB

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OBJECTIVES: To assess the feasibility of use of medical-transcription data for real-world clinical evidence generation in the US. **METHODS:** Majority of clinical practices in the US are experimenting digitization of patient medical records for two reasons: patient-management/care-delivery and billing/administrative/legal documentation purposes. Increasingly, physicians are using medical-transcription services, where physicians dictate details of patient visits and send the voice-recording-device to medical-transcription organization which processes voice-data and delivers electronic-files back to clinics; physicians review/revise/append the electronic-documentation and adds data to their patient-database-repository for future use. This pilot study assessed the utility of de-identified medical-transcription data in evaluating patient-physician dynamics and real-world treatment patterns/outcomes and documented adverse-events(AEs) using random set of adult SLE patients who initiated belimumab (a recently-launched biologic) within the past 2years as part of usual care. SLE was chosen specifically because of its complex clinical management issues. **RESULTS:** Nineteen belimumab patient transcription-records (de-identified) were reviewed (mean age:39.4yrs; female:95%). Top-4 clinical-manifestations at belimumab-start were: musculoskeletal(68%)/mucocutaneous(53%)/constitutional(42%)/renal(21%). Physicians discussed belimumab-attributes (specifically, infection-risks/AEs/etc), asked patients to do their own research on belimumab, and cited insurance/reimbursement-issues prior to belimumab-start in 58%, 26% & 26% of cases respectively; 11% of patients asked for belimumab. Top-3 documented-reasons for belimumab-start were: steroid-sparing(32%), control autoimmune diathesis(11%), control SLE-flares(16%). In 47% of patients, belimumab (at initiation) replaced another medication (majority:steroids/immunosuppressants); concomitant SLE-medications were: antimalarials(84%)/oral-steroids(68%)/Immunosuppressants(47%). Average belimumab-duration was 8.1months (overall data availability/patient:23.8months). During the observation period, 42% had >=1AE (e.g., diarrhea/rash/bronchiolitis/alopecia/upper-respiratory-track-infection), 42% discontinued belimumab (but 26% re-started) and 47% had some physician-documented improvement in outcomes (e.g., joint-pain/rash/energy level/fatigue). One patient had documented steroid-stoppage post-belimumab initiation. **CONCLUSIONS:** Medical-transcription data may provide documented real-world evidence of treatment dynamics and clinical status/outcomes associated with patient care. In this random cohort of SLE patients using belimumab, belimumab appears to provide some demonstrable benefits in almost half of the patients.

PRM53

UPDATE OF THE PATIENT-REPORTED OUTCOME AND QUALITY OF LIFE INSTRUMENTS DATABASE (PROQOLID): INCLUSION OF E-PRO INFORMATION

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OBJECTIVES: In 2002, PROQOLID was launched to provide an overview of existing PRO instruments and a facilitated access to the instruments and their developers through the structured presentation of synthesized, reliable, and constantly updated data. With the constant growth of electronic capture of patient-reported outcomes, detailing information about modes of data collection (i.e., paper vs. electronic) in PROQOLID might become a crucial step in updating the database. The objective of this study was: (1) To review how e-PROs are currently reported in PROQOLID; and (2) To propose (if needed) ways of clarifying and updating e-PRO information. **METHODS:** PROQOLID was searched to retrieve current information about e-PROs using an advanced search engine. **RESULTS:** The e-PRO information was found under the category "mode of administration." Three options could be chosen: computer-administered, electronic-administered, and IVR (Interactive Voice Response) version. Out of the 751 instruments in the database, 37 (5%) were reported with e-PRO information. Information about existing translations of electronic versions was clearly specified for three questionnaires. To clarify and update e-PRO information in PROQOLID, several recommendations are proposed: (1) To create a new category, i.e., mode of data collection, in order to differentiate it from the "mode of administration" category; (2) To categorize each mode of data collection into five subcategories [i.e., Hand-Held Device, IVR, Internet web-data capture, Pen, and Tablet]; and (3) To provide a list of all translations available in each mode of data collection. **CONCLUSIONS:** This review has shown that PROQOLID already includes e-PRO information. Recommendations are given on how to modify the organization and content of the database to present the information on electronic capture of PROs.

PRM54

USEFULNESS OF A COMMERCIAL HOSPITAL CLAIMS DATABASE TO IDENTIFY CURRENT ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR TREATMENT PATTERNS IN PATIENTS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION IN JAPAN

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OBJECTIVES: Access to large-scale public health claims databases is limited due to privacy concerns and lack of a unique identifier in Japan. Since such databases were not originally designed for outcomes research, we assessed the usefulness of one of the commercial databases in identifying treatment patterns in routine clinical practice. **METHODS:** Treatment patterns for patients with exudative age-related macular degeneration (AMD) using anti-vascular endothelial growth factor (anti-VEGF) was selected as an example to enhance our understanding of real-world clinical practice. A retrospective open-cohort study of patients diagnosed with AMD and treated from January 2010 to December 2012 at community hospitals employing Diagnostic Procedure Combination payment system was conducted by using hospital claims database provided by Medical Data Vision, Co., Ltd. Strengths and weaknesses of using the database were also identified. **RESULTS:** During the study period, 248 patients were diagnosed with AMD and received ranibizumab, 19 patients received pegaptanib, and two patients received aflibercept. Among the patients who received ranibizumab, the average number of ranibizumab injections per year was 3.21±2.38. The strength of the database was granularity of data including daily medication and medical procedural histories that allow us to obtain key parameters of analyzing treatment patterns. A major weakness was no unique identifier for patients; thus, a patient would be recorded as two different entries in the database if s/he visited two different hospitals. **CONCLUSIONS:** The results show that the commercial hospital claims database was useful to understand treatment patterns of exudative AMD at non-university hospital settings. Since treatment guidelines are usually written based on published clinical trial evidence, this type of database research provides an understanding of real life clinical practice and its associated patient outcomes, contributing to better adherence and future updates of treatment guidelines.

PRM55

COMPARISON OF THE PRICES USED IN THE MANUFACTURERS' BUDGET IMPACT ANALYSES AND THE PRICES FROM REIMBURSED DRUGS LIST

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OBJECTIVES: To compare official prices and refunding limits of the selected drugs with the prices and limits used in the manufacturers' Budget Impact Analyses (BIAs) submitted in the reimbursement applications and in the manufacturers' documentations from request for removing, altering the level or method of financing of medicines to AHTAPol and to verify the accuracy of their assumptions. **METHODS:** Prices and limits proposed in BIAs in years 2007-2011 and official prices and limits for the same medicine were compared. Only BIAs for medicines which had been reimbursed for at least one year were included in the analysis. The official prices and limits were obtained from reimbursed drugs list published in Ministry of Health's Orders. **RESULTS:** In the studied period, 72 drugs were included in the analysis. Among them, 51,39% (37/72) were from reimbursement applications and 48,61% (35/72) were from requests for removing, altering the level or method of financing of medicines, respectively. As a result, 13% (9/72) of the prices proposed in the BIAs were underestimated. Median and mean difference (MD) between official prices and prices used in BIAs for the same medicine were 95% and 91% respectively. The overestimation was found in 39% BIAs (28/72); median = 117%, MD = 124%. Rest of the prices were equal 49% (35/72). Limits were underestimated in 8% (6/72) of the BIAs. Median and mean difference between official prices and prices used in BIAs were 97% and 98% respectively. Overestimation of the limits was found in 57% (41/72) of the BIAs; median = 133%, MD = 117%. Rest of the limits were equal 35% (25/72). **CONCLUSIONS:** Among the contradictory prices and limits official ones were higher than the prices assumed in BIAs for the same medicines. There is a strong need for further research.

PRM56

DEVELOPING A PUBLICATION STRATEGY IN THE CONTEXT OF OUTCOME RESEARCH: A REVIEW OF THE LITERATURE

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OBJECTIVES: Many public health decisions are made based on information contained in medical publications. Therefore developing a publication strategy is a benefit for the pharmaceutical industry as it ensures an efficient dissemination of drug efficacy and safety evidence and an ethic development of the publications. In the context of outcome research, a publication strategy should take into consideration specific aspects related to the field (e.g., dealing with local, regional and global levels) and is important to ensure that unbiased information is provided to medical decision makers on time for the good of public health. A literature review was conducted to investigate if published guidelines on the development of a publication strategy in the context of outcome research exist. **METHODS:** A literature search of English articles was conducted on MEDLINE and Scopus. Search terms included "publication strategy" OR "publication planning" OR "publication coordination" AND "health economics" OR "health outcome" OR "outcome research" OR "medical economics". Independent extraction of articles was performed using predefined data fields. **RESULTS:** The search provided four citations; all were discarded after reviewing the abstracts. However, a simple search for the keywords "publication strategy" OR "publication planning" returned 85 hits in fields as various as psychology, political science, environmental science and medicine. None of the citations was specific to outcome research. **CONCLUSIONS:** The results of the literature search showed that the development of a publication strategy is an important concept through many different domains. However, no published guideline on the development of a publication strategy in the context of outcome research was found. A publication strategy specific to outcome research publications will be presented including recommendations regarding the key aspects that should be covered in an efficient outcome research publication strategy such as a critical assessment of published literature, identification of gaps, and development of a strategic plan.

PRM57

TELLING THE INSIDE STORY: ACTIVITY AND PERFORMANCE METRICS FOR A TYPICAL INTERNATIONAL MULTI-LANGUAGE MULTI-CENTER NON-INTERVENTIONAL STUDY WITH THE INTRIAL DATA CAPATURE SYSTEM

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OBJECTIVES: Getting insight into the technical and logistical challenges of a typical global non-interventional EDC study by analyzing the pure log file numbers: from application scalability to data handling and processing. **METHODS:** To analyze EDC activity and performance metrics, a global oncological observational study managed via the INTrial EDC application was selected. System log files were used for quantitative and qualitative performance/workflow-related aspects and time measurements. **RESULTS:** Study parameters: The study ran for 4 years and was conducted in 39 countries with 6 languages, 382 sites, 3395 patients and 1612 users. The electronic Case Report Form for a single patient consisted of up to 2513 fields with a total number of 1,574,627 filled-in fields for the whole study. 24,382 translations were imported into the EDC system. Using 845 possible system queries per patient, 163,703 of these were commented and resolved, 30,451 manual queries were inserted. In total, 4,938,215 page calls took place for reading purpose and 582,052 for writing purpose (average of 3,781 page calls per day, 2.6 calls per minute). 6,060,981 field entries or changes (value or status) were carried out (average: 4,151 changes per day). Performance: Time between real data collection and data entry by site: 25% within 5 days, 22% from 6 to 20 days and 24% from 21 to 60 days. 92% of all manual queries had been commented by the site. Average time for resolving site comments for system queries: 29 days. Average time for translation processing: 19 days. **CONCLUSIONS:** A suitable technical system like INTrial can help to improve and optimize the study workflows. Easy to use data entry and data management functionalities and additional tools like multi language support, translation import or archiving are substantial – always in combination with a well trained and enthusiastic study team and established procedures.

PRM58

4-VALENT VACCINE PATIENTS – STATISTICAL ASSESSMENT OF A NEW ESTIMATION METHODOLOGY

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OBJECTIVES: The objective was to estimate the number of patients in Germany who received a 4-valent vaccine in 2011. This estimation was based on data collected through a sample of GP/Pediatrician practices (Vaccine Analyzer [VA] sample (0.43%; 1.13%). **METHODS:** The VA-sample was compared to the German population by age/gender. This comparison shows a disproportional distribution of the VA-sample. A disproportional sample distribution may result in biases of final estimates. Hence, we opted for a methodology to mitigate estimation biases that would result from a straight-forward projection methodology. The VA-sample was restricted to eligible practices. For the projection of the patient sample counts to the universe, a specific formula was used. The assumption is that the sampling ratio in terms of doses equals the sampling ratio in terms of patients. This assumption is theoretically valid as per medical recommendation one dose per patient shall be used. In summary, the estimation of total number of universe patients can be considered feasible from statistical point of view. **RESULTS:** The methodology to estimate total patient numbers is statistically valid and utilizes data sources in an efficient way. The assumption with regard to the conversion of patients into doses is in line with empirical findings. The stratified projection caters to disproportional distribution of VA-sample doctors. **CONCLUSIONS:** The usage of patient age information from the VA-sample is theoretically feasible. The empirical validation with independently sourced German Longitudial Prescription data of statutory insured patients shows differences, which is a certain weakness. As most vaccine-prescriptions are not patient-based the coverage is only 0.07% at paediatricians and 0.39% at GPs. However, VA-age distributions show an overall correlation of 80% which let the usage of VA-age distribution appears feasible. The suggested estimation method is methodologically sound and delivers results confirmed by observation, and statistically preferable to straightforward projection methods which are prone to bias.

PRM59

APPLICABILITY OF JAPANESE HEALTH CARE DATABASE TO CLINICAL TRIAL PLANNING FOR DYSLIPIDAEMIA DRUG

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OBJECTIVES: Clinical trial simulation (CTS) is encouraged to prevent clinical trials (CT) from failing. Health care database (HDB) is a potential source for baseline characteristics in CTS. The study evaluates, 1) overlapping between distribution of baseline characteristics extracted from Japanese HDB and also from two Japanese CTs for dyslipidaemia drugs, and 2) applicability of HDB as a sampling frame (SF) for baseline data in CTS for dyslipidaemia drug development. **METHODS:** We extracted data from MinaCare HDB which contains both insurance claims and health check-ups of people insured by employment-based insurances as of April 2013 and built two SFs according to eligibility criteria of the protocol in two CTs (Protocol-A and Protocol-B) conducted by Pfizer Japan Inc. Distribution of patient characteristics at screening, such as body mass index (BMI) and low density lipoprotein cholesterol (LDL-C) levels, were compared between SFs (n=1663 for Protocol-A, n=5011 for Protocol-B) from MinaCare HDB and CTs, for Protocol-A (n=165) and Protocol-B (n=459), respectively. **RESULTS:** For both two protocols, we found similar distribution of age, sex, weight, and BMI when comparing descriptive statistics (e.g., mean, standard deviation (SD)). However, LDL-C in CTs was higher than in SFs; e.g., in Protocol-A, patients without prescription for dyslipidaemia showed LDL-C (mg/dL) of 169.9±19.2 from the CT vs. 160.2±16.5 from the SF. Among the patients with prescription, LDL-C was 132.3±31.0 from the CT vs. 118.4±31.0 from the SF. A similar difference was observed for Protocol-B. This finding showed non-weighted sampling from the SF would cause biases in CTS. At the same time, this result suggested that various CTS's assumptions by weighted sampling might be useful. Further evaluation is recommended. **CONCLUSIONS:** The present study provides relevant information that there is considerable similarity in the demographics between SFs from Japanese HDB and Japanese CTs, suggesting usefulness of HDB with application of weighted sampling with CTS.

RESEARCH ON METHODS – Modeling Methods

PRM60

DOES IT MATTER? DISCOUNTING AND ITS ROLE IN ANALYSING THE COST-EFFECTIVENESS OF PREVENTATIVE INTERVENTIONS

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OBJECTIVES: The UK runs a human papillomavirus (HPV) vaccination programme for girls aged 12-13 years to protect them from cervical cancer (CC). When long-term health benefits such as these occur, with costs occurring at the outset, cost-effectiveness analyses are very sensitive to the discount rate used. In view of this, the National Institute for Health and Care Excellence (NICE) will consider analyses with discount rates of 1.5% for costs and outcomes. Therefore, we modelled the cost-effectiveness of vaccination with the AS04-adjuvanted HVP-16/18 vaccine (BV) compared with HPV-6/11/16/18 (QV) with discount rates of 1.5%. **METHODS:** A published lifetime Markov cohort model replicating the natural history of oncogenic and low-risk HPV infection was adapted to the UK and run for a cohort of 100,000 girls aged 12. Vaccine efficacy against vaccine-type and non-vaccine type HPV was obtained from each vaccine's respective clinical trials. Lifetime protection was assumed for both vaccines. Input data were obtained from the literature, public databases and expert opinion. All costs were updated to 2012 values and reflected an NHS perspective. The incremental cost effectiveness ratio (ICER) of vaccinating with the BV vs. the QV was evaluated. Sensitivity analyses were performed on key variables. **RESULTS:** The model estimated that compared with QV, BV saved an additional 277 CIN1 cases, 1,460 CIN2/3 cases, 53 CC cases and 23 deaths, but did not protect against 7,747 GW cases. Discounting at 1.5% results in +54 QALYs gained and £2.4 million saved. However, applying a discount rate of 3.5% results in -52 QALYs and £1.1 million saved. Sensitivity analyses showed results were robust. **CONCLUSIONS:** Applying a discount rate of 1.5% for both costs and outcomes focuses the appraisal on the long-term outcomes, such as CC and CC-death, of the vaccination programme, and to the finding that the BV was shown to dominate QV.

PRM61

INVESTIGATING THE VALIDITY OF THE UKPDS OUTCOMES EQUATIONS IN CURRENT CLINICAL PRACTICE

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OBJECTIVES: The UKPDS 68 equations are routinely used to assess the benefits associated with glucose control in type 2 diabetes mellitus (T2DM) cohorts. Their validity has been questioned because they were derived from a cohort of newly diagnosed T2DM subjects and diabetes management practices have evolved considerably. The objective of this study was to re-calibrate the equations to contemporary health care data and assess their continued relevance. **METHODS:** We utilized data from The Health Improvement Network (THIN) database over the period 1/1/2004 to 31/12/2009. We selected patients either aged > 64 years with HbA1c >7.5% and diabetes duration >10 years or aged >55 years with at least 1 established cardiovascular risk factor. Weibull survival equations were fitted to the following endpoints; myocardial infarction (MI), stroke, congestive heart failure (CHF), ischemic heart disease (IHD), amputation, blindness and end-stage renal disease (ESRD) using R. Missing data was modeled using multiple imputation. **RESULTS:** Data were available on 68,990 T2DM subjects meeting the inclusion criteria with mean age 66.1 years, 46% female, 8.8 years duration of diabetes; with mean body mass index (29.7m/kg^2), HbA1c (8.0%), systolic blood pressure (147.5mmHg), total cholesterol (5.1mmol/l) and HDL cholesterol (1.3mmol/l). Log hazards (standard error) associated with unit changes HbA1c were 0.097(0.011) for MI, 0.084 (0.008) for CHF, 0.051 (0.009) for stroke, 0.112(0.02) for blindness, 0.043 (0.007) for ESRD and 0.225 (0.017) for amputation. These estimates were statistically consistent (at the 95% level) with the original UKPDS log hazards except for IHD (non-significant in the THIN database) and ESRD (non-significant in UKPDS). **CONCLUSIONS:** In general, the UKPDS equations retain their validity for assessing the relationship between HbA1c and macrovascular and microvascular complications. It is likely that use of UKPDS equations will overestimate the incidence of IHD and under-estimate the incidence of ESRD.

PRM62

VARIANCE REDUCTION THROUGH ANTITHETIC VARIATES AS A MEANS OF DEVELOPING COMPLEX VBA MODELS WITH REASONABLE COMPUTATION TIMES

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OBJECTIVES: Modelling chronic conditions such as diabetes necessitates the development of complex models, raising issues of computational intensity and execution time. While the use of compiled languages such as C++ is more computationally efficient, concerns may exist regarding their transparency compared to commonly used VBA in Microsoft Excel. This study investigates the application of antithetic variates to the pseudo-random numbers of Monte Carlo simulation, to provide reductions in stochastic uncertainty, through the introduction of negatively correlated pairs of simulation replicates, as a means of developing complex VBA models with reasonable computation times. **METHODS:** A

simulation model of type 2 diabetes, based on the UKPDS 68 outcomes equations, was executed with and without the application of antithetic variates. The impact of the technique was evaluated through comparison of total cost and benefit estimates, predicted over a long-term horizon of 40 years. **RESULTS:** An approximate four-fold reduction was observed in the Monte Carlo Error (MCE) associated with estimated mean incremental costs and benefits, when antithetic variates were applied over 1,000 simulations of 1,000 individuals. For a fixed number of runs (1,000), the number of replicated individuals required to achieve 99% accuracy (MCE/mean<1%) in incremental cost and benefit estimates fell from approximately 500 and 550 respectively, to fewer than 50 with antithetic variates. Similarly, for a fixed cohort size (1,000) the same level of precision was produced with fewer than 10% of the simulation runs required otherwise. **CONCLUSIONS:** The use of antithetic variates can improve the precision of modelling output; reducing the number of simulation runs and thus computation time required to perform analyses. The use of such variance reduction techniques should be pursued in the simulation of chronic conditions, as a means of achieving manageable run times and facilitating the extensive scenario and sensitivity analyses required as part of economic evaluations.

PRM63

MODELLING THE ADENOMA AND SERRATED PATHWAY TO COLORECTAL CANCER (ASCCA)

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OBJECTIVES: Most models developed for colorectal cancer (CRC) screening evaluations are based on the adenoma-carcinoma pathway only. Currently, there is increasing evidence that serrated lesions can also develop into CRC. This study aimed to develop a model that reflects both the adenoma-carcinoma pathway and the serrated pathway to CRC and that includes characteristics of polyps. **METHODS:** The Adenoma and Serrated pathway to Colorectal CAncer (ASCCA) model was built using the scientific literature, expert opinion, data from the Dutch COCOS trial and Dutch cancer registry data. A flexible model structure was chosen to examine the impact of two alternative natural history assumptions: (i) all CRCs arise from adenomas and (ii) 15% of CRCs arise from serrated lesions. The two model versions were calibrated manually using a systematic, step-by-step approach. **RESULTS:** Calibration resulted in 19 parameter sets for the adenoma-carcinoma pathway and 13 for the serrated pathway, matching the age- and sex-specific adenoma and serrated lesion prevalence in the COCOS trial and several other intermediate model outcomes. For the first natural history assumption, progression rates from advanced adenoma to CRC between 1.6% and 2.7% were found to produce model-based age-standardized incidence rates within the 95% confidence interval of the Dutch incidence in 2009. For the second assumption, these progression rates were between 1.3% and 2.2%. Mean duration from adenoma to CRC was 24 years. **CONCLUSIONS:** The ASCCA model will be used to evaluate the (cost-)effectiveness of different screening and surveillance strategies for CRC. Future analyses will evaluate the upcoming Dutch screening program using the two calibrated model versions. The implication of different test accuracies for different types of polyps with their characteristics can be taken into account in a straightforward manner. Furthermore, the impact of structural as well as parametric assumptions concerning the serrated pathway can be addressed.

PRM64

MICROSIMULATION OR COHORT MODELLING? A CASE STUDY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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OBJECTIVES: Markov models are commonly used to study time dependent disease progression. While most models are cohort based, due to their limitation of dealing with heterogeneities, continuous variables, and dynamic strategies, individual-based microsimulation is being increasingly used. The objective was to compare microsimulation to cohort approach in modeling COPD, while validating the two approaches against findings from TORCH trial. **METHODS:** We developed both models to study COPD progression in a cohort defined by the characteristics of TORCH patients. The microsimulation randomly generated a large number of patients and tracked each patient's the lung function (FEV1), exacerbations, and mortality, based on individual's characteristics and disease history. The cohort model included four COPD stages and death; it modeled exacerbations as events, assuming no impact on transitions or future exacerbations. Both models were populated by published data and results were compared against TORCH findings. **RESULTS:** The mean decline in FEV1 over 3-year was 126 ml in microsimulation, 49 ml in cohort model, compared to 117 ml in TORCH. The annual rates of moderate and severe exacerbations were 0.94 and 0.18 in microsimulation, 1.12 and 0.18 in cohort model, compared to 1.13 and 0.19 in TORCH. The 3-year mortality was 17.4% in microsimulation, 12.2% in cohort model, and 15.2% in TORCH. Microsimulation required simulating at least 3500 patients to obtain stable estimates, which took 4 minutes to run each scenario. It would take 300 hours to run 5000 scenarios for sensitivity analysis, while the cohort model took less than 1 minute. **CONCLUSIONS:** In COPD, patient heterogeneity and disease history can be conveniently captured in microsimulation, while parameter uncertainties are easily assessed using cohort approach. The cohort approach is simple to develop, but its inherent Markovian property cannot fully represent COPD pathology. Microsimulation is flexible in mimicking COPD progression, but it is computational expensive.

PRM65

SIMULATING PATIENT POPULATIONS – DIFFICULTIES IN CONTROLLING THE ROLL OF THE DICE

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OBJECTIVES: In developing probabilistic models to analyse cost-effectiveness, it is possible to control many model parameters using random seeds so that output differences should be due to the interventions being modelled rather than due to chance differences in the model parameters. However, at the point of intervention, the simulated patient effectively enters a parallel universe where outcomes may legitimately be better or worse irrespective of the intervention. The purpose of this study was to present an example of reduced health outcomes contrary to expectation. **METHODS:** Using a model developed to evaluate the impact of different MRI-based breast cancer surveillance strategies, the total benefits measured for individual simulated patients were compared between surveillance and no surveillance. Random seeds were used to ensure model parameters were matched between different model runs. Model structure ensured that later detection of cancer could not be associated with a better outcome. For breast cancer occurrence, random seeds were matched until the first incidence. Individuals could have multiple cancers. **RESULTS:** Across 7 surveillance strategies, compared to a situation of no surveillance, life expectancy was unchanged for between 97.7% and 99.0% of individuals. Depending on the surveillance strategy, between 0.98% and 2.2% of individuals had increased life expectancy, and between 0.04% and 0.1% of simulated individuals experienced a reduced life expectancy. A larger number of individuals had reduced life expectancy due to surveillance, but this is attributable to the detection of DCIS which does not always develop into invasive cancer. **CONCLUSIONS:** When comparing interventions using probabilistic models, chance variation can result in poorer outcomes despite the intervention. Although these anomalies are not apparent in summary figures as there may be an "on average" benefit, their occurrence is legitimate and should not be artificially prevented.

PRM66

ADHERENCE TO DISEASE-SPECIFIC RECOMMENDATIONS FOR PHARMACOECONOMIC STUDIES IN RHEUMATOID ARTHRITIS

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OBJECTIVES: Previous research has demonstrated wide varieties in modelling methods of pharmacoeconomic (PE) studies focussing on biological drugs for the treatment of rheumatoid arthritis (RA). To eradicate this variety, disease specific guidelines were presented in 2002 by OMERACT-ILAC. The objective of this study is to assess whether recently published PE studies adhered to these recommendations. **METHODS:** A literature review was conducted for PE studies evaluating TNF-α inhibitors use in RA. Four different databases (e.g. Embase, NIHR-EED) were searched for PE studies published that focus on Adalimumab between October 2003 and May 2013. Methodological quality of included studies was checked against the CHEC-checklist. Data extraction forms were used to retrieve information such as study outcomes (QALY's, costs, ICER) and modelling methods and parameters (e.g. time horizon, sources for costs and effectiveness data). Finally, information retrieved from all studies was compared to recommendations proposed by the OMERACT-ILAR guideline to assess adherence to these recommendations. **RESULTS:** Nine studies were identified that met all inclusion criteria and were included in our analysis. All studies met at least 12 of the 19 items of the CHEC checklist for quality and 3 studies met all 19 items. Study outcomes varied considerably in QALY's calculated, costs and ICER's. Patient subtypes, modelling methods, sources for cost and effectiveness data also varied significantly. Only 2 of the 12 recommendations published in the OMERACT-ILAR guideline were unanimously implemented in all 9 studies of our review. Only 1 study was found to contain all elements of guideline recommendations, albeit with some limitations **CONCLUSIONS:** We demonstrate that modelling methods still widely differ and adherence to disease-specific guidelines for the conduct of PE studies in RA is very low. Development of strict disease-specific guidelines in RA and subsequent adoption by re-imbursement agencies is vital to ensure comparability,validity and credibility of future PE studies.

PRM67

MODELING A SWITCH FROM TRIVALENT TO QUADRIVALENT INFLUENZA VACCINE IN CANADA AND THE UNITED KINGDOM

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OBJECTIVES: Current trivalent influenza vaccines (TIVs) contain only one of the two currently circulating influenza B lineages (Victoria and Yamagata). Worldwide, in about half of all influenza seasons since co-circulation of the two B lineages commenced, the dominant B lineage did not match the one chosen for inclusion in the TIV. Quadrivalent influenza vaccines (QIVs) would help address this problem by including both B lineages each season. We modeled the impact of a country-wide switch from TIV to QIV on the yearly population-wide rates of influenza cases and influenza-associated events, in both Canada and the UK. **METHODS:** We calculated projections using a dynamic transmission model which incorporates four interacting influenza strains, transmission-rate seasonality and age-specific mixing within the population, run over a 40-year time horizon. Influenza vaccine coverage rates in Canada and the UK were taken from public sources, TIV efficacy was obtained from a meta-analysis (Tricco et al., in press), and QIV efficacy was assumed to be similar to TIV without B lineage mismatch. **RESULTS:** Across Canada, the model estimates that a switch from TIV to QIV would, in an average influenza season, avert 9% (relative) of influenza cases (=237,000 cases), 9% (=86,000) of general practitioner (GP) visits, 9% (=12,000) of emergency room (ER) visits, 8% (=2,500) of hospitalizations, and 7% (=330) of deaths. Across the UK, the model estimates that 0.7% (=70,000) of influenza cases, 0.8% (=19,000) of GP visits, 0.8% (=600) of ER visits, 0.8% (=800) of hospitalizations, and 3% (=270) of deaths would be averted. **CONCLUSIONS:** In both Canada and the UK, a country-wide TIV-QIV switch is predicted to bring about a clear reduction in the burden of influenza. The relatively greater impact of the switch in Canada is due principally to that country's higher vaccine uptake among people younger than 65 years.

PRM68

HEALTH ECONOMIC ANALYSIS OF PNEUMOCOCCAL VACCINATION – EXAMPLE FROM BULGARIA

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OBJECTIVES: To evaluate cost-effectiveness of pneumococcal vaccination of children with 10-valent (PHiD-CV) compared with 13-valent pneumococcal conjugate vaccine (PCV-13). **METHODS:** A Markov cohort model which simulates in a Bulgarian birth cohort the disease process of invasive disease (ID) (meningitis and bacteremia), community acquired pneumonia (CAP), and acute otitis media (AOM) over life-time caused by S. pneumoniae and non-typeable Haemophilus Influenzae (NTHi). The cohort model essentially considers the perspective of the health care payer. Bulgarian specific epidemiological and demographic data and data from other country sources were obtained for the model. Base case assumptions include estimates of pneumococcal and NTHi infection rates as well as vaccine efficacy based on published literature, 94% vaccine coverage, herd protection and a (3+1) vaccination schedule. One-way sensitivity analyses performed to assess the impact of changes in key model assumptions. **RESULTS:** PHiD-CV and PCV-13 are projected to prevent 29.4 and 29.9 cases of invasive diseases respectively and 437 and 434 bacteremia hospitalizations respectively . PHiD-CV in comparison with PCV-13 is projected to prevent additional 9393 cases of AOM, 426 myringotomies and 2801 GP visits. Vaccinating a birth cohort with PHiD-CV is expected to generate 41 more QALYs compared to PCV-13. The estimated total savings for health care system are 1.77 mil Euro. The PHiD-CV is dominant in comparison with PCV-13. Sensitivity analyses indicate that GP visits for AOM and efficacy vs. AOM due to Streptococcus Pneumonia non-Vaccine Types Sp nVT have biggest impact on results. **CONCLUSIONS:** Overall, PHiD-CV is expected to have betterI impact and under the given assumptions, PHiD-CV dominates PCV-13 because it also has a larger cost offsets.

PRM69

CORRELATING COST EFFECTIVENESS OUTPUT WITH PATIENT LEVEL DATA INPUT VIA THE IMS CORE DIABETES MODEL (CDM)

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OBJECTIVES: Analysing patient level data (PLD) within cost-effectiveness (CE) models offers the potential to better understand patient profiles associated with greatest health economic benefit. The objective of this study was to contrast the application of average treatment efficacy profiles compared to patient level treatment efficacy in assessing the CE of insulin glargine (IG) versus Neutral protamine Hagedorn (NPH) in Type 2 diabetes mellitus (T2DM) **METHODS:** This study used the IMS Core Diabetes Model (CDM), a validated and established diabetes model to evaluate the CE of switching to IG from NPH using published effectiveness data from a large population based cohort. Average HbA1c reduction after switching from NPH was -0.18% and weight gain was 0.5kg. Annual diabetes specific therapy cost was £573 (IG) versus £320 (NPH). A PLD extract was obtained from NHANES and the CE of IG versus NPH assessed applying (a) overall mean treatment effects (MTE) and (b) baseline HbA1c, BMI and sex adjusted treatment effects (ATE). Costs (2012 UK£) and benefits were discounted at 3.5%. **RESULTS:** For the MTE and ATE scenarios, the incremental cost effectiveness ratio (ICER) was £28,925 and £57,279 respectively. For MTE scenario, 765 (41.1%) of subjects were CE at the £20,000 willingness to pay (WTP) and 47 IG subjects (6.1%) were both cost saving with increased health benefit. Using ATE, 525 (28.2%) were CE at the £20,000 WTP threshold with 164 (31.2%) of IG subjects identified as both cost saving with increased health benefit. The odds ratio (OR) of being both cost saving with greater health benefit was significantly associated with age, OR=0.89(0.87-0.93) and baseline HbA1c, OR=6.11 (4.64-8.03). **CONCLUSIONS:** The identification of patient characteristics associated with greater potential for health gain and reduced cost is an important goal. The analysis of PLD alongside simulation model output provides an additional mechanism for informing health care decision-making.

PRM70

COMPARISON OF MARKOV AND DISCRETE EVENT SIMULATION MODELING TECHNIQUES WITH APPLICATION TO COST EFFECTIVENESS ANALYSES

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OBJECTIVES: To assess the bias introduced to absolute costs, absolute QALYs and the incremental cost effectiveness ratio (ICER) associated with Markov models, compared with discrete event simulation (DES) models. To investigate how such biases are a function of cycle length and half-cycle correction. **METHODS:** A hypothetical three health state model was constructed using both Markovian and DES approaches. Costs and utility were assigned to each health state and the ICERs between two treatment strategies were estimated. Six Markov models using different cycle lengths (1 month, 3 month, 1 year), and with and without half cycle correction were constructed. Differences in the absolute costs and QALYs generated between each Markov model were compared with the DES approach and the ICERs generated by each model were compared. **RESULTS:** Markov model simulation was shown to introduce biases in the absolute costs and QALYs when compared with a DES approach. The bias was related to the duration of the time cycle with the results converging to the DES values as the time cycle was reduced. The initial bias in cost fell from 14% to less than 1%; QALY bias was consistently below 1%. The ICERs show bias between 2.4% and 9.6% when using a 1 year cycle and between 0.6% - 5.4% when using a 1 month cycle. The half-cycle correction reduced absolute bias between 2% - 10%, the ICERs were not affected. The time cycle duration was the primary parameter in reducing bias. **CONCLUSIONS:** Markov models introduce bias due to the simplifying assumptions of fixed cycle length and half cycle correction; DES models do not suffer the same biases. It is suggested that when the ICERs produced are close to the Willingness to Pay threshold, Markov models should be analyzed with shorter cycle length or a DES approach adopted to ensure conclusions are robust.

PRM71

MODEL-BASED ECONOMIC EVALUATIONS IN ALZHEIMER'S DISEASE : A REVIEW OF MODELING METHODS

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OBJECTIVES: To review the modeling-based economic evaluations (MB2E) of acetylcholinesterase inhibitors (ACE) and memantine (MEM) used in the field of Alzheimer's disease (AD). **METHODS:** A systematic literature search was carried out based on several electronic databases such as Medline or the Cochrane Library up to November 2012. Modeling frameworks used to depict the natural history of AD and incorporation of treatment effects were qualitatively described and compared. **RESULTS:** More than thirty MB2E were identified with several local adaptations based on ten original modeling frameworks. First published MB2E were either Markov state-transitions models or partition failure time survival models while most recent MB2E relied on discrete events simulations. The hallmark of the disease, the cognitive dimension, was first introduced to model the disease progression mainly based on the Mini Mental State Examination (MMSE) scale. The two other fundamental-functional and behavioral-dimensions were taken into account as a second step. Models relied on distinct clinical milestones and risk equations to extrapolate intermediate clinical endpoints from clinical trials (mainly on cognition and function) into long-term final endpoints. These latter were delay in severity, loss of patient autonomy, institutionalization, burden of care and quality-adjusted life years. Differences occurred as well on the way inter-patient heterogeneity was incorporated with a trend towards more micro-simulations technics. Eventually, predictors and inter-relations between the several dimensions of the natural history of the disease seemed not to be fully captured in the model structures with challenging needs to assess the resulting potential biases. **CONCLUSIONS:** Advanced modeling methods in the field of AD were being introduced to better capture the continuous, progressive and multivariate natural history of AD. Further work is warranted given the emerging early diagnosis technics, neuropathological biomarkers and targeting therapies.

PRM72

THE COST-EFFECTIVENESS OF SEQUENTIAL FIRST- AND SECOND-LINE TREATMENTS IN METASTATIC RENAL CELL CARCINOMA USING REAL-WORLD DATA AND A PATIENT-LEVEL SIMULATION MODEL

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OBJECTIVES: Previous cost-effectiveness analyses of targeted therapies in metastatic renal cell carcinoma (mRCC) have been based on randomised trials and evaluate just one single treatment-line. The aim of this study was to estimate the real-world cost-effectiveness of sequential first- and second-line treatments for patients with mRCC using a patient-level simulation (PLS) model. **METHODS:** Based on patient-level data from a Dutch population-based registry, a PLS model was developed that comprised entities (i.e. patients with mRCC), attributes assigned to the entities (i.e. prognostic factors), and events (i.e. second-line treatment or death). Patients were repeatedly simulated from the model and time-to-event was estimated using a lognormal distribution. A separate sampling process was used to determine which type of event occurred. Time to death following second-line treatment was modelled using a Weibull distribution. Lifetime health care costs were modelled using patient-level data from the registry. **RESULTS:** In current daily practice, 50% (341/686) of patients did not receive any targeted therapy and 42% (291/686) received sunitinib as first-line therapy. In the second line, 31% (33/107) were treated with sorafenib and 31% (33/107) with everolimus. Mean overall survival (OS) was 13.6 months and mean costs were €69,622 for all patients. In a strategy where all patients are treated according to clinical guidelines, mean OS was 15.2 months and costs were €91,059. This meant an increase in OS (1.6 months) and costs (€21,437) compared to current practice, with an incremental cost-effectiveness ratio of €159,107 per life-year gained. Probabilistic sensitivity analyses showed the robustness of these results. **CONCLUSIONS:** A complete disease model and real-world data are essential in estimating real-world cost-effectiveness. Our PLS model allows comparisons between treatment strategies spanning multiple treatment lines, which will ultimately help to reveal the optimal strategy. For example, guidelines-based treatment appears to increase both OS and costs compared to current daily practice.

PRM73

THE ROLE OF SIMULATION MODELING IN PLANNING LONG-TERM CLINICAL TRIALS IN TYPE 2 DIABETES

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OBJECTIVES: Long-term cardiovascular outcomes studies are routinely undertaken to demonstrate safety in all new diabetes therapies. Given that diabetes models are extensively validated to contemporary outcomes trials they offer the potential to inform on design of new trials. The objective of this study was to use an established diabetes model to explore the relationship between levels of glycaemic control, major adverse cardiovascular events (MACE) and sample size. **METHODS:** The IMS CORE Diabetes Model (CDM) a validated and widely used simulation model was initiated with patient level data (PLD) drawn from NHANES. The model was run with a five-year time horizon and the sample sizes required to detect a difference in MACE (defined as myocardial infarction, stroke or CV death) at the 5% level as a function of change in HbA1c evaluated. **RESULTS:** PLD from NHANES was available on 1853 subjects with mean (SD) age 63.6(12.1) years, 53% male, duration of diabetes 9.6(8.5) years, baseline HbA1c 7.4% (1.8), systolic

blood pressure 134.9mmHg (22.0) and total cholesterol of 189.8 mg/dl (48.7). The expected five-year cumulative MACE event rate was 9.2% and HbA1c reductions of 0.5%, 1.0% and 1.5% produced relative risk reductions of 7.5%, 9.0% and 10.6% respectively. At the 5% level, the number of patients required to detect a significant reduction in MACE events was 17,786, 11,758 and 1,912 for HbA1c reductions of 0.5%, 1.0% and 1.5% respectively. On average, each half-unit change in HbA1c required an additional 7,937 subjects to detect a significant difference in MACE event rate. **CONCLUSIONS:** Given the requirement to extensively validate health economic models to contemporary outcomes studies it is an obvious extension to use these models to inform on the design of clinical trials. These models offer considerable flexibility in the evaluation of sample size requirements in terms of expected changes in modifiable risk factors.

PRM74

DEVELOPING REALISTIC PATHWAYS IN COST-EFFECTIVENESS MODELS FOR PSORIASIS: WHAT TO DO WHEN A BIOLOGIC FAILS

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OBJECTIVES: Clinical studies indicate switching to a second biologic or combination therapy with an immunosuppressant after failure of first biologic can be effective in patients with moderate to severe plaque psoriasis not responding to the first biologic. **METHODS:** A systematic literature review was performed to assess treatment pathways included in cost-effectiveness (CE) estimates of biologic treatments of moderate to severe psoriasis and compare these pathways with those recommended in psoriasis treatment guidelines. **RESULTS:** Twenty-one CE modeling studies were identified. Of these 10 estimated incremental cost per responder for >=1 biologics over time horizons varying from 12 weeks to 18 months. Treatment pathways were considered not relevant in these studies. In 11 studies with time horizons up to 10 years where treatment pathways were considered, 5 studies included a switch to non-systemic therapy or best supportive care after failure of the initial biologic. In 6 of 11 studies, failure of the initial biologic was followed by monotherapy with a second-line biologic - one of the recommendations in current treatment guidelines. In only 1 of 6 studies that considered treatment sequencing was the efficacy of the second-line biologic adjusted downwards compared to first line treatment. None of the cost-effectiveness analyses included dose titration with the first-line biologic or combination therapy with a biologic plus methotrexate or phototherapy after failure of the first-line biologic as recommended in some treatment guidelines. **CONCLUSIONS:** In most long term CE studies, failure of the first biologic was followed by biologic monotherapy of the second, without efficacy adjustment. Some treatment guidelines support dose titration or combination treatment after failure of a first-line biologic. Nevertheless, these options were not included in the published CE models with time horizons up to 10 years. For decision makers there may be a need for more extensive models where such strategies are allowed.

PRM75

DECISION ANALYTIC MODELS USED IN ESTIMATING THE COST-EFFECTIVENESS OF DRUG-ELUTING STENTS VERSUS BARE-METAL STENTS: A SYSTEMATIC REVIEW

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OBJECTIVES: Drug-eluting stents (DES) and bare-metal stents (BMS) are both used widely in percutaneous coronary interventions. However, cost-effectiveness analyses of DES versus BMS conflict about whether the reduction in repeat revascularizations of DES versus BMS offsets the initial higher treatment costs of DES. A systematic review was performed to examine whether modelling methods influenced the cost-effectiveness of DES versus BMS. **METHODS:** We reviewed modelling studies published until January 2012 that compared the costs and consequences of DES versus BMS. General information (e.g. funding) and modelling methods used, related to the framing of the economic evaluation (e.g. population and intervention characteristics, time horizon) and parameterisation of the models were extracted from the relevant studies for each of the individual analyses performed in the studies. Associations between these characteristics and the incremental costs and effectiveness were explored using regression analysis. We also examined whether the results were associated with the quality of the models based on the Philips et al. (2006) checklist. **RESULTS:** Fifteen eligible studies accounted for 498 separate analyses, in which the incremental cost-effectiveness ratios ranged from DES being dominated by BMS to DES being dominant. The most important predictors significantly associated with these differences were several population and procedure characteristics, funding and assumptions concerning stent efficacy. The results and conclusions of individual studies corresponded with the findings of this meta-level systematic review. Overall quality of the models was moderate (55%±17%) and significantly negatively associated with repeat revascularizations avoided. **CONCLUSIONS:** Models are important to obtain valid estimates of the cost-effectiveness of DES versus BMS, and framing decisions (e.g. time horizon) and quality of the models both influence incremental costs and effects. The most influential parameters are identified with this systematic review and we showed the need of examining those parameters and of performing a quality check when interpreting the results.

PRM76

EXPLORATORY STRUCTURAL EQUATION MODELS: A SIMULATION STUDY EXPLORING GEOMIN AND TARGET ROTATION TECHNIQUES ON VARIATIONS OF ESEM MODELS

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OBJECTIVES: This simulation study evaluates the impact of Geomin and Target rotation criteria on factor loading matrices in the recently developed exploratory structural equation models (ESEM), a method that can be considered a strong alternative to the exclusive use of exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) in patient related outcomes measurement. By combining the steps of EFA and CFA in one unified approach, ESEM saves significant time and effort usually invested in separate iterations of EFA and CFA. **METHODS:** One hundred replications of ESEM models were carried out for variations of sample size and latent factors. *Simulation study 1* examined the behavior of ESEM parameter estimates by changing the values of rotation constant (0.01, 0.001 and 0.0001) in Geomin rotation for a *three-factor single group* model and for N=300 and 1000. Simulation study 2 evaluated the behavior of ESEM parameter estimates for multi-group models using three- and four-factor models for N=150 and 500 per group. Bias, Mean Square Errors (MSE) and standard errors were used to evaluate accuracy of parameter recovery. Item parameters were generated from 27 items belonging to a pilot graduate creativity instrument. **RESULTS:** For study 1, Geomin rotated parameter estimates of factor loadings, means and covariances produce higher MSEs than the follow up Target rotations. In study 2, the parameter estimates for ESEM Geomin show small sample size bias for some parameters while the standard errors produced correct coverage for all parameters under Target rotation method for large N=500 per group. **CONCLUSIONS:** Overall, there was accurate recovery of parameter estimates in the smallest sample of 300 especially in the multi-group models specifically when Geomin rotations were employed. This bodes well for analysis of real data and for the study of measurement invariance across groups. Future studies could include the examination of number of items affecting recovery of parameter estimates.

PRM77

METHODOLOGICAL APPROACHES FOR MODELING CARDIOVASCULAR EVENTS IN COST-EFFECTIVENESS ANALYSES BASED ON OUTCOME TRIALS

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OBJECTIVES: Historically, cardiovascular (CV) endpoints, including myocardial infarction and stroke, have often been included indirectly in cost-effectiveness analyses (CEA) based on surrogate endpoints from clinical trials, such as cholesterol levels, blood pressure or glycemic control. With the availability of outcomes trials sufficiently powered to show differences in CV endpoints, there is an increasing need to incorporate these data directly into CEA. This study investigated approaches available in the published literature for modeling CV endpoints directly based on outcomes data. **METHODS:** A systematic review of cost-effectiveness models for cardiovascular interventions published in the past 5 years was conducted in PubMed and Embase using a predefined search strategy. Only studies in English language directly integrating trial data on CV endpoints from randomized clinical trials were considered. For each study that met the inclusion criteria, clinical input characteristics and the modeling approach were summarized and evaluated. **RESULTS:** Twenty-three papers were identified for final review, including studies of antithrombotic, heart failure, and lipid lowering therapies. Methodologically, decision trees, Markov models (cohort and individual patient), discrete event simulations as well as hybrids of these approaches were used. Event rates were incorporated either as constant rates, time-dependent risks, or risk equations based on patient characteristics. Although potentially more accurately reflecting the trial data, risks dependent on time and/or patient characteristics were only used where feasible (major event rates >1%/year) and practical (models with fewer than seven health states). Models incorporating data from infrequent events or with numerous health states generally preferred constant event rates. **CONCLUSIONS:** When the risk of CV events is low and/or the disease state is explicitly modeled in detail, constant events rates were most common. For heterogeneous populations or when CV event risk is high, simpler model structures were generally accompanied by patient- or time-dependent event rates where permitted by the available data.

PRM78

TWO-WAY SENSITIVITY ANALYSIS: SHOWING THE IMPACT OF CORRELATED PARAMETERS IN COST-EFFECTIVENESS ANALYSES

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OBJECTIVES: Correlated parameters are a common feature in economic models, but no standard sensitivity analysis (SA) exists to show their impact on cost-effectiveness. The one-way SA only varies one parameter at a time and ignores correlation while the probabilistic SA is typically used to address overall uncertainty. The objective of this study is to propose a standard method for visualising the impact of one variable consisting of two correlated parameters in cost-effectiveness analysis. **METHODS:** A model evaluating the cost-effectiveness of a cancer product was used. Using the Cholesky decomposition, 1,000 correlated random draws were generated from the distributions of the intercept and slope of a linear function determining survival in the model. Each pair was inputted in the model to yield the percentage of simulations below accepted thresholds. Results were visualised using R in a scatter plot with both parameters on a separate axis. Shaded areas represented the percentage of simulations below accepted cost-effectiveness thresholds and an ellipse was added representing 80% of the simulated parameter combinations. A conventional one-way SA was performed for comparison. **RESULTS:** The one way SA found wide ranges of incremental cost-effectiveness ratios (ICER) for the intercept and slope parameters (£10,000 - £50,000 per QALY gained). The method described above found that 78% of the simulated pairs resulted in ICERs below £20,000 per QALY gained, and 93% in ICERs below £30,000. The scatter plot visualised the combined uncertainty and their impact on the ICER. A limitation is that the visualisation only allows for 2 correlated parameters. Also, the use of R to generate the graph complicates incorporation of this SA in Excel models. **CONCLUSIONS:** A method was demonstrated to show the impact of correlated parameters in cost-effectiveness analyses. This method may be especially helpful when assessing the uncertainty around parametric survival fits.

PRM79

ASSESSING THE SIGNIFICANCE OF HBA1C DURABILITY IN COST EFFECTIVENESS ANALYSIS OF 2ND LINE ORAL THERAPIES IN THE MANAGEMENT OF TYPE 2 DIABETES

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OBJECTIVES: Due to the progressive nature of type 2 diabetes mellitus (T2DM), therapy escalation or intensification is often required to maintain acceptable levels of glycaemic control. The objective of this study was to assess how differential dual therapy failure rates influence the cost effectiveness (CE) results in T2DM. **METHODS:** This study used the IMS Core Diabetes Model (CDM), a validated and established diabetes model, to evaluate the CE of metformin+ sulphonylurea (M+S) compared to metformin + DPP-4 (M+D). Efficacy data for dual therapy was sourced from a published systematic review; HbA1c and BMI change of -0.8% and 0.199kg/m^2 (M+D) and -0.79% and 0.707kg/m^2 (M+S) respectively were applied. Rates of severe hypoglycaemia were 0.1612 and 1.538 per 100 patient years and 4.596 and 68.769 per 100 patient years for non-severe events in M+D and M+S respectively. Insulin rescue therapy was initiated at an HbA1c threshold of 7.5%. Base case analysis assumed M+D and M+S had the same HbA1c durability; lifetime CE was assessed assuming improvement in durability favouring M+D applied in 10% increments with costs (US$) and benefits discounted at 3.5%. **RESULTS:** In the base case analysis, annual HbA1c increase was 0.26% with mean time to therapy escalation of 5 years; and a predicted cost per quality adjusted life year (QALY) of $211,948. Mean annual increments in HbA1c for M+D of 0.182%, 0.13% and 0.1% were necessary to achieve costs effectiveness at willingness to pay (WTP) thresholds of $100,000, $70,000 and $50,000 respectively. Published HbA1c durability for M+D of 0.052% per year was associated with a cost per QALY of $33,427. **CONCLUSIONS:** This analysis demonstrates that the annual rate of increase in HbA1c exerts considerable influence over predicted CE and is therefore an important variable to study when assessing the CE of new interventions for the management of T2DM.

PRM80

NUTRIECONOMIC EXPLORATORY ASSESSMENT OF A DAILY CONSUMPTION OF PLANT STEROLS-ENRICHED DAIRY PRODUCTS ON STATIN'S INITIATION DELAY: A CONSUMER PERSPECTIVE APPROACH

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The efficacy of plant sterols in reducing plasma LDL-cholesterol has been demonstrated. In 2009, the European Food Safety Agency stated that for an intake of 1.5-2.4g/day plant sterols, an average reduction of LDL blood cholesterol from 7% to 10.5% can be expected and such a reduction is of biological significance in terms of reduced risk of coronary heart disease. In France, the consumption of plant-sterols enriched products (PSEP) was part of the official dietary recommendations for hypercholesterolemic subjects when the study was designed. **OBJECTIVES:** The objective was to assess the cost-effectiveness of a daily consumption of PSEP, in the context of a healthy diet, on statin's initiation delay from the consumer perspective, in the *eligible*at risk French population. **METHODS:** A 1 year cycle Markov model was built to estimate the benefit (i.e. delay/avoid statins' initiation) in a French population aged between 45 and 65 years and at risk of drug treatment according to the French Drug Agency recommendations. Information on the evolution of cholesterol level and the different cardiovascular disease risk factors was retrieved in the literature. Costs of statin treatment duration avoidance (i.e. price of PSEP fully paid by the consumers) was estimated according to age and gender. **RESULTS:** The *eligible*population included in the model was respectively 49% and 66% among the French male and female population between [45;65 y]. Based on the selected assumptions, and assuming that healthy diet is already integrated in lifestyle habits, daily cost per statin free life year due to substitution of usual dairy product by a PSEP was estimated at 0.71€/day and 1.01€/day respectively for male and female. **CONCLUSIONS:** This exploratory work allowed getting a first estimation of the cost-effectiveness of the daily consumption of PSEP, from the consumer perspective in accordance with official dietary recommendations for cholesterol management.

PRM81

GENERATING THE COST-EFFECTIVENESS FRONTIER WHEN COSTS AND/OR BENEFITS ARE CORRELATED ACROSS STRATEGIES

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OBJECTIVES: The cost-effectiveness efficiency frontier is typically generated by plotting the costs and benefits for a variety of technologies, often summarised as the mean across a large number of simulations. However, the mean across simulations may mask correlations between technologies within simulations. We sought to investigate these issues using a HTA comparing 19 different interventions. **METHODS:** We compared 19 different breast cancer surveillance strategies for women aged less than 50 years with a BRCA1 mutation. We calculated the cost-effectiveness efficiency frontier for 5,000 simulations and also based on the mean costs and benefits for each strategy. We also investigated the probability of a strategy appearing on the frontier and correlations between whether or not different strategies appeared on the frontier. **RESULTS:** The efficiency frontier based on means included 6 strategies. This was the cost-effectiveness efficiency frontier in only 22 (0.44%) of 5,000 simulations. Forty four other frontiers were more likely to be generated by simulations. Two strategies not on the frontier of means had a substantial probability of being on the frontier. Some strategies were negatively correlated such that the appearance of one strategy on the frontier never or seldom co-occurred with another. These negative correlations also occurred between strategies that appeared on the frontier of means. **CONCLUSIONS:** The cost-effectiveness frontier generated by the average costs and benefits of each technology may mask inter-dependencies between technologies. Parameter values that render one technology efficient may render another inefficient, and vice versa. There can also be uncertainty about which interventions appear on the frontier, and the adoption of approaches to select competing interventions solely on the basis of being on the efficiency frontier may be unreasonable.

PRM82

VALIDATING AN INDOLENT NON-HODGKIN'S LYMPHOMA (NHL) COST-EFFECTIVENESS ANALYSIS MODEL USING TWO SOFTWARE TOOLS: KEY IMPLEMENTATION CONSIDERATIONS AND RESULTS

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OBJECTIVES: The ISPOR-SMDM Modeling Good Research Practices Task Force highlights the importance of model transparency and validation, including cross validation, as a means to establishing trust and confidence in economic models. (1) To investigate how a technical model validation can be conducted by reconstructing a previously-developed Microsoft Excel cost-effectiveness model using TreeAge; and, (2) to validate the model by comparing the results of two implementations. **METHODS:** An Excel-based cohort model on indolent NHL was reconstructed in in TreeAge using the same model structure, clinical inputs, and costing assumptions. Lifetime costs, life-years, quality-adjusted life-years, and incremental cost-effectiveness ratios (ICERs) were projected and compared for bendamustine-rituximab (Ben-R) versus fludarabine-rituximab (Fdb-R) in relapsed indolent NHL patients in Colombia. All costs were in 2013 Colombian pesos. The base-case results and sensitivity analyses were compared between the two software tools and key implementation considerations were identified. **RESULTS:** Key differences in the two software tools were identified and implementation differences will be described, including handling of survival inputs and application of one-time and per-cycle costs. The TreeAge model produced more favorable results compared to the Excel model. The total costs for Ben-R and Fdb-R were $223,400,660 and $208,115,352 in the TreeAge model, respectively, while in the Excel model they were $291,192,912 and $260,463,392. The ICERs were $11,582,974/LY and $13,815,417/QALY in the TreeAge model and $23,286,360/LY and $27,956,124/QALY in the Excel model. However, once the differences between the two models were accounted for in implementation, the reconstructed TreeAge model produced approximately the same results compared to the original Excel model (23,381,795/LY vs. $23,286,360/LY). **CONCLUSIONS:** There are inherent differences in model implementation in Excel vs. TreeAge that should be considered when performing double implementation and when interpreting the model results. Model validation using two software tools is a practical way to ensure proper and intended implementation.

PRM83

RELATIONSHIP BETWEEN MODELLING APPROACH AND REPORTED OUTCOMES: CASE STUDIES OF MODELS FOR THE TREATMENT OF SCHIZOPHRENIA

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OBJECTIVES: Different modeling approaches have been used to estimate the cost-effectiveness of antipsychotics used to reduce psychotic symptoms of schizophrenia. This study systematically reviewed schizophrenia modelling studies, to examine the relationship between the modeling approach used in schizophrenia studies and their reported outcomes. **METHODS:** A systematic literature review of MEDLINE, EconLit, Embase, and the Cochrane Library and an Internet search identified published results of schizophrenia modeling studies from 2000 to 2011. Two independent reviewers performed searches according to a prespecified protocol limited to English-language articles from any country. **RESULTS:** Eighty-three publications reported 80 individual modelling studies that met the inclusion criteria. Fifty-seven studies reported results of 71 pairs of antipsychotic drug comparisons (drug A vs. drug B) as incremental cost-effectiveness ratios (ICERs), such as cost per quality-adjusted life-year (QALY), which allowed a comparison of results. The majority of the economic evaluations used a Markov (23 studies) or decision-tree model 23 studies); 9 studies used a discrete-event simulation (DES) model, and 2 studies used a microsimulation model. Among the 11 comparisons with contradictory results, we focused on the following drug comparisons of atypical antipsychotics with the most studies: risperidone long-acting injection versus oral olanzapine, oral risperidone versus oral olanzapine, oral risperidone or oral olanzapine versus ziprasidone, and oral olanzapine versus oral aripiprazole. Overall, model structure, time horizon, and patient population did not affect study results. Differences among studies with contradictory results generally reflected definition of response and relapse rates in the health states, validity of clinical data sources for transition probabilities, and assignment of utilities to estimate QALYs. **CONCLUSIONS:** The cost-effectiveness results of the majority of models were in agreement regardless of the model structure. In models with contradictory results, most differences could be explained by definition of response, relapse, discontinuation, or adverse-event rates and/or by the selection of sources.

PRM84

LITERATURE REVIEW AND ASSESSMENT TO POPULATE A DECISION-ANALYTIC MODEL EVALUATING A NOVEL PROGNOSTIC IN EARLY LUNG CANCER

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OBJECTIVES: A novel prognostic test is being developed to predict cancer-related mortality in early non-small cell lung cancer (NSCLC) to inform the use of adju-

vant chemotherapy (ACT). The collection and assessment of data inputs for a U.S. economic model evaluating this prognostic will be reported. **METHODS:** Medline and Tuft's CEA Registry were searched for model parameters using the following terms and MeSH headings: NSCLC, adjuvant chemotherapy, recurrence, utilization, economics, cost, quality of life, utility, cost-effectiveness/-utility/-benefit. Inclusion criteria were randomized controlled trials (RCTs), meta-analyses, heath technology assessments, North American and European studies, quality of life analyses, and early lung cancer. Results were limited to full text and English articles. We also assessed relevant references listed in these articles. **RESULTS:** The search yielded one meta-analysis and 7 RCTs assessing ACT in resected NSCLC. These studies report survival (HR 0.75-0.95 favoring ACT), ACT toxicity (30-85% experiencing grade 3-4 toxicity), and stage distribution (Stage IA-7.6%, IB-29.9%, II-35.3%, III-27.2%). They also include disease free survival (HR 0.66-0.93 favoring ACT), but not stratified by NSCLC stage. Monthly cost of NSCLC was found in two studies (initial $5,255-11,496, continuing $2,602-3,733, terminal $9399-16,470). Two studies reported the U.S. cost of ACT toxicity ($4,629-9,516 per grade 3-4 event). Three studies reported utility values specific to early NSCLC including one with values related to ACT and toxicity with values varying from 0.60 to 0.75. Data reporting current U.S. ACT utilization was not identified. **CONCLUSIONS:** Early NSCLC literature contains the majority of data inputs necessary for this model. Limitations exist, specifically regarding recurrence by stage, current ACT utilization and cost of health care resources. These limitations can be overcome using expert opinion, assumptions for guideline adherence and/or conducting observational studies to inform the model.

PRM85

ANALYSIS OF CAUSAL RELATIONS IN STROKE REGISTRY DATA

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OBJECTIVES: Stroke–one of the leading causes of death and disability–represents substantial clinical and economic burden. Understanding treatment patterns and causative relations may help e.g. to identify outcomes predictors and cost drivers. **METHODS:** We used Polish Hospital Stroke Registry data on patient baseline characteristics (demographics, risk factors, prestroke disability, stroke severity), hospital management, treatment outcomes and drugs (pre-admission, during hospitalisation, and prescribed at discharge). We used inferred causation approach that deducts causal (not associative) interpretations from patterns of (conditional) independence. In this primary analysis we used 5000 observations from 2007/2008 year, binary variables and assumed no hidden variables. We used Tetrad 4.3.10-6 with PC algorithm. Variables were grouped into five tiers, a priori forbidding some directions of causal influence. Large number of variables led us to a restrictive significance level (α=0.0001). **RESULTS:** New insight can be gained from existence, lack of, and the direction of causal relations. Our results: confirmed (without imposing prior knowledge) the use of cardiovascular drugs in relation with underlying risk factors and natural sequence of drug management (drugs used prior to, in acute stroke and at discharge); surprisingly suggested no causal relation between some clinical characteristics and drug use (e.g. history of stroke/diabetes and oral anticoagulants) or acute stroke treatment (e.g. aspirin, thrombolysis, stroke unit based treatment) and mortality/post-stroke disability; determined the causal direction between some risk factors (e.g hypertension and diabetes, gender and AF) or patient history and prestroke disability (history of stroke or age over 75 and impaired disability); could not unambiguously discover the causal-relation between stroke unit based treatment and unproven efficacy drugs use. **CONCLUSIONS:** Apart from statistical or econometric approach, causal-type reasoning can be used both to confirm the intuition, and to detect new patterns in data. Further research should include the possibility of hidden variables and try to quantify the causal relations.

PRM86

HOW TO SELECT THE RIGHT COST-EFFECTIVENESS MODEL? A SYSTEMATIC REVIEW AND STEPWISE APPROACH FOR TRANSFERRING AN EXISTING HEALTH ECONOMIC MODEL FOR RHEUMATOID ARTHRITIS

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OBJECTIVES: To a) to perform a systematic literature review to identify existing models for cost-effectiveness analysis of disease modifying anti rheumatic drugs in Rheumatoid Arthritis, and b) to develop and test a method for the selection of a model that is transferable to the Dutch health care setting by simple adaptation. **METHODS:** We searched Medline and Embase to identify relevant studies in the English language between 1-1-2002 and 31-8-2012. For studies that met the inclusion criteria, we applied a 3-step approach in model selection. First, models that did not meet all minimal methodological requirements based on the OMERACT criteria were excluded. Second, the models were assessed based on their fit when transferred to the Dutch health care setting. Transferability factors as published by Welte et al., except for those that were deemed transferable by simple adaptation, were used for this ranking procedure. Finally, the remaining models underwent a general quality check using the Philips checklist. Models showing good fit and high quality were considered to be transferable to the Dutch health care setting using simple adaptation. **RESULTS:** The systematic literature search resulted in 498 papers, which included 33 unique health economic models. Only six models passed the OMERACT methodological requirements. Two of these models had imperfect transferability fit according to Welte. The remaining four models were, according to Philips, of good quality and were expected to be transferable by a simple adaptation. **CONCLUSIONS:** This study introduces a stepwise approach to the identification and selection of health economic models that are transferable by a simple adaptation. This approach can be applied in various therapeutic areas, provided that the minimal methodological requirements are defined accordingly. Availability of health economic models coupled with structured model selection could improve the efficiency, quality and comparability of health economic evaluations.

PRM87

EXTERNAL VALIDATION OF THE SYREON DIABETES MODEL

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OBJECTIVES: The Syreon model was developed to predict the long term effects of screening, treatment and control of type 2 diabetes. After a successful internal validation the model's outcomes needs to be compared to outcomes of cohorts that were not used for the modeling exercise. The objective of this study was to demonstrate the methods and results of the external validation. **METHODS:** As a first step, we identified the applicable clinical trials and cohort studies which had not been used to build the model and simulated the patient cohorts for each study according to the published demographic, epidemiologic characteristics and treatment patterns. The incidence rates of the predicted and observed outcomes were calculated for comparison and the results were evaluated using statistical methods and expert opinion. **RESULTS:** 92 validation analyses were performed. The differences between the estimated and measured values of the incidences were within the range of 44% and -100%. The slope of the fitted linear regression line was 0.5326 while the R^2 value was 0.6956. The macular oedema submodel presented the best fit and the estimated values from the foot ulcer submodel had the lowest accuracy compared to values observed in other studies. **CONCLUSIONS:** In overall the model performed well, however it frequently underestimated the incidence of the outcomes observed in the studies. This is most likely due to the limited information about the patient characteristics from the studies under evaluation. In most cases the information published about the population characteristics, treatment patterns and effectiveness were not sufficiently detailed to precisely match the model's input parameters. Without sufficient information average values were used as input parameters, and this way the model presumably simulated healthier patient cohorts than the ones participated in the studies.

PRM88

DISENTANGLING EFFECTS ON FATAL AND NON-FATAL CARDIOVASCULAR EVENTS OVER TIME

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OBJECTIVES: Within acute coronary syndromes (ACS), the risk of experiencing fatal and non-fatal cardiac events is highest immediately after diagnosis and decreases over time. Visual inspection of survival curves from pivotal ACS trials suggest three potential risk periods. The highest risk (unstable disease) period typically lasts up to 10 days from diagnosis. Patients then become more stable but are still at a high risk of events until approximately 30 days from diagnosis. Beyond 30 days patients are considered stable and at a lower risk of events. Different agents may be best suitable for different periods and may affect different events. The objective of this research is to estimate a model which enables the effects on fatal and non-fatal events following an ACS episode to be disentangled and that distinguishes between periods of disease without accurately knowing how long these periods are. **METHODS:** A Markov model is estimated which distinguishes between three time periods and between fatal and non-fatal events. A likelihood function is derived as well as a Bayesian procedure to estimate the model parameters. The approach is tested using simulated data. Subsequently, event free survival data and overall survival data comparing ticagrelor with clopidogrel are taken from the Kaplan-Meier curves presented in the publication of the PLATO trial and model parameters are estimated based on these data. **RESULTS:** Using simulated data the model mimics the data generating process perfectly and the approach seems quite powerful in distinguishing periods and differences with patient numbers of 500 and above. **CONCLUSIONS:** When applied to the PLATO study we conclude from the model that ticagrelor lowers the probability to experience an event in the unstable and stable high risk disease periods.

PRM89

A DE NOVO ECONOMIC MODEL TO ASSESS THE COST AND QUALITY OF LIFE CONSEQUENCES OF AN INTERVENTION FOR LEVODOPA INDUCED DYSKINESIA AMONGST PATIENTS WITH PARKINSON'S DISEASE

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OBJECTIVES: Emergence of long-term side effects of treating Parkinson's disease (PD) patients with levodopa, particularly dyskinesia (levodopa induced dyskinesia - LID), limit the ability to optimally treat symptoms and consequences of PD. PD-LID interferes with performance of activities of daily living, ambulation and balance and increases health care costs. There are no approved treatments and no studies examining cost-effectiveness of an intervention for PD-LID. Objective of the present study is to develop a de-novo economic model to identify the value drivers for a drug to be cost-effective for treatment of PD-LID. **METHODS:** The model combines a short-term (6 months) decision tree, to determine initial response to the drug, with a long-term Markov approach to model transition of patients across LID severity over lifetime. The model classifies LID severity using modified Abnormal Involuntary Movement scale (mAIMS) with disease states defined as mild (0-12), moderate (13-18) and severe (19-24). Disease state specific costs included costs of drug treatments, consultations/visits, paramedical services, laboratory tests, radiological examinations, hospitalizations, community/social services and unpaid services. State specific utilities were calculated and assigned based on literature. **RESULTS:** The model suggests that initial response to the treatment, ability to improve and halt worsening dyskinesia health states are the greatest value drivers of the treatment for PD-LID. More than 90% of costs were driven by medical costs. A treatment for PD-LID that results in 6-month response rate of at least 50%, 25% increase in the probability of dyskinesia improving and 25% reduction in the probability of dyskinesia worsening results in a 0.28 QALY gain per patient. **CONCLUSIONS:** This economic analysis suggests that a health care intervention that could improve the clinical parameters of dyskinesia can have significant beneficial impact on costs and utilities. Further studies are required

to characterize the underlying disease progression parameters and strengthen these assessments.

PRM90

OVERVIEW OF HEALTH ECONOMIC MODELS IN TYPE 2 DIABETES MELLITUS (T2DM); A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: To identify and compare economic models developed to evaluate the cost-effectiveness of treatments for type 2 diabetes mellitus (T2DM), and their use in health care decision-making. **METHODS:** This research updates two previously published systematic reviews. The current systematic literature review was performed according to a pre-defined search strategy and review criteria in six commonly used databases from September 2008 to January 2013. In addition, websites of Health Technology Assessment (HTA) organizations across nine countries and major disease conferences' proceedings were also reviewed. For each identified model, key information was extracted and assessed. **RESULTS:** Overall, 2262 citations were identified; 122 full text publications, 169 conference proceedings and 106 HTA reports met the pre-defined inclusion criteria. Among these, 27 models were identified; 6 from full text publications, 18 models from conference proceedings, and 3 models from HTA reports. Most of the included models applied a similar model structure, either using Markov-modelling or micro-simulation techniques, and were based on similar key data sources. A key challenge of T2DM economic modelling is to appropriately predict the long-term progression of relevant risk factors and translate these into clinical and economical consequences of diabetes-related complications. In line with previous findings, the UKPDS risk equations were most commonly used for the above purposes in the newly identified models. Among published studies and HTA submissions, T2DM economic models that are widely published and accepted by HTAs include CARDIFF and CORE. **CONCLUSIONS:** The most commonly employed models in HTA submissions, namely CARDIFF and CORE, have similar techniques to forecast future costs and health outcomes. Hence, the focus for decision makers should be to consider the appropriateness of the critical assumptions regarding data inputs that impact the results.

PRM91

NETWORK META-ANALYSIS WITH FRACTIONAL POLYNOMIALS FOR REPEATED TROUGH FEV1 MEASURES IN COPD: ACLIDINIUM BROMIDE 400 µG BID VERSUS TIOTROPIUM 18 µG QD

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OBJECTIVES: To estimate the relative efficacy of aclidinium bromide 400 µg BID (AB400), to tiotropium bromide 18 µg QD (TIO18) by means of lung function in patients with COPD, within the first 24 weeks of treatment and illustrate the repeated measures network meta-analysis (NMA) models. **METHODS:** A systematic literature search using a predefined strategy in MEDLINE, EMBASE and the Cochrane Library identified 16 unique placebo-controlled RCTs reporting FEV_1 trough: TIO18 (n=13) and AB400 (n=3). The development of trough FEV_1over time for AB400, TIO18 and placebo (PLA) was modeled with fractional polynomials, and the difference between the parameters of these polynomials within a trial were synthesized across studies with a Bayesian NMA. This type of NMA allows for the simultaneous analysis of outcomes at multiple time points. The within-trial correlation was not available from the publications of the included studies, and as such a sensitivity analyses was performed assuming different values for the correlation. **RESULTS:** Given the fractional polynomial parameters obtained with the NMA model, the corresponding treatment effects over time for AB400 vs TIO18, AB400 vs PLA and TIO vs PLA were estimated. The model with $t^{-0.5}$and log(t) had the best fit according to the deviance information criterion (DIC). These polynomials and within study correlation were used for the modeling of the outcomes over time. AB400 is equally efficacious compared to TIO18 during the first 24 weeks, as the 95% CrI of the difference in CFB between the treatments includes zero while the mean is <15mL. Furthermore, the probability that each treatment was best was calculated as a function of time. **CONCLUSIONS:** This analysis demonstrates the use of the proposed NMA models and suggests that maintenance treatment with AB400 results in comparable improvements in lung function, as TIO18 in COPD patients over a 24 weeks period.

PRM92

EVPI CURVES IN PRACTICE

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When making decisions about the allocation of scarce health-care resources it's not only important to consider the estimated cost-effectiveness (CE) with current evidence, but also the value of additional research. Expected value of perfect information (EVPI) is the amount a decision maker should be willing to pay to eliminate uncertainty surrounding the decision about which option is optimal for different levels of the CE threshold (λ). Although EVPI analysis is being requested increasingly by reimbursement agencies there is still limited literature on the interpretation of EVPI curves. The typical 'textbook' example represents just one of the possible shapes that the curve can take. **OBJECTIVES:** To explore and explain different shapes of EVPI curves based on the position of alternative treatment choices on the incremental cost-effectiveness plane. **METHODS:** A hypothetical probabilistic decision model was developed in which two interventions were compared. Key input parameters were varied to force the model outcomes into different quadrants on the incremental CE plane. The population EVPI, based on a hypothetical number of future patients and the estimated lifetime of the new intervention, was plotted. **RESULTS AND CONCLUSIONS:** The result of this study demonstrates a number of scenarios where the EVPI curve takes a different form compared to the one illustrated in the typical 'textbook' example. For example, when the majority of the plotted outcomes are spread over the northern quadrants the traditional EVPI peak is absent, and this could be explained by the fact that the reduction in decision uncertainty does not outweigh the increased value of opportunity loss. Further, plots spread over the eastern quadrants present a maximum EVPI at zero λ which then gradually decreases. This study may inform the interpretation of EVPI curves, and add value to the analysis of the value of additional research.

PRM93

MODELING MEDICATION ADHERENCE IN COMPARATIVE EFFECTIVENESS RESEARCH

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OBJECTIVES: Real-world patients do not exhibit the level of medication adherence seen in clinical trials. Hence, the effectiveness of medications in routine practice may differ. It is important to understand the manifestations of suboptimal medication adherence in a population to assess the potential of adherence-improving interventions and the real-world value of medications. The objective of our study was to compare the clinical outcomes of an adherence naïve framework versus a dynamic adherence framework using the case of statins for primary prevention of cardiovascular disease versus no statin use. **METHODS:** Statin adherence was categorized as PDC≤.20, .20<PDC<.80 and PDC≥ .80 based on a longitudinal epidemiological cohort study of US medical and pharmacy claims. Yearly adherence transitions were incorporated into a Markov microsimulation using Treeage software. Tracker variables were used to store adherence transitions which were then used to adjust probabilities of cardiovascular events (MI, stroke, acute angina) over the patient's lifetime. Statin effectiveness was adjusted between 0% and 100% of trial-based risk reduction. A total of 10,000 microsimulations were used to estimate incremental effectiveness as CV events avoided and quality-adjusted life-years (QALYs). **RESULTS:** In the 10,000-patient statin user cohort simulated by the adherence-naïve model, it was estimated that statin use resulted in 1,162 CV events avoided and 0.39 QALYs gained over a lifetime horizon. The dynamic adherence model estimated that 42% of patients exhibited highest adherence, 40% exhibited intermediate adherence and 18% exhibited low adherence. This model simulated that overall, statin use resulted in 366 events were avoided and 0.18 QALYs gained. **CONCLUSIONS:** A Markov microsimulation used to simulate changes in patients' medication adherence over time reveals differential risk reduction and effectiveness in terms of CV events and QALYs gained. The framework presented here is useful for comparing drugs in which optimal effectiveness and costs may be similar, but differential adherence may affect outcomes.

PRM94

CAUSAL ANALYSIS OF LONGITUDINAL PATIENT TURNOVER DATA AT HEPATITIS-C

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OBJECTIVES: In recent years the financer in Hungary (NHIFA) has established a detailed and stabile patient turnover database, which reflects time dependent changes. Meanwhile, statistical methods of longitudinal data revealing causal relationship have been becoming widespread. By these new methods, analyses similar to assessment of randomized clinical trials have become available. In our research we studied the causal effects of the strategy of treatment, especially the frequency of retreatment of responder patients on features of status, events and costs of patients diagnosed Hepatitis C. **METHODS:** Causal inference on longitudinal (e.g. patient path) data is possible using the methods of Robins (1999). It makes therapy history exogenous, i.e. independent of the actual status of the patient via dynamical, time dependent reweighting of individual patient paths. Consequently, patient paths can be analyzed similarly to cohort data assessment of randomized clinical trials. The method can be used to confirm the results of RCTs. It can substitute RCTs, too, e.g. if RCTs are ethically impossible. **RESULTS:** We obtained by applying Robins' method that repeated combination therapies decreased the risk of liver related complications and the development of hepatocellular carcinoma. The method applied to cost analysis revealed that despite repeated therapies the costs of newly developed cirrhosis and tumor are higher than the corresponding costs of patients with sustained viral response. **CONCLUSIONS:** Robins'method is appropriate for measuring the causal effects of certain factors of care on patient pathways, especially if patient turnover data are supplemented with physiologic, diagnostic and lab information found in clinical registers.

PRM95

APPROPRIATE EVIDENCE SOURCES FOR POPULATING DECISION ANALYTIC MODELS WITHIN HEALTH TECHNOLOGY ASSESSMENT (HTA): A SYSTEMATIC REVIEW OF HTA MANUALS AND HEALTH ECONOMIC GUIDELINES

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OBJECTIVES: Decision analytic modellers use numerous types of evidence for populating model parameters. Detailed methodological advice on which type of data is to be used for what type of model parameter is required. We aim at reviewing existing HTA manuals and health economic (modelling) guidelines in order to gain advice on appropriate evidence sources for populating models. **METHODS:** We identified manuals and guidelines via the International Network of Agencies for Health Technology Assessment (INAHTA) and by hand search. We included documents from Europe, the USA, Canada, Australia and New Zealand as well as transnational guidelines written in English or German. We systematically sum-

marised recommendations on appropriate evidence sources for different model parameters in a narrative manner. Additionally, information on advantages and disadvantages of sources, on evidence identification methods and on data quality issues was extracted. **RESULTS:** Twenty-eight documents fulfilled our inclusion criteria. We identified a large variety of evidence sources for informing model parameters on clinical effect size, natural history of disease, resource use, unit costs and health state utility values. They comprise research and non-research based sources. The documents do not provide structured advice on the hierarchy of evidence and on the limitations of evidence sources. The information is presented fragmentarily and is not tailored to specific model types. **CONCLUSIONS:** The usability of guidelines and manuals for modelling could be improved by addressing the issue of appropriate evidence sources in a more structured and comprehensive format.

PRM96

MODELLING UNCERTAIN FUTURE EVENTS IN COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: When the appropriate time horizon exceeds the evidence time horizon in a cost-effectiveness decision model, numerous uncertainties arise. One potential source of uncertainty is that of a possible future event that may affect one or more model parameters, e.g. a price shock or the emergence of a new comparator. These uncertain future events (UFEs) are rarely accounted for in health technology assessment and there is a dearth of guidance regarding how they should be modelled. The objective of this study is to describe the circumstances under which UFEs could meaningfully impact cost-effectiveness estimates and to explore and demonstrate appropriate modelling techniques using a motivating example. **METHODS:** Drawing on examples from HTA and other relevant literature, a framework is proposed to outline: when to take explicit account of uncertain future events for the purposes of reimbursement decisions, how different future events may affect value-of-information analysis and what modelling methods are likely to be useful when incorporating UFEs. Taking the example of a decision model seeking to estimate the cost-effectiveness of an early interventional strategy for patients with non-ST-elevation acute coronary syndrome, a future price change is simulated and the framework is applied. **RESULTS:** UFEs are shown to impact 'accept or reject' reimbursement decisions only in very specific circumstances where there is the potential to incur irrecoverable costs, whereas their role in value-of-information analysis is invariable. The applied example shows that the reimbursement recommendation for future populations may change with the occurrence of the future event and that there is value in reducing the uncertainty regarding the nature of the future event. **CONCLUSIONS:** UFEs will only impact expected costs-effectiveness sunder specific and rare circumstances. When it is appropriate to include a future event in a decision model, the uncertainty surrounding its likelihood, timing and magnitude should also be quantified.

PRM97

TECHNICAL ERRORS IN COST-EFFECTIVENESS MODELS: EVIDENCE FROM THE SINGLE TECHNOLOGY APPRAISAL PROGRAMME IN ENGLAND AND WALES

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OBJECTIVES: Modelling for cost-effectiveness studies often relies upon the use of spreadsheets. However, research has shown that approximately 90% of spreadsheets contain technical errors. Furthermore, cost-effectiveness models rely on accurate transcription between many data sources, which increases the risk of errors further. The objective of this analysis was to ascertain the incidence of reported technical errors in cost-effectiveness models submitted to NICE as part of the Single Technology Assessment (STA) programme, which are subject to rigorous assessment by Evidence Review Groups (ERGs). **METHODS:** NICE guidance documents were searched for a wide range of technical error types using the HTAinsite database. Reports were included if the ERG had identified technical errors in the manufacturer's submission and this had been noted at committee level. Included appraisals were analysed to identify categories of errors identified. **RESULTS:** Of the 102 completed STA Guidance documents searched, 39 appraisals met the inclusion criteria of the study, representing a technical error incidence of 38.2% (95% CI: 28.8 – 48.4%). Within these studies, 47 errors were identified in the following areas: computation (47%), logic (17%), transcription (13%) and data handling (9%). Error causes could not be determined in 15% of cases. The magnitude of effect caused by technical errors was difficult to determine, because corrected models often include additional changes to parameters or model structure. **CONCLUSIONS:** The incidence of technical errors identified in the STA programme was lower than has previously been observed in studies of spreadsheet validity although this analysis assumes that ERG groups will identify all technical errors. The true incidence of errors may be higher than reported by this analysis. Use of best-practice methods and increased awareness of the causes and identification of technical errors may help to reduce their pervasiveness.

PRM98

THERAPY ESCALATION THRESHOLDS AND THE POTENTIAL FOR BIASED COST EFFECTIVENESS ANALYSIS WHEN FAILING TO SAMPLE BASELINE HBA1C IN TYPE 2 DIABETES

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OBJECTIVES: Due to the progressive nature of type 2 diabetes mellitus (T2DM), patients inevitably require therapy escalation or intensification. In health economic analyses, sampling input parameters is routinely undertaken for probabilistic analysis but non-sampled analysis (mean values) is still commonplace. The objective of this study was to assess how sampling baseline HbA1c in combination with therapy escalation thresholds influences predicted costs and quality adjusted life expectancy (QALE) in T2DM economic evaluations. **METHODS:** This study used the IMS Core Diabetes Model (CDM), a validated and established diabetes model, to evaluate the cost effectiveness of metformin+ sulphonylurea (M+S) compared to metformin + DPP-4 (M+D). Baseline HbA1c was set to 8.0% (non-sampled scenario) with standard error of 0.8 (sampled scenario). Efficacy data for dual therapy was sourced from a published systematic review; HbA1c and BMI changes of -0.8% and 0.199kg/m^2 (M+D) and -0.79% and 0.707kg/m^2 (M+S) respectively were applied. Insulin rescue therapy was applied to both arms at HbA1c thresholds of 6.5%, 7.0% 7.5%. The model was run over a lifetime and costs (US$) and benefits were discounted at 3.5%. **RESULTS:** Total incremental costs were $7,667, $9,571 and $11,644 for M+D versus M+S using sampled baseline HbA1c for therapy escalation thresholds of 6.5%, 7.0% 7.5% respectively; and were $5,258, $2311 and $206 lower using non-sampled values, respectively. A similar pattern was observed for QALE, in which incremental QALE gains were 85%, 42% and 1% lower with non-sampled compared to sampled baseline HbA1c for escalation thresholds of 6.5%, 7.0% 7.5% respectively. **CONCLUSIONS:** The importance of probabilistic analysis within cost effectiveness models extends beyond quantifying the effects of parameter uncertainty. When treatment decision rules are dependent on patient attributes that are subject to variability (such as HbA1c) then failing to accommodate this within the model can significantly bias predicted costs and QALE.

PRM99

MARKOV MODELS IN NON METASTATIC PROSTATE CANCER – AVAILABILITY OF INPUT FACTORS AND STRUCTURURAL UNCERTAINTY

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OBJECTIVES: This study aims at reviewing structural differences in Markov Models comparing different treatment strategies for Non-Metastatic Prostate Cancer related to scope, time-horizon, perspective, assumptions and the selection of parameters for the model. **METHODS:** There is an abundant literature on Prostate Cancer. There are however few well performed RCT's comparing different options for management for NMPCa.[1] Due to the lack of conclusive clinical evidence on the best treatment for localised prostate there has been a considerable interest in the modelling of prostate cancer in decision analytic models and economic evaluation.[2] The literature review in this paper focuses on the limited number of papers on economic evaluation related to the condition. In addition there are several articles presenting Markov Models. The evaluation was based on selected items from "Consolidated Health Economic Evaluation Reporting Standards (CHEERS)". **RESULTS:** In NMPCa there are Markov models ranging from two to five health states [9]. The choice of model originates from the underlying assumptions, the aim/scope of the study or the availability of data to feed into the model. The insufficient clinical evidence and few preference based studies of health state values where the most influential elements in structuring the models Little attention is paid to the structural differences in the analysis and the discussions in the available papers. Structural uncertainty is viewed as external to the model and difficult to evaluate unless the structural choices are made transparent.[10]. **CONCLUSIONS:** Models in NMPCa differ in complexity and structure. The ability to evaluate the use of different models is highly dependent on transparency in the different building blocks. The CHEERS framework provided a useful tool in the evaluation input factors and the different Markov Model structures,

PRM100

BAYESIAN EVIDENCE SYNTHESIS OF SAFETY DATA: A ROBUST OPTION?

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OBJECTIVES: Particularly in the context of HTA evaluations where both post-marketing and pre-marketing data may be considered, the evidence to be synthesized can be sparse, partial and heterogeneous for safety outcomes. The Bayesian option has increasingly appeared as an unrivalled option for such challenging evidence synthesis cases but implementation in practice may be questioned. This work aims at determining how Bayesian meta-analysis or mixed treatment comparison of safety data can be optimized especially regarding the choice of prior distributions and model parameterization. **METHODS:** Based on the latest developments from the DIA working group on Bayesian methods for safety data applied to specific real-world cases of both direct meta-analysis and mixed treatment comparisons (MTC), different model parameterizations and different forms of informative and non-informative prior distributions are tested, with various weights allocated to the clinical data vs. the observational information. **RESULTS:** As opposed to the NICE parameterization of network meta-analysis, the 2-way predictor parameterization of MTC as proposed by the DIA working group provides more robust analysis based on non-informative priors. In the case of informative prior results, the most robust option was seen for equal total weight of clinical vs. observational data. Results of all meta-analyses appeared to be consistent across different model and prior specifications, even with low number of studies (<10). **CONCLUSIONS:** Bayesian evidence synthesis can leverage all available information in a robust manner for both direct and indirect comparisons, with fair quantification of uncertainty. Specific guidance on MTC model parameterization for safety data could complement the current NICE guidelines.

PRM101

THE ROLE OF HALF-CYCLE CORRECTION IN THE MODELS USED FOR HEALTH TECHNOLOGY ASSESSMENT

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OBJECTIVES: To analyse the half-cycle correction and its effect on the final results of Markov models. **METHODS:** In our analysis we focus on the half-cycle correction, which is a method used to deal with the inaccuracy caused by inadequate cycle

length in Markov models. The benefits of half-cycle correction has been widely published in the international literature. We measured the importance of half-cycle correction in the models submitted to the Hungarian HTA Office. We examined when it is adequate to use half-cycle correction and how big role should it have in the process of modelling. **RESULTS:** Our experience shows that only 11% of the submitted models incorporated half-cycle correction. In more than half of these cases the value of the incremental cost-effectiveness ratio (ICER) changed by less than 1% when half-cycle correction was used compared to the base-case scenario. We also found the possibility that in some cases the added benefit of half-cycle correction is not considerable. **CONCLUSIONS:** The necessity of using half-cycle correction is essential in models, when the cycle length is half year or longer and if the number of the cycles of the models is less than 200. In most cases the half-cycle correction results in only a little change in the cost-effectiveness ratio of the submitted models, therefore half-cycle correction should be executed carefully.

PRM102

A REVIEW OF CLINICAL TRIAL SIMULATION METHODS

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OBJECTIVES: Randomized controlled clinical trials are the gold standard for determining causal inference. However, trials are expensive, and the results can be difficult to interpret. Our objective was to evaluate methods for clinical trial simulation to understand how the simulation approach can be used for improved trial planning and interpretation of trial results. Our primary focus was trials of type 2 diabetes and cardiovascular disease. **METHODS:** We systematically searched the MEDLINE database for clinical trial simulation studies. We used the MeSH terms: Markov model, Markov chains, simulation, simulation model, microsimulation, computer model, and required type 2 diabetes mellitus and cardiovascular diseases. We restricted the search to studies of humans published in English and found 92 publications. We also considered innovative clinical trial simulation methods from other areas to gain context. **RESULTS:** A number of established techniques — notably, the Archimedes Model, Markov models, and observational analyses— are used for clinical trial simulation. Markov model-based simulations are widely employed, but have structural limitations with regard to the physiological detail they can capture (e.g. multiple comorbidities). Retrospective, observational methods for clinical trial simulation are gaining utility as more databases become available. However, observational methods remain vulnerable to unknown biases. Finally, large-scale simulation models (such as the Archimedes model), with physiological underpinnings, provide accurate and clinically detailed trial simulations. These models are used to simulate trials of therapies not yet marketed, or to forecast late stage trials. Model-based simulations require validations to ensure accuracy. **CONCLUSIONS:** Clinical trial simulation is an increasingly powerful tool, complementing real-world clinical trials. Large scale simulation modeling has been shown to be valuable for estimating and interpreting clinical findings. Recent studies suggest that future developments will leverage both large-scale simulation models and increasingly rich real-world evidence.

PRM103

PROTOTYPE MODEL IN METASTATIC CASTRATE-RESISTANT PROSTATE CANCER (MCRPC): A TOOL TO POSITION NEW TREATMENTS IN THE PATIENT PATHWAY?

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OBJECTIVES: New treatments registered in mCRPC are expected to alter the way patients are currently treated. It is hence essential for developers of any new treatment not only to position it within the current therapeutic landscape, but also to anticipate what this landscape will resemble at time of launch. To address this issue, we developed a modeling tool that recast a new treatment's value into the evolving therapeutic landscape. **METHODS:** We conducted a literature review of existing health economic models in mCRPC, including recent HTA reports and conference abstracts. Technical and contextual elements were leveraged to build a flexible prototype economic model for new treatments. The model encompasses disease management from asymptomatic mCRPC to patient's death. It aims at describing the future management of mCRPC in including the current way patients are treated and the following innovative features: flexibility to alter the target population definition and size and to add new therapies. New therapies' effectiveness and their expected positioning within the treatment pathway of mCRPC patients are assessed through the model. **RESULTS:** We have created a dynamic prototype model to position new options in the current and future therapeutic landscape for treatment of mCRPC in Europe. Economic models identified in literature were addressing specific reimbursement questions and were not flexible enough to be re-used for our purpose of assessing therapeutic landscape evolution. However, some technical elements on costs and effectiveness could be leveraged for our model. The tool itself enabled to identify information gaps: epidemiology and real-life data were missing for some new treatments. These could be simulated and introduced in our easily-actualizable tool. **CONCLUSIONS:** An actualizable modeling and simulation tool was developed in mCRPC. This tool enables dynamic identification of the best public health and economic outcomes out of a new potential therapeutic alternative.

PRM104

A REVIEW OF METHODS USED IN HEALTH ECONOMIC MODELS OF CHRONIC MYELOID LEUKEMIA INTERVENTIONS

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OBJECTIVES: To describe the methods adopted by economic models of CML interventions, assess their strengths and limitations, and develop best practice recommendations. **METHODS:** Examples of different economic modeling approaches used to assess the cost effectiveness of CML interventions were identified in MEDLINE and EMBASE. The studies were reviewed to map the method employed, how and why these approaches were selected, and lessons learned by the authors. **RESULTS:** A total of unique CML models were reviewed. The large majority of these models were published in the last 10 years, with almost half being published in 2011. All but 1 of the models adopted a Markov structure, based around the following health states: chronic phase; accelerated phase; blast phase; and death. In line with best practice recommendations, over 75% of studies modeled progression and survival based on response to treatment. Extrapolation of trial data used a wide range of statistical models. Contrary to best practice recommendations, the fit of these models to the trial data and the validity of the extrapolation were not always tested. A variety of approaches were employed to estimate the health related quality of life associate with health states, including the direct valuation of health states, the use of standard health instruments (such as EQ5D), and mapping methods. **CONCLUSIONS:** Several approaches to the economic modeling of CML interventions were identified in the literature. A number of examples of good practice were identified, including the use of disease response outcomes when modeling progression and survival, and the systematic testing of the fit of survival distributions to trial data. Key challenges facing CML modeling are the validity of extrapolations of trial data given the long time periods over which these extrapolations are required, and the lack of data against which to validate them.

PRM105

MODELLING THE NATURAL HISTORY OF SCHIZOPHRENIA: COMPARISON OF NAÏVE VERSUS ADVANCED STATISTICAL METHODS

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OBJECTIVES: The literature provides little guidance on statistical methods for estimating parameters of Markov models using longitudinal data. We compared the commonly used naïve (based on raw data) and advanced approaches to estimate two model parameters: transition probabilities and hospitalisation rates. Both the naïve and advanced approaches were applied using data from the European Schizophrenia Cohort (EuroSC) to populate a Markov model in schizophrenia. **METHODS:** EuroSC is a 2-year observational study of patients with schizophrenia (n=1,208), with 5 visits at 6-month intervals. Patients were classified into 8 health states at each visit according to severity of symptoms assessed using the Positive and Negative Syndrome Scale (PANSS). For each health state, both model parameters (hospitalisation days and transition probabilities) were estimated based on raw data by pooling all time intervals (i.e. naïve approach). Similarly, for advanced methods, transition probabilities were estimated using multi-state models while hospitalisation days were estimated using two-part Generalised Estimating Equations (GEEs). Advanced methods adjusted for patient characteristics and included random effects to account for repeated measures. **RESULTS:** The naïve approach showed that the average number of hospitalisation days in a 6-month interval ranged from 4.20 in health state 1 to 19.43 in health state 8. Results from the two-part GEEs provided a range from 4.21 in health state 1 to 14.7 in health state 8. GEEs tended to provide narrower confidence intervals. With regards to transition probabilities, differences between the naïve approach and the multi-state model were mostly seen in the second decimal place. **CONCLUSIONS:** While the naïve approach is frequently used for its simplicity, it has a number of shortcomings including: not accounting for repeated measures and not allowing for adjustment of patient characteristics. To increase the robustness of results, we recommend using statistical models that recognise and account for the unique distributional characteristics of data.

PRM106

SURVIVAL ANALYSIS WITH COVARIATES IN COMBINATION WITH MULTINOMIAL ANALYSIS TO PARAMETRIZE TIME TO EVENT FOR MULTI-STATE MODELS

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OBJECTIVES: Recent ISPOR Good practice guidelines as well as literature encourage to use a single distribution rather than the latent failure approach to model time to event for patient level simulation models with multiple competing outcomes. Aim was to apply the preferred method of a single distribution on time to event in combination with a multinomial distribution on type of event for parameterizing the primary tumor component of a patient level head and neck cancer model. **METHODS:** Data on patients treated with radiation therapy as first line therapy for head and neck tumor at two university hospitals in The Netherlands between 25-02-1980–13-12-2010 was used (nUMCG=277 & nVUMC=736). Several distributions were tested for model fit, using QQ-plots, AIC, and simulated versus actual data plots to judge best fit. Covariates tested for inclusion were age, gender, tumor location dummies, nstage and tstage. The final model was applied in the patient simulation model. Multinomial regression with the same covariates and time of event added as a covariate was applied on type of event, distinguishing death, loco regional recurrence and metastasis as events. All analyses were performed in R. **RESULTS:** The LogNormal distribution showed best fit. The final model had the following coefficients for the location parameter (se in brackets): Intercept, 8.2 (0.38), Age -0.026 (0.0053), Tstage -0.38 (0.062), Nstage -0.21 (0.076), Locd1 -0.91 (0.22) , Locd2 -0.28 (0.15), Locd3 -0.72 (0.22). Locd refers to location dummies. The estimated value for Log(sd) was -0.44 (0.038). The multinomial model had age, tstage and time of event as significant covariates **CONCLUSIONS:** A disadvantage of this method is that a single distribution has to be fit to a time of event which is the result of different interacting stochastic processes. The resulting distributions showed acceptable fit and could be implemented straightforwardly in the patient level simulation model.

PRM107

EXTRAPOLATING SURVIVAL IN A HETEROGENEOUS PATIENT POPULATION WITH METASTATIC MELANOMA; A CASE STUDY OF INTEGRATING STATISTICAL AND CLINICAL CONSIDERATION

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OBJECTIVES: While the follow-up time on Ipilimumab trials is in excess of 4 years, HTA models often require survival to be extrapolated to 10 years and beyond. However, patient level data on prognostic factors are rarely available; hence extrapolation methods assume a homogeneous study population and are based on statistical considerations only. Such approaches are criticized for disregarding clinical reality and may be biased. In this study a survival extrapolation model that accounted for heterogeneity was developed based on both statistically and clinically relevant considerations. The method was applied on survival data in patients with Metastatic Melanoma. **METHODS:** Survival data were taken from a randomized controlled clinical trial that compared dacarbazine plus placebo versus dacarbazine plus ipilimumab. Two parametric models were explored to extrapolate survival: a model assuming no heterogeneity in patients and another model that divided patients into three subgroups based on cancer stage observed at baseline and additionally included subpopulations of *a priori* unobserved long-term survivors. Survival of the subpopulations was extrapolated and summed to obtain survival in the overall population. Subgroup formation was guided by expert opinion of oncologists. The statistical and clinical validity of the models were assessed. **RESULTS:** Among commonly used distributions (exponential, Weibull, lognormal) the lognormal distribution fitted the survival data best in the no-heterogeneity model whereas Weibull distribution was used for the heterogeneity model. For statistical validity, both models fitted the data reasonably well. However, the no-heterogeneity model underestimated the long tail of the survival curves. The no-heterogeneity model implied decreasing mortality over time while the heterogeneity model implied increasing mortality, which is more clinically relevant. **CONCLUSIONS:** The no-heterogeneity model fitted the data reasonably well but was not relevant for extrapolation from a clinical perspective. The heterogeneity model captured the long tail of the survival curve best, and provided a statistically and clinically relevant model.

PRM108

BIVARIATE INDIRECT COMPARISON META-ANALYSIS MODEL IN ECONOMIC EVALUATION OF CANCER TREATMENTS

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OBJECTIVES: A three-state Markov model for cost-effectiveness analysis of cancer treatments requires information on both progression-free survival (PFS) and overall survival (OS). However, data is not always available on both of these outcomes. The objective of this study is to perform a Bayesian bivariate indirect comparison meta-analysis (BICMA) to obtain estimates of both PFS and OS for use in a cost-effectiveness analysis when data on these outcomes is incomplete. **METHODS:** In a UK Health Technology Assessment report on cost-effectiveness assessment of docetaxel with prednisone/prednisolone for the treatment of hormone-refractory metastatic prostate cancer, a two-state Markov model was specified using OS data from a single randomised controlled trial that did not report PFS. We propose the use of a Bayesian BICMA model that jointly estimates OS and PFS, and which in turn allows for the specification of a three-state Markov model incorporating a post-progression phase. Survival data for the trials included in the BICMA were reconstructed from survival curves, presented in the articles reporting the trials, using the method proposed by Guyot et. al. (*BMC Med Res Methodol* 2012;12:9) using the DigitizeIt and R software. **RESULTS:** The Bayesian BICMA model was designed to jointly model the correlated outcomes: OS and PFS using either non-informative or informative prior distribution on the correlation between the outcomes. An informative prior distribution on the correlation between PFS and OS was based on external evidence using prostate cancer trials presented in Halabi et. al. (*Clin Oncol* 2009;27(17):2766-71). Modelling the correlated outcomes jointly using this bivariate model allows prediction of PFS for the comparison of interest. **CONCLUSIONS:** In the absence of evidence on PFS, required for the specification of a three-state Markov model, the proposed method allows PFS to be constructed thus eliminating the need to reduce the cost-effectiveness analysis to a two-state Markov model.

PRM109

THE DETERMINANTS OF INNOVATION – A BRIEF STUDY OF ISSUES INFLUENCING INNOVATION IN THE PHARMACEUTICAL INDUSTRY

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OBJECTIVES: To examine factors determining the level of innovation in an organisation, examining two factors – market size and the strength of intellectual property rights for a particular drug class **METHODS:** The pharmaceutical industry is used as a case study as it not only relies heavily on R&D, but, with the division between brand name and generic drugs, can provide insight into how the removal of intellectual property rights might affect innovation. The estimation models were based on an economic model for innovation and market size developed by Acemoglu and Linn (2004). Drug approval data obtained from the US FDA was used for the innovation variable; a measure for market size was constructed using prescribed medicines expenditure data from the US Medical Expenditure Panel Survey. The analysis focussed on examining the relationships between the variables using various statistical estimation techniques, starting with a simple OLS log-log model, more general negative binomial and gamma models, as well as fully flexible non-linear smoothing regressions in the form of feed-forward neural networks. **RESULTS:** Brand name approvals increased by 2.64% and generic approvals by 4.2% for a 1% increase in income-based market size. The presence of generic drugs and, thus, weak intellectual property rights did not appear to have a negative effect on research and marketing activity by brand name drugs. Estimates were small, significant, and positive (feed-forward neural networks indicated an even stronger positive relationship between brand and generic approvals), suggesting that the presence of generic drugs might further innovation. **CONCLUSIONS:** It was shown that market size does affect the rates at which pharmaceuticals aim to bring their products to the market. While brand manufacturers react positively to increased market size, weak property rights do not appear to affect innovation output negatively.

PRM110

CROSSOVER ADJUSTMENT IN ONCOLOGY TRIALS USING A RANK PRESERVING STRUCTURAL FAILURE TIME MODEL (RPSFTM): WRAPPING BOOTSTRAPS AROUND ESTIMATES OF LIFE EXPECTANCY FOR CE MODELS

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OBJECTIVES: Oncology trials increasingly permit switching from standard care (SC) to the new treatment following disease progression. Methods to remove the effect of the active treatment in the SC arm are used by HTA agencies to estimate what the effect of the SC would've been had crossover not occurred. One method is using RPSFT models to derive counterfactual survival times without crossover. For CE modeling, these counterfactual survival times need to be parametrically extrapolated to estimate life expectancy. It is known that the RPSFT approach introduces additional uncertainty and e.g. the standard error of a hazard ratio calculated from counterfactual survival times needs to be inflated. Traditional methods of parametric survival analysis don't account for this increased uncertainty which could influence allocation decisions. **METHODS:** A dataset of 400 patients was simulated assuming a Weibull distribution for PFS and OS with 70% of the patients in the SC arm switching after progression. Life expectancy was calculated in two scenarios. In scenario 1 the RPSFTM adjusted OS had Weibull parameter estimates and covariance calculated directly from the counterfactual survival times. In scenario 2 the data was bootstrapped 1000 times. For each iteration a new RPSFT model, associated counterfactual survival times and Weibull functions were fitted. The mean and covariance of these 1000 parameter estimates was taken. **RESULTS:** Mean incremental life expectancy after adjusting for cross-over was the same with and without bootstrapping. When PSA was run, larger confidence intervals in the scenario with bootstrapping indicated, the traditional approach failed to account for the increased uncertainty and underestimated the probability of the new treatment being less efficacious (0.4% without compared to 13.4% with bootstrapping). **CONCLUSIONS:** Failing to appropriately reflect the uncertainty underlying parameter estimates of crossover adjusted survival times could impact HTA decisions when appraisals are based on the likelihood of a treatment being cost effective.

PRM111

THE USE OF DATA FROM PUBLISHED KAPLAN-MEIER SURVIVAL CURVES IN NICE HTAS

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OBJECTIVES: Reporting of survival outcomes from clinical trials is often limited to median survival times, hazard ratios, Kaplan-Meier curves and numbers at risk. The numerical results are not always sufficient for meta-analysis and cost-effectiveness analysis. Further information can be obtained by digitizing and analysing the Kaplan-Meier curves. The most basic analysis approach is to fit a non-linear model to the Kaplan-Meier curve and use this to estimate parameters such as the mean survival time. Methods have recently been developed for estimating individual patient data (IPD) from Kaplan-Meier curves. Once individual patient data is estimated, standard survival analysis approaches can be used to estimate parameters and also provide estimates of uncertainty in the curve fits. The objective of this study was to review the methods commonly used and assess the impact of the improved methods, where IPD is estimated, on the inferences drawn. **METHODS:** We conducted a systematic review of the methods that have been used in NICE HTAs to obtain data from published Kaplan-Meier curves. We examined the frequency of each method, how results were used and any feedback from Evidence Review Groups. Improved methods, estimating IPD, were applied to a selection of studies where this was not conducted in the original analysis. The impact of the improved methods on the conclusions of the studies was assessed. **RESULTS:** The review showed that most HTAs used non-linear models to approximate the Kaplan-Meier curves. It also showed that the improved methods, estimating IPD, can have a significant impact on conclusions drawn from survival results. **CONCLUSIONS:** The estimation of IPD from Kaplan-Meier curves is a valuable method that is currently underutilised. It has the potential to provide better estimates of survival parameters and to improve the characterisation of uncertainty in such estimates. This is especially important when survival curves are extrapolated.

PRM112

A BAYESIAN DYNAMIC MODEL OF ASTHMA IN THE REAL LIFE

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OBJECTIVES: Evolution of asthma disease severity over time can be highly dependent on the prescription patterns and drug compliance of patients. The purpose of the modeling is to analyze longitudinal observational data of cohort of asthma patients to describe and quantify the dynamics of adherence, prescriptions, and outcomes and their interaction over time. **METHODS:** We explored and analyzed 5 different observational studies following asthma patients in France over up to 2 years. Main patients' demographics along with prescriptions, ACT and 3-level GINA control scores could be defined every quarter and exacerbations at a given quarter were adjucated based on hospital admissions. Medication possession ratios could be defined quarterly and used as a proxy for adherence. A patient-

level dynamic Bayesian inhomogeneous Markov model with quarterly time-step was then developed to jointly describe prescriptions and outcomes over time in relation with adherence proxy using medication possession ratio, adjusting for patients demographics and seasonality. Internal and external validation was performed. **RESULTS:** . Such Bayesian model could be fitted to the available data with different parameters informed by one or another data source. Treatment switches were associated with severity at the previous quarter while adherence was significantly improved when patients are switched and when they are less controlled in the previous quarter. Risk of exacerbations was depending on the control score and season at the present quarter and on the risk of exacerbation at the previous quarter. Control was significantly improved by a better adherence and to a lesser extent by a treatment escalation and improved severity at the previous quarter. **CONCLUSIONS:** This Bayesian dynamic model allowed quantifying the most important interactions between drug uses and effects on control and exacerbations over time, hence providing a powerful tool for real-world outcomes predictions in asthma patients.

PRM113

UNCERTAINTY QUANTIFICATION OF LARGE-SCALE HEALTH ECONOMIC SIMULATION MODELS

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OBJECTIVES: Large scale simulation models (e.g. Archimedes Model, MISCAN) are increasingly used to predict cost-effectiveness of medical interventions and to drive reimbursement decisions. These models are complex and involve hundreds of parameters and inputs. Quantification of parameter uncertainties using traditional sampling-based approaches (e.g., Monte Carlo sampling and its variants) can be prohibitively expensive for these models. **METHODS:** We overcome the limitations of traditional probabilistic sensitivity analysis through a 4-step process. First, we conduct a thorough survey of all parameters and their confidence intervals. Second, we use local sensitivity analysis to evaluate the effects of each parameter on the outcome of interest. Third, based on results from single-parameter sensitivity analysis, we rank and identify a group of parameters that have the largest effects on the outcome. We then employ response surface (RS) approximation methods to create a mathematical model of the model predictions for these parameters. We use Latin Hypercube sampling (LHS) to generate data points and multivariate adaptive regression splines (MARS) to build the response surface approximations. Fourth, we sample parameters from their joint distributions, and then use the constructed response surface to calculate the probability distribution of the predicted outcomes. **RESULTS:** We apply the above methodology to quantify uncertainties in predictions of the Archimedes Model for effectiveness of colorectal cancer (CRC) screening by colonoscopy (COLO) and fecal immunological test (FIT). We started out with 200 parameters and identified 20 parameters that have significant influences on predicted effectiveness of CRC screening. We conclude that there is a 89% chance that COLO will save more life years FIT, after accounting for parameter uncertainties. Similarly we estimate that there is a 61% probability that FIT is more cost effective than colonoscopy. **CONCLUSIONS:** We have developed a robust and efficient methodology for quantifying parameter uncertainties of large-scale simulation models used for cost-effectiveness analysis.

RESEARCH ON METHODS – Patient-Reported Outcomes Studies

PRM114

CATALOGUE OF EQ-5D SCORES FOR CHRONIC CONDITIONS IN DENMARK

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OBJECTIVES: EQ-5D catalogues have been developed and tested in US and UK. The current study aims to develop a Danish preference-based EQ-5D 3L scores catalogue for around a hundred of the most common monitored chronic conditions. The development is based on experiences from the US and UK, but adding new factors of importance such as health habits, BMI, social networks and stress. **METHODS:** The marginal disutility estimates will be calculated using CLAD and OLS regression on a single source population from a random sample: the National Danish Health Survey Data from 2010 which is a self-administrated survey with approx. 38.000 respondents age ≥16. The survey data is combined with data from national registers containing individual health data e.g. diagnosed chronic conditions during hospitalization, medication, use of hospitals as well as socio-economic data. The catalogue differs from UK and US catalogues' by adding health habits information and by using ICD-10 classifications from registers as well as it is based on Danish EQ-5D tariffs. The marginal disutility is calculated for each chronic condition controlling for age, gender, ethnicity, income, education and comorbidity etc. **RESULTS:** Marginal disutility estimates (EQ-5D) for around a hundred ICD-10 chronic conditions are presented and compared. It is expected that this new knowledge will contribute and qualify prioritization debate, when results are published and combined with knowledge of for example factors of importance and burden of disease in costs. **CONCLUSIONS:** The catalogue will provide scientist with an "off-the-shelf" tool for use in health economic evaluations. Marginal disutilities estimates can be used to estimate QALY's in CEA for a wide variety of conditions in Denmark.

PRM115

PATIENT PREFERENCES ON TREATMENTS FOR ERECTIL DYSFUNCTION DEFINED BY MEANS OF DIFFERENT ATTRIBUTE GROUPS: THE METHOD OF ADMINISTRATION IS THE MOST VALUED ATTRIBUTE AND THE ORODISPERSIBLE TABLET IS THE MOST PREFERRED LEVEL

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OBJECTIVES: Phosphodiesterase type 5 inhibitors (PDE5i) for the treatment of erectile dysfunction (ED) have similar pharmacologic profile. Patient preferences may influence the outcome of treatment. The objective was to assess patient preferences on treatments for ED by applying Conjoint Analysis. **METHODS:** Seven attributes were selected through a literature review and a consultation with 25 patients treated of ED and 5 experts: effectiveness (E), rapidity of onset (R), duration of effect (D), adverse events (AE), methods of administration (MA), price (P) and interaction with alcohol and food (I). 3 groups of scenarios were selected using "Orthogonal Design": Phase 1, 9 scenarios with 4 attributes (R, D, MA, I); Phase 2, 16 scenarios with the 7 attributes; Phase 3, 9 scenarios with 4 attributes (E, MA, P, I). It was applied the "Order of simulated preference" method by using cards with symbols and text. Interactions of age, comorbidity and frequency of sexual intercourses with preferences were studied. **RESULTS:** The set of 16 scenarios was very difficult for patients. A total of 314 patients participated in Phase 1, 99 in Phase 2 and 178 in Phase 3. Order of preferred attributes: Phase 1: MA (57.99%), D (16.68%), I (14.57%) y R (10.76%); Phase 2: MA (40.53%),E (21.98%), R (8.98%), P (8.11%), D (7.46%), AE (6.67%),I (6.25%); Phase 3: MA (53.9%), I (22.45%), P (12.50%), E (11.14%). The preferred MA in the 3 phases was the orodispersible tablet with reference to pill and injectable. No statistically significant associations were found with age, comorbidity and frequency of sexual intercourse. **CONCLUSIONS:** . Patients gave more importance to the attribute "method of administration" in any of the three phases performed. The preferred MA was orodispersible tablet over pill and injectable.

PRM116

CHOOSING HEALTH STATES FOR ELICITATION OF POPULATION PREFERENCES FOR THE EQ-5D

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OBJECTIVES: The EQ-5D-3L descriptive classification defines a total of 243 health states which presents a problem when seeking to establish social preferences. As it would be challenging to value all 243 health states, a subset is chosen but the basis for this selection varies across national valuation studies. The aim of this study was to choose health states based on the most commonly found health states experienced by the Irish population. **METHODS:** EQ-5D data from four different datasets were combined to determine what health states are prevalent in Ireland. Data from a general population study of health (SLAN), an over 70 population cohort, a rheumatoid arthritis and psoriatic arthritis cohort. The most commonly experienced health states were determined and these were arranged on a 5 dimensional lattice. Health states were chosen using the Manhattan distance metric. **RESULTS:** A total of 12,520 ratings of self-reported EQ-5D health states were included. Fifty two per cent of the cohort had perfect health (11111). Ninety five per cent of states include at least one '1' and no '3'. 126/243 health states were not experienced in these datasets. The Manhattan distance between health states was measured. The imposition of such a metric facilitated the identification of clusters of states and associated centroids. Distance sampling was used to identify states within the clusters. A simple random sampling strategy was also used across the lattice to ensure coverage of health states outside of the cluster **CONCLUSIONS:** Previous population preference elicitation studies have used theoretical approaches to health states elicitation, which could lead to health states being directly valued which are rarely experienced in the population. The approach presented here uses the information already known about the population, to inform choice of health states for population valuation of health using the EQ-5D.

PRM117

HEALTH UTILITIES INDEX (HUI®): POPULATION REFERENCE STATISTICS

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OBJECTIVES: To describe HUI reference statistics available from clinical and general population health studies. **METHODS:** Reviews of published literature, unpublished reports and corporate databases were used to identify summary statistics or data available for calculation of summary statistics. Published examples illustrate the use of HUI reference statistics for health-related quality of life (HRQL) scores to assess the health of patients relative to general populations and of general populations between countries. **RESULTS:** Summary statistics of HRQL scores were compiled from published clinical studies (n=5), population health surveys (n=6), or provided by investigators of individual studies (n=3). Statistics from four sets of published results were used to identify health problems among patients treated for acute lymphoblastic leukemia in childhood in a recently published study. Results from the Joint Canada/US Survey of Health (JCUSH), conducted at the same time in both countries using the same survey methodology are presented here in brief. The mean HUI3 score in Canada (0.88) was slightly higher than in the US (0.87) ($p<0.05$). However, the mean HUI3 score for those with less than a high school education in Canada (0.81) was much higher than the mean for the same group in the US (0.74) ($p<0.05$). HUI Mark2 (HUI2) and HUI Mark3 (HUI3) summary statistics by country, gender, race and age groups are presented in 43 tables on the HUI web-site (www.healthutilities.com). **CONCLUSIONS:** The results highlight the usefulness of continuous preference-based measures of population health such as the HUI3. Population reference data enable international comparisons of population health and provide normative data with which to interpret results from clinical studies. The publicly available summary statistics of interval-scale preference-based measures for the HRQL of reference populations provide valid, reliable and cost-effective results for clinical and general population studies.

PRM118

PATIENT PREFERENCES IN THE CHOICE OF DISEASE MODIFYING DRUGS FOR MULTIPLE SCLEROSIS

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OBJECTIVES: There is a variety of disease modifying drugs available for the treatment of multiple sclerosis (MS). These drugs are associated with different characteristics in key attributes such as side effects, mode of administration etc. The current study was carried out to assess the importance of treatment characteristics for patients' preferences in an ecologically valid design. **METHODS:** In a discrete choice experiment (DCE), MS patients from 38 neurological practices in Germany (n=1,153) were asked to choose the most and the least preferred drug (best-worst-scaling) among hypothetical multi-attribute alternatives with varying levels of the following key attributes: mode of administration, local and systemic side effects, frequency of administration, and required monitoring of the patient. This design (Case-3, multi-profile case) simulates a real choice situation between different hypothetical multi-attribute pharmaceutical treatment alternatives. **RESULTS:** On average, patients (~75% female) were 42 years of age with 9.6 years of disease duration, and ~90% reporting prior experience with parenteral modes of administration. Count analysis (Flynn & Louviere, 1992; Orme, 2009) yielded that mode of administration was the most important attribute guiding patients' preferences, with 'oral application' being most desired (selected as best option in 63% of the cases). Notably, the studied systemic side effects, such as flu-like symptoms or gastrointestinal disorders were only half as important as mode of administration for patients' choice. The second most relevant attribute was frequency of administration, with 'administration once a week' being the most preferred attribute level (in 47% of the cases). **CONCLUSIONS:** Our data indicate that for MS patients, the most important attributes of MS disease modifying drugs are route of administration (oral being the number one choice by majority) and frequency of administration (with intake once a week being the most preferred), probably because these aspects meet the patients' need for low treatment burden in daily life.

PRM119

RELIABILITY AND VALIDITY OF A THAI VERSION OF LAM EMPLOYMENT ABSENCE AND PRODUCTIVITY SCALE (LEAPS)

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OBJECTIVES: Work-loss disability from ailments especially depression become shortcoming in economic development thus demands early reverts. No reliable tool to evaluate work-loss diability in Thai developed. We assessed reliability and validity of Thai version of Lam Employment Absence and Productivity Scale (LEAPS),direct patient report outcome subsequent to ailments. **METHODS:** An original LEAPS was officially acquired,validated by language experts, distributed to field-test from patients age above 18 years with ailments seeking treatment at hospital. The scale reliability employed item-scale and inter-item consistency with standardized Chronbach's alpha coefficient. The scale discrimination for patient with income or non-income job was determined and compared using area under curve for Receiver Operating Characteristics (AuROC) with Chi-square test. **RESULTS:** There were seven main LEAPS items with five responder choices. Of 201 patients, 86(42.8%) male,115(57.2%) female, mean (SD)age of 39.6(15.2) years recruited from 3 hospitals. 132(65.7%) and 69(34.3%) patients were classed in income job and non-income job respectively. Background education were graduate 76(38%), vocational certificate 35(17.5%), high school 42 (21%) and primary education 42(21%). 74 (37.2%) of patients had been diagnosed with co-morbidities whom 13(18%) and 61(82%) were psychological and physical illness respectively. Overall 120(60%) of patients complained about their health problems which demanded medical treatment within one week, where 58(29%) reported the condition not interfere with daily activities whereas 36(18%) indicated that the conditions were severe and needed hospitalization. The responder to LEAPS was 94.5%. Reliability test for overall internal consistency Chronbach's alpha coefficient were 0.834 with AuROC of 0.78,95%CI:0.72-0.85. The AuROC for non-income generating vs income-generating group of 0.82,95%CI:0.71-0.92 vs 0.77,95%CI:0.69-0.86 were not significant different (p=0.528) with corresponding Chronbach's alpha coefficient of 0.811 vs 0.842 (p=0.667). **CONCLUSIONS:** Thai version Lam Employment Absence and Productivity Scale(LEAPS) is reliable to use among Thai patients. The scale is robust with consistency among Thai patients with employment and loss productivity regardless of income-generating job and highly predictive for work-loss disability.

PRM120

A SYSTEMATIC REVIEW OF PATIENTS' TREATMENT SATISFACTION AND/OR PREFERENCE PATIENT-REPORTED OUCOMES MEASURES USED IN CLINICAL TRIALS

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OBJECTIVES: To determine the availability of Patient Reported Outcome (PRO) instruments measuring Patient's Treatment Satisfaction and/or Preference for drug therapies. **METHODS:** The authors conducted a systematic review of the published literature using established biomedical literature databases (Medline and Embase), ClinicalTrials.gov as well as a PRO specific database (PROQOLID). The instruments identified through the various sources were selected according to specific criteria: 1) Include: PRO instruments of Treatment Satisfaction or Preference as a sole concept OR PRO instruments with at least two domains of Treatment Satisfaction or Preference; 2) Exclude: Evaluation of biomarker control OR No information found on the PRO instruments. **RESULTS:** The systematic literature review identified a total of 720 articles on biomedical databases and 1634 closed clinical trials on Clinicaltrials.gov. The search in PROQOLID identified ten PRO instruments. From an initial review, 130 instruments were considered of particular relevance. Upon detailed review, 88 PRO instruments met selection criteria - nine of which were solely designed for a specific study. Of these 88 PRO instruments, 31 were generic (35%). The most disease-specific measures were for use in diabetes (n = 11; 13%)), then 7 pain instruments (8%), 5 respiratory questionnaires (6%), 2 urological questionnaires (2%) and 2 treatment specific instruments (2%). The remaining 30 (34%) instruments covered individual conditions ranging from anaemia to osteoporosis. **CONCLUSIONS:** There are at least 88 patient's treatment satisfaction/preference instruments published for possible use in clinical trials; 31 of which are useful for evaluating satisfaction / preference for drug therapies without reference to a specific therapy area. For those disease-specific measures, assessment of content validity and psychometric properties should be assessed before chosing the most appropriate measure for a given study.

PRM121

DUAL BACK TRANSLATION VERSUS SINGLE BACK-TRANSLATION METHODOLOGY WHEN TRANSLATING PATIENT REPORTED OUTCOMES (PRO)

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OBJECTIVES: To determine whether dual back-translators improve the translation process for Patient Report Outcomes (PRO). **METHODS:** Four (4) PROs were translated using dual back-translators. The two back-translators worked independently, possessing no knowledge of the other's back-translation. The translated PROs were: a physical assessment questionnaire containing 1507 words with medical terminology, a physical assessment questionnaire with simple terminology containing 593 words, a COPD questionnaire containing medical concepts with 713 words, and a cancer treatment questionnaire containing colloquial terminology and 403 words. Instances of the following scenario were tallied during analysis: one back-translation accurately reflected the source, the other back-translation inaccurately reflected the source, but revealed an error in the forward translation. The same PROs were analyzed again, focusing only on one of the back-translators to compare the number of forward translation revisions that occur when using a single back-translator. **RESULTS:** After analysis, 184 forward translation revisions occurred when using dual back-translators. 11 out of the 184 were a revision to a forward translation where one back-translation was correct despite the other back-translation being incorrect. This occurred 4 times amongst Slavic family languages, 3 times amongst Indian languages, 3 times amongst Southeast Asian languages, and once with Chinese. No such revisions occurred amongst Latin and Germanic language families. After analysis of the translated PROs with just one back-translator, a total of 180 forward translation revisions occurred. **CONCLUSIONS:** A second back-translation improves the translation process if the readability of the text of higher difficulty, and if Slavic, Asian and Indian language translations are required. However, the low number of revisions resulting from one incorrect back-translation, while using dual back-translators, demonstrates that one back-translator is acceptable. Since dual back-translators revealed the need for only 4 more forward translation revisions than the single back-translator, the quality output is similar.

PRM122

MOBILE PHONE USE IN PATIENT REPORTED OUTCOMES – A LITERATURE SEARCH

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OBJECTIVES: To demonstrate the increased use of mobile phones to collect patient reported outcomes in research and to show that they are a valid method of data collection. **METHODS:** A literature search was conducted looking at articles published between 2009 and 2013 that referenced electronic diaries of some description. Articles were pulled out that specifically referenced mobile or cellular phones. **RESULTS:** Twenty-four of out of 157 articles found specifically referenced mobile. The studies referenced in these articles were carried out on populations with an age range of 8 years up to 70 and were split into 12 therapy areas including metabolic and genetic disorders, pain, weight management, sexual activity, respiratory and alcohol related. Population size ranged from 15 to 994 (mean 145.6; SD-180), and subjects reported for a minimum of 7 days (up to 6 reports per day) to a maximum of 365 days (mean 107.9 days; SD-112.6). Notably, 17 out of the 24 studies allowed the subjects to use their own mobile phone for the reporting and 11 referenced smartphones specifically. **CONCLUSIONS:** All concluded that mobile phones were suited to collect data from subjects. It was noted that the use of mobiles was acceptable as they are used them in everyday life and found to be convenient; the technology was also inexpensive to implement. The fact that 70.8% of the studies allowed the subjects to use their own mobile phones for the reporting emphasises the practicality of using mobile phones in patient reported outcomes. Although the mean age of all the studies was relatively low, the age range was very wide and researchers can be confident that older populations could use mobile phones to collect these data. The rapid adoption and technical evolution of mobile technologies and ubiquitous nature show that this technology is a valid means to collect patient reported outcomes.

PRM124

EXPLORING THE FEASIBILITY OF THE INSTRUMENT USED IN DETERMINATION OF WILLINGNESS-TO-PAY PER QUALITY-ADJUSTED LIFE-YEAR IN MALAYSIA

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OBJECTIVES: The lack of empirical and well-accepted cost-effectiveness (CE) threshold is recognized as one of the most important barriers in using Health technology assessment (HTA) in policy decisions and this is no exception in Asia Pacific region. HTAsiaLink, a network of HTA organizations in Asia has embarked on first collaborative research on determining the CE threshold across 4 countries in Asia Pacific region namely Korea, Japan, Malaysia, and Thailand. This pilot study aimed 1)to explore the feasibility of the instrument/methods used 2)to examine the value of a quality-adjusted life-year (QALY) associated with improving quality of life in mild, moderate and severe health condition, and extending life during terminal illness. **METHODS:** Five EQ-5D health states with different health severity (11121, 11212, 11323, 11223

and 22332) were used. For improving quality of life scenarios, willingness-to-pay (WTP) to avoid being in the given health state for a given duration was determined to ensure the similar magnitude of QALY gained (0.2 and 0.4QALYs) across health conditions. Similarly, in extending life during terminal illness and life saving scenarios, WTP for increasing life expectancy for given 0.2 and 0.4QALYs were examined. Data were analysed using Predictive Analytics Software (PASW v18.0). **RESULTS:** The mean WTP/QALY value for 199 adult was estimated at MYR10,505 (SD:17311) for mild, MYR10,906 (SD:15,101) for moderate and MYR14,981 (SD:21,774) for severe health condition. For terminal illness with extended life scenario, it was estimated at MYR19,611 (SD:27,054). Participants took mean of 29.74 minutes (SD:6.77) to response. One-third (32.2%) of the respondents felt the questionnaire was difficult to answer and 7% rated it as very difficult. **CONCLUSIONS:** The instrument used was feasible for determining the value of WTP/QALY. However, further revision of the questionnaire may be required to simplify the research task. This study also suggested that the threshold for Malaysia to be MYR10,505(0.35GDP)–MYR19,611(0.66GDP) per QALY.

PRM125

EPRO MIGRATION AND USABILITY TESTING OF PATIENT-REPORTED OUTCOME (PRO) MEASURES

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OBJECTIVES: In recent years there has been an increase in interest surrounding the adaptation of traditional paper-based PRO measures to create 'ePRO' (electronic PRO) versions. Questionnaires in this format are intended to be administered to patients via a tablet or PDA device, website or other electronic media. In collaboration with Isis Outcomes, PharmaQuest Ltd. has managed a series of ePRO migration and translation studies. The aim of the study presented here was to produce versions of the Oxford Hip Score (OHS) and Oxford Knee Score (OKS) that can easily be completed by patients through electronic media, and that are conceptually equivalent to the original paper-based measures. **METHODS:** The adaptation process consisted of 3 main steps. Firstly a draft ePRO version was produced and discussed to resolve any formatting issues. The draft was then tested for conceptual equivalence with the paper-based measure via cognitive debriefing interviews with patients from the target population. Finally, a series of usability questions were used to assess the patients' experience of completing the ePRO measure. **RESULTS:** Overall, no comprehension issues were reported during the cognitive debriefing step for these questionnaires, although the clarity of some instructions was questioned. The feedback from usability testing varied predominantly by age group, with older respondents generally reporting more difficulty in using the ePRO device. However, a large majority of respondents reported that the ePRO version was preferable to a paper questionnaire. **CONCLUSIONS:** Cognitive debriefing feedback confirmed that the ePRO versions presented here were conceptually equivalent to the paper questionnaires. The ePRO versions were generally well received by patients, although the usability testing highlighted the importance of clear instructions and intuitive software.

PRM126

LOCALIZATION OF ACTIVITIES AND EQUIVALENCE OF MOVEMENT IN CLINICAL OUTCOMES ASSESSMENTS

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OBJECTIVES: Clinical Outcomes Assessments (COAs) frequently include questions to assess patients' ability to perform specific activities. Some activities may not be applicable in the target country, necessitating adaptation during translation. When requiring adaptation, a tendency exists to substitute an equally recognizable, but non-equivalent, activity. Consideration of movements and exertion, as well as cultural appropriateness, is imperative. Failure to do so can impede data pooling across languages in multinational trials. **METHODS:** Languages observed were Eastern European, Indian, Middle Eastern, Asian, and Southeast Asian, all of which presented difficulties in adapting "Western" activities. The activities analyzed appeared in actual patient questionnaires that underwent linguistic validation. Alternatives were recommended by linguists and cognitive debriefing subjects. **RESULTS:** In Arabic for Egypt, "bocce" was deemed inapplicable. "Billiards" was suggested as an appropriate alternative as both require standing and light exertion. "Bocce" also posed difficulties for Indian languages. The initial alternative was "cricket," however, cricket requires higher exertion and running. A suitable alternative was "playing marbles," as the Indian version requires standing, light movement, and no running. Questionnaires also may assess one's ability to complete personal hygiene tasks, such as "getting in and out of a bathtub." In Indian languages, cognitive debriefing subjects did not understand "bathtub," as a majority of the target sample do not have "bathtubs" at home. A suitable alternative was "to sit on and get up from a small stool in order to take a bath with a tumbler." This activity replicated both the source movement and exertion with a culturally appropriate activity. **CONCLUSIONS:** Adaptation of Western activities in COAs requires consideration of the movement and exertion involved in the source, as well as maintaining cultural appropriateness and familiarity to the respondent. This is essential when creating a localized questionnaire that will yield sound data across languages.

PRM127

ITEM REFINEMENT AND PSYCHOMETRIC TESTING OF A NOVEL SURVEY FOR EVALUATING PATIENT PERCEPTION AND PREFERENCE FOR HAEMOPHILIA A TREATMENT

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OBJECTIVES: Haemophilia A treatment involves replacement of missing clotting factor (FVIII) by intravenous infusion prophylactically or on-demand. Treatment adherence is influenced by patients' beliefs about their condition, treatment and side effects; mode of administration can also be a significant barrier. This study aimed to assess the psychometric properties of a survey evaluating patient perception and preference for haemophilia A treatment. **METHODS:** A 40-item survey (derived from existing literature) was developed to assess patient perception and preference for haemophilia A treatment and delivery systems in five European countries. Item refinement and analyses involved: 1) item response and dimensionality analyses using classical test theory; 2) finalisation of items based on data analysis and clinical relevance; 3) scoring development; 4) psychometric testing of the resulting scores including 4a) Rasch analysis, factor analysis, item-level discriminant validity tests and item response distributions; 4b) internal consistency reliability; and 4c) known-groups validity. **RESULTS:** A total of 273 male patients with haemophilia A completed the survey. The results support the survey's construct, known-groups; item-level convergent and divergent validity; and internal consistency reliability. A five-factor solution was observed with the following subscales: 1) Ease of using clotting factor treatment; 2) Impact of clotting factor treatment; 3) Risk associated with clotting factor treatment; 4) Burden of clotting factor treatment; and 5) Influence of others on treatment choices. Twenty-seven items were deleted based on redundancy identified through poor psychometric performance and low clinical relevance, and one item was added (to provide a rating on ease of use of treatment which was considered missing from a content validity perspective) resulting in a 14-item scale. **CONCLUSIONS:** A sequential process of item evaluation and reduction resulted in a short, patient-completed 'Perceptions of clotting factor treatment' survey - a brief, psychometrically tested method assessing patient perceptions and preference for clotting factor treatment in haemophilia A.

PRM128

VALIDATION OF THE MULTIPLE SCLEROSIS INTERNATIONAL QUALITY OF LIFE QUESTIONNAIRE IN ELECTRONIC FORM USING ITEM RESPONSE THEORY

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OBJECTIVES: The Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL) has been validated in paper and pencil form. Validating patient-reported outcomes using Item Response Theory (IRT) along with Classical Test Theory (CCT) methods are becoming progressively more common. The current study examined the psychometric properties of the MusiQoL among patients diagnosed with multiple sclerosis (MS) using an online version of the instrument. **METHODS:** Data were used from a 2012 US survey of patients self-reporting a diagnosis of MS (N=1,000). The online survey collected information on patients' demographics, disease and treatment history, and health outcomes. Participants also completed the Multiple Sclerosis Rating Scale Revised (MSRS-R) and the abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9). Internal consistency and concurrent validity were examined for the domain-specific scores and the composite total score of the MusiQoL. IRT (one and two-parameter graded response models) analyses evaluated item discrimination and item difficulty. **RESULTS:** Among 1000 patients with MS, 82.8% were female, the mean age was 48.7 (SD = 11.29), and 76.7% were currently using a disease-modifying medication. Internal consistency (Cronbach's α) of the total scale of the MusiQoL was 0.913 and the domain scores ranged from 0.824 to 0.944. The total score of the MusiQoL were moderately-to-strongly correlated with MSRS-R (r=-0.551), and adequately correlated with the subscales of the TSQM-9 (r=0.138 to 0.348). Items varied in their discrimination (range: 1.507 to 4.814) and difficulty (range: -2.875 to 2.362) parameters. Majority of the MusiQoL domains best discriminated at lower levels of health-related quality of life (HRQoL). **CONCLUSIONS:** IRT and CCT are both helpful means for evaluating the psychometric properties of the MusiQoL. The MusiQoL in electronic form is reliable and valid for evaluating HRQoL in patients with MS, but performs best when discriminating among respondents with poorer HRQoL.

PRM129

FUNCTIONAL OBSERVATION WITH TTO IN CHRONIC DISEASES

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OBJECTIVES: Ageing population will result in an increased social burden of chronic diseases. Therefore we evaluate the impact of three chronic diseases (Diabetes Mellitus;DM, Hypertension;HT, Rheumatoid Arthritis;RA) on quality of life (QoL) in Hungary with EuroQoL-5D-3L (EQ-5D) EuroQoL-Visual Analogue Scale (EQ-VAS) and Time Trade Off (TTO). TTO is useful in health planning, economic evaluation as it is a utility measure when health state is based on the willingness to trade off lifetime **METHODS:** A total of 468 patients were interviewed with EQ-5D, EQ-VAS and TTO. 253 patients with RA, 110 patients with DM and 105 patients with hypertension filled out the questionnaires. In TTO patients need to choose between two alternatives: living with the actual health state for ten years or living with perfect health state for Y years. We used the ping-pong method to find the minimum Z period of time which is offered in exchange for perfect health. **RESULTS:** The EQ-5D mean scores were according to our expectations: RA had lowest (0,525;SD:0,32); DM had 0,73;SD:0,26 and HT had highest (0,769;SD:0,26). In contrast TTO was lowest in DM (0,74;SD:0,24); RA was 0,769;SD:0,21 and HT was 0,815;SD:0,21. TTO results are higher than EQ-5D index scores in all disorders. Moderate correlation (0.2<r<0.7) was observed in all cases between EQ-5D, VAS and TTO at 0.01 significance-level opposed to HT where correlation was lower (r=0,18). **CONCLUSIONS:** The low correlation between EQ-5D and TTO in HT could be due to the lacking disease awareness in many subjects, TTO needs special consideration in such patients. TTO is an easy method to use but some of the patient could not understand the question or they had difficulties to accept the concept of giving up life-years, some needed longer explanation. The answer on the EQ-5D depend only on patient's health state however the answer of the TTO depend on health, social state and religion.

PRM130
VALIDATION OF THE WHOQOL-OLD IN TAIWAN
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OBJECTIVES: To examine the psychometric properties of the WHOQOL-OLD in Taiwan. **METHODS:** Five questionnaires including the WHOQOL-BREF, WHOQOL-OLD, Geriatric Depression Scale (GDS-15), Barthel Index (BI), and Mini-Mental State Examination (MMSE) were used. A total of 524 participants (M = 76.2, SD = 7.5, ages ranged from 60 to 99) from northern and southern Taiwan completed these questionnaires. Cronbach's alpha, correlation analysis, and factor analysis were conducted to examine internal consistency reliability, content validity, criterion validity, and construct validity. **RESULTS:** Among the participants, 180 (34.4%) were male, and 344 (65.6%) were female. The results showed that the originally designed 6-factor model of the WHOQOL-OLD was supported. Fit indices (CFI = 0.93, IFI = 0.93, NNFI = 0.92 and RMSEA = 0.06) were acceptable. The internal consistency coefficients (Cronbach's alpha) ranged from 0.72 to 0.95 for the 6 domains. Content validity coefficients were in the range of 0.41 to 0.80 for item-associated domain correlations. Except for the DAD domain (Death and dying), other domains showed moderate to high inter-domain correlations (Pearson's correlation ranges from 0.24 to 0.70) and provided good criterion related validity with GDS-15 and WHOQOL-BREF (Pearson's correlation ranges from 0.23 to 0.55). **CONCLUSIONS:** The results showed that the psychometric properties of WHOQOL-OLD were acceptable. The WHOQOL-OLD module is a useful instrument for the old people in Taiwan.

PRM131
DEVELOPMENT OF AN INTERVIEWER-ADMINISTERED VERSION OF THE ASTHMA CONTROL QUESTIONNAIRE (ACQ-IA) FOR 6-10 YEAR OLD PATIENTS IN 11 LANGUAGES
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OBJECTIVES: The Asthma Control Questionnaire (ACQ) was developed and validated to measure the adequacy of asthma control in patients 11-70 years. Since younger children may have difficulty reading and understanding the instructions, questions and response options, an interviewer version (ACQ-IA) for 6-10 year old patients was developed and validated in UK English. If children had difficulty understanding an ACQ question, standardised alternative wording was added (in UK English, alternatives were needed for questions 2-4 and 6). The objective was to develop the ACQ-IA in a further 11 languages [English (Australia), French (Belgium), Korean, Norwegian, Portuguese (Brazil, Portugal), Spanish (Argentina, Guatemala, Peru and the USA), and Swedish] based on the adult ACQ versions, using the methodology developed for the UK ACQ-IA. **METHODS:** First, the concept of each question was defined. For each language there was: (1) forward/backward translation of ACQ-IA instructions; (2) testing of instructions with interviewers; (3) Cognitive interviews with children (6-10yr) with symptomatic asthma (n=5) to identify questions difficult to comprehend; (4) Development of alternative wording for these questions; (5) Testing of the alternatives on a different sample of children (n=5). **RESULTS:** In all languages at least three questions required alternative wording. Most frequently children had problems understanding medical terms such as "asthma," "symptoms," "wheeze," and "short-acting bronchodilator." "Asthma" was usually replaced by "difficulty in breathing" and "symptoms" was followed by examples in brackets (hard to breathe, cough, wheeze). For "wheeze", "whistling sound when you breathe" was the most common alternative. Children usually know their "short-acting bronchodilator" as their "rescue" or "emergency" medicine. **CONCLUSIONS:** Cognitive interviews with children were crucial for identifying ACQ questions difficult for 6-10 year olds to understand and for formulating the alternative wording in each language. The validity of this novel methodology for the ACQ-IA cultural adaptation has been further supported by these successful adaptations.

PRM132
STRUCTURAL VALIDATION OF THE CHRONIC VENOUS INSUFFICIENCY QUALITY OF LIFE QUESTIONNAIRE-14 (CIVIQ-14) : A CONFIRMATORY FACTOR ANALYSIS
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OBJECTIVES: The aim of this study was to confirm the factorial structure of the short version of the CIVIQ questionnaire using Vein Consult Program (VCP) results. **METHODS:** The VCP was an international study aiming to evaluate the impact of chronic venous disease (CVD) on cost and quality of life. The factorial structure of CIVIQ-14 was evaluated using two methods: confirmatory factor analysis (CFA) and multitrait/multi-items matrix. CFA was performed based on the 3-dimensional structure of CIVIQ-14 established in a previous study. 6 indices from CFA were used to assess stability: Chi², Root Mean Square Approximation (RMSEA), Adjusted Goodness-of-Fit Index (AGFI), Standardized Root Mean square Residual (SRMR), Normed-Fit Index (NFI) and Comparative-Fit Index (CFI). In addition, VCP results were also used to evaluate the psychometric properties of the questionnaire. Prior to data analysis, missing data were replaced using multiple imputation and a bootstrap was conduct to take the country-effect into account. **RESULTS:** A total of 47149 questionnaires from 17 countries were available in the VCP, of which 1438 were excluded for more than 50% missing values. Results from the CFA showed an acceptable adjustment of the CVIQ-14's 3-dimensional structure to VCP data. Within absolute-fit indices, both AGFI and SRMR proved the model to be relevant (AGFI=0.905; SRMR=0.034) while RMSEA was slightly over threshold (RMSEA=0.079; threshold=0.07). Relative-fit indices were consistent with absolute indices, with NFI=0.95 and CFI=0.95. Multitrait/mutli-items analysis agreed with CFA, showing all items to be more correlated to their dimensions score, with correlation coefficient superior to 0.4. Evaluating psychometric properties of the scale, Cronbach's alpha proved internal consistency (α>0.8 in all dimension). **CONCLUSIONS:** Confirmatory factor analysis on VCP data supported the stability of the CIVIQ-14 questionnaire factorial structure. An attempt has been made to evaluate the psychometric properties of the questionnaire, but, due to VCP's transversal design, the full process hasn't been achieved.

PRM133
PATIENT REPORTED OUTCOMES WITH MULTIPLE SCLEROSIS IN SLOVAKIA
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OBJECTIVES: The current prevalence of Multiple Sclerosis (MS) in Slovakia ranges from 100 till 150 cases per 100 000, actualized by 112 cases with insurance data. There are approx. 6 100 MS diagnosed MS patients. The objective of this paper was to find out all possible data about patients and for patients. **METHODS:** We conducted a research in collaboration with MS patient organizations. No HCP were involved, patient investigators were trained. A. Demography, treatment and socioeconomics (53 items), B. Specific questionnaire (31 items). We disseminated 500 questionnaires, 356 valid questionnaires were at the end evaluated, 78% women, 20% men (2% n. a.), average age 48.5 ± 11.9 , range 23-78 y, median 49.5 y, 52% college/gymnasium, 24% university, equal w + m (p=0.460). **RESULTS:** First symptoms related to SM raised average in the age of 30.9 ± 9.2 y (median 30 y), 12% before the age of 20, 18% after 40 , 41% were diagnosed until 6 months of the first visit by physician, another 21% in 1 y. 30% were diagnosed after more than 2 y. 45% EDSS 4-6.5, 33% EDSS 0-3 and 16% EDSS 7-9.5 (6% did not announced), 60% impaired with walking, 10% wheelchair, 2% in bed, 51% with assistance by daily activities, 9% by any activity. With rising EDSS MS therapy declines and other therapy is rising. **CONCLUSIONS:** The patients with MS in Slovakia, even with a relatively generous support from health care and social care and with available conventional or disease modifying therapy (DMT) suffer a significant decrease of their QoL.

PRM134
RELIABILITY AND VALIDITY OF THE PEDIATRIC QUALITY OF LIFE INVENTORY GENERIC CORE SCALES FOR DUTCH CHILDREN WITH FUNCTIONAL CONSTIPATION
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OBJECTIVES: Although psychometric properties of the Quality of Life Inventory™ (PedsQL) version 4.0 Generic Core Scales have been established in different pediatric populations, it has not been validated in patients with functional constipation (FC). The primary objective of the current study was to determine the reliability and validity of the Dutch translation of PedsQL in children with FC in The Netherlands. **METHODS:** The PedsQL was administered to 189 children and adolescents (aged 5-18 yrs) who met the Rome III diagnosis criteria for FC and 257 parents (of patients aged 2-18 yrs) recruited from 12 hospitals. Missing responses, internal consistency and reliability (Cronbach's alpha), discriminant validity (t-test comparisons between children with FC and a separate sample of healthy children [from the literature]) and construct validity (Pearson correlation between *a-priori*hypothesized relationships between the PedsQL and disease-specific indicators, including the GI-module and the Defecation Disorder List), and inter-rater reliability between self- and parent-reports (Intraclass Correlations Coefficients, ICC) were assessed. **RESULTS:** The PedsQL showed minimal missing responses (5% child-, 0% parent-report) and achieved good to excellent internal consistency reliability for the Total Score (α 0.86 child, 0.88 parent), Physical Health Summary Score (α 0.75 child, 0.83 parent), and Psychosocial Health Summary Score (α 0.79 child, 0.85 parent). It also distinguished between healthy references and children with FC (d=0.28-0.57 child, 0.49-0.85 parent). The PedsQL was correlated to disease-specific reference measures (r varied from 0.23 to 0.57 child, 0.25 to 0.45 parent) consistent with the *a-priori* hypotheses. ICC's between child and parent-reports ranged from 0.70 to 0.72. **CONCLUSIONS:** The results showed good initial measurement properties of the Dutch version of the PedsQL generic core scales in patients with FC. It could be considered as a valuable tool for measuring health related quality of life in Dutch speaking patients aged 2 to 18 years with FC.

PRM135
PILOT TESTING OF THE POLISH PRE-FINAL VERSION OF "DISABILITIES OF THE ARM, SHOULDER AND HAND" (DASH) QUESTIONNAIRE
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OBJECTIVES: To perform a pilot testing of the translated and culturally adapted Polish pre-final version of the DASH questionnaire in a population from a target setting. **METHODS:** Thirty patients (20 men), medium age 41.1 years (range 13 -79) from Rehabilitation Centre STOCER (Konstancin-Jeziorna) took part in pilot testing. The studied population was heterogeneous in terms of side affected (right: 13, left:13, both: 4), diagnosis (20 different diagnoses, most common - brachial plexus injury, n=6) and treatment (both conservative and surgical). Subjects completed questionnaires and were asked if there were questions that were difficult to respond or difficult to understand. After that each patients had to explain in his/her own words the meaning of five randomly chosen questions and their answers. We analyzed: number of missing items by question, number of missing items by patients and distribution of responses for each item. **RESULTS:** Understanding of randomly chosen questions and answers was appropriate. All items, except one, had high frequency of present answers (86.7% - 100%). Item 21 (sexual activity) was omitted by 60% of respondents. Number of missing items by patients ranged from 0 to 6. Five patients (16.7%) had more than 10 percent of the items left blank. Three from these persons were 60 years of age and over and could characterize with

worse cognitive function. Fifteen items had responses with ≥ 35% frequency and three items (turning a key, recreational activities with force, recreational activities with moving arm freely) had responses with ≥ 50% frequency. **CONCLUSIONS:** Patients had no complaints about understanding or difficulty of the adapted version of the questionnaire. Still, there were some items with missing answers (most often - sexual activity). Although, we provide some evidence of content validity, additional testing for the retention of psychometric properties of the translated questionnaire is recommended.

PRM136

IMPACT ON THE ESTIMATED ICER OF INCLUDING AGE-SPECIFIC BASELINE HRQOL IN A MODEL

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OBJECTIVES: For models that simulate patients over a long span, such as from birth to life expectancy, the baseline HRQoL can be incorporated. Typically this means that younger people have a higher utility than older people. The aim of this study was to investigate the impact of including age-specific baseline utilities in a model that simulated women at elevated risk of developing breast cancer from ages 20 to 85. **METHODS:** A model was developed to evaluate the impact on costs and benefits of breast cancer surveillance in a population of women with a BRCA1 mutation. Women were modelled from age 20 to 85. QALY reductions were associated with the treatment of cancer and were stage-specific. The model was evaluated incorporating age-specific baseline QALYs and also where all ages had a baseline QALY of 1. The impact of age-specific baseline QALY inclusion was evaluated in terms of the ICERs for different surveillance strategies. **RESULTS:** The incremental cost of each intervention and the interventions included in the cost-effectiveness efficiency frontier were unaffected by the choice of baseline HRQoL. However, both the average and incremental cost-effectiveness ratios were changed. For interventions on the cost-effectiveness efficiency frontier, all ICERs were less than €100,000/QALY when age-specific baseline HRQoL values were used. ICERs reduced by an average €11,520 when a uniform baseline HRQoL was used. **CONCLUSIONS:** The use of age-specific baseline HRQoL in a cost-effectiveness model needs to be carefully considered. Inclusion of age-specific baseline HRQoL can favour interventions with an impact at a younger age. Whether age-specific or uniform baseline data are used in a model, the alternative should be considered in a sensitivity analysis.

PRM137

EQ-5D-5L CROSSWALK VALUE SET FOR POLAND

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OBJECTIVES: To estimate EQ-5D-5L crosswalk value set for Poland, based on Crosswalk methodology developed by EuroQol Group. **METHODS:** Based on the data from 3691 respondents from 6 European countries, EuroQol Group has developed a method of obtaining interim values sets for the EQ-5D-5L by means of mapping to the available EQ-5D-3L values sets ("crosswalk" methodology). A significant part of the data in this study came from Polish respondents (n=972; 26.3%). Poland is the first Central European country with EQ-5D-3L time trade-off based social values set published. In order to obtain interim EQ-5D-5L values set, we applied Crosswalk methodology, developed by EuroQol Group, to available Polish EQ-5D-3L values set. **RESULTS:** Estimated Polish values for 3125 EQ-5D-5L health states will be presented. Both, EQ-5D-5L and EQ-5D-3L values sets have the same range (from -0.523 to 1.000), but different means (0.448 vs. 0.380) and medians (0.483 vs. 0.403), respectively. Participation of states worse than dead is less in EQ-5D-5L (5.38%), than in EQ-5D-3L (13.17%) values set. **CONCLUSIONS:** As long as value set based on preferences directly elicited from representative Polish general population sample is not available, estimated crosswalk values set should be used in EQ-5D-5L studies in Poland in order to calculate health state utilities.

PRM138

CROSS (-WALK) AT YOUR OWN PERIL! COMPARING AND CONTRASTING CEA RESULTS WHEN INDIVIDUAL-LEVEL UTILITIES ARE DERIVED FROM EXTERNAL MAPPING ALGORITHMS RATHER THAN ACTUALLY OBSERVED RESPONSES

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OBJECTIVES: Existing studies exploring the validity of using mapping algorithms to predict utilities in external datasets have found mixed results. We apply a series of published EQ-5D mapping algorithms to individual patient level data from a trial which in fact collected this outcome, with a view to assess the impact of using predicted versus actual EQ-5D values on the results of a cost-effectiveness model. **METHODS:** The RITA-3 trial compared early interventional strategy for patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) against a conservative strategy. EQ-5D data were collected at baseline, 4 months, 12 months and yearly thereafter. A range of other clinical and quality of life outcomes were also collected including the Seattle Angina Questionnaire (SAQ), SF-36 and the Canadian Cardiovascular Society (CCS) Functional Classification of Angina. Using mapping algorithms found in the published literature, we predicted EQ-5D scores using these outcome measures. We then explored what effect the predicted utilities had upon cost-effectiveness estimates in a model compared to those with the actual EQ-5D data. The comparisons were made across five patient subgroups. **RESULTS:** The cost-effectiveness estimates varied according to the original outcome measure used to map and the patient subgroup. The EQ-5D values predicted using CCS scores produced cost-effectiveness estimates much higher than those with the actual EQ-5D data in the trial, whilst the estimates using EQ-5D values predicted using SAQ scores were lower. The values predicted using SF-36 scores gave cost-effectiveness estimates very similar to those with the EQ-5D data, irrespective of the patient subgroup. **CONCLUSIONS:** Analysts should take caution when mapping EQ-5D values from algorithms that have not been externally validated, especially where these algorithms have used clinical outcomes or disease-specific measures of health-related quality of life. Our results suggest that mapping from generic outcome measures might be reasonable.

PRM139

LOST IN TRANSLATION: TRANSLATABILITY OF PSYCHIATRIC TERMS – THE EXAMPLE OF THE MINI–INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW (M.I.N.I.)

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OBJECTIVES: The Mini-International Neuropsychiatric Interview (M.I.N.I.) is a short, structured diagnostic interview, developed by psychiatrists and clinicians in the USA and Europe, for DSM-IV and ICD-10 psychiatric disorders. The objectives of our study were: 1) To determine if the psychiatric terms used in the M.I.N.I. are translatable worldwide, especially in non-western countries, and 2) To review strategies used to culturally adapt psychiatric terms. **METHODS:** We reviewed the records of all linguistic validation projects involving the M.I.N.I. **RESULTS:** We retrieved 67 language versions, representing 47 countries. The analysis of the translations' content revealed three types of results, depending on the existence (or not) of corresponding psychiatric terminology in the target languages. The standard methodology (forward/backward and clinician review) was used in all countries and adapted, depending on the context. In all western and westernized countries (e.g., Europe, Russia, etc., totaling 49 languages), the psychiatric terms used in the M.I.N.I. were easily translated (i.e., existence of an agreed-upon corresponding terminology). In languages where psychiatric terms do not exist (e.g., certain Sub-Saharan languages), all the clinician-directed parts (titles and clinician-directed instructions/algorithms), which are capitalized in the original instrument, were left in English, and the patient-directed parts were translated in the target languages. In languages where there is a partially agreed-upon terminology (e.g., Thai), the titles as well as the algorithms were translated with corresponding English equivalents between brackets, when necessary. Moreover, in order to follow the typographical conventions of the M.I.N.I., in languages with no capital letters (such as Kannada or Malayalam), the translations used bigger font size. **CONCLUSIONS:** This review showed that terms used to describe psychiatric disorders had no equivalents in some countries, especially in Africa. Translation was not always possible and was even judged to be culturally and linguistically irrelevant in countries where psychiatry is only taught in English.

PRM140

HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN PATIENTS TREATED BY NOVEL ORAL ANTICOAGULANTS (NOACS): REDUCED VERSION OF THE SAWICKI QUESTIONNAIRE

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OBJECTIVES: Sawicki questionnaire is a 32-item specific measure for the evaluation of the change in the measure of the Quality of Health Related Life (HRQOL) experienced by patients treated by Novel Oral Anticoagulants (NOACs) versus traditional Oral Anticoagulant Therapies (OAT). The objective of this research focuses on the application of the Rasch model in selecting the most appropriate items of Sawicki questionnaire. **METHODS:** Sample was composed of 689 Atrial Fibrillation (AF) patients in whom an attempt of electrical or pharmacological cardioversion was scheduled within a 4 months inclusion period from baseline (CARDIOVERSE study). Data were analyzed with WinSteps version 3.75 using the Rasch Partial Credit Model. Statistical criteria taken into account for the selection of those items with better psychometric properties were: model-fit and separation statistics, Differential Item Functioning (DIF), unexpected responses and item content. The results were compared with those of the original version of the questionnaire in CARDIOVERSE sample. **RESULTS:** Misfiting items were deleted, resulting in a 12 items version rated on a 4-point Likert-scale. This short form of the questionnaire showed good model fit and represented an accurate measure of the construct. Infit MNSQ ranged from 0.90 to 1.15 (M=1.02; SD=0.09) and outfit MNSQ ranged from 0.90 to 1.18 (M=1.02; SD=0.08). Person separation index and item reliability were 2.11 and 0.99 respectively and item-person map showed that the test was on-target and covered the wide range of the ability scale. Finally, the criterion validity of the short version by age, sex and risk groups was similar to the original version of the questionnaire. **CONCLUSIONS:** Short version of Sawicki questionnaire has adequate psychometric properties in terms of goodness-of-fit-test and reliability. This version makes it possible to have a new short and appropriate HRQoL measure for the study of the effect in QoL experienced by patients treated by NOACs.

PRM141

VALIDITY OF QOL IMPACT ATTRIBUTIONS TO SPECIFIC DISEASES: A MULTITRAIT-MULTIMETHOD COMPARISON

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OBJECTIVES: To test convergent-discriminant validity of quality of life (QOL) impact attributions to arthritis and respiratory conditions using the multitrait-multimethod (MTMM) approach. **METHODS:** Chronically-ill adults (N=601) with osteoarthritis (OA) and respiratory (asthma, COPD) disease completed Internet-based surveys. Ages ranged from 18-93 (median=58), 66.5% female and 20.7% non-white. QOL impact was measured using 3 methods: QOL Disease Impact Scale (QDIS) and disease severity with specific attribution to each condition, specific

symptoms (joint pain, shortness of breath), and generic physical (PCS) and mental (MCS) summary measures (SF-36). The resulting 10X10 correlation matrix (3 disease-specific, 2 generic) for each disease was evaluated to test convergent validity (correlations > 0.40 between different methods of measuring the same disease) and discriminant validity (significantly lower correlations between different diseases measured by the same method). The MTMM matrix was also analyzed using principal component analysis (PCA) to test for disease versus methods factors. **RESULTS:** The MTMM matrix yielded strong evidence that patients discriminated the impact of one condition from the other. In support of convergent validity, disease specific QOL impact, severity and symptom measures (joint pain for OA, SOB for respiratory) correlated substantially for asthma (0.516 - 0.765) and OA (0.465 - 0.774). In support of discriminant validity, different diseases measured by the same method correlated significantly lower (0.264 - 0.286). PCA yielded two disease-specific factors (OA and respiratory) with high loadings across methods for OA (0.748 - 0.871 and respiratory (0.687 - 0.890) and low secondary loadings (0.085 - 0.262). Generic PCS and MCS measures correlated lower than disease-specific measures, as hypothesized. 2-method (QOL impact, severity) MTMM validations replicated these results across 37 pairs of over-sampled comorbid conditions. **CONCLUSIONS:** Results strongly support the convergent-discriminant validity of survey measures of QOL impact based on attributions to OA and respiratory disease and suggest that disease-specific attributions may improve the validity of QOL impact attributions for other common pairs of comorbid conditions.

PRM142

ESTIMATING THE ASSOCIATION BETWEEN THE OXFORD HIP SCORE (OHS) AND EQ-5D UTILITY VALUES USING DIRECT AND RESPONSE MAPPING METHODS

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OBJECTIVES: Mapping algorithms can translate disease-specific or generic health-related quality of life measurements into values obtained from preference-based instruments such as the EuroQol 5-dimension questionnaire (EQ-5D). The Oxford Hip Score (OHS) is a disease-specific instrument widely used by orthopaedic surgeons to assess outcomes from hip surgery. There is an algorithm for estimating mean EQ-5D scores from the OHS, but this was developed using early response mapping methods and has limited external validation. We have developed a new mapping algorithm to translate OHS results into EQ-5D domain responses and utilities in a large UK dataset using direct and response mapping methods. **METHODS:** OHS and EQ-5D responses were extracted from the publicly available National Patient Reported Outcomes Measures (PROMs) database. The sample of complete data pairs (n=126 862) was split into estimating (n=51 800, years 2009–10) and external validation (n=75 062, years 2010–12) samples. EQ-5D utilities were estimated directly using ordinary least squares regression and two-part models. EQ-5D responses were estimated using ordered and multinomial logit models. For the two-part and the multinomial logit models, the expected value method was used to calculate utilities. Performance was evaluated using mean square error (MSE) and mean absolute error (MAE). **RESULTS:** The two-part models and the ordered or multinomial regressions performed better than ordinary least square regression. In external validation, the MSE (MAE) was 0.0319 (0.1286) for the two-part model and 0.0315 (0.1249) for response mapping. For EQ-5D index values >0.5 (better health states), response mapping predictions had a slightly smaller MSE and MAE than direct method predictions. Both indirect and direct approaches predicted higher MSE and MAE when EQ-5D <0.5. **CONCLUSIONS:** Response mapping between OHS and EQ-5D was similar or slightly more predictive than direct mapping. Further research is needed to improve the performance of these techniques in poorer health states.

PRM143

META-ANALYSIS OF QUALITY OF LIFE IN CORONARY HEART DISEASE

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OBJECTIVES: A large number of quality of life (QoL) values for patients with coronary heart disease (CHD) are available in the literature. From the abundance of QoL values in CHD, only preference-based values can be directly applied in cost-utility analysis (CUA). In this study we performed a multivariate meta-regression analysis of the preference-based QoL values in CHD. Our aim was to obtain a summarized QoL estimate while accounting for study-level covariates and for the correlation between multiple outcomes both within and between studies. **METHODS:** Studies were considered eligible for this analysis if they reported mean QoL values, standard deviations and the instrument for measuring QoL (e.g. EQ-5D, SF-6D). Additionally, studies reporting separate values of SF-36 and SF-12 QoL instruments were included. The scores of the SF-36 and SF-12 QoL were mapped onto EQ-5D and SF-6D values. Mapped preference-based values were added to the base-case data set that consisted only of published preference-based QoL values. Finally, a multivariate meta-regression model was used in order to estimate pooled, instrument-specific QoL in CHD. **RESULTS:** Our systematic search identified 35 eligible studies reporting 43 preference-based QoL values in CHD as well as 46 studies reporting QoL scores of SF-36 and SF-12. Following instrument-specific QoL estimates were obtained when conducting the analysis on the base-case data set: 0.77 (EQ-5D UK), 0.79 (EQ-5D US), 0.65 (SF-6D), 0.85 (15D), 0.44 (HUI3) and 0.63 (QWB). Age was the only study-level covariate that showed an influence on instrument-specific QoL estimates. Significant heterogeneity was observed when the analysis was conducted on the expanded data set. **CONCLUSIONS:** This study represents the first meta-analysis of QoL in CHD. Given the abundance of QoL values in CHD on the one hand and the requirement for single, accurate QoL values in CUA on the other hand, pooled estimates of QoL could be highly applicable in CUA.

PRM144

THE 'WOUND-QOL': A SHORT QUESTIONNAIRE MEASURING QUALITY OF LIFE IN PATIENTS WITH CHRONIC WOUNDS

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OBJECTIVES: To develop a short questionnaire measuring health-related quality of life (HRQoL) in patients with chronic wounds. **METHODS:** Three validated instruments assessing HRQoL in chronic wounds, the Freiburg Life Quality Assessment for wounds (FLQA-w), the Cardiff Wound Impact Schedule (CWIS), and the Würzburg Wound Score (WWS), were filled in by 154 leg ulcer patients in a prospective study under routine care. For implementation in the new, shorter questionnaire Wound-QoL, those of all 92 items were selected that covered the core content of the three questionnaires and showed good psychometric properties (e. g. number of missing values, inter-item correlations). Internal consistency, convergent validity regarding four generic HRQoL measures such as the EQ-5D, and responsiveness of the Wound-QoL were analysed using the longitudinal study data on the selected items (so-called virtual validation). Subscales were determined with factor analysis. Item, instruction, and response scale wording of the Wound-QoL were harmonized. **RESULTS:** Seventeen items were included in the Wound-QoL questionnaire which could be attributed to three subscales on everyday life, body, and psyche. Both global score and subscale scores were internally consistent with Cronbach's alpha values between 0.71 and 0.91. The global score showed significant convergent validity (r=0.48 to 0.69, depending on the criterion) and responsiveness regarding change in generic HRQoL (r=0.18 to 0.52); the same was true for the subscale scores. **CONCLUSIONS:** The Wound-QoL for measurement of HRQoL in chronic wounds proved to be internally consistent, valid, and responsive in the virtual validation analysis.

PRM145

MAPPING FROM PDQ-39 AND PDQ-8 ONTO EQ-5D UTILITY INDEX IN PATIENTS WITH PARKINSON'S DISEASE: EXTENDED ANALYSIS

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OBJECTIVES: To develop an algorithm for mapping of disease-specific health related quality of life scores to the EQ-5D utility index for patients with PD. **METHODS:** EQ-5D and Parkinson's disease Questionnaire (PDQ) data were obtained for 117 UK PD patients (HY stages 1-4) via a cross-sectional survey of practicing clinicians and their patients. The EQ-5D utility index (UK Tariff) was regressed on PDQ-39/PDQ-8 summary indices (SI) and PDQ-39 domains/PDQ-8 questions using OLS regression. Analysis on PDQ-39 domains/PDQ-8 questions was repeated using OLS with backward elimination. Two-part models (TPM) were conducted on PDQ-39/8 SI and domains/questions respectively consisting of a logistic regression on whether EQ-5D<1 followed by either OLS, GLM with gamma distribution and log link or identity link functions and GLM with Gaussian distribution with log link for the remainder. Mapping equations were used to predict utilities which were subsequently compared to those observed. Models were compared using RMSE values. **RESULTS:** Compared to simple OLS [RMSE 0.1685-0.1924], a model with backward elimination of variables did not improve predictive power. Out of the TPMs the best fitting models were GLM with gamma distribution and identity link function [RMSE 0.1666-0.1929] and GLM with Gaussian distribution and log link function [RMSE 0.1683-0.1912]. All models produced better results utilising the domains of PDQ-39 or individual questions of PDQ-8 than with the SI. **CONCLUSIONS:** All mapping algorithms estimated utilities for patients with HY stage 1-4 with reasonable accuracy. Therefore, mapping functions reported could be used for predicting EQ-5D scores from either PDQ-39 or PDQ-8 when EQ-5D data were not collected. However, simple OLS, TPMs with gamma family and identity function and Gaussian family and log functions resulted in the best prediction and the smallest RMSE values. Further validation is needed to ascertain whether these mapping functions perform well for more advanced patients in HY stage 5.

PRM146

PATIENT-REPORTED OUTCOME MEASURES FOR SYSTEMIC LUPUS ERYTHEMATOSUS CLINICAL TRIALS: A CONTENT VALIDITY AND PSYCHOMETRIC PERFORMANCE REVIEW

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OBJECTIVES: Patients with Systemic Lupus Erythematosus (SLE) experience unmet medical needs and many inflammatory symptoms resulting in humanistic and economic burden. This study aimed to create a conceptual model of patient and economic burden, and review patient-reported outcomes (PROs) used to measure such concepts in SLE clinical trials. **METHODS:** An SLE conceptual model was developed from structured review of published articles from 2007-June 2012 identified from literature databases (MEDLINE, PsycINFO, EconLit) plus other sources (PROLabels, FDA/EMA websites, Clinicaltrials.gov). PROs targeting key symptom/impact were identified from the literature. In the context of FDA guidance, the PROs were subject to in-depth review and assessed for face and content validity, and psychometric properties to determine appropriateness for use in SLE trials. **RESULTS:** Pain, fatigue, cognition, daily activities, emotional well-being, physical/social functioning, and work productivity were in the conceptual model identified as key SLE concepts. Of the 63 articles reviewed, 31 reported PRO data. From these and the other sources, 14 PROs were selected for review including SLE-specific health-related quality of life (HRQoL) measures (n=3), work productivity (n=1), and generic measures of fatigue (n=3), pain (n=2), depression (n=2) and HRQoL (n=3) as these were deemed salient for patients with SLE in the literature. The FACIT-Fatigue, BPI-SF (pain) and LupusQoL demonstrated the strongest face validity, conceptual coverage and psychometric properties measuring key concepts in the conceptual model. All PROs reviewed,

except for the Lupus-specific HRQoL measures, lacked SLE patient involvement during development limiting their content validity. The HADS, SF-36v2, EQ-5D-3L and WPAI:Lupus showed suitability for SLE economic models. **CONCLUSIONS:** SLE is a condition associated with clear unmet medical needs and considerable burden to patients. This review highlights the current availability and future need for both disease-specific and generic patient-reported measures of relevant domains of disease signs and symptoms, HRQoL and work productivity.

PRM147

MODE EQUIVALENCE OF INTERACTIVE VOICE RESPONSE (IVR) AND PAPER VERSIONS OF THE BRIEF PAIN INVENTORY (BPI) "WORST PAIN" ITEM IN METASTATIC CASTRATE RESISTANT PROSTATE CANCER (MCRPC) EVALUATED CONCEPTUALLY USING QUALITATIVE METHODS

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OBJECTIVES: The BPI "pain at its worst in the last 24 hours" item is often administered as a primary or key secondary endpoint in clinical trials using an IVR daily diary. However, evidence of equivalence between the validated paper version and IVR has not been published. This study evaluated conceptual equivalence between IVR and paper version of this item using qualitative methods. **METHODS:** Twenty-six patients with mCRPC in a non-randomized expansion cohort (N=144) of phase 2 study XL184-203 were interviewed to confirm their comprehension of the BPI "worst pain" item administered using an IVR simulation by the interviewer and presented on paper. Patient interpretation of the item's meaning in both modes was elicited and compared to identify similarities between the modes. Patients were also interviewed regarding the usability of IVR during the trial. **RESULTS:** Patients (median age = 68; range 44-81) had ECOG performance status of 0 (38%) and 1 (62%). Nearly all patients answered the IVR version of the question as intended – by considering the past 24 hours (72%; 18% did not specify); including non-cancer related pain (96%); and reporting pain experienced with analgesia (100%). Patients did not interpret the paper version of the pain question differently from the IVR version; 4 patients spontaneously stated that the paper version was the same as the IVR version they had used. All patients reported that the IVR was easy to use to answer the diary. **CONCLUSIONS:** This study provides important qualitative support of conceptual equivalence between an IVR and paper version of the BPI "worst pain" item. These results confirm that this item is well understood by patients, and that they interpret the question similarly whether administered via IVR or on paper. The results also show good usability and acceptability of IVR administration of this important item in clinical trials.

PRM148

A COMPARISON OF THE RELATIVE WEIGHTS OF HEALTH DOMAINS ON GLOBAL RETROSPECTIVE AND EXPERIENCED HEALTH AND WELL-BEING

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OBJECTIVES: Are the relative weights of different dimensions of health different when determined by their impact on subjective well-being (SWB; 2 types of self-report: retrospective global evaluation, momentary experience) and health (3 types of self-report: retrospective global evaluation, future prospect, momentary experience). **METHODS:** The study population consisted of persons experiencing psychosomatic, psychological and somatic illness, and members from public. The experience sampling study took 6 days, during which momentary self-reports of health and SWB were obtained. In addition, participants completed retrospective global evaluations of health (EQ-5D), SWB (Life Satisfaction Scale) and preference for a future prospect of health (time trade-off). Regression analysis was used to determine relative weights of EQ-5D dimensions on the outcomes. **RESULTS:** A total of 139 participants were included. Some/moderate problems in usual-activities and anxiety/depression were associated with the largest drop in health for all three types of self-report. Moderate anxiety/depression had a larger impact than moderate problems in usual-activities in momentary as compared to retrospective health-reports. Moderate problems in usual-activities and anxiety/depression and self-care were associated with a drop in retrospective and momentary SWB. Moderate problems in usual-activities was associated with the largest drop in retrospective SWB, while moderate anxiety/depression was associated with the largest drop in momentary SWB. Comparing the relative weights, it was shown that anxiety/depression was more important relative to usual-activities in momentary experiences than in retrospective evaluations. **CONCLUSIONS:** Relative weights of health domains are different, depending on the type of self-report (global or momentary) and concept of value (health or SWB) used. Most notably, the relative weight of anxiety/depression is larger when using a momentary measure, and when taking SWB as the outcome of interest. This finding warrants further discussion and research on the place and value of momentary measures of experience and SWB as outcome in health (economic) evaluation.

PRM149

PATIENT SURVEY: INVESTIGATION ON WHAT IMPACTS PATIENT SATISFACTION, DROP-OUT AND COMPLIANCE IN PATIENT DIARIES

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OBJECTIVES: Patient Reported Outcomes (PROs) play an important role in patient-centered research where compliance is important. To better understand patient preferences when participating in PROs, survey research was conducted in 2013. This presentation investigates what impacts patient satisfaction, drop-out and compliance. **METHODS:** An internet-based survey was administered to a global sample of patients who participated in at least 1 clinical trial that included patient diaries in the past 2 years. The survey asked questions about the most recent trial with a diary focusing on the patient's diary experience. **RESULTS:** A total of 398 patients provided complete responses. On a scale of 1-7 (1=Very Bad; 7=Very Good), mean satisfaction rating=5.4. Satisfaction was categorized for sub-group analysis purposes: Positive Satisfaction (75%); Ok Satisfaction (16%); Negative Satisfaction (9%). Time per diary entry had the biggest impact on satisfaction. Those whose diaries took <=30 minutes had the highest percentage of positive satisfaction (78%) and those whose diaries took >30 minutes had the lowest percentage of positive satisfaction (46%), $p<0.001$. Patients who were negatively satisfied had the highest percentage (44%) of reporting dropping out or considering dropping out due to diary effort, $p<.0001$. Patients who were negatively satisfied had the highest percentage (67%) of reporting non-compliance with completing diaries ($p<0.01$). Time per diary entry impacted compliance where those patients whose diaries took >30 minutes had the highest percentage of reporting non-compliance (68%), $p=0.03$. **CONCLUSIONS:** When planning patient diaries, it is important to consider the patient population and preferences. As the results show that satisfaction is linked to drop out and compliance, it is important to keep patients satisfied. As time per diary was found to impact satisfaction, it is important to keep patient burden and their experience in mind when developing ePRO instruments and selecting mode of administration. . Satisfied patients lead to higher compliance, retention and data quality.

PRM150

CAN WE USE THE EQ-5D ONLY FOR ASSESSING THE QUALITY OF LIFE OF PATIENTS WITH OSTEOPOROSIS?

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OBJECTIVES: Osteoporosis is a chronic disease which has impact on specific aspects of health such as pain, physical functioning, social and mental functioning and loss of personal independence. Generic questionnaire EQ-5D explores similar dimensions and therefore is usually used as a questionnaire for assessing the concurrent validity of the specific osteoporosis questionnaires. The objective of this study was to explore for a potential correlation between the similar dimensions of the specific osteoporosis questionnaire QUALEFFO-41 and EQ-5D. **METHODS:** Analyzed data were a part of the study that included 50 patients with osteoporosis and vertebral fractures conducted during the period June 2010 - October 2011. The correlation between the questionnaires was assessed using the Spearman's correlation coefficient. **RESULTS:** Strong correlations were found between EQ-5D index / VAS score and QUALEFFO-41 total score (ρ=-0.73 and ρ =-0.57, $p<0.001$, respectively). The EQ-5D dimensions "Pain/discomfort", "Mobility", "Activities", "Anxiety/Depression" similar to QUALEFFO-41 dimensions "Pain", "Physical function", "Leisure, social activities", "Mental function" were also strongly correlated (ρ=0.42, ρ =0.76, ρ =0.46 and ρ=0.32, $p<0.001$, respectively). **CONCLUSIONS:** Strong correlations between similar dimensions of the compared questionnaires were notified. Negative values of the Spearman's correlation coefficient indicated that total score of the QUALEFFO-41 were scored in the reverse order. There was only one QUALEFFO-41 dimension ("General health perception") that is not similar to any of the EQ-5D dimensions. Although there was a strong correlation between the total scores of compared questionnaires, the results of the EQ-5D questionnaire should be observed with caution, because it does not contain all important dimensions that osteoporosis affects.

PRM151

VALIDITY, RESPONSIVENESS AND RELIABILITY OF THE ARTHRITIS-SPECIFIC WORK PRODUCTIVITY SURVEY ASSESSING WORK PRODUCTIVITY WITHIN AND OUTSIDE THE HOME IN PATIENTS WITH PSORIATIC ARTHRITIS

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OBJECTIVES: The arthritis-specific Work Productivity Survey (WPS) estimates arthritis-related productivity limitations at workplace and within home, and on social activities, during the preceding month. There is an unmet need for an instrument assessing similar limitations in psoriatic arthritis (PsA). Following its validation in rheumatoid arthritis, this analysis aimed to assess the psychometric properties of WPS in adult-onset active PsA. **METHODS:** WPS comprises 9 questions evaluating employment status, workplace and household productivity. Psychometric properties were assessed using data from RAPID-PsA (NCT01087788). The WPS was completed at baseline and every 4 weeks (wks) until Wk24. Validity was evaluated via known-groups approach, comparing patients (pts) with a worse vs better health state, defined by the 1st and 3rdquartiles cut-off of pt scores to DAS28(CRP), HAQ-DI, SF-36 and PsAQoL. The responsiveness and reliability were assessed comparing WPS mean changes in ACR20 or HAQ-DI MCID=0.3 responders vs non-responders at Wk12. Comparisons were conducted in the Randomized Set (observed cases) using a non-parametric bootstrap-t method. **RESULTS:** Results confirmed the discriminant validity of WPS. Compared to pts with a better health state, pts with a worse health state had significantly more days of household work lost, household work with reduced productivity, social activities missed, outside help hired and a significantly higher interference rate of arthritis. Similarly, employed pts with a worse health state had significantly more work days lost or with productivity reduced by $\geq$50%, and higher interference of arthritis on work productivity. WPS was also responsive to clinical changes, with responders reporting significantly larger improvements at Wk12 in WPS scores vs non-responders. The effect sizes for changes in productivity in responders were moderate ($0.5<SRM<0.8$) or small. **CONCLUSIONS:** These analyses demonstrate that the WPS is a valid, responsive and reliable instrument for measurement of productivity within and outside the home in adult-onset PsA.

PRM152
TRANSLATION AND CULTURAL ADAPTATION OF THE POLISH VERSION OF "DISABILITIES OF THE ARM, SHOULDER AND HAND" (DASH) AND QUICKDASH QUESTIONNAIRES
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OBJECTIVES: To translate into Polish and adapt culturally DASH and QuickDASH outcome measures. **METHODS:** We followed recommendations issued by Insitute for Work and Health (IWH, 2007). Two forward translations were made – by an informed (T1) and uninformed translator (T2). Discrepancies were discussed and resolved with participation of the third unbiased investigator and a synthesis of translations was produced (T12). Two native speakers, totally blind to the original version, translated back T12 version into English (BT1 and BT2). Eight experts: 2 orthopedic surgeons, physiotherapist, sworn translator, 2 English native speakers, psychologist and a Polish language specialist formed an Expert Committee (EC). Committee consolidated all the versions, review all the translations and reached a consensus on any discrepancy found. Decisions were made to achieve semantic, idiomatic, experiential and conceptual equivalence with the original version. **RESULTS:** We report 65 discrepancies raised by Expert Committee members and their solutions. The Polish pre-final versions of DASH and QuickDASH questionnaires, ready for pilot testing, were produced. Written reports from all stages of the process were submitted to the IWH Cross-Cultural Adaptation Review Committee for approval. **CONCLUSIONS:** Numerous translation discrepancies were resolved by discussion by Expert Committee. The Polish pre-final versions of DASH and QuickDASH questionnaires were produced and used in pilot testing.

PRM153
LINGUISTIC TRANSLATION AND CULTURAL ADAPTATION OF FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY-TUBERCULOSIS INSTRUMENT INTO ARABIC LANGUAGE
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OBJECTIVES: Functional Assessment of Cancer Therapy- General (FACT-G) was adapted to develop a disease specific subscale for pulmonary tuberculosis (PTB) patients in Iraq. The current study aimed to linguistically validate Functional Assessment of Chronic Illness Therapy- Tuberculosis (FACIT-TB) measurement scale into Arabic language and to produce a translated version which was conceptually equivalent to the original U.S. English version for use in clinical practice and research. **METHODS:** The linguistic validation process comprised of general procedures derived from internationally accepted guideline for linguistic validation and cultural adaptation of FACIT measurement system; including 1) Forward translation, 2) Reconciliation, 3) Back translation, 4) Review, 5) Spelling and grammatical verification. Furthermore, the translated questionnaire was pretested at Thoracic and Respiratory Diseases Specialist Center in Baghdad, Iraq. **RESULTS:** Issues encountered during the linguistic validation process of FACIT-TB into Arabic language pertained to linguistic and semantic nuance were resolved. Pretesting was completed in seven Arabic-speaking TB patients with a mean age of 40.14 years. In addition, respondent need about 15.35 minutes (range 10-20 minutes) to complete the questionnaire. In general, respondent reported no significant problem with understanding the content of the Arabic version of FACIT-TB. Furthermore, they reported no culturally-irrelevant item. The instrument was found to be comprehensible, clear and relevant to the value of PTB patients in Iraq. **CONCLUSIONS:** Linguistic validation of FACIT-TB into Arabic language was completed according to a recognized and rigorous double-back translation method to achieve, to the greatest degree possible, equivalence of meaning and measurement between the two different country versions. It will provide an additional parameter to evaluate the effectiveness of TB program for patients in Iraq. Health care providers in the national TB control program should make a judicious utilization of this instrument in helping patients to cope with their illness and in predicting TB treatment outcomes.

PRM154
ESTIMATING THE SOCIAL DISTRIBUTION OF HEALTH IN ENGLAND
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OBJECTIVES: To develop a model of quality adjusted life expectancy (QALE) in England and estimate the social distribution of both mortality and morbidity by socio-economic characteristics such as gender, ethnicity and deprivation. METHODS The 2011 wave of the Health Survey for England (HSE) is used to model EQ-5D as a function of gender, ethnicity, index of multiple deprivation and other relevant characteristics using appropriate regression techniques to account for the skewness of the EQ-5D distribution. Previous waves of the HSE are used to validate the model. ONS life tables and the ONS longitudinal study data are used to model life expectancy as a function of the same characteristics. The two models are combined to give a multivariate prediction model for QALE as a function of these characteristics. This prediction model is combined with population level aggregate data on the key characteristics and used to estimate a population QALE distribution. **RESULTS:** There is a substantial social gradient in the health distribution as represented by QALE in England. The QALE differential between most and least disadvantaged fifths of the social distribution is 12 years, compared with a difference of 5 years in life expectancy when morbidity differentials are not taken into account. **CONCLUSIONS:** The QALE prediction model allows us to estimate quality adjusted life expectancy distributions for various subsets of the population, and shows that focusing on life expectancy alone substantially underestimates the degree of health inequality. Our model can be used both for obtaining a more accurate picture of the overall level of health inequality in society and for evaluating the overall impact of population health interventions on health inequality.

PRM155
USING STRUCTURAL EQUATION MODELING TO DETECT RESPONSE SHIFT AND TRUE CHANGE IN HEALTH-RELATED QUALITY-OF-LIFE SCORES OF BREAST CANCER PATIENTS AFTER SURGERY
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OBJECTIVES: This study aimed to capture response shift and true change in health-related quality of life (HRQOL) scores of breast cancer patients after surgery. **METHODS:** A data set from a prospective study to identify predictive factors of HRQOL (Taira N, Shimozuma K, *et al*: Breast Cancer Res Treat, 2011) was analyzed, which included HRQOL scores of physical well-being (PWB) and emotional well-being (EWB) scales of the FACT-G in 191 female breast cancer patients during a two-year postoperative period (at baseline [1 month after surgery]), 6, 12, and 24 months postoperatively). Oort's structural equation modeling approach was used to investigate three aspects of response shift: (a) a change in the respondent's internal standards of measurement (i.e., recalibration); (b) a change in the respondent's importance of values (i.e., reprioritization) and (c) a redefinition of the target construct (i.e., reconceptualization). **RESULTS:** All three aspects of response shift were observed. Recalibration and reprioritization were occurred in three items of PWB ('nausea', 'trouble with family', 'side effects'). Reconceptualization was observed from PWB to EWB in two items ('nausea' and 'pain') and from EWB to PWB in two items ('sadness' and 'nervousness'). True change, which was calculated after adjustment of response shift, was observed in PWB (the across occasion difference of common factor mean [alpha] = 0.238, $P < 0.001$) during first 6 months, and in PWB (alpha = 0.605, $P < 0.001$) and EWB (alpha = 0.234, $P < 0.05$) during first 12 months, while observed data analyses indicated statistically significant change in PWB and EWB during first 12 months. **CONCLUSIONS:** Captured response shifts in this study may be affected by various pre- and post-operative events such as notification of cancer and/or received treatments. These results will help improve reliability of HRQOL measurements in a longitudinal study.

PRM156
FACTORIAL INVARIANCE OF THE WHOQOL-OLD ACROSS GENDER, AGE, AND RESIDENT AREA IN TAIWAN
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OBJECTIVES: To examine the factor invariance of the WHOQOL-OLD across gender, age, and resident area for the old people in Taiwan. **METHODS:** Data were collected from 512 Taiwan elderly people (M = 76.2, SD = 7.5, ages ranged from 60 to 99) including 177 males and 335 females. 232 aged from 60 to 75 and 279 aged from 76 to 99. 334 live in the southern rural area and 176 live in the northern metropolitan area. To examine the factorial invariance of the WHOQOL-OLD, the sample was divided into two groups on different gender, age, and resident area. First, a baseline six-factor model was tested for different gender, age, and resident area respectively. Second, multi-sample analysis was conducted across gender, resident area, and age. Specifically, equal constrains on factor loadings, error variances, and factor variances were imposed. Model comparisons by using Chi-square difference tests were conducted to examine the factor invariance across gender, age, and resident area. **RESULTS:** Multi-sample analysis revealed that the factor loadings were invariant across different gender, age, and resident area groups respectively. Besides, when imposing equal constrains on the factor loadings, item variances and factor variances, the model fit indices revealed that the only complete factor invariance model was across gender but not age and resident area groups. **CONCLUSIONS:** This study suggests the underlying factor construct of the WHOQOL-OLD are similar to different degree across different gender, age, and resident area groups. We conclude that the WHOQOL-OLD is a practical measurement tool for different gender, age, and location groups for the old people in Taiwan.

PRM157
A REVIEW OF COGNITIVE INTERVIEWING METHODOLOGIES DURING LINGUISTIC VALIDATION OF CLINICAL OUTCOME ASSESSMENTS (COAS)
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OBJECTIVES: Per ISPOR and FDA guidelines, conducting cognitive interviews during the linguistic validation of COAs is recommended to increase comprehension and conceptual equivalence between language versions. However, multiple methods are available to conduct cognitive interviews, partially enabled by the increased availability and ease of technology to facilitate the interviews. This poster will review the various methodologies that can be used to conduct cognitive interviews. **METHODS:** A review of cognitive interview methodologies from past projects as well as potential alternative methods was conducted, including: 1) in-person interviews, 2) telephone interviews, and 3) interviews via video conferencing. Consideration was given to ease of scheduling, cost, and quality/comphrensiveness of feedback. **RESULTS:** Each methodology presented pros and cons, including: 1) in-person interviews enable the interviewer to gauge the respondent's body language, signaling where he/she may be having difficulty with an item but are unable to verbalize feedback; however, the interviews are more costly and present organizational challenges (i.e. scheduling, travel, etc.); 2) telephone interviews enable easier scheduling of interviews and reduce cost, but do not allow the interviewer to gauge the body language of the respondent and respondents may not feel comfortable providing feedback over the telephone; 3) interviews via video conferencing may enable easier scheduling of interviews, allow an interviewer to gauge the body language of the respondent, and provide a lower-cost alternative, but the availability of the technology can present challenges in certain regions. **CONCLUSIONS:** There are various ways of conduct-

ing cognitive interviews during the linguistic validation process of COAs. Further research is required to develop industry guidelines to ensure that the interviews are able to achieve their purpose: garnering accurate and meaningful feedback from respondents in order to increase comprehension and cross-cultural equivalence of multiple language versions.

PRM158

DEFINING STANDARDS OF CLINICIAN QUALIFICATIONS FOR THE LINGUISTIC VALIDATION OF CLINICAL OUTCOME ASSESSMENTS (COAS)

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OBJECTIVES: As the linguistic validation of COA instruments often includes a review of medical terminology, it is important to confirm that the in-country clinician reviewer has sufficient qualifications to ensure quality as well as to elicit the highest level of conceptual equivalence in a linguistic validation project. This poster will consider each type of COA (Clinical Outcomes Assessment) and recommend guidelines for the qualifications of medical reviewers. **METHODS:** An examination was conducted of past linguistic validation projects involving an in-country review step with a medical professional. A review was completed of COAs (Clinician-Reported, Caregiver-Reported, as well as Patient-Reported questionnaires and diaries) within various therapeutic areas. This review also included an analysis of the specific background of each in-country clinician reviewer. **RESULTS:** In the examination of linguistic validation projects that included a medical review step, it was determined that the experience level of clinician reviewers varied between projects. In an effort to standardize this step, a minimum experience requirement based on study needs and project type is proposed. **CONCLUSIONS:** After a thorough review of past linguistic validation projects, it is suggested that an in-county clinician reviewer should, at a minimum, encompass the following qualifications: 1) 2+ years experience diagnosing and/or treating the patient population; 2) M.D. or relevant equivalent in the target country; 3) Native-language and/or advanced medical terminology training in the target language/country. Implementing minimum qualifications standards will help to ensure that an in-country medical reviewer will conduct a high-quality review for linguistically validated COAs.

PRM159

EVALUATION OF THE PSORIASIS AREA AND SEVERITY INDEX (PASI) AS PATIENT RELEVANT OUTCOME IN THE BENEFIT ASSESSMENT OF PSORIASIS THERAPIES

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OBJECTIVES: Psoriasis vulgaris is one of the most frequent chronic diseases in dermatology and can cause a high disease burden and reduction of quality of life. The severity of psoriasis is determined by the clinical parameter PASI (Psoriasis Area and Severity Index). It is the most often cited measurement to determine the efficacy of therapies. Since the assessment of patient relevant treatment benefit gains importance in treatment evaluation, the objective of the study was to test to what extent PASI improvements agree with patient relevant benefit parameter. **METHODS:** A multicenter longitudinal observational study was conducted in n = 218 patients with psoriasis vulgaris. Data collection took place at the beginning of psoriasis treatment and between three and eight weeks after treatment. In addition to PASI, physician and patient data were collected, e.g. socio-demographics, clinical features, dermatological quality of life (DLQI), and assessment of treatment. **RESULTS:** Each level of PASI (50, 75, 90) showed relevant improvements in patient reported outcomes. The satisfaction with the treatment and the patient benefit was greater, the higher PASI was reached. This effect was not seen for DLQI. However, improvements were only significant for PBI for all levels of PASI. Furthermore, results showed that not only changes in PASI but also its absolute value at the end of treatment has an impact for the patient reported assessment of therapy. Values < 3 in comparison to < 5 resulted in better values of PBI and higher treatment satisfaction. **CONCLUSIONS:** The clinical reduction of the severity of psoriasis vulgaris correlates with the improvement of the quality of life and with the patient defined treatment benefit. However, the PASI does not completely reflect the patient relevant outcome in the benefit assessment. Therefore, it is recommended to make additional elicitation of patient defined objectives and benefits in the evaluation of psoriasis therapies.

PRM160

THE INFLUENCE OF CHOICE TASK LAYOUT ON THE OUTCOMES OF A DISCRETE CHOICE EXPERIMENT

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OBJECTIVES: To test to what extent the presentation of choice tasks contrasting display in words or graphics, influences the attribute estimates, relative importance and participation probability and the conclusions drawn from a Discrete Choice Experiment (DCE). **METHODS:** A DCE questionnaire was sent to the parents of 2,500 newborn babies aged 6 weeks at maximum. Each questionnaire contained two versions of the same 9 choice tasks, one in which the levels were presented in words, and one with graphic attribute levels. The DCE consisted of five attributes: vaccine effectiveness, frequency of severe side effects, protection duration, location of vaccine administration, out-of-pocket costs. Choice consistency was estimated, panel-mixed logit models were conducted to estimate the relative importance of the attributes and internal sample validation was calculated. **RESULTS:** In total 13% answered consistent on all choice tasks, 19% answered inconsistently in one choice task, and 51% answered inconsistently in more than two choice tasks. Respondents who were presented with word choice tasks at first were significantly more consistent compared to respondents that were presented with graphic choice tasks at first. Although out-of-pocket costs was the most important and frequency of severe side effect was the least important attribute in both datasets, the relative importance of the other attributes differed. All results differed by educational level. Estimated and observed choices showed higher correlation in the word dataset. **CONCLUSIONS:** The presentation of the choice tasks by either using words or graphics influences study outcomes. The use of graphics to present attribute levels in choice tasks seems less preferred by respondents and showed a reduced validity. Besides extensive pilot testing, discussions about the presentation of the choice tasks should be included in the focus group stage of the designing process. Extensive research on respondents' interpretation of choice tasks should be conducted to enable the formation of choice task presentation guidelines.

PRM161

SIMILARITIES AND DIFFERENCES ACROSS SAME LANGUAGE QUESTIONNAIRES FOR DIFFERENT COUNTRIES: LINGUISTIC VALIDATION OF THE ASTHMA SYMPTOM DIARY (ASD) AND KIDNEY DISEASE AND QUALITY OF LIFE (KD-QOL-36)

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OBJECTIVES: Prior to use in an international study, the Asthma Symptom Diary and Kidney Disease and Quality of Life underwent linguistic validation into over 30 languages. This involved linguistic validation work on common languages targeted for different countries via the forward / backward translations or adaptation steps and cognitive debriefing step. This study aims to investigate similarities and differences in the translation of key terms and wordings and determine potential patterns across groups of languages. **METHODS:** This investigation was carried out as follows: 1) Identification of key terms and words; 2) Collation and comparison of the translations across the same language versions; 3) Identification of similarities and differences; and 4) Review of discussions and issues from the translation process. **RESULTS:** The linguistic validation process was shown to be able to identify and resolve important cross-cultural differences. Key findings included the identification of potential recurring translation issues between same language groups. Within the German, French and Spanish languages, technical terminology was translated alike whilst there were differences in the way non-technical, socially constructed wordings, emotions and symptoms were translated due to such factors as idiomatic formulations and cultural differences. Across the English languages, the text was simplified or elaborated as part of the adaptation process. Across the Russian and Chinese languages there were differences in the way technical and disease-specific terms were translated. **CONCLUSIONS:** With the insight of the linguistic validation process, important differences were identified and resolved between technical terms and general wordings across same language groups. Cognitive debriefing is highly recommended and this will ensure appropriate comprehension across cultures and facilitate International comparison and pooling of data.

PRM244

DETERMINING THE MAGNITUDE OF A DETECTABLE AND A RELEVANT TREATMENT BENEFIT IN AESTHETIC MEDICINE USING A PHOTOGUIDE AND THE INTERNET

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OBJECTIVES: Photoguides are used as measures of treatment effect. To interpret the results, an understanding of what change is "enough" is required. The purpose of this study was to determine the Patient Detectable Difference (PDD) and Patient Relevant Difference (PRD) in scar severity using a discrete choice experiment with paired comparisons of scar photos via the internet. **METHODS:** Patients were asked to select the scar most like their own from a 5-photo photoguide as the referent. Each patient was then presented with a randomly selected scar from a scar library previously scored on severity by clinicians. For the PDD, patients were asked if the random scar was better, worse, or about the same. For the PRD, patients were asked if they would undergo treatment to "get" the random scar as opposed to keeping the referent scar. Each exercise was repeated five times. Optimal cutoff scores for PDD and PRD were based on a random intercept logistic model (RILM). **RESULTS:** Using a series of RILM estimations across 514 participants, the PDD was calculated as 15.4 points on a 100-point scale (area under curve = 0.85, sensitivity = 0.83, specificity = 0.73). In subgroup analyses by gender and scar source, the PDD ranged from 9.5 to 22.0 points. The replicate analysis adjusting for directionality of preference (improvement only) showed a PRD of 26.9 points (area under curve = 0.97, sensitivity = 0.90, specificity = 0.93), which ranged from 19.5 to 32.0 in the subgroups. **CONCLUSIONS:** Results show that, as expected, scar patients report detectable differences in scar severity that are smaller than what they report as relevant differences necessary to choose treatment. The Internet-based approach using a discrete choice experiment is a novel method to quantify the threshold of detectable and relevant differences in scar severity using a photoguide.

PRM162

PARENT RATINGS OF ABILITY TO CONSENT FOR CLINICAL TRIALS IN FRAGILE X SYNDROME

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OBJECTIVES: Advances in understanding the neural underpinnings of intellectual disabilities (ID) such as fragile X syndrome (FXS) have led to clinical trials testing medications addressing disease-specific targets. Individuals with ID ought to have a voice in consenting for clinical trials, but the extent to which they are capable of doing so is unknown. We discuss the importance of involving individuals with ID in the consent process and report results from a study of parents' perceptions of their child's ability to consent. **METHODS:** A survey was conducted with 422 families who had a child with FXS. Parents rated items assessing their child's abil-

ity to understand and complete six consent tasks. They also provided information about themselves (maternal education, willingness to enroll child in a clinical trial) and their child (age, autism status, thinking/reasoning ability, gender). **RESULTS:** Factor analysis confirmed that the six items comprise a single factor. However, we found a clear hierarchy of difficulty; the least difficult tasks were "understands that this medication is different from his/her regular treatment" and "realizes that he/she can choose to participate in the study or withdraw at any time." The most difficult were "can make a decision about study participation" and "understands and weighs potential benefits and risks of participating in the study." Although 29% of parents reported that their son was not at all capable of participating, the remainder exhibited a range of decisional skills. Factors associated with this variability include gender, autism, cognitive ability, age, and parents' willingness to enroll their child in clinical trials. **CONCLUSIONS:** Parents rate many individuals with FXS as able to participate in the consent process, but they will likely need support to maximize effective participation. We conclude with a brief review of strategies to support more inclusive participation in the consent process for people with ID.

PRM163

RESULTS OF A STUDY USING A TABLET PC TO COLLECT PROS IN ELDERLY POPULATION

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OBJECTIVES: Primary objective of the Percepolis study was to look at patient's perception regarding their Erythropoiesis Stimulating Agents (ESA) treatment of anemia in chronic kidney disease. Many discussions arose at the set-up of the study regarding the best collection method of PROs as target population was old. The following factors helped to make a decision towards ePRO: - Clinical data were collected using an eCRF and previous experience of studies using PROs showed it was difficult to mix method of collecting data, - PRO was the primary endpoint of this study and needed to be carefully monitored, - Most elderly people use new technologies (cellular phone, PC), - Twenty questionnaires needed to be equally distributed. **METHODS:** This is a 6-month multicenter prospective Non-Interventional Study (NIS). Patients had to complete questionnaires at baseline and around 6-month in order to analyze the importance they gave to their ESA treatment characteristics. Technology used was the Tablet PC Samsung Galaxy Tab and specific interface was developed on the Operating System (O.S.) Android to maximize ease of use of the device for patients and investigators. For example, patients only had to select an answer on the screen to display the next question using the tactile functionnalities of the device. When connecting to the electronic data capture system, O.S. was detected in order to fit the screen's display of the HTML pages. **RESULTS:** A total of 789 patients were included, 93% patients answered at least one questionnaire at baseline, 87% after 6 months of treatment. Mean age of the study population was 73 years old (± 13 years). Most PROs (95%) were answered using the Tablet PC. **CONCLUSIONS:** ePROs can be used in elderly population as long as tools are adequately developed to simplify use of devices. ePROs also allowed following online study recruitment and questionnaires data entry.

PRM164

HOW BURDENSOME IS COMPLETION OF ELECTRONIC PATIENT-REPORTED OUTCOMES (EPRO)? ITEM COMPLETION TIMES AND QUALITATIVE EVIDENCE FROM STUDIES IN FOUR DIFFERENT HEALTH CONDITIONS

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OBJECTIVES: The patient burden of completing large numbers of patient-reported outcome (PRO) items is often a concern; particularly when PROs must be completed daily, or at multiple timepoints over long studies. However, as ePRO and mPRO (technology that utilizes patients' personal tablets and smartphones) methods advance, PRO completion becomes quicker and easier. How long does it actually take patients to complete ePROs? How burdensome do patients find ePRO completion? **METHODS:** ePRO allows collection of the time taken to complete a set of PRO items. We summarise data from four qualitative studies across a range of health conditions (fibromyalgia, a women's health condition, pediatric constipation and pediatric irritable bowel syndrome). In all four studies, small samples of patients (n=20-65) completed an ePRO diary daily for 5-9 days during pilot testing prior to cognitive debriefing. Completion times and missed days were collected. During the cognitive debriefing interviews patients were asked how burdensome the PRO completion was and if they had difficulty fitting it into their daily routine. **RESULTS:** The PROs being developed had 15-35 items, but two included skip patterns, reducing the item burden. Average completion times ranged from 2.5-5.5 minutes per diary. For diaries without skip patterns, mean 'per item' completion times were calculated to range from 9.4-15.7 seconds. The majority of patients (93-100%) reported that the PRO was quick and easy to complete and not burdensome. Missed diary rates were consistently low with only 0-12% of patients missing more than one diary completion in the two studies where this information was collected. **CONCLUSIONS:** These data provide evidence that patients (including children) can complete ePRO diaries very quickly, don't find this burdensome, and are happy to complete relatively large numbers of items daily. If ePROs are carefully designed, using skip-patterns and event driven items, completion burden can be reduced even further.

PRM165

HARMONIZING MEASUREMENT OF ADHERENCE ACROSS THE 4-ITEM AND 8-ITEM MORISKY MEDICATION ADHERENCE SCALE USING CROSS-SECTIONAL DATA FROM PATIENTS TREATED FOR IRRITABLE BOWEL SYNDROME

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OBJECTIVES: The 4-item Morisky Medication Adherence Scale (MMAS-4) and the more recent 8-item version (MMAS-8) have been both validated, and their concurrent validity has been assessed among hypertensive patients, but the extent to which the two scales can be compared against one another has not been determined. The current analysis assessed whether adherence scores obtained with the two scales on different patients can be compared or integrated across studies. **METHODS:** Data were taken from the 2011 and 2012 US National Health and Wellness Survey (NHWS). The NHWS is a large cross-sectional survey representative of the total adult population in several major markets; current analyses were limited to the US (n~75,000/year). Respondents self-reported physician diagnosis of various health conditions, including 9,633 who reported a diagnosis of IBS. Adherence was measured with MMAS-4 in 2011 and MMAS-8 in 2012. The two adherence scales were evaluated by comparing the frequency distributions of the MMAS scores in the two scales, Cronbach's alpha and inter-item correlations, and the creation of a new 4-item scale including the questions in MMAS-8 that best matched the questions in MMAS-4. **RESULTS:** In IBS patients, both MMAS-4 and -8 scores are Poisson-like distributed, with median at zero (high adherence). Chronbach's alpha was 0.64 for MMAS-4 and 0.70 for MMAS-8, while average item-test correlations were 0.70 and 0.59, respectively. The reduced 4-item scale created out of MMAS-8 is also Poisson-like distributed, Cronbach's alpha was 0.67 and the average item-test correlation was 0.71. **CONCLUSIONS:** Data obtained with the two MMAS show similar qualitative and quantitative characteristics, suggesting that it may be appropriate to integrate data sources using the two different versions, particularly when the responses to the subset of 4 MMAS-8 items are available. Future research should confirm that the scales can be integrated in different therapeutic areas.

PRM166

USING FEEDBACK FROM PATIENTS IN DETERMINING SUITABILITY OF THE PERCEIVED DEFICITS QUESTIONNAIRE (PDQ) AND THE RESOURCE UTILIZATION IN DEMENTIA-LITE (RUD-LITE) FOR USE IN CLINICAL TRIALS IN PRODROMAL ALZHEIMER'S DISEASE

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OBJECTIVES: Many instruments used to assess outcomes of treatment for Alzheimer's disease (AD) have no published evidence for their content validity in mild cognitive impairment (MCI) or prodromal AD (pAD). The objective of this project was to evaluate the content validity of AD patient reported outcome (PRO) instruments in this population. **METHODS:** Two waves of interviews were conducted: First, 11 patients with MCI and their informants/ (carers) evaluated several AD PROs (Alzheimer's Disease Medication Administration Questionnaire (ADMAQ), Abbreviated Resource Utilization in Dementia-Lite (RUD-Lite), Perceived Deficits Questionnaire (PDQ), and Abbreviated Dependence Scale (AB DS); Second, 8 patients with pAD reviewed the modified PDQ, and their carers reviewed the RUD Lite. Interviews were transcribed and analysed. **RESULTS:** Results of Wave 1 identified the PDQ and the RUD-Lite as the most promising measures for this cohort. Some minor modifications were suggested for the PDQ, and a separate section was added to the RUD-Lite. Results of Wave 2 showed pAD carers viewed the content of the RUD- Lite as less relevant because the patients are not functionally restricted enough to utilize resources at this early stage of the disease, although the newly added domain for the pAD population was understood and applicable. The modified PDQ was more acceptable to pAD patients than the original version. **CONCLUSIONS:** Even well-established measures for AD patients should have their content validity evaluated prior to their use in pAD or MCI populations. In this study, we found that the PDQ and RUD –Lite needed modifications to be more relevant in early stage patients.

PRM167

RECOMMENDATIONS FOR THE SUCCESSFUL LINGUISTIC VALIDATION OF CLINICAL OUTCOME ASSESSMENTS FOR LIMITED PATIENT POPULATIONS

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OBJECTIVES: Timeline and budget considerations for the linguistic validation of Clinical Outcome Assessments (COAs) can vary substantially depending on patient population requirements and target locales. Rare diagnoses and/or small populations of native speakers of a language can lead to a small pool of eligible patients for cognitive debriefing respondents. This review highlights considerations necessary to promote successful linguistic validation projects and mitigate the potential impact of small patient populations that, in turn, can affect study timelines as a whole. **METHODS:** To assess possible steps to take during study planning and the linguistic validation process, a literature review and examination of past linguistic validation projects were completed. This focused on trials in which a small patient population limited the number of eligible cognitive interviewing respondents, and the issues and solutions associated with each project. **RESULTS:** In order to meet timeline and budget requirements, it is crucial that sufficient steps are taken to ensure cognitive interviewing populations are fully evaluated during a trial's planning stages. Solutions for helping achieve this include: 1) Identification and possible inclusion of broader patient populations with conditions with similar symptoms; 2) Extended timeline consideration for rare diseases or small native-speaking populations at study start; 3) Selection of more general COAs (e.g. not specific to the diagnosis in the case of rare conditions) so cognitive interviewing may be performed on healthy respondents or a broader group of patients. **CONCLUSIONS:** When choosing COAs for global use, an analysis of the intended patient population – including prevalence rates of the condition and size of the native-speaking population – is recommended in order to integrate projected linguistic validation timelines into the overall study plan. It is also recommended that study teams discuss this with their language services team for guidance on timelines and assistance in planning to ensure targeted study milestones are met.

PRM168

USING MOBILE TECHNOLOGY (MHEALTH) TO DEVELOP THE VALUE STORY FOR NEW DRUGS, DEVICES AND THERAPIES: OPTIMISING USER ENGAGEMENT AND ADDRESSING PAYER CONCERNS

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OBJECTIVES: This research explored the feasibility of using mobile technology (mHealth) to capture data such as resource utilisation and patient reported outcomes to support the market access of new products. The main objectives were to understand best practices in engaging end users to optimise data collection, and to explore payer opinions on the validity of using mHealth for data collection and its usefulness in the decision making process. **METHODS:** Secondary research was conducted to identify best practices in optimising end user engagement with mHealth solutions. Studies that led to successful outcomes were analysed in detail to understand the key engagement success factors. Qualitative primary payer interviews were conducted in several key European markets to understand the validity of using mHealth to collect data including perceived challenges of leveraging this data to support market access decisions. **RESULTS:** Research showed that interventions that are personalised through data, analytics and behaviour change methodologies are most successful in engaging end users when using mHealth. Payers highlighted several key concerns of using mHealth; namely, data quality and sustainability/scalability. These concerns should be considered and addressed by health care companies who wish to use mHealth as a data platform to support payer decisions. **CONCLUSIONS:** mHealth is a tool that holds promise for many different parts of the health care value chain. This includes leveraging mHealth to support the market access targets of new products, by collecting and using data to enhance the communication of the products' value. The findings from this research highlight best practices to engage users in order to optimise data collection as well as provide insights from payers on the key concerns of doing so.

PRM169

THE INFLUENCE OF HAQ UTILITY MAPPING ALGORITHMS ON THE COST-EFFECTIVENESS OF SECOND LINE BIOLOGICS FOR TREATMENT OF RHEUMATOID ARTHRITIS

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OBJECTIVES: In 2010, the National Institute for Health and Clinical Excellence (NICE) performed a multiple technology assessment for second line biologic treatments (following the failure of a TNF inhibitor and disease modifying antirheumatic drugs (DMARDs)) for the treatment of rheumatoid arthritis (RA). The Birmingham RA Model (BRAM) was used to obtain incremental cost-effectiveness ratios (ICERs) of £21,100/quality-adjusted life year (QALY) for rituximab versus DMARDs and £130,600 for abatacept versus rituximab. Adalimumab, etanercept and infliximab were dominated by rituximab. NICE recommended rituximab, unless contraindicated, in which case all the other biologics were recommended. The BRAM used in the NICE assessment used a linear regression model to translate Health Assessment Questionnaire (HAQ) scores into EQ-5D scores, however other algorithms exist. The objective of this study was to understand how the algorithm used to map from HAQ to EQ-5D affects the ICERs generated by the model. **METHODS:** The BRAM used in the NICE assessment used a linear regression model to translate Health Assessment Questionnaire (HAQ) scores into EQ-5D scores, however other algorithms exist. The objective of this study was to understand how the algorithm used to map from HAQ to EQ-5D affects the ICERs generated by the model. **RESULTS:** The ordering of the effectiveness of treatments did not change with the mapping algorithm used, however there was substantial variation in the magnitude of the ICER. The ICER for rituximab versus DMARDs varied from £21,594/QALY to £32,039/QALY depending on the exact algorithm used. The ICER for abatacept versus rituximab varied from £124,776/QALY to £167,687/QALY. **CONCLUSIONS:** The cost-effectiveness results of the BRAM are heavily influenced by the choice of mapping algorithm. In future modelling, the choice of algorithm should be justified, and appropriate sensitivity analyses presented. Further research is needed to identify the most appropriate algorithm(s) for use in health technology assessment.

PRM170

USING RASCH ANALYSIS TO CO-CALIBRATE SCORES FROM OUTCOME MEASURES SPECIFIC TO ASTHMA (ALIS), CHRONIC OBSTRUCTIVE PULMONARY DISEASE (LCOPD) AND PULMONARY HYPERTENSION (CAMPHOR)

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OBJECTIVES: Disease-specific patient-reported outcomes (PROs) are designed to be highly relevant to a single disease. It is widely believed that comparisons of outcomes between patients with different diseases is only possible using generic PRO measures. The present study employs a novel method of using Rasch analysis to co-calibrate scores from different disease-specific PROs allowing scores to be compared across diseases. **METHODS:** Three samples of patients completed the Asthma Life Impact Scale (ALIS), the Living with COPD scale (LCOPD) or the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR), depending on their illness. Each scale utilises the needs-based model of QoL and the scales share 8 common items. The three samples were analysed separately for fit to the Rasch model and then combined and re-analysed. **RESULTS:** The ALIS was completed by 140 asthma patients (mean age=50.6, males = 29.3%); the LCOPD by 162 COPD patients (mean age=69.3, males = 43.8%) and the CAMPHOR by 91 patients (mean age=52.6, males = 29.7%). Each of the scales fit the Rasch model individually (ALIS $Chi^2 = 0.05$; LCOPD $Chi^2 = 0.32$; CAMPHOR $Chi^2 = 0.92$). The combined dataset also fit the Rasch model at first run ($Chi^2 = 0.24$). One common item showed misfit ($Chi^2<0.001$) and non-uniform differential item functioning (DIF) by disease ($Chi^2<0.001$). This item was removed from the analysis and the final co-calibrated scale showed good fit to the Rasch model ($Chi^2=0.48$) with minimal DIF by age, gender or disease. **CONCLUSIONS:** The results showed that it was possible to co-calibrate scores on the ALIS, LCOPD and CAMPHOR. As disease-specific measurement has advantages over generic assessment related to relevance and reproducibility, the results have the potential to enhance PRO measurement in respiratory research.

PRM171

THE E-HEALTH IMPACT QUESTIONNAIRE: DEVELOPING A TOOL TO MEASURE THE EFFECTS OF USING HEALTH-RELATED WEBSITES

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OBJECTIVES: The internet is a valuable resource for accessing health information and support. This study aimed to develop a tool (the eHIQ) to measure the impact of using health-related websites which contain experiential and factual information. **METHODS:** A multi-method study with four stages. Stage 1: Themes concerning the impact of using health-related websites were identified through qualitative secondary analysis of interviews exploring patient and carer experiences of health and a relevant literature review. Stage 2: Questionnaire items based upon identified themes were constructed and assessed using expert and patient opinion. Stage 3: Items were administered online and subjected to exploratory factor analysis. Stage 4: The reduced questionnaire and appropriate reference measures were administered online to test convergent validity and external reliability. **RESULTS:** Sixty-seven items were constructed according to the key themes identified through relevant literature and qualitative analysis. Following expert and patient refinement, two independent item pools were entered into psychometric testing. The first item pool (eHIQ-Part 1) related to general views of using the internet in relation to health and second item pool (eHIQ-Part2) related to the impact of using a specific health-related website. Analysis confirmed three domains present in eHIQ-Part 1 and six domains present in eHIQ-Part 2. These domains were tested further during Stage 4 and were found to have high convergent validity, internal consistency and good test-retest reliability. **CONCLUSIONS:** Developing the eHIQ through the use of qualitative analysis and patient-expert opinion enhanced face and content validity. The eHIQ demonstrates good psychometric properties and will enable the measurement of the effects of using health-related websites across a range conditions.

PRM172

DESIGN OF LUPUS IMPACT TRACKER (LIT) VALIDATION STUDY IN FIVE EUROPEAN CLINICAL PRACTICE SETTINGS

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OBJECTIVES: Physicians treating systemic lupus erythematosus (SLE) use a variety of tools to monitor disease activity and organ damage however these do not capture the functional burden experienced by patients. Studies suggest that communication between physicians and patients need to be optimized. The Lupus Impact Tracker (LIT), a brief, disease specific 10-item patient reported outcome tool, was developed to assess the impact of SLE on patients daily functioning and well-being. This study aims to evaluate the cross-cultural validity, acceptability and feasibility of the LIT in European clinical practice settings. Potential effect of LIT on communication during the consultation will also be assessed. **METHODS:** This is a prospective, observational, multicenter cross-sectional validation study of SLE patients on standard of care from hospital/clinical settings in five European countries (France, Germany, Italy, Spain and Sweden). 625 patients enrolled to obtain at least 500 evaluable cases irrespective of disease severity. Before the visit, patients will complete self-reported questionnaires: SF-36, Global Evaluation of Change (GEC), care satisfaction and LIT. During visits, physicians will record patient data, assess disease activity using the SELENA-SLEDAI and Physician Global Assessment (PGA), and disease damage using the SLICC/ACR damage index. After the visit patients and physicians complete LIT feedback questionnaires. Analyses will be performed using descriptive statistical methods with no specific hypothesis suggested. **RESULTS:** Psychometric evaluation of LIT in US clinical settings found the tool reliable and valid. Evaluation for use in European clinical practice settings is thus needed. Cross-cultural validity of LIT across countries will be analyzed using differential item functioning (DIF) analysis. Data from the Lupus Impact Tracker-(Patient and Physician) Feedback Questionnaires will be tabulated and summarized. **CONCLUSIONS:** We need improvement of the patient/physician interaction in lupus care. The LIT may be a valid and acceptable tool for use with SLE patients in European clinical practice settings.

PRM173

DEVELOPMENT OF A QUESTIONNAIRE TO EVALUATE FOOD-RELATED WELL-BEING

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OBJECTIVES: To screen food-related products and support allegation demands, evaluating food-related concepts with appropriate tools is essential. In the absence of such a tool, we developed a specific questionnaire providing insight into the way a person links food to well-being in terms of pleasure, joint comfort, digestive comfort, prevention and immunity. **METHODS:** Semi-directive interviews were conducted with 40 healthy subjects to explore three themes: food, well-being and food-related well-being, and determine the basis of the interview guide for focus group discussions. Twenty-four group discussions (199 subjects in total) were conducted with healthy subjects (n=12) and subjects with joint, digestive or repetitive infection complaints (n=4 per complaint), to investigate definition and experience of food-related well-being. Qualitative analysis was performed to identify concepts of interest. Based on the designed conceptual model and discussion with the scientific committee, items were generated using subjects' verbatim expression. Face-to-face cognitive interviews were conducted with 29 healthy subjects to ensure comprehension and appropri-

ateness of the resulting test questionnaire. After revision, the pilot questionnaire was created. **RESULTS:** Concepts elicited during group discussions revolved around pleasure and health. The test questionnaire consisted of 199 items divided into six modules: "grocery shopping", "cooking", "places where meals are eaten", "conviviality", "eating and drinking", and "eating habits and health". Items within the first five modules assess subject behaviour and benefits (pleasure, psychology, digestion, physical condition); the module "eating habits and health" assesses beliefs. Cognitive interviews led to minor rewordings, removal and addition of items. The resulting pilot questionnaire consisted of 174 items distributed across the 6 aforementioned modules. **CONCLUSIONS:** We developed a unique tool that comprehensively assesses the full picture of well-being related to food and eating habits in the general population. A validation study is underway to establish the scoring and ascertain the psychometrics of the instrument before it can be used in clinical studies.

PRM174

METHODOLOGY AND DEVELOPMENT OF 'POLISH DICTIONARY OF QUALITY OF LIFE TERMS'

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Lack of an established Polish terminology is a serious limitation of the development of health-related quality of life (HRQoL) studies in Poland. **OBJECTIVES:** To develop Polish dictionary of terms used in the studies of HRQoL. **METHODS:** In February 2012, HRQoL Special Interest Group of ISPOR Poland Chapter took on the task of preparing Polish dictionary of HRQoL terms. Following steps were planned: (1) preparation of a list of target English-language terms, (2) preparation of a reference list of translations typically used in Polish literature, (3) step-by-step translation of English terms by individual experts (4) analysis and approval of proposed translations by Expert Committee, (5) re-analysis of key terms, (6) preparation of pre-final vocabulary, (7) reviews by Review Committee, (8) preparation and publication of the final version. The list of English terms was based on following sources: popular English-language HRQoL textbooks, key words from papers published in leading peer-reviewed journals in the field, ISPOR guidelines concerning patient-reported outcomes, websites of generic HRQoL instruments. The reference lists of translations used in Polish literature was based on pharmacoeconomics and psychology textbooks, EBM dictionaries and HRQoL papers published in Polish peer-reviewed journals. Expert Committee was comprised of seven Polish investigators with vast experience in the field of HRQoL studies. Review Committee was formed by three authorities in the field of psychometrics, statistics and epidemiology. **RESULTS:** Till June 2013, there were 13 meetings of Expert Committee: three focused on the development of methodology and ten - on analysis and approval of proposed translations. Initially, we identified 1640 English terms from different sources. After removal of duplicates, final English list comprised of 1314 terms. Pre-final version of vocabulary, ready for peer-review, consists of 1051 proposed Polish translations. **CONCLUSIONS:** We anticipate, that dictionary prepared by the ISPOR Poland Chapter will support practical usage of PRO in Poland.

PRM175

MAPPING THE OXFORD HIP SCORE (OHS) TO EQ-5D: A TEST OF MODEL PERFORMANCE

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OBJECTIVES: The lack of preference-based utility data places great importance on the accuracy of mapping functions. The objective of this study is to assess the predictive accuracy of statistical models which address the unique properties of EQ-5D. **METHODS:** A large dataset from the Patient Reported Outcome Measures (PROMs) programme reporting EQ-5D and OHS values for patients who have undergone total hip replacement, during April 2010 and March 2011, was used to develop 6 mapping functions using different statistical methods: Ordinary Least Squares (OLS), standard Tobit, adjusted Tobit, two-part logit (TPL), response-mapping and censored least absolute deviation (CLAD). Three different model specifications were investigated, including the total OHS, individual item score and individual item responses. Each model specification was examined using goodness-of fit measures. The predictive accuracy of each model was analysed using the mean absolute error (MAE) and mean squared error (MSE). Model performance was compared in an internal and external validation. **RESULTS:** The OHS individual item response variables proved to give the best model fit and were therefore used across all models. The OLS and TPL models consistently demonstrated the highest predictive accuracy, providing the lowest MSE and the closest estimation of the mean EQ-5D. The response-mapping approach was the poorest predictor in estimating individual values; however it was able to predict the median with perfect precision. Models using Tobit and CLAD frameworks provided the poorest predictions. **CONCLUSIONS:** The OLS and TPL models proved to be the most accurate in predicting EQ-5D on an individual level, whilst the response-mapping model is recommended for predicting the median. Using inaccurate mapping functions such as the Tobit models developed in this study can have a substantial impact on CEA results and reimbursement decisions.

PRM176

TRANSLATION AND CULTURAL ADAPTATION OF THE SF-6D QUESTIONNAIRE FOR USE IN ARABIC-SPEAKING COUNTRIES

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OBJECTIVES: The use of pharmacoeconomic evaluations, e.g. cost-utility analysis (CUA), in resource allocation is gaining attention in Arabic –speaking countries. The Short Form-6D (SF-6D) is a generic preference-based measure of health-related quality of life (HRQoL) that can be used to generate health-state utilities for use in CUAs. The objective of this study is to translate and culturally-adapt the SF-6D for use in Arabic-speaking countries, with particular focus on Egypt and the United Arab Emirates. **METHODS:** The study followed the International Quality of Life Assessment (IQOLA) methodology. Two forward translations, one consensus and one backward translation were undertaken. The translators (professional linguists and bilingual pharmacoeconomists) reported the difficulties encountered in the translation process. An advisory committee of six researchers and three clinicians, who are native Arabic speakers and proficient in English language, assessed the consensus version for accuracy, cultural compatibility and cognitive burden. The difficulties encountered during the process were categorized as grammatical, idiomatic, semantic/conceptual, and cultural. The backward translation was completed by a professional medical translator, reviewed and assessed by the committee. **RESULTS:** Five items raised discussion during the process for grammatical (1 item), semantic (1 item), idiomatic (1 item) and cultural (2 items). For example, "emotional problems" had to be culturally adapted and "down-hearted and low" had to be substituted. The committee members approved the forward translation as linguistically and grammatically accurate. Minor changes were made to the forward translation to improve cultural appropriateness. The Backward translation did not reveal major problems and equivalence to the original was confirmed following committee review. **CONCLUSIONS:** The translation and cultural adaptation of the SF-6D into Arabic resulted in a conceptually equivalent and culturally appropriate version. Psychometric validation and a valuation survey will be needed to assess its validity for use in the target populations.

PRM177

ASSESSING MEASUREMENT EQUIVALENCE OF DIFFERENT FORMS OF ADMINISTRATION OF THE CAMBRIDGE PULMONARY HYPERTENSION OUTCOME REVIEW (CAMPHOR) USING RASCH ANALYSIS

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OBJECTIVES: Electronic formats of patient-reported outcome (PRO) measures are now routinely used in clinical trials. Their use promises a range of benefits such as improving access to patients, increasing compliance, reducing missing data and avoiding errors associated with data entry. When changing from paper and pen to an electronic administration it is necessary to establish their equivalence. This is the first study to evaluate the use of Rasch analysis for this purpose. **METHODS:** Three groups of US patients with pulmonary hypertension participated. A clinical sample completed an electronic version of the CAMPHOR (*e-sample*) and two different samples completed the pen and paper administration (*pp1* and *pp2*). Analyses were conducted on the CAMPHOR activity limitations and quality of life (QoL) scales. The three databases were analysed separately for fit to the Rasch model. Data were then combined, re-analysed and assessed for differential item functioning (DIF). **RESULTS:** The three datasets were matched randomly for sample size (n=147). Mean age (years) and percentage male respondents were as follows: *e-sample* (51.7, 16.0%); *pp1* (50.0, 14.0%); *pp2* (55.5, 40.4%). After minor adjustments to the three datasets, fit to the Rasch model was achieved (Chi^2 values for activity limitations and QoL respectively were *e-sample* (0.11, 0.07); *pp1* (0.18, 0.12); *pp2* (0.40, 0.30)). Fit was also achieved for the combined sample after minor adjustments (activity limitations Chi^2 = 0.21, QoL Chi^2 =0.12). Importantly, no evidence of DIF by mode of administration was found. **CONCLUSIONS:** Equivalence of the electronic and pen and paper administrations of the CAMPHOR was established. The results showed how the Rasch model can be utilized to determine the equivalence of alternative formats of PRO measures. This methodology has the added advantage of avoiding the need for complex study designs such as matching samples for disease severity or repeated administration of alternative formats of questionnaires.

PRM178

MODELLING THE RELATIONSHIP BETWEEN THE WOMAC OSTEOARTHRITIS INDEX AND EQ-5D

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OBJECTIVES: Economic evaluation typically is conducted using health state utilities to estimate treatment benefits. However, such outcomes are often missing from studies of clinical effectiveness. This study aims to bridge that gap by providing appropriate methods to link values from the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) to the EQ-5D utility instrument. **METHODS:** Patients from a large registry of Spanish patients (n=7072 observations) with knee or hip osteoarthritis who completed both WOMAC and EQ-5D was used. A mixture model approach was used based on distributions bespoke to the EQ-5D UK value set to estimate EQ-5D as a function of WOMAC pain, stiffness and function subscores. **RESULTS:** A five class mixture model provides very close fit to the observed data at all levels of disease severity. The overall mean (0.542 vs 0.542), median (0.620 vs 0.636) and the percentage of observations at full health (15 vs 14.8) were very similar between the observed data and the estimated model respectively. Stiffness has limited relationship to EQ-5D, whereas functional disability and pain are strong predictors. **CONCLUSIONS:** EQ-5D can be reliably estimated from WOMAC subscale scores without any systematic bias using the results based on a bespoke mixture model method.

PRM179

DIFFERENTIAL ITEM FUNCTIONING IN A SATISFACTION ITEM BANK

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OBJECTIVES: In the last years, the assessment of patient satisfaction has become an area of great interest due to its implications, especially in the management of chronic diseases. Across the board, satisfied patients tend to have better adherence to medication. It affects a patient's prognosis and treatment costs. High-risk hypertension and Diabetes Mellitus (DM) (types I and II) are two chronic diseases with high prevalence. The objective of this research was to examine Differential Item Functioning in a previously developed Satisfaction with Treatment item bank between these chronic diseases as a first step to improve the item bank. **METHODS:** The sample consisted of a total of 283 patients diagnosed with DM and 1.517 high or very high-risk hypertensive patients. Uniform DIF between both samples was investigated using Winsteps. The presence of DIF in thirteen items from a satisfaction bank was analyzed. **RESULTS:** Ceiling effect was detected and an item-person map showed that the test was off-target and didn't cover the highest range of the ability scale. DIF was present between patients with Diabetes Mellitus (I and II) and high-risk hypertensive patients. Differences above one logit were found in three items, two related to adverse-events, which diabetes patients found harder to endorse, and one to oversights, harder to endorse for high-risk hypertensive patients. A difference in the same direction was found in two more items pertaining to convenience, with differences in this case larger than 0.75 logits. **CONCLUSIONS:** This study represents a psychometrically valid initial effort to improve patients with chronic diseases satisfaction assessment. The DIF analysis has allowed improving the item satisfaction bank, selecting those items which could provide better information in order to develop a satisfaction questionnaire better tailored to specific patients. Future research is recommended considering different chronic pathologies and to reduce the ceiling effect associated with the satisfaction measures.

PRM180
THE IMPACT OF DSM-5 ON THE DEVELOPMENT OF DRUGS TO TREAT SCHIZOPHRENIA
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OBJECTIVES: In May 2013, the American Psychiatric Association released the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), a classification system for psychiatric and certain neurologic conditions. DSM-5 brings significant changes to many diagnostic categories as compared to the previous DSM-IV-TR. The objective of this review was to examine the changes in the Schizophrenia criteria and discuss the impact these changes may have for industry. **METHODS:** A line-by-line review of the DSM-5 and DSM-IV criteria was undertaken. Significant changes were highlighted and discussed from the point of view of sponsors of clinical trials for psychopharmacologic agents being developed to treat Schizophrenia. **RESULTS:** The primary diagnostic criteria for Schizophrenia in DSM-5 are little changed. The major change in the so-called "active-phase symptoms" is with the mix of symptoms that can meet this criterion. Five key symptom areas must be present to meet criteria. In DSM-IV, any two symptoms were sufficient and in some limited cases, even just one was enough (bizarre delusions or Schneiderian first-rank auditory hallucinations – conversing voices). According to the DSM-5 criteria, there always must be at least two symptoms to meet Criterion A, and one of the two must be either delusions, hallucinations, or disorganized speech. Other important changes include changes to the course specifiers, the elimination of Schizophrenia subtypes, and the addition of an optional framework for clinicians to rate the severity of the primary symptoms. **CONCLUSIONS:** The changes in DSM-5 pose both challenges and opportunities for industry. The changes in the DSM-5 criteria may translate into changes for how we go about developing medical products to treat psychiatric disorders, including Schizophrenia. There will need to be an investment in research and education, and sponsors must examine the possibility of developing new endpoints and outcome assessments for use in clinical trials.

PRM181
THE VALUE OF PILOT TESTING PRO SYMPTOM DIARIES PRIOR TO CONDUCTING COGNITIVE DEBRIEFING INTERVIEWS IN CHILDREN/ADOLESCENTS: QUALITATIVE AND QUANTITATIVE INSIGHTS
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OBJECTIVES: To pilot test daily electronic symptom diaries in pediatric chronic constipation (CC) and irritable bowel syndrome with constipation (IBS-C) for approximately one week prior to cognitive debriefing interviews. **METHODS:** Separate child and parent eDiary measures of CC/IBS-C symptoms were developed based on concept elicitation interviews with children with CC/IBS-C and their parents. The eDiaries were completed by 36 children/adolescents (aged 6-17 years) with CC/IBS-C and 30 parents (of 6 month-11 year old children with CC/IBS-C) for 5-9 days prior to cognitive debriefing. Children and parents were trained to use the eDiary and following the pilot test, children and parents were interviewed separately about their experiences completing the eDiaries and the symptom items. Item descriptive statistics were calculated using the eDiary data collected during the pilot test. **RESULTS:** Both eDiaries were well understood, all items were considered relevant, and no symptoms were identified as missing from the eDiaries. During cognitive debriefing, the children were able to reflect on their experiences of completing the eDiary as opposed to considering hypothetical scenarios to debrief the items. Although 9 children and 15 parents reported challenges with transmitting data, mean compliance rates were high (94% and 92%, respectively), indicating low levels of missing data and that the eDiaries were easy to use overall. Mean completion times were 3.72 minutes for children and 3.96 minutes for parents, providing further evidence of low burden. All item responses were normally distributed and demonstrated expected patterns of response (e.g., most reported 0 or 1 bowel movement daily). **CONCLUSIONS:** Pilot testing eDiaries prior to cognitive debriefing interviews, especially with children, provides respondents with the experience of completing the eDiary, facilitating a more informed qualitative interview. Pilot testing also provides preliminary quantitative item performance data and important insights about the usability of eDiaries.

PRM182
THE IMPACT OF DSM-5 ON THE DEVELOPMENT OF DRUGS TO TREAT AUTISM SPECTRUM DISORDER
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OBJECTIVES: In May 2013, the American Psychiatric Association released the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) which is a classification and diagnostic system for psychiatric and certain neurologic conditions. DSM-5 brings significant changes to many of the diagnostic categories as compared to the previous edition of the manual. The objective of this review was to examine the changes in the Autism Spectrum Disorder (ASD) criteria and discuss the impact of these changes for industry. **METHODS:** A line-by-line review of the DSM-5 criteria for Autism Spectrum Disorder and the DSM-IV criteria for Pervasive Developmental Disorders was undertaken. Significant changes were highlighted and discussed from the point of view of sponsors of clinical trials for psychopharmacologic agents being developed to treat these conditions. **RESULTS:** The changes to the diagnostic criteria for what were known in DSM-IV as pervasive developmental disorders (PDD) are sweeping. ASD, now in a section of the DSM titled "Neurodevelopmental Disorders," is a single entity in DSM-5 with several levels of severity that effectively replaces the five PDDs that were separately classified in DSM-IV. Notable changes include the addition of severity levels to the ASD criteria, changes to the social interaction and social communication criteria, and the addition of hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment, as an illustrative example of restrictive, repetitive patterns of behavior, interests, or activities. **CONCLUSIONS:** The numerous and significant changes in DSM-5 pose both challenges and opportunities to industry. We need to take a careful look at DSM-5 to understand what the changes mean for how we go about developing medical products to treat psychiatric disorders. This means the need for investment in research, education, and new ways of approaching the development of endpoints and outcome assessments in clinical trials.

PRM183
ESTIMATING THE IMPACT OF ENDOGENOUS SUBSTANCE ABUSE ON SELF-REPORTED HEALTH STATUS
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OBJECTIVES: The impact of addictive substance abuse (SA) on overall well-being, such as patient's self-reported health status, may suffer from endogeneity bias. The purpose of this study is to estimate the impact of SA on patient's health status using the instrumental variable (IV) approach. **METHODS:** The sample was extracted from the 2011 Substance Abuse and Mental Health Services Administration (SAMHSA) data for 36,347 adult US respondents who indicated SA status. Treating SA as exogenous, a single-equation probit model was used. Treating SA as endogenous, bivariate probit models were employed using different IVs. The outcome variable was the self-reported health status (1=better than good; 0=fair or poor). Other exogenous variables controlled in the model were respondents' age, gender, race, marital status, education level, employment status and family income. IVs were respondents' age at SA initiation, SA frequency and substance availability. Exogeneity, over-identification and weak instrument tests were performed to ensure the validity and appropriateness of the IVs. **RESULTS:** About 50% of the respondents were between 18-25 years old. Over 56% indicated SA and approximately 36% had initiated SA before age 18. The single-equation probit suggested that SA was associated with at least a 2% decrease in overall health status ($p<0.01$), compared those who never had SA. After adjusting for endogeneity bias, the negative relation between SA and health status increased by at least two-fold ($p<0.01$). All tests indicated that the IVs used were valid and the results were significant. **CONCLUSIONS:** The findings suggest that estimating the impact of SA on health status should consider adjusting the endogeneity bias induced by individual characteristics and environmental factors such as age at SA initiation, frequency of SA use and substance availability in the community. Further investigations on the effect of SA abstinence durations on health status should be explored to strengthen their associations.

PRM184
THE IMPACT OF DSM-5 ON THE DEVELOPMENT OF DRUGS TO TREAT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER
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OBJECTIVES: In May 2013, the American Psychiatric Association released the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) which is a classification system for psychiatric and certain neurologic conditions. DSM-5 brings significant changes to many diagnostic categories as compared to the previous edition of the manual. The objective of this review was to examine the changes in the Attention-Deficit/Hyperactivity Disorder (ADHD) criteria and discuss the impact these changes may have for industry. **METHODS:** A line-by-line review of the DSM-5 and DSM-IV criteria for ADHD was undertaken. Significant changes were highlighted and discussed from the point of view of sponsors of clinical trials for psychopharmacologic agents being developed to treat ADHD. **RESULTS:** One of the more notable changes to ADHD criteria in DSM-5 is in the age of onset cutoff. To meet DSM-IV criteria, symptoms had to be present before age 7. In DSM-5 this was changed to 12. Additionally, symptoms present before the age of onset cutoff had to cause impairment to meet the DSM-IV criteria, but in DSM-5 there is no such requirement. Another significant change lies in the fact that while DSM-IV did not make a distinction between childhood and adult ADHD, in DSM-5, from age 17 on, only 5 of 9 symptoms in one or both categories are required, rather than 6. Several other changes related to differential diagnosis and functional impairment were noted as well. **CONCLUSIONS:** The significant changes in DSM-5 pose

both challenges and opportunities for industry. The changes in the DSM-5 criteria may translate into changes for how we go about developing medical products to treat psychiatric disorders, including ADHD. There will need to be an investment in research and education, and sponsors must examine the possibility of developing new endpoints and outcome assessments for use in clinical trials.

PRM185
THE IMPACT OF DSM-5 ON THE DEVELOPMENT OF DRUGS TO TREAT MAJOR DEPRESSIVE DISORDER
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OBJECTIVES: In May 2013, the American Psychiatric Association released the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), a classification system for psychiatric conditions. DSM-5 brings significant changes to many diagnostic categories as compared to the previous edition. The objective of this review was to examine the changes in the Major Depressive Disorder (MDD) criteria and discuss the impact these changes may have for industry. **METHODS:** A line-by-line review of the DSM-5 and DSM-IV criteria for MDD was undertaken. Significant changes were highlighted and discussed from the point of view of sponsors of clinical trials for psychopharmacologic agents being developed to treat MDD. **RESULTS:** The primary symptom criterion for MDD remains unchanged, requiring five of nine symptoms, over a two-week period. The changes of note have to do with the differential diagnoses and specifiers. One change that received significant attention in the time leading up to the publication of DSM-5 was the elimination of the bereavement exclusion, which discounted bereavement after the loss a loved one within the first two months as part of the normal grief process. In terms of specifiers, a new addition in MDD is "with anxious distress," referring to episodes of depression characterized by at least two of five symptoms of anxiety. DSM-5 notes that this is associated with "greater likelihood of treatment nonresponse."Therefore, this is a factor sponsors may wish to consider in developing their trial inclusion/exclusion criteria. **CONCLUSIONS:** The significant changes in DSM-5 pose both challenges and opportunities for industry. The changes in the DSM-5 criteria translate into changes for how we go about developing medical products to treat psychiatric disorders, including MDD. There will need to be an investment in research and education, and sponsors must examine the possibility of developing new endpoints and outcome assessments for use in clinical trials.

PRM186
PATIENT NETWORKS AS A DATA SOURCE FOR PATIENT REPORTED OUTCOMES RESEARCH. CARENITY EXPERIENCE
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OBJECTIVES: To explore the potential of online patient networks (PN) as a viable source of PRO data for clinical research. Several PNs have emerged in the last few years in different European countries, and as a natural meeting point for chronic patients with an active engaged with their communities, they represent a promising source of patient reported data. In this original, the experience with the French PN "Carenity" is described. **METHODS:** Given the great heterogeneity of the users of "Carenity", and the fact that the test was computer-led by definition, a Computer Adaptive Test (CAT) was considered the best choice. The authors decided to use a culturally adapted version of CAT-Health system, which measures generic health-related quality of life (HRQoL). However, in absence of a calibration for the French population, a selection of the best items was used, using the Spanish calibration as a reference. All patients in the PN were invited to participate in the test. A score was estimated for the test using the Spanish parameters, as a rough approximation of the real score. Age, sex and the main pathology of the subjects were also collected. **RESULTS:** Preliminary results from the first week of data collection show 601 patients answered (Women: 404, Men: 140). The most frequent reported pathologies and their t-scores were multiple sclerosis (N:92,M:37.91,SD:5.85), fibromyalgia (N:81,M:36.65,SD:4.99), ankylosing spondylitis(N:60,M:37.74,SD:5.32) and both types of diabetes (I: N:53,M:50.38,SD:10.94, II: N:41,M:48.12,SD:10.04). Significant differences ($p<0.05$) were found in diabetes patients by sex, and between both types of diabetes and the other 3 most common pathologies. **CONCLUSIONS:** Carenity PN seems to be a fast way to obtain PRO scores directly from patients. Preliminary results show differences in the expected direction.

RESEARCH ON METHODS – Statistical Methods

PRM187
DEFINING THE PROPER METHODOLOGY TO USE IN A DATA-PEEK FOR POWER (DPP)
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OBJECTIVES: Late phase research is conducted outside the RCT setting where there is uncertainty as to how many subjects are needed to find differences between groups. Due to the lack of real-world information (non-RCT) in late phase designs, there are no tangible inputs for power calculations. This research defines a bias-free method to examine data while determining sample size. **METHODS:** As an example of the application of a DPP, a study examining the decrease of HGbA1c values in two different insulin delivery methods was examined in patients with several comorbid conditions. Literature examined found little to no data and a DPP was used to determine effect size (ES) and standard deviations (SDs) once 30 patients had been enrolled in each group. The DPP procedure was: 1) Determine the test statistic; 2) Identify the power formula most appropriate to the test statistic; 3) Determine the ES, variation and assumptions needed for the data-peek in the form required by the formula; 4) Construct a matrix of possible sample size values; and 5) Select a sample size that is obtainable and answers the research question. **RESULTS:** Data for group A demonstrated a mean reduction of 2.75% ±0.760, group B mean reduction of 3.01% ±0.636. Exact power analysis showed 113 subjects per group would be needed. A matrix of likely sample size based on these values ranged from 44 to 193 per group. Based on this DPP, a sample of 120 per group was selected as the sample size that would deliver clinically meaningful results. **CONCLUSIONS:** A DPP is useful in late phase research to define appropriate sample size where no data exist. It is important to note that DPP methods do not require significance testing, but the benefit is no need for a correction for multiple comparisons at the time of the final analysis.

PRM188
FAULTY CONNECTIONS: CAN CRITICISMS OF NETWORK META-ANALYSIS IN NICE SUBMISSIONS BE AVOIDED?
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OBJECTIVES: To assess 1) how network meta-analyses (NMAs) included within manufacturer submissions to the National Institute for Health and Care Excellence (NICE) have been criticised by its Evidence Review Groups (ERGs); 2) how some of these criticisms might be avoided in future submissions; and 3) the extent to which such avoidance might increase the likelihood of a new intervention being approved. **METHODS:** We reviewed the ERG reports of all NICE technology appraisals published since January 2007 to identify those where the manufacturer's submission included an NMA. Subsequently, all criticisms made by the ERG of such analyses were analysed to seek common themes; and assess how often any one type of criticism was associated with a rejection by NICE. **RESULTS:** A total of 181 NICE technology appraisal reports were evaluated. These covered 243 separate interventions, 83 (34%) of which were drugs for cancer. Overall 37–64% of submissions cited NMAs, of which 43–83% were criticised, with this proportion having increased over time. Avoidable criticisms related to flaws in the systematic review methodology used to identify relevant RCTs for the analysis; inappropriate pooling of data from heterogeneous studies; and use of suboptimal statistical approaches in conducting the NMA. Unavoidable criticisms related to the lack of RCTs available for competitor drugs in the population of interest. However, no association was found between flaws in the NMA and a decision by NICE not to approve the use of the intervention. Instead, such rejection was associated mainly with a lack of evidence of clinical efficacy or cost-effectiveness in the target population. **CONCLUSIONS:** Most criticisms of NMAs could be avoided by a more rigorous and transparent approach to conducting and reporting the underlying systematic review and statistical analysis. However, rejection of submissions remains a considerable risk where the underlying evidence is weak.

PRM189
METHODOLOGICAL CHALLENGES IN COMPARING TOPICAL THERAPIES IN DERMATOLOGY IN THE ABSENCE OF HEAD TO HEAD STUDIES
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OBJECTIVES: German HTA agency requires evidence about the additional benefit of a new pharmaceutical versus an appropriate comparator as basis for price negotiations. This is challenging when head-to-head studies (H2HS) or randomized placebo-controlled trials (RPCTs) are missing and particularly in dermatology, where topical therapies in registration trials are usually compared to their individual vehicle. The aim of this research was to describe different approaches to assess the additional benefit of a new topical therapy under these limitations. **METHODS:** For ingenolmebutate-gel (IMG) and the appropriate comparator diclofenac-hyaluronic-acid (DHA) bibliographic literature search was conducted for RCTs followed by sequential screening on H2HS, comparable endpoints, RPCTs, common bridge comparator, H2HS of vehicles alone, RPCTs of vehicles. The similarity of vehicles was assessed by comparison of efficacy and safety profile. The lack of H2HS demands to conduct the following approaches depending on the comparability of vehicles: 1. An adjusted indirect comparison due to Bucher 1997 (vehicles are placebo-like or adequately similar) 2. Linkage of direct comparisons due to Wells 2009 (possible when H2HS or RPCTs of vehicles are available) 3. Mixed treatment comparison (MTC) (prerequisites as mentioned for Bucher). **RESULTS:** 5 RCTs for IMG versus 3 RCTs for DHA were identified with comparable endpoints. No RPCTs for topical therapies or for their vehicles, no H2HS of vehicles, no bridge comparator and no clear evidence for the adequate similarity of both vehicles could be detected. Therefore, the prerequisites of all available statistical methods are not met and cannot thoroughly be applied. Notwithstanding these limitations, Bucher (RR[95%KI]: 4.14[2.03;8.47]) and MTC both favor IMG significantly while Wells showed non-inferiority (RR[95%KI]: 0.8[2,03;8,47]) in the primary endpoint of IMG versus DHA. **CONCLUSIONS:** A definition of adequate similarity for vehicles by German HTA agencies is needed to enable the use of methodologically sound indirect comparisons or MTCs in reimbursement dossiers.

PRM190
USE OF MULTIVARIATE BAYESIAN EVIDENCE SYNTHESIS TO REDUCE UNCERTAINTY AROUND CLINICAL EFFECTIVENESS AND QUALITY OF LIFE ESTIMATES
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OBJECTIVES: In health technology assessment, decisions about reimbursement of new health technologies are largely based on effectiveness estimates. These estimates are sometimes also used to predict the health-related quality of life outcomes, such as EQ-5D, as part of economic evaluation. However, sometimes these effectiveness estimates are not readily available. When many alternative instruments measuring these outcomes are being used (and are not all reported) or an extended follow-up time of clinical trials is needed to evaluate long-term endpoints (and drug development is at an early stage), data on relevant outcomes may be limited. The aim of this study was to develop methodology that would allow synthesis of all available evidence to assess interventions early and reduce uncertainty around relevant outcomes. **METHODS:** Bayesian multivariate meta-analysis

methods have been developed for synthesis of diverse sources of evidence: multiple outcomes (including surrogate, potentially short-term endpoints) and other external evidence. These methods were applied to an example in rheumatoid arthritis where outcomes such as the Health Assessment Questionnaire (HAQ), the Disease Activity Score (DAS-28) and the American College of Rheumatology (ACR20) are synthesized. External information about correlations between the outcomes was included in the form of informative prior distributions. Estimates of HAQ were then mapped onto EQ-5D. Also in an alternative approach, the multivariate framework was applied to model jointly the utility estimates and the clinical effectiveness outcomes. **RESULTS:** The use of multivariate meta-analysis led to reduced uncertainty around the effectiveness and utility estimates. Combining the HAQ with DAS-28 gave a 19% reduction in the uncertainty around the estimate of HAQ and also 16% around the estimate of EQ-5D. **CONCLUSIONS:** By allowing all relevant data to be incorporated in economic evaluations of new health technologies, this multivariate approach to meta-analysis can lead to reduced uncertainty and hence more efficient decision-making in health care.

PRM191

NETWORK META-ANALYSIS OF MULTIPLE OUTCOMES: A SIMULATION STUDY AND APPLICATION

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The usefulness of a multivariate approach to compare treatments in the context of pairwise meta-analysis has been widely demonstrated in the literature. However, this approach has not yet been considered for multiple treatment comparisons. We believe that extending such methodology to network meta-analysis (NMA) will increase the primary evidence base allowing us to compare more interventions across multiple outcomes measures. Borrowing strength between outcome measures using multivariate NMA can also potentially increase the precision of relative treatment effect estimates and reduce the impact of outcome reporting bias.**OBJECTIVES:** To extend standard NMA to incorporate multiple outcomes of interest and evaluate the use of multivariate NMA models through simulated and real datasets. **METHODS:** We developed a random effects multivariate NMA model to account for the correlation between multiple outcome measures. The potential benefits of this method were demonstrated in a simulated example comparing univariate and bivariate NMAs for continuous outcome measures. We further explored the application of our multivariate NMA model using a case study comparing anti-obesity pharmacological interventions for waist circumference, weight change and BMI change from baseline. **RESULTS:** The simulation study showed that through use of multivariate NMA the precision in mean relative treatment effects increased compared to a standard univariate NMA. This held true under multiple scenarios testing model parameters including both within- and between-outcome correlations. Similar findings were obtained from the application to the example dataset in obesity. **CONCLUSIONS:** Our method proves particularly useful in reducing uncertainty around relative effectiveness estimates when the outcomes included for analysis are highly correlated. However, the advantages of the multivariate NMA are limited where there is little correlation between outcome measures. Further work will explore the applicability of multivariate NMA methods to different types of outcomes such as binary outcome measures.

PRM192

HANDLING VARIABILITY IN TIME ENDPOINTS IN MULTI-CENTRE TIME AND MOTION (T&M) STUDIES: A CASE STUDY OF ERYTHROPOIESIS-STIMULATING AGENTS FOR ANAEMIA MANAGEMENT IN 13 CENTRES IN ITALY

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OBJECTIVES: In multi-centre Time and Motion (T&M) studies, time endpoints can be highly variable due to differences in centre practices. Our aim was to assess the impact of the type of analysis employed on the results of a T&M study. **METHODS:** Data from 13 centres were analyzed in relation to each of the following: drug preparation, distribution, and injection, using three methods. Base case methodology included a random intercept generalized linear mixed effect model assuming gamma distribution with log link function to account for potential centre clustering effect and non-normality of the outcome measure. The two alternative methods were: standard linear regression (assuming time data are normally distributed) and gamma regression with log link function (assuming time data are positively skewed), both of which do not account for centre clustering effect. Sample means and variability as measured by 95% confidence interval (CI)) were also compared. **RESULTS:** For the base case, mean time was 0.53 min (95% CI: 0.33-0.85) for "preparation", 0.30 min (95% CI: 0.22-0.40) for "distribution", and 0.81 min (95% CI: 0.59-1.11) for "injection". Mean time resulting from the standard linear regression was markedly higher for "preparation": 0.66 (95% CI: 0.59-0.73), and similar for "distribution" and "injection": 0.34 (95% CI: 0.30-0.37) and 0.84 minutes (95% CI: 0.79-0.88), respectively. Using the gamma regression yielded similar results to standard linear regression: 0.65 (95% CI: 0.59-0.71), 0.31 (95% CI: 0.29-0.34), and 0.83 minutes (95% CI: 0.79-0.88), respectively. The base case scenario detected a "centre-clustering" effect, hence producing substantially wider CIs compared to both alternative methods which ignore dependence in the data. **CONCLUSIONS:** Although mean task times remained relatively stable across the various methods, 95% CIs were substantially wider for random intercept model. If "centre-clustering" is detected, random effects regression models must be employed to produce valid confidence intervals around point estimates.

PRM193

BAYESIAN NETWORK META-ANALYSIS TO ASSESS RELATIVE EFFICACY AND SAFETY OF CANAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) INADEQUATELY CONTROLLED WITH METFORMIN

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OBJECTIVES: To assess the relative efficacy and safety of canagliflozin (CANA), a sodium-glucose co-transporter (SGLT) inhibitor, as add-on to metformin, compared to sulphonylureas (SU), pioglitazone, DPP-4s, GLP-1s and dapagliflozin. **METHODS:** Bayesian network meta-analysis was conducted based on a systematic literature review described separately. Outcomes of interest included HbA1c, weight and hypoglycaemia. Networks were based on treatment- and dose-specific nodes where possible. Non-informative priors were used; selection of fixed versus random-effect model was based on DIC. Studies causing inconsistency (identified through the comparison of direct and indirect evidence in the network) were identified with a clinical expert and excluded from the base case. **RESULTS:** 25/17/7 studies reported results at 26/52/104 weeks (w) respectively. HbA1c-reduction (2) at 26w/52w was best for exenatide 2mg and liraglutide 1.8mg. CANA 300mg had a higher reduction versus DPP-4s (h=-0.11 to -0.39) and dapagliflozin 10mg (==-0.12 to -0.38) across all time points; while CANA 100mg conferred at least as large reductions (==0.01 to -0.30 and 0.00 to -0.26 respectively). The analysis at 104w was conducted based on the pooling of SUs. CANA 300mg and 100mg ranked first/second before liraglutide 1.2mg/1.8mg (s=-0.11/-0.13 and -0.02/-0.04 respectively). Both CANA doses had higher weight-reductions than SU, DPP-4s and pioglitazone, and provided reductions comparable to GLP-1s and dapagliflozin. Odds ratios for hypoglycaemia versus SU ranged from 0.03 to 0.11 for DPP-4 and SGLT. **CONCLUSIONS:** NMA of add-on therapies to metformin suggests that CANA 300mg is associated with increased HbA1c-reduction versus DPP-4s and dapagliflozin while CANA 100mg provides at least similar effects. Additionally, results suggest increasing relative efficacy of CANA over time versus liraglutide and CANA reached at least as large HbA1c reductions as liraglutide at 104w. Weight reduction was comparable to GLP-1s and substantially higher than all other classes. All classes showed significantly less risk of hypoglycaemia compared to SU.

PRM194

ESTIMATING CHRONIC DISEASE PREVALENCE FROM CLAIMS DATA: REDUCING BIAS BY ACCOUNTING FOR DISEASED INDIVIDUALS WHO DO NOT GENERATE CLAIMS

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OBJECTIVES: Claims data are often used to estimate the prevalence of chronic diseases, typically by dividing the number of patients with disease-related claims (e.g., ≥1 or ≥2 claims) by the number of studied individuals. Such estimates will have a downward bias because not all diseased patients will generate disease-related claims within their enrollment period. This downward bias can be substantial for underserved diseases that lack effective treatments. We explored whether an empirical Bayes estimator for the number of diseased individuals who do not generate claims could improve the accuracy of claims-based prevalence estimates. **METHODS:** As an example, we studied the prevalence of a rare dermatological condition without any FDA-approved therapies. After accounting for enrollment time, individuals in a large nation-wide claims database were identified as having 0, 1, 2, 3, etc., disease-related claims. These counts were modeled using a mixture of Poisson distributions, with an unknown mixing distribution. Empirical Bayes approaches, which are frequently used to estimate numbers of unobserved species in ecological experiments, were used to estimate the number of diseased individuals without claims, and to provide adjusted prevalence estimates. **RESULTS:** Out of over 4 million individuals with at least one year of continuous enrollment, n=2,026 had disease-related claims, comprised of n=1,422 with one claim, n=317 with two claims, n=134 with 3 claims, etc. The traditional method for estimating prevalence identified 4.9 cases per 10,000 persons. After applying the empirical Bayes approach, the estimated prevalence increased to 7.9 cases per 10,000 persons, and became closer to published prevalence estimates based on non-claims data sources. **CONCLUSIONS:** In this example application, prevalence estimates based on claims data were increased by over 60% by using empirical Bayes approaches to account for large numbers of diseased individuals who did not generate claims. The increased prevalence estimates were more consistent with the published literature.

PRM195

APPLICATION OF COPULAS IN ECONOMIC EVALUATION

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OBJECTIVES: To analyse the applicability of copulas distribution in economic evaluation. **METHODS:** We have analyzed data from an observational prospective study of patients with allergic rhinitis in Spain (n=498). Main data were direct cost (€2012) and Health Related Quality of Life (SF-12). We have calculated the goodness of fit for copulas (Gumbel copula, Clayton Copula, Frank Copula, Normal Copula, Plackett Copula and T copula) based on the empirical process comparing the empirical copula with a parametric estimate of the copula derived under the null hypothesis. We have used inversion of Kendall's tau method to fit copulas. A multivariate independence sample was generated to compare with copulas results. This process was replicated for a 100 times to obtain p-values by bootstrap method. **RESULTS:** Marginal distribution of direct cost was a 3-parameter Gamma distribution (shape=1.856, scale=0.00324, location=10.97). Marginal distribution of Health Related Quality of Life was associated to a 1- gamma (shape 2.9253 and scale 0.16104). P-value range were 0.093 to 0.144 for independent distribution, 0.004 to 0.031 for Gumbel copula, 0.246 to 0.522 for Clayton Copula, 0.545 to 0.814 for Frank Copula, 0.463 to 0.716 for Normal Copula, 0.373 to 0.628 for T Copula and 0.549 to 0.847 for Plackett Copula. Frank Copula and Plackett Copula had the best goodness of fit. Kendall's Tau for Fran Copula showed a correlation of -0.4212. **CONCLUSIONS:** Copulas distribution allows us to adjust better the non-lineal relation between cost and effectiveness. Furthermore, this kind of approach could improve probabilistic sensitivity analyses.

PRM196

VALIDATION OF DISEASE STATES IN SCHIZOPHRENIA: COMPARISON OF CLUSTER ANALYSIS BETWEEN THE UNITED STATES AND EUROPEAN POPULATIONS

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OBJECTIVES: A set of disease states for patients with schizophrenia was previously published using a statistical clustering method, applied to Positive and Negative Syndrome Scale (PANSS) data from US patients. While factor analyses of the PANSS have shown remarkable stability of the structure across international populations, it is unknown whether similar multidimensional disease states would also be stable. Using data from the European Schizophrenia Cohort (EuroSC), a 2-year observational study in 1,208 schizophrenia patients, we examined the factor structure of the PANSS and identified disease states using the same clustering method as previously. **METHODS:** A principal component analysis (PCA) was conducted using the Kaiser criterion and varimax rotation on PANSS items, followed by a *k*-means cluster analysis on PANSS scores for items most strongly correlated with the PCA domains. For each cluster, a level (low, moderate, high) was assigned to each domain based on the cluster centres values. Kappa statistics were used to measure the agreement in assignment between the published and the derived states sets. **RESULTS:** Five factors accounting for 56% of total variance were obtained from the PCA (positive symptoms, negative symptoms, cognitive impairment, mood disorder, and hostility). As in the analysis of patients in the initial US study, rates of change in root mean squared distance became small after six clusters. When assigning the two sets of states based on levels of positive, negative, and cognitive impairment, the simple, Cicchetti-Allison, and Fleiss-Cohen weighted Kappa statistics (95% CI) were, 0.418 (0.401-0.435), 0.568 (0.553-0.584), and 0.692 (0.676-0.709), respectively. **CONCLUSIONS:** The factor structure, number of discrete states, and combinations of levels of symptoms in states were similar in US and European populations. Resulting moderate-to-substantial agreement in assignment suggests that disease states obtained using *k*-means clustering from the PANSS generalise across international populations.

PRM197

EVALUATING OVERALL SURVIVAL IN ONCOLOGY TRIALS WITH SUBSEQUENT THERAPIES: A METHODOLOGICAL REVIEW AND APPLICATION IN NON-SMALL CELL LUNG CANCER

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OBJECTIVES: The use of subsequent therapies has the potential to confound assessment of overall survival (OS) in oncology trials, in particular for trials in early lines of therapy and for malignancies with several registered or investigational treatment options. Standard intent-to-treat analysis is biased, since treatment choices are likely to be influenced by events associated with mortality risk, such as disease progression. We review and compare available statistical methods to obtain unbiased estimates of OS effects in presence of subsequent therapies. **METHODS:** Marginal structural modeling methods include inverse-probability of censoring weighting (IPCW) and inverse-probability of treatment weighting (IPTW). These methods explicitly model both treatment choices and effects of treatments on mortality. Rank-preserving structural failure time models (RPSFT) instead depend on parametric assumptions regarding the effect of investigational and subsequent therapies on survival, and require non-standard estimation methods such as G-estimation or iterative parameter estimation (IPE). We compare the results with the different methods with data from the Lux Lung 1 trial of the tyrosine kinase inhibitor afatinib in non-small cell lung cancer. **RESULTS:** IPCW and IPTW require detailed information on covariates that influence treatment choices and are sensitive to model misspecification. RPSFT may not yield a single estimate of treatment effects due to limitations of the G-estimation procedure. All methods were consistent with a potential OS benefit from afatinib, but the hazard ratio varied from 0.583 (p=0.038) with the pre-specified IPCW method to 0.894 (0.281) with RPSFT/IPE. **CONCLUSIONS:** The proposed methods for obtaining unbiased OS estimates in presence of subsequent therapies rest on assumptions that cannot be tested empirically. There is currently no accepted standard method; pre-specification of model choice is of importance as well as testing alternative methods. Care should be taken to avoid unbalance in subsequent therapy and to record specific information on administered treatments with potential OS effects.

PRM198

QUANTIFYING HEALTH CARE EFFICIENCY: A REVIEW OF PUBLISHED TIME AND MOTION STUDY DESIGN PARAMETERS REFERENCED IN PUBMED BETWEEN 2008-2013

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OBJECTIVES: To review design characteristics of T&M studies applied to health care, with a focus on choice of study design, statistical methodology, and handling of multi-centre data. **METHODS:** A PubMed search was performed using key search terms including "time and motion" (MeSH Term) AND any of the following: cost (analysis), (health) economics, observation(al), and prospective. Articles (English; 2008 or later) were selected based on the following criteria: (1) observational study using T&M methodology; and (2) task-based data collection. Studies that measured broad aggregate health care professional tasks/hospital workflows, in the absence of task- or event-specific timings, were excluded. **RESULTS:** Of 191 identified abstracts, 151 were excluded during screening; upon review, 21 of 40 remaining were retained for detailed assessment. Half (48%) were applicable to Europe, of which 2 were multi-country studies. Medical interventions studied were: drug (48%), diagnostic process (14%), medical procedure (24%), and IT systems to improve clinical management (e.g. EMR) (14%). The majority (86%) of studies were hospital-based, 86% were observational, and 14% employed hybrid methods, including chart review or survey. Only 20% used independent observers. Three quarters (76%) reported descriptive statistics. Of 9 multi-centre studies, one used a random effects regression model to account for "centre clustering", and 8 reported pooled data (3 of which used a "mean of centre averages" approach). Eleven studies (52%) compared two groups, of which 3 applied an analytical design aiming to defect statistical differences, and 2 reported a sample size calculation. **CONCLUSIONS:** This review of T&M studies revealed that descriptive designs are most common (analytical designs using power calculations seem rare). Multi-centre comparator studies rarely use random effects regression models to account for "centre clustering", though considered the method of choice to produce valid confidence intervals around point estimates. In general, statistical methodology is scarcely reported, affecting overall study credibility.

PRM199

THREE TOOLS TO REDUCE THE IMPACT OF COMMON DECISION-MAKING BIASES WHEN CONSIDERING SUBGROUP ANALYSES

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OBJECTIVES: Subgroup analyses of randomized trial data are performed to provide estimates of average treatment effects for patients with specific characteristics. They inform adoption and re-imbursement decisions by identifying groups of patients with favourable risk-benefit or cost-effectiveness ratios. They may also inform decisions regarding the conduct and design of future clinical studies. However, subgroup analyses are essentially observational (patients are not randomized between subgroups) and there is a risk that the differences observed between subgroups may be due to chance rather than reflecting true effects. This risk is exacerbated as typically the same data are used to both select relevant subgroups and to estimate subgroups effects leading to biased estimates and underestimation of uncertainty. This tendency increases as the number of subgroups tested increases. A number of measures are recommended to reduce the risk of bias including: pre-specification, consideration of biological plausibility, and correction of inference for multiple testing. However, the risk of bias is not obviated by pre-specification, correction for multiplicity may lead to discounting of true subgroup effects, and biological plausibility may not be a particularly specific test. In addition, common cognitive and process biases associated with decision-making such as the action imperative, optimism bias, anchoring, and group think may further lead to the inherent uncertainty in subgroup analyses to be effectively underestimated. **METHODS AND RESULTS:** We demonstrate three techniques that may help to counteract these biases: graphical inference methods clearly illustrate the inherent uncertainty in subgroup analysis; Bayesian shrinkage estimation can reduce the effect of anchoring on the observed subgroup effects and encourage consideration of regression to the mean; and reframing exercises (for example, considering the credibility of biological plausibility arguments as if they had been mooted *a priori*) may counter optimism bias. **CONCLUSIONS:** These techniques are illustrated using a published subgroup analysis from the PLATO trial (NCT00391872)

PRM200

PARAMETER IMPORTANCE ASSESSMENT IN A HEALTH ECONOMIC EVALUATION MODEL FOR HEART FAILURE

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OBJECTIVES: Along with uncertainty around the parameters and the initial parameter value assumptions used in health-economic evaluation models, an analysis of the uncertainty around the model inputs/outputs is essential. Parameter importance analysis (PIA) provides an explicit framework to quantitatively identify the contribution of each uncertain input to the output uncertainty. There are several methods available to be used in PIA. The objectives of this research were to investigate different PIA methods with the pros and cons of each method and identify the most robust method with respect to different initial parameter value assumptions. **METHODS:** A health economic model for heart failure is developed to serve as a basis to implement different PIA methods. Six alternative methods are applied: One-way sensitivity analysis, rank correlation analysis, analysis of covariance (ANCOVA), dominance analysis, standardized regression analysis and expected value of perfect parameter information (EVPPI) analysis. Initial parameter assumptions are varied and the robustness of each method is assessed with respect to how close the parameter importance rankings are with different initial parameter assumptions. **RESULTS:** Each technique/initial parameter values' assumption combination generates a different ranking for the importance of the parameters that explain the uncertainty around the expected net monetary benefit with £20,000/QALY. EVPPI is the most robust method with respect to different initial parameter assumptions. However it is the most demanding method in terms of computation time. On the opposite side, one-way sensitivity analysis is the least computation time demanding method; however the importance rankings are very susceptible to change with different initial assumptions. Other Monte-Carlo simulation based methods (e.g. ANCOVA, dominance, standardized regression and rank correlation analysis) are alternative PIA methods, which generate rather robust rankings with different initial parameter assumptions. These alternative methods require substantially less computation times compared to EVPPI with high consistency and robustness to different initial value assumptions.

PRM201

ADJUSTING FOR TREATMENT SWITCHING IN CLINICAL TRIALS WHEN ONLY SUMMARY DATA ARE AVAILABLE – AN EVALUATION OF POTENTIAL METHODS

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OBJECTIVES: Treatment switching is an important problem in Health Technology Assessment (HTA), particularly in oncology, which can often bias trial results. Although a variety of statistical approaches have been advocated for adjusting trials subject to treatment switching these all assume that Individual Patient Data

(IPD) is available. In many situations, especially when Indirect Comparison (IC) methods are required to estimate head-to-head effects, it is often the case that IPD is only available for one trial, and summary data for the other. A variety of potential methods are evaluated for the adjustment of such summary data using simulation methodology. **METHODS:** A review of HTA submissions to NICE in which both ICs were used and in which trials were subject to treatment switching was undertaken. A series of simulation studies were undertaken to assess the potential level of bias associated with the methods that are most commonly used for the analysis of such trials. Two broad approaches to adjusting summary data for treatment switching were then evaluated on the simulated data – calculation of Adjustment Factors (AFs), and re-creation and analysis (including bootstrapping) of IPD using scanned survival curves. **RESULTS:** The most commonly reported methods of analysis for studies only presenting summary data were Intention-to-Treat (ITT) and Per Protocol (PP) analyses. Results from the simulation studies indicated that these may be subject to between 0.5% and 140% levels of bias depending on trial characteristics, and that the use of AFs or re-created IPD had potential scope for reducing this. **CONCLUSIONS:** Treatment switching can be associated with considerable levels of bias, and methods for adjusting using summary data, can go some way to compensating for this when IPD is not available as is often the case in Indirect Comparisons (IC). Further extension to a Network Meta-Analysis (NMA) setting is under investigation.

PRM202

MULTIPLE IMPUTATION TECHNIQUES FOR SURVEY DATA WITH MULTIPLE RATING SCALES

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OBJECTIVES: Large scale survey data presents a number of challenges to imputation, not least the high number of variables and complexity of the data set. Data may suffer from sparsity in responses, and some questions may be conditional upon previous responses. In addition, survey data commonly contain results from multiple rating scales, which are summed (either directly or weighted) during analysis. We aim to develop a method for the multiple imputation of missing data from complex surveys. **METHODS:** We propose an adaptation of multiple imputation for survey data which contains multiple rating scales, whereby scale summary scores are used within the prediction models. The method is applied to data gathered from a large multinational survey, with data sets from 9 countries. Analysis uses a logistic regression model on each of the 9 data sets, and results are compared from a complete case analysis approach with those from multiple imputation. **RESULTS:** The proposed approach reduces the size of the prediction models from 135 predictors to a maximum of 72. Distributions of imputed data are seen to be consistent with observed data. Results from the regression analysis with multiple imputation are similar to, but show lower standard errors than, results for complete case analysis; for the same regression models a 39% reduction in the standard error is observed. **CONCLUSIONS:** Our adaptation makes multiple imputation practical for large scale survey data with multiple rating scales. For the data considered, analysis of the multiply imputed data shows greater power and efficiency than complete case analysis. The adaptation of multiple imputation makes better use of available data and can yield substantively different results from simpler, less valid techniques.

PRM203

STRUCTURAL FAILURE TIME MODELING OF OVERALL SURVIVAL EFFECTS IN ONCOLOGY TRIALS WITH SUBSEQUENT THERAPIES

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OBJECTIVES: Subsequent therapies can confound the evaluation of overall survival (OS) in oncology trials. We evaluated the application of rank-preserving structural failure time modeling for the estimation of OS effects in presence of subsequent therapies through Monte Carlo simulations. Results were demonstrated for a clinical trial: the Lux Lung 1 study of afatinib vs. placebo in non-small cell lung cancer. **METHODS:** In accelerated failure time models, covariates are assumed to affect survival times rather than hazard rates. Counterfactual survival times can therefore be computed, i.e. how long patients would have survived without the investigational or subsequent therapies. The parameters of structural failure time models can be obtained by G-estimation, whereby counterfactual survival times are calculated with hypothetical treatment effects and OS is compared between treatment arms. The G-estimate is the set of hypothetical effects that generate the most similar survival in both study arms. Branson & Whitehead (2002) developed an alternative estimation method for trials with cross-in from placebo to active treatment based on iterative parametric regressions; we extend this framework to the application with subsequent therapies. **RESULTS:** Simulation showed that standard methods are biased in the presence of subsequent therapies affecting overall survival. This includes intent-to-treat analysis, censoring at start of subsequent therapies and subgroup analysis in patients never receiving subsequent therapy. G-estimation often failed to identify parameter values when more than one treatment effect was included in the model. Iterative parameter estimation produced unbiased estimates in simulation studies and predicted a small numeric but non-significant survival benefit of afatinib. **CONCLUSIONS:** Structural failure time models can be useful to obtain unbiased estimates of OS in presence of subsequent therapies. However the assumption of proportionality in survival times cannot be tested empirically and non-standard estimation procedures are required.

PRM204

THERE IS MORE TO DECISION MAKING THAN COSTS AND EFFECTS: HANDLING PRACTICAL CONSTRAINTS IN THE VALUE OF INFORMATION FRAMEWORK

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OBJECTIVES: Whether new medical technology is implemented may depend on the balance between costs and effects, but also on practical constraints. Examples are a fixed health care budget and a maximum clinically acceptable risk of adverse events. However, the impact of compliance with such constraints cannot be handled explicitly in the current value of information (VOI) framework. Our objective was to demonstrate proper handling of constraints by extending the VOI framework through separation of cost, effect, and constraint components. **METHODS:** The proposed VOI extension was investigated in a simulation study comparing two hypothetical drugs and their side effects. The VOI extension was also applied to a clinical study concerning the cost-effectiveness of carotid intima-media thickness measurements to improve treatment guidance of patients at high risk of cardiovascular disease. Results of the standard VOI analysis, considering only costs and effects, were compared with results from the extended VOI analysis explicitly considering constraints. **RESULTS:** Standard VOI results may under- or overestimate the value of additional research compared to extended VOI results. In our clinical example, with penalties of $2 and $5 per dollar budget exceedance, standard values for the Expected Value of Perfect Information (EVPI) of $24, and $1,490 were found, with corresponding values of $239, and $565 for the extended EVPI. Ignoring the budget constraint in the standard EVPI analysis therefore resulted in a underestimation of $214 ($2 penalty) and an overestimation of $925 ($5 penalty) of the EVPI per patient. **CONCLUSIONS:** When decision-maker's criteria go beyond costs and effects, standard VOI results may not reflect the actual value of additional research accurately and may therefore jeopardize optimal research prioritization. Determination of the extended VOI, through separation of cost, effect, and constraint components, is straightforward and can support optimal research prioritization regardless of the complexity of the decision criteria considered.

PRM205

MEASURING TREATMENT EFFECTS ON RARE EVENTS USING META-ANALYSIS: AN ASSESSMENT OF EXISTING METHODS

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OBJECTIVES: Meta-analysis combines results from independent studies to produce robust statistical estimates. This technique is widely used in health care to synthesise treatment effects from clinical studies. However, when dealing with rare events such as rare adverse events, existing meta-analysis methods might not produce good treatment effect estimates, especially when there is no event occurrence in one or both arms of a study. The objective of this study is to compare the performance of various methods in estimating effect size for rare events. **METHODS:** An assessment of meta-analysis methods providing pooled odds-ratios as effect size estimates was conducted for different scenarios. The Inverse Variance Weighted, Peto, Mantel-Haenszel and logistic methods were assessed, with constant, "treatment arm" or empirical continuity corrections added when needed. The scenarios were created using different values of odds-ratio, baseline risk, and group imbalance. For each scenario 5,000 simulations of 10 studies were generated using R software. Coverage, bias and statistical power were used to compare the methods. **RESULTS:** The most commonly used continuity correction is outperformed in every scenario by the two other corrections. The inverse variance method, most commonly used in meta-analysis, performs poorly when the event probability is smaller than 0.10: it is not recommended for sparse data. Peto's method performs well in some scenarios but leads to biased results with high odds ratios and high imbalance. The logistic method is highly biased when baseline risk is low and true odds ratio is high. Under other scenarios it performs well but is most often outperformed by other methods. The Mantel-Haenszel method with empirical correction performs constantly well over the scenarios. **CONCLUSIONS:** These findings may be used to develop guidelines on when to use which method for conducting meta-analysis with rare events. Next steps will be to assess the use of mixed models and Bayesian techniques.

PRM206

METHODOLOGY FOR ESTABLISHING INTERNAL AND EXTERNAL VALIDITY WHEN PROPENSITY SCORE MATCHING IS USED

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OBJECTIVES: Propensity score matching (PSM) is an approach commonly used when treatment and control groups are thought to be different on key study variables. When the control group is larger than the treatment group, (as large as 20:1) a good match might be easy to obtain. However, differences may exist between the matched controls and the unmatched controls, indicating poor generalizability of study results. **METHODS:** Groups for the analysis are the unmatched controls (UM), the matched controls (MC) and the treatment cohort (TRT). Analysis methods for these groups in a fully crossed method and interpretation of the results will determine internal (IV) and external validity (EV). Analysis comparing the groups against the outcomes variable will determine if variables need to be controlled for in models that may be developed. **RESULTS:** After the PSM is conducted MC and TRT groups should be compared on the matched variables. Differences at this stage would indicate a poor match and a low level of IV. MC and UM should also be compared on the variables used for matching, as well as the outcome variables of interest. Significant differences on the matched variables would indicate low EV and poor generalizability of results, while differences of MC and UM groups and UM and TRT groups on the outcome variables would indicate that statistical models would need to address covariates as potential confounding effects would be present. Analysis methods can be fit statistics (chi-square or equivalence tests) or typical inferential methods with adjusted p-values greater than 0.05. **CONCLUSIONS:** It is important that research studies maintain good IV and EV. This is often complicated in research where the controls vastly outnumber the treatment group. Proper statistical analysis can go a long way to test and clarify data to make the results as meaningful as possible.

PRM207
NOVEL USE OF MULTIVARIATE JOINT MODELLING TO IDENTIFY PATIENT LEVEL FACTORS ASSOCIATED WITH TREATMENT FAILURE – EXAMPLE OF BOTOX TREATMENT FOR PATIENTS WITH OVERACTIVE BLADDER
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Detrusor overactivity (DO) is characterised by the symptoms of overactive bladder (OAB) including incontinence, urgency, and voiding episodes; though, identification of a cardinal symptom still remains unclear, where treatment efficacy is often evaluated across multiple outcomes. As a result, ascertainment of the most patient impacting symptom is crucial. Joint modelling allows us to evaluate the association between surrogate outcome measures such as patients' symptom profiles and time to perceived treatment failure. **OBJECTIVES:** To determine the most associated OAB symptom with patients' perceived time of treatment failure using a novel application of a joint modelling framework. **METHODS:** To account for the potential correlation between symptoms, we applied a joint model of multivariate longitudinal and time-to-event data to a randomised clinical trial of patients receiving botulinum toxin for DO. We investigate the association of incontinence, urgency and voiding episodes collected at baseline, 6 weeks, 3 months, and 6 months, on patients' perceived time of treatment failure. **RESULTS:** The multivariate joint model was applied to 122 patients (270 data points) with 69 (56.6%) patients reporting treatment failure. The results identified urgency as the most impactful surrogate measure on patients' perceived time of treatment failure, with an estimated hazard ratio of 1.26 (95% CI: 0.97 to 1.64) for every additional urgency episode. Incontinence, voiding episodes and the interaction between symptom measures had a non-significant association. However, in this example, sensitivity to the model choice produced inconsistent estimates due to the limited nature of the data set and therefore results should be interpreted cautiously. **CONCLUSIONS:** This approach illustrates the advantage of applying a joint modelling framework to identify symptoms most associated with time to treatment failure. With an increasing need to identify and assess core symptoms for varying medical conditions, the novel use of a joint modelling approach would appear to be extremely promising.

PRM208
USING MULTI-CRITERIA DECISION ANALYSIS TO SUPPORT ALLOCATION DECISIONS IN LARGE TRANSLATIONAL RESEARCH PROJECTS
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OBJECTIVES: Large translational research projects often have abstract objectives, such as reducing the burden of disease and health care costs from type-2 diabetes (T2DM). Such an abstract objective entails: i) a very large number of possible strategies to reach the objective and ii) a lack of detailed data and high levels in uncertainty. Currently, no methods to support project selection and resource allocation decisions in such a setting are available. **METHODS:** As a case study, we supported a resource allocation decision for the remaining funds in a large Dutch translational research consortium with the aforementioned objective, and compared the results to the decision made at the start of the project. We used the problem structuring, model building methods from multi-criteria decision analysis to identify four different alternative research strategies, and a set of evaluation criteria. Consequently, we used a combination of judgment from experts involved in the project and previously published data on the burden of disease and health care costs to evaluate the alternatives. Finally, a decision analysis was performed using Stochastic Multicriteria Acceptability Analysis for ordinal data (SMAA-O), which allows for the combined use of quantitative and qualitative (ranked) data. **RESULTS:** Using our method, it was decided to allocate remaining resources to the identification of biomarkers and development of technologies that can be used in the prevention of macrovascular complications in T2DM patients. This decision differed from the one made at the start of the project, which was not supported by any formal decision analysis. **CONCLUSIONS:** Our study shows that our method using SMAA-O can be a practical and valuable tool to support decisions on the allocation of research funds within large translational research consortia.

RESEARCH ON METHODS – Study Design

PRM209
CONFRONTING HETEROGENEITY: USING SYSTEMATIC REVIEW EFFECTIVELY FOR META-ANALYSIS
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OBJECTIVES: The pooling of treatment effects estimated from several trials via meta-analysis or network meta-analysis can be confounded by differences across studies; however, advanced methodologies are available to address many of these issues. Systematic reviews of interventions typically generate a large volume of data and lead to assimilation of a large amount of knowledge by the reviewers. Identifying key variances between trials can be difficult and important nuances can be missed by a meta-analyst. We have designed a novel checklist that highlights key areas of heterogeneity to be considered when designing and undertaking meta-analysis. **METHODS:** It is important to identify differences early on; hence we have developed a checklist that can be applied to the results of a systematic review of randomised controlled clinical trials. Components of the checklist fall into four domains where heterogeneity may be present: population, interventions, outcomes, and risk of bias. Sections documenting the feasibility of network meta-analysis and recommendations for analysis design are also included. The checklist has been retrospectively applied to a recent NICE technology appraisal; percutaneous vertebroplasty and percutaneous balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures (TA279). **RESULTS:** The checklist identified the following sources of heterogeneity in the nine included studies: inclusion criteria, endpoint definitions, endpoint reporting, presence of cross-over, differences in interventions, risk of bias; and within-trial imbalances in baseline characteristics. The checklist suggests that a quality network meta-analysis of this data should exclude one study with high risk of bias, avoid grouping sham procedures and optimal pain management, and control for baseline pain-score to address imbalance across arms. Meta-regression to control for differences in endpoint definitions or inclusion criteria would likely have been infeasible given the low number of studies. **CONCLUSIONS:** Applying the checklist improved our ability to identify sources of confounding to be addressed or highlighted as caveats in a meta-analysis.

PRM210
IMPLEMENTATION OF INTERNATIONAL CHART REVIEW STUDIES: AN ASSESSMENT OF KEY DESIGN AND OPERATIONAL CONSIDERATIONS FOR SUCCESSFUL CONDUCT
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OBJECTIVES: There is an increased need to conduct international chart review studies (chart reviews) since health care databases with required information are not consistently available. Chart reviews offer an alternative for the effective capture and analysis of real-world patient-level data on patient characteristics and outcomes, treatment patterns, treatment effectiveness and safety. For successful implementation, awareness of significant multi-national design and operational considerations is necessary. **METHODS:** A critical review of 13 recent chart reviews conducted in Europe and North America on treatment patterns, clinical outcomes and/or drug utilization and safety was undertaken. Design and operational challenges, opportunities, and learnings are delineated. **RESULTS:** All studies collected data retrospectively. Two studies collected certain information prospectively. Four studies were categorized as post authorization safety studies. Therapeutic areas varied across the studies with 8 studies being in oncology. Sample size ranged from 20-2,000 patients, number of countries ranged from 1-6, and number of sites ranged from 4-375. All studies included at least 1 European country. Across studies, key design considerations include confirming the eligibility and study periods that permit evaluations of recent care patterns yet allow for sufficient follow-up time, case ascertainment and sampling frame methodologies, and safety reporting in the context of retrospective source data. Additionally, key operational considerations include balancing science and practicality in site selection, ambiguous multinational ethical/regulatory requirements, country variations for informed consent, data collection designed to minimize site burden, and effective yet cost-efficient site management for quality data. **CONCLUSIONS:** International chart reviews are proving to be an effective methodology for capturing tailored, patient-level data. These studies can be used to address a myriad of research objectives. Through conduct and assessment of recent chart reviews, the design and operational considerations involved can be understood with opportunities for improvement learned. These lessons will help for better planning and overcoming these challenges.

PRM211
GENERATING AND MAINTAINING MOMENTUM IN POST-AUTHORISATION STUDIES
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OBJECTIVES: Some observational studies fail to gain momentum while others move smoothly to successful completion. This study set out to determine which factors drive physician motivation in prospective observational studies. **METHODS:** A web based survey was designed using input from structured literature review, investigators and experienced observational study researchers. It comprised 35 questions covering: Scientific and clinical factors (7), Study requirements (11), Operational considerations (6), Financial and legal considerations (4), Personal and professional factors (7). Respondents were asked to rate factors on a scale -5 to +5 (+5 represented very motivational and -5 very de-motivational). Free form comments were also invited. The survey was e-mailed to investigators (n=1160) identified from Citeline® as having performed both prospective observational studies and clinical trials in the last 5 years. **RESULTS:** Overall response was 15% (n=174), Europe (55%) and North America (45%) covering Community care (34%), University hospitals (29%), General hospitals (24%) and dedicated research facilities (13%). Most respondents had experience of >5 clinical trials in the last 5 years (81%) but fewer had similar experience with observational studies (40%). Responses indicate that not all physicians are equally motivated by the same factors. However most important motivational factors were in the scientific and clinical, financial and legal domains including studies which advance medical knowledge and / or patient management and acceptable honoraria. Less important factors were in the personal and professional domain including opportunities to speak at conferences or publish the data. Investigators more experienced in observational research placed greater motivational value on advancing medical knowledge and/ or patient management than less experienced colleagues. **CONCLUSIONS:** The findings provide good insight into which factors really motivate physicians and more customised motivational approaches are likely to minimise study risks. Further sub analyses of the survey data may identify more detailed strategies to pursue.

PRM212
RESEARCH IN HAEMOPHILIA B – STUDIES IN A RARE DISEASE IN TIMES OF REQUIREMENTS FOR HIGH EVIDENCE LEVELS
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OBJECTIVES: Haemophilia B (HB), a rare disease, occurs in approximately 1:30,000 males and requires individualized therapy with factor IX (FIX) concentrate. Payers in European countries request studies with high levels of evidence for decision making. The objective was to determine the status quo of current studies concerning HB, new FIX products and new therapeutic modalities regarding clinical and real-life evidence. **METHODS:** A systematic literature research was conducted

in EMBASE and MEDLINE, search terms ‚hemophilia B' and ‚FIX'. Inclusion criteria: journal articles (JA), conference abstracts (CA), English language, published between January 2009 and March 2013, studies only. Screening of titles, abstracts and full texts was performed subsequently. Registered trials (RT) concerning HB or FIX were identified in ClinicalTrials.gov. Analysis comprised age group, sponsor, research topic, recruitment status, and study design. **RESULTS:** Screening of 1,639 hits yielded 31 JA describing 35 studies, and 62 CA. FIX was the topic of 21 studies (60.0%) and 29 CA (46.8%). A total of 7 studies focused on various aspects of HB, 6 on haemophilia studies with separate data on HB. Gene therapy was the main focus of 2 JA and 11 CA (17.7%). Screening of 173 hits from ClinicalTrials.gov yielded 47 RT, 42 unpublished. Overall 32 unpublished RT (76.2%) concerned FIX, and 4 (9.5%) gene therapy. Randomized study design was described in one study (2.9%) and 4 RT (9.5%), and 3 studies (8.6%) and 7 RT (16.7%) were prospective observational comparative. **CONCLUSIONS:** Randomized study design or comparator arms were uncommon, and payers' requirements for evidence were not met. Therefore, randomization, comparison to standard of care and documentation of outcome should be discussed. Development of refined statistical methods and exploitation of complementary data like real-life data may help to fill actual evidence gaps in rare diseases.

PRM213

THE ROLE OF DSM IN THE EMA AND FDA AUTHORIZATION PROCESS FOR PSYCHIATRIC DRUGS

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OBJECTIVES: In May 2013, the American Psychiatric Association released the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). This is significant for clinicians, researchers, and developers of psychopharmacologic drugs. The previous version of the DSM, the DSM-IV-TR, was published in 2000 and the last time the diagnostic criteria were revised was in 1994, when the DSM-IV was published. The objective of this review was to determine how much of a role DSM has played in the drug approval process in Europe and the US. **METHODS:** For drugs authorized since 2000, summaries of product characteristics (SPCs; EMA) and approved labels (FDA) were reviewed to determine how frequently the DSM is mentioned in the "clinical particulars" or "indications" sections and how frequently DSM criteria are mentioned in the clinical trials sections of the SPCs or labels. The review focused on schizophrenia and psychotic disorders, mood disorders, and for the FDA, attention-deficit/hyperactivity disorder as well. **RESULTS:** For EMA-authorized products, 8 EPARs met the criteria with 10 indications in total. The DSM was never mentioned in the indications or posology sections, but in 7 (70%) of the descriptions of pharmacodynamic properties (section 5.1), DSM criteria were cited as the study inclusion criteria. For FDA-approved products, 17 labels with 22 indications met the review criteria. The DSM was mentioned in 10 of the indications sections (45%) and DSM criteria were cited as inclusion criteria in 20 instances (91%). **CONCLUSIONS:** Regulators in Europe and the US rely heavily on DSM diagnostic criteria, in the sense that these often serve as inclusion criteria for pivotal clinical trials. Given significant changes to the criteria in many diagnostic categories, regulators and sponsors need to familiarize themselves with the document and evaluate their use of DSM criteria going forward.

PRM214

PODCASTS AS A LEARNING TOOL IN A RESEARCH METHODS COURSE FOR PHARMACY STUDENTS

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OBJECTIVES: Podcasts (recorded lectures) can be beneficial for all students, particularly English as a second language students who face language barriers when learning in another language. There is limited study on pharmacy student perceptions and podcasts, none from an international perspective. The primary objective was to describe pharmacy students' perceptions on the usefulness of podcasting and a secondary objective was to compare perceptions between native versus non-native English speakers in a pharmacy research course. **METHODS:** All first year pharmacy students (n=157) attending a Research Methods course in 2012 were invited to participate in a survey, which utilized a 4-point Likert Scale (1= strongly disagree, 2=disagree, 3=agree, and 4=strongly agree). Podcasts covered all course topics such as Applied Statistics, Odds Ratio and Relative Risk, Case Reports, Observational Studies, Randomized Controlled Trials, and Economic Evaluations. Descriptive statistics and t-tests were utilized to analyze the data in SPSS. The study was approved by the Institutional Review Board. **RESULTS:** A total of 73% of the class completed the survey (40.2% Caucasian, 32% Asian and 25% African American). A total of 24.1% identified themselves as non-native English speakers, 94.6% lived in the US for greater or equal to 5 years and 66.1% communicated in English at home. The majority of students agreed/strongly agreed that podcasts helped them to prepare for exams (92.9%), podcasts were a useful learning tool (91.2%), promoted understanding of course material (89.3%), helped with missed concepts (96.4%), and facilitated note-taking at their own pace (92.2%) with mean scores 3.34, 3.27, 3.27, 3.48 and 3.48, respectively. Results of the t-test revealed that there is no statistically significant difference between native versus non-native English speaking students in their perceptions of podcast usefulness ($p>.05$). **CONCLUSIONS:** Podcasts are beneficial to a majority of students, despite their language background. Podcasts have the potential to be a valuable learning tool for students taking a research methods course.

PRM215

GRADE FOR QUALITY ASSESSMENT OF EFFICACY AND EFFECTIVENESS STUDIES ON ANTI-TNFS TREATMENT OF RHEUMATOID ARTHRITIS

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OBJECTIVES: Assess the quality of evidence on experimental and observational clinical research through the same approach named GRADE (Grading of Recommendations Assessment, Development and Evaluation) **METHODS:** We evaluated the primary endpoint of a random sample from efficacy and effectiveness studies included in a systematic review on the treatment of rheumatoid arthritis with anti-TNFs. The quality assessment was conducted in accordance with the recommendations of the GRADE Working Group available at: www.gradeworkinggroup.org/toolbox/index.htm. It assigns at first high quality for trials and low quality for observational studies. **RESULTS:** The assessment of 8 efficacy and 8 effectiveness studies showed respectively that the quality of evidence were high in 5 and 0; moderate in 3 and 2; low in 0 and 2; and very low in 0 and 4. The risk of bias was present in 3 and 5; imprecision results in 0 and 5; elevated magnitude of effect in 6 and 4; controlled confounding bias in 0 and 3; presence of dose-response gradient in 0 and 1. Indirect evidence and inconsistencies were not found in any of the studies. **CONCLUSIONS:** The quality of evidence of 3 trials and 4 observational studies were downgraded, while 2 observational studies had the quality assessment increased.

PRM216

WHAT VALUE CAN OPERATIONAL FEASIBILITY STUDIES BRING TO POST MARKETING OBSERVATIONAL STUDIES (PMOS)? EXAMPLE OF FEASIBILITY STUDY PERFORMED IN EASTERN EUROPE TO ASSESS HEPATITIS C VIRAL DISEASE/PATIENT MANAGEMENT IN REAL WORLD SETTING

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OBJECTIVES: Operational feasibility studies provide a good opportunity to assess practicality of large full-scale studies. They are an almost essential pre-requisite and should be well designed with clear objectives. Conducting a pilot study can enhance the likelihood of success of PMOS and potentially help to avoid serious design flaws. The objective of this research is to assess the value of feasibility studies prior to PMOS implementation and highlight the importance of local physicians' feedback. **METHODS:** A feasibility study in 6 Eastern European countries was conducted via collection of physician surveys to assess local standard of care. The feasibility questionnaire was developed to assess operational aspects, such as availability of patient population, site experience and time and willingness to participate. The 37 physicians who received the questionnaire were selected through PubMed; they were all experts who have published regarding HCV infection and were provided with the protocol synopsis **RESULTS:** Out of the 37 selected physicians, 18 gastroenterologists, hepatologists, and infectious disease specialists in Bulgaria, Croatia, The Czech Republic, Hungary, Poland and Romania completed the questionnaire. The participating Physicians were working exclusively in public institutions. The average number of HCV patients seen by year is 140 and out of them 78 are treated by Interferon. They specified that they can enrol 2 eligible patients per month on average. They see their patients frequently during treatment initiation (bi-weekly or monthly). However, the follow-up varies from one country to another (quarterly or semi-annually). Physicians indicated that patient records and data regarding blood tests and procedures are accessible for 100% of the cases. Over 60% of the sites were familiar with Patient Reported Outcomes. Overall, 12 physicians were interested in participating in the Study. **CONCLUSIONS:** The result of this survey helped us documenting routine medical practice and confirming the study design and methodology to be implemented.

PRM217

USE OF SURROGATE OUTCOMES IN HEALTH TECHNOLOGY ASSESSMENTS (HTAS)

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OBJECTIVES: This study analyzes how frequently surrogate outcomes are used in HTAs and if the validity of these outcomes are discussed and reported within the HTAs. A surrogate outcome is defined by the National Institutes of Health as a biomarker intended to substitute for a clinical endpoint. A surrogate outcome is used when a clinical endpoint of interest is not ideal or does not occur often enough to perform meaningful statistical analysis. It is appropriate to use a surrogate outcome only when there is a strong correlation with the clinical endpoint. Before using surrogate outcomes researchers should confirm that the surrogate outcome is biologically plausible, has a magnitude of association with the clinical endpoint, and reflects changes in the relevant clinical endpoint. **METHODS:** Context Matters (CM) analyzed 1,056 HTAs spanning 38 disease conditions. Each HTA had a primary outcome that could be classified as either a surrogate outcome or a clinical endpoint. Data was analyzed for eight HTA agencies: AHRQ, DERP, SMC, HAS, PBAC, NICE, CADTH, and HIS Scotland. For those HTAs using a surrogate outcome as the primary outcome, CM then determined if the HTA agency reported the use of the surrogate and/or discussed the surrogate outcome's validity. **RESULTS:** Ninety-one percent of HTAs used a surrogate outcome (966 HTAs), but only 11% (109 HTAs) identified it as a surrogate outcome and/or discussed its validity. The agencies that discussed the use of the surrogate outcome most often were AHRQ, DERP, and HIS Scotland at 48.1%, 28.6%, and 29.0% of the time, respectively. **CONCLUSIONS:** Surrogate endpoints are prevalent in HTAs, but the agencies rarely discuss the validity of these endpoints. All agencies failed to discuss the use of the surrogate endpoint in over 50% of their reviews. HTA agencies are not following best practice use of surrogate outcomes.

RESEARCH ON METHODS – Conceptual Papers

PRM218

PROPOSAL OF ECONOMIC EVALUATION GUIDELINE IN JAPAN

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OBJECTIVES: Use of economic evaluation of health care technologies is intensively discussed in the government in Japan. In order to make evaluation results comparable, standardized method of evaluation is required. We proposed an economic evaluation guideline in Japan. **METHODS:** We organized a research team for developing guideline. After reviewing guidelines in HTA agencies in the world and current debate on issues, we investigated HTA reports and methodology of economic evaluation studies in several drugs, devices and procedures. Based on the review of these information, the research group discussed and proposed economic evaluation guideline suitable for Japan. **RESULTS:** Proposed guideline consist of 13 items: 1) Objective; 2) Perspective of analysis; 3) Comparators; 4) Method of analysis; 5) Time horizon; 6)Choice of outcomes; 7) Source of clinical data; 8) Costs; 9) Productivity loss; 10) Discounting; 11) Modeling; 12) Uncertainty; and 13) Budget impact analysis. Guideline sentences are classified into 3 levels, principal, recommended, and optional. **CONCLUSION:** This guideline is a proposal by a research team. However, it will be needed in the near future for using economic evaluation of health care technologies. Proposed guideline should be tested by adopting individual studies.

PRM219

DEALING WITH ZERO CELLS IN SPARSE NETWORKS IN BAYESIAN NETWORK META-ANALYSIS

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OBJECTIVES: Bayesian Network Meta-Analysis (NMA) models for binary data are well established and special precautions do not usually need to be taken in the case of zero cell counts. Furthermore, trials with zero cells in both arms are usually excluded from the analysis. However, in sparse networks with only one trial per comparison and zero cells in unique link studies, their inclusion may be mandatory. Zero frequencies may result in numerical instability and/or large variances. The objective of this study was to investigate the effect of different methods dealing with zero cells in sparse networks in Bayesian NMA. **METHODS:** A review was conducted to identify methods dealing with zero cells for binary outcomes in sparse networks in a Bayesian setting. The identified methods were applied to a sparse network with six treatments and one study per comparison. The outcome was grade 3+ Adverse Events and measured by Odds Ratio. A fixed effects model was fitted with binomial likelihood. The performance of the methods was assessed by the residual deviance and the Credible Intervals' (CrI) width was compared. **RESULTS:** We identified three methods: apply a continuity correction (a constant factor of 0.5 or the reciprocal of the opposite treatment size), use of informative priors on treatment effects and placing a distribution on the baseline model. We applied all methods and combinations of them. The model fit was adequate for all methods (residual deviance [10;12.3] for 12 datapoints). The use of different informative priors improved the variability estimates. CrI widths were reduced up to 15 times with respect to the original model with vague priors. **CONCLUSIONS:** Although the debate on the inclusion of studies with zero events in NMA is still open, our research shows that methods are available to address this issue. However, no clear recommendations can be provided.

PRM220

QUALITY ASSESSMENT OF OBSERVATIONAL STUDIES FOR SYSTEMATIC REVIEWS

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Observational studies are frequently included in systematic reviews, especially in those disease areas where RCTs are limited. While there are very specific tools for and guidance on assessing the quality of RCTs, the assessment of observational studies is less standardized. OBJECTIVE: To understand and assess the different tools used to review the quality of observational studies and to make recommendations based on our evaluation. **METHODS:** First, a systematic review of literature from 2005-present was conducted in Embase and Medline to determine the frequency of use of quality assessment for observational studies and the type of tools used to conduct the assessment. Second, we reviewed documentation from NHS guidance on quality assessment of non-randomized studies. Finally, we reviewed two years of approved HTA submissions to see what methods of assessment have been used for submissions. **RESULTS:** A total of 1429 articles were screened. Compared to a similar study on older literature, our review found an increase in the use of quality assessment for observational studies. However, we found that many studies continue to devise their own tool or adapt existing tools rather than use a tool in its entirety. Downs and Black, MOOSE, and STROBE were the most referenced tools, although STROBE was not originally intended for such use. Guidelines centered on "non-randomized" studies were mixed and were not always found to be applicable to observational studies, but instead mostly to single-armed clinical trials. **CONCLUSIONS:** There is still a need for guidance and standardization for observational studies assessment for use in systematic literature reviews. Although quality assessment of observational studies is still not standardized, there are a few methods becoming more frequent in the literature but are difficult to compare across systematic literature reviews because they have often been adapted by each author.

PRM221

AN APPROACH FOR QUANTIFICATION OF PATIENT ADVOCACY GROUP INPUT IN THE HTA PROCESS

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Patient input in HTA pathways by the appropriate disease Patient Advocacy Group (PAG) uses principally humanistic and social studies as an evidence base followed by critical evaluation against traditional CEA (Cost Effective Analysis) via a scientific process. Patient and Public Involvement (PPI) in HTA is associated with a low evidence base potentially limiting its value. Research presented at ISPOR 2012 by the same authors concluded a need to improve and standardize PAG input integration in HTA decision making. To investigate the way different forms of knowledge / experience are used by PAGs in NICE HTA for guideline development and new technology review. We will look at: 1) Influence of PAG structure, resource capability, internal process and the impact of PAG advisory board physician representatives on scientific validation of patient input in HTA participation, and 2) Part I results will inform further research into selection and ranking criteria of social derived data compared with CEA. An iterative PPI best practice approach will be followed. Selection criteria: Five UK PAG groups (Neurological, Autoimmune, Rare disease, Cardiovascular and Oncology) will be invited to participate. The NICE PPI Unit will nominate groups when needed. Inclusion criteria: 1) willingness to participate, 2) prior involvement in guideline / new technology assessments; and 3) presence of medical advisory board. Research elements: Application of GRIPP criteria (Guidance Reporting Involvement Patient Public) to ensure a strong evidence base will guide development of an on-line survey and subsequent focus groups and interviews. The survey, designed for SAP review, will study: size of PAG, internal process for HTA involvement, previous HTA involvement, data submitted, PAG knowledge gaps and involvement of medical advisory board. Follow up by focus groups and interviews with PAG and advisory board members to identify insights/ themes.

PRM222

JUGGLING JURISDICTIONS: METHODS FOR CONDUCTING MODULAR SYSTEMATIC REVIEWS?

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A crucial component of a systematic review is a clear description of the disposition of studies throughout the various steps of the review process (de-duplication, abstract review, full paper review and final inclusion). This is commonly achieved using a PRISMA diagram that shows the number of inclusions and exclusions at each stage of the review. This may be supplemented with details of the reasons for exclusion. To create the PRISMA diagram it is necessary to keep an on-going count of exclusions and inclusions throughout the review process. However, this can pose a challenge where the scope of a systematic review changes from the original specification. This may happen where the set of licensed treatments or HTA requirements vary between jurisdictions or over time. In these cases, it may be time consuming to recreate the on-going counts of exclusions that correspond to the modified scope. We present a methodology for conducting a modular systematic review in which PRISMA diagrams and other descriptions of study disposition can be generated corresponding to any subsequent changes of scope. This is achieved by splitting the review into a set of 'component-reviews' defined by mutually exclusive treatment search terms that comprise the full set of possible intersections between the individual treatments. Throughout the systematic review process separate counts of abstracts, papers and studies are maintained for each of these component-reviews. The results from the component-reviews can then be combined to reflect any final review scope (based on individual treatments). We will illustrate the methodology with an example review of the comparative efficacy of licenced thiazolidinedione's (TZDs) versus placebo in patients with type 2 diabetes mellitus (T2DM) where there are two TZDs licensed in the USA (pioglitazone and rosiglitazone) but only one in Europe (pioglitazone).

PRM223

SOCIAL NETWORK ANALYSIS OF AUTHORSHIP NETWORKS AND THE IDENTIFICATION OF EXPERT ADVISORS

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OBJECTIVES: Systematic reviews are often supplemented with the use of external experts to provide guidance on the nuances of the area. This can help add context if a review is used to support trial design or health economic model development. The ideal expert would have a deep understanding of the area and be well connected to those individuals conducting trials. The aim of the current research was to assess whether social network analysis of coauthor networks could be used to rapidly and objectively identify individuals with the qualities desired in an external expert. **METHODS:** Publication lists from a recent systematic review of rheumatoid arthritis were used to produce a list of links between authors and publications. This was then imported into the Gephi program for social network analysis. Within Gephi, matrix multiplication was used to transform this network into a coauthorship network. Eigenvector centrality was then used to infer the amount of access individual authors have to the research community as a whole. The use of eigenvector centrality as a measure of influence within the author network was then validated by correlating the centrality scores of a random sample of authors against independent ratings of desirability of those individuals' expertise. **RESULTS:** The coauthor network for rheumatoid arthritis, while not completely connected, showed a high degree of connectivity (mean degree: 26, network diameter: 5). Eigenvector centrality allowed the identification of key experts, with the highest scoring experts each providing direct access to approximately half of the whole network. Eigenvector centrality measures were a reliable predictor of mean desirability scores from ten raters ($F(1,9)=20.35$, $p=0.0015$, R-squared=0.69). **CONCLUSIONS:** Social network analysis of coauthor networks provides an efficient and robust method for the identification of expertise, and can be used as part of the systematic review process.

PRM224

SYSTEMATIC REVIEW APPROACHES FOR HTA: HORSES FOR COURSES?

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Systematic reviews aim to identify, select, synthesize and appraise all high quality research evidence relevant to a particular research question, and are widely accepted as the gold standard for providing the best evidence for use in decision making. They are essential, routine components of submission data packages for health technology assessments (HTAs) of products undergoing evaluation for reimbursement and market access. Additionally, systematic reviews are often the source for clinical evidence used in health economic modelling to evaluate cost-effectiveness. Thus, they represent a substantial investment of resources, and incorrect or incomplete reviews could invalidate the proposed clinical and economic value of a product set out in a health technology submission and result in unfavourable reimbursement decisions and/or delayed market access. There are a number of best practice criteria set down for systematic reviews; the most widely recognised being from the Cochrane group. However, when carrying out a systematic review for HTA purposes researchers should be aware of the additional requirements set out by each agency. The Cochrane, UK National Institute for Clinical Excellence (NICE) and Germany's Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesenis (IQWIG) methodological guidelines for conducting and reporting systematic reviews were analysed and an 'inclusive' checklist of requirements was developed to ensure the systematic review and meta-analysis met the broad set of HTA requirements and minimise the risk of having to repeat the procedure or create the need for a HTA review group to carry out its own review, which could potentially lead to an unfavourable reimbursement decision or a restriction on use. An awareness of specific HTA systematic review requirements can help optimise the preparation of a data package for HTA submission and hence maximise the chances of success.

PRM225

CAN A MULTI-CRITERIA DECISION (MCD) OPTIMISATION MODEL HELP DECISION MAKERS IN THE OPTIMAL SELECTION OF VACCINES WHEN EXPANDING THEIR UNIVERSAL MASS VACCINATION PROGRAMME? THE CASE OF POLAND

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OBJECTIVES: The model aims to determine the optimal allocation of financial resources amongst various paediatric vaccines accounting for changes in budget and availability of new vaccines over time. This approach aims to inform decision makers who are seeking to extend their national immunisation programmes about the optimal mix of vaccines and sequence of their introduction, meanwhile accounting for their preferences in clinical and cost outcomes. **METHODS:** An MCD optimisation model was developed in Microsoft *Excel* that considered availability of new vaccines and budget changes over time, optimal mix of vaccines in previous years, budget investment time horizon, cumulative outcomes time horizon, maximal achievable vaccination coverage, specific target populations. The optimal mix of vaccines within an available portfolio was determined by manually programmed linear optimisation based on a defined objective function and budget constraints. The objective function includes maximisation of prevention of disease cases, GP visits, hospitalisations, deaths, and cost savings in disease management. A multi-criteria approach allows for redistributing weights across clinical and cost outcomes in the objective function. Vaccination against rotavirus, varicella, influenza and pneumococcal disease was evaluated, based on disease incidences and direct medical costs from Poland. Relative risk reductions induced by vaccination were based on randomised controlled trials and post-marketing surveillance data. **RESULTS:** Dependent on the definition of objective function, the allocation of budget across a portfolio of vaccines resulted in different recommendations. If deaths-avoided was weighted at maximum, pneumococcal vaccine was ranked first, followed by rotavirus and influenza vaccination. If cost savings received the maximum preference, vaccination against influenza was ranked first, rotavirus second, pneumococcal third, and varicella fourth. The use of a weighted objective function resulted in different vaccines introduction sequences. **CONCLUSIONS:** The use of an MCD optimisation model provides a tool to inform decision makers about the optimal allocation of financial resources over time.

PRM226

DON'T MAKE ME WAIT: THE VARIANCE REDUCTION TECHNIQUE FOR FASTER MONTE CARLO SIMULATIONS IN COST EFFECTIVENESS MODELS ON WEB

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With the rapid pervasion of internet technologies, demand for making health economic evidence, such as mathematical models, accessible through the web increases. Long running computations such as Monte Carlo simulation can impair user experience because of longer waiting time. Our aim is to employ mathematical techniques to reduce the computation time of probabilistic cost effectiveness Monte Carlo models, thus increasing their acceptance when used on the web. We employ the variance reduction technique to reduce computation time while obtaining outcomes with the same Monte Carlo error. The control variate approach is applied. It utilizes information about errors in estimates of known mean Net Monetary Benefit (NMB) quantities to reduce errors in estimation of the cost-effectiveness acceptability curve. The NMB mean value is calculated based on the deterministic counterpart of the model. The said technique has been applied to the published probabilistic decision tree-based Excel model for evaluating cost-effectiveness of breast cancer screening. In this model, different types of probability distributions can be chosen to model uncertainty of disease incidence, mortality rate and intervention effectiveness. By applying the control variate approach we were able to achieve outcome with the same error while performing 50% less simulations as compared to the plain Monte Carlo method. Such performance improvement is yet another step towards increasing user acceptance of web based health economic models with Monte Carlo simulations.

PRM228

SIMULATED TREATMENT COMPARISONS – AN ALTERNATIVE APPROACH TO INDIRECT COMPARISON WHEN STANDARD METHODS ARE NOT FEASIBLE OR APPROPRIATE

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Health technology assessments (HTAs) rely on comparative evidence about new treatments and competing therapies, which are typically derived using indirect or mixed treatment comparisons (ITC/MTCs). These are not always feasible or appropriate, particularly in rapidly evolving therapeutic areas, like oncology. For instance, some comparisons may not be possible due to incomplete evidence networks; or, heterogeneity between studies due to differences in design or population may make an MTC inappropriate. There is, therefore, a need for alternative techniques, such as Simulated Treatment Comparisons (STCs). This technique is designed to derive comparisons between treatments after adjustment for differences between the populations of the two studies. This targeted comparison requires individual patient-level data (IPD) for at least one of the treatments (the index), and are appropriate when the trials used for the comparison are sufficiently comparable in design and methods, but differ in the profiles of their population in measured risk factors. The differences can be adjusted analytically using IPD via regression equations. This produces endpoint estimates for the index treatment that reflect the profile of the comparator population. These can then be contrasted with published results for the comparator to obtain a measure of difference between treatments. Since only measured risk factors can be included in the adjustment, the potential for residual confounding remains. Another potential bias is a possible "study effect" whereby other differences between studies distort the comparisons. This can be assessed using the reference groups of the trials, if these received the same treatment. STCs have been used in HTA submissions, and it is likely that its use and that of other alternative techniques will increase particularly in areas with rapid drug development. In the presence of heterogeneity or incomplete evidence networks, STCs can provide comparative evidence where these may be otherwise deemed unavailable due to limitations of ITCs/MTCs.

PRM229

THE USE OF EUROPEAN ELECTRONIC HEALTH RECORDS TO INVESTIGATE CANCER TREATMENT PATHWAYS

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RCTs remain the gold standard for evaluation of drug efficacy and safety. However, the only way of identifying treatment pathways and improving understanding of costs and outcomes at different stages of care is via longitudinal observational studies. Observational data from electronic health records (EHRs) are increasingly being used to support pharmaco-epidemiological research. Coverage, data quality and validity of UK EHR databases such as the Clinical Practice Research Datalink (CPRD) have improved in recent years, and many papers confirm the validity of data in diagnoses such as cancer. Published data show that recording of cancer diagnosis and mortality in primary care electronic records is generally consistent with Cancer Registry (CR) data in England. The use of "read codes" in CPRD to identify an event (cancer diagnosis or referral to secondary care) and the possibility of anonymous linkage to secondary care databases (e.g. Hospital Episode Statistics [HES] for information about hospital management as an in- or out-patient, to other CR data, and accurate mortality tracking by the Office for National Statistics [ONS]) allows the data and diagnosis to be validated against multiple sources, as well as identifying treatment pathways in both secondary and primary care. There are some limitations, e.g. not all patients identified in GP practices via the CPRD are linked to other databases. Management data such as secondary care prescribing are difficult to access (not available in HES) but may be available from reviewing anonymized patient notes or by connecting to other datasets. For example, IMS Health links CPRD data with hospital pharmacy audit data and HES data. However these data have only become available recently, are expensive to access and currently patient population coverage is low. We will provide a detailed description of the possibilities for integrated database use to map treatment pathways for cancer patients.

PRM230

SHOULD THERE BE AN OPTION TO "UNREFER" NICE SINGLE TECHNOLOGY APPRAISALS: CASE STUDY OF ARIPIPRAZOLE FOR BIPOLAR I DISORDER IN ADOLESCENTS

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Single technology appraisals (STAs) are a key component of the development of NICE technology appraisals guidance, but are a time and resource intensive process. Societal costs are incurred during STAs by holding the NICE Appraisal Committee, via payment to the evidence review group (ERG) and in the opportunity costs of other technologies which are not appraised. In addition, the drug manufacturer also incurs substantial costs in preparation of their submission and throughout the STA process. Recently aripiprazole, an atypical antipsychotic drug for the treatment of manic episodes in adolescent bipolar I disorder, was subjected to an STA and received positive guidance. It was apparent to the ERG from the outset of the appraisal that the conclusion would be positive as: the drug had a small acquisition cost; was already in widespread use; would shortly be going generic; and had a profile similar to its comparators. As the budget impact over a 5-year period estimated by the manufacturer was less than the payment received by the ERG, it was unlikely that the STA represented efficient use of resources. Given a fundamental role of NICE is in assessing cost-effectiveness, the option of un-referring STAs in rare circumstances has appeal. It is proposed that if certain criteria are met then it would be more cost-effective to not proceed with an STA. These include: small patient population, commonly used in current clinical practice, patent expiring in

the near future, and similar levels of efficacy and acquisition cost as key comparators In rare circumstances conducting an STA may not be cost-effective. It is possible that this can be predicted early in the STA process and we propose criteria to aid in this decision. When these criteria are met the possibility of "unreferring" the topic is likely to be the most cost-effective option.

PRM231

THE 2013 REVISION TO NICE'S DISCOUNTING GUIDELINES: DIFFERENTIAL DISCOUNTING HAS GONE BUT UNJUSTIFIED SELECTIVE APPLICATION REMAINS

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OBJECTIVES: To call attention to the problems resulting from the National Institute for Health and Care Excellence's (NICE) recent revision to their methods guidance on discounting, which recommends applying a lower discount rate than the reference case rate in selected cases. **METHODS:** NICE's reference case discount rate for costs and health effects is 3.5%. In 2011 NICE amended their economic appraisal guidelines recommending differential discounting of costs and health effects at 3.5% and 1.5% respectively in selected cases. A recently published article in Value in Health criticised this amendment on a number of grounds, including ambiguity over what are the eligible selected cases; the lack of rationale for selective application of differential discounting; the apparent inconsistencies that unjustified selective application give rise to; and, the size of the differential between the two discount rates. In April 2013 NICE published a comprehensive revision of their methods guidelines, in which equal discounting of costs and effects at 1.5% in selected cases is now recommended. **RESULTS:** While NICE's new 2013 guidance no longer includes an unjustified differential between the discount rate on costs and health effects, it still recommends the application of lower discount rates in selected cases. The revised guidance still offers no rationale for such selective application of lower discount rates. This means that many of problems described in the recently published critique of the 2011 amendment still apply to the new 2013 guidance, including a particularly worrying potential for age discrimination. **CONCLUSIONS:** NICE's selective application of lower discount rates in certain cases is not justified and leads to inconsistencies in the appraisal of different interventions. NICE is urged to again revise their discounting guidance, this time ensuring all interventions are treated equally and are subject to the same discount rates.

PRM232

A FLEXIBLE MULTI-STATE MODELLING FRAMEWORK FOR THE SIMULATION OF CANCER PROGRESSION AND CANCER CARE

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Most cost-effectiveness models for evaluation of cancer care compare interventions within a single treatment line. However, to investigate the full impact of a new treatment, also downstream effects must be taken into account. Furthermore, most models are based on observed clinical states, whilst these observations depend on the timing of examinations and the choice of diagnostic test. To evaluate the potential of new treatments and diagnostics, the underlying disease process needs to be modeled including the interaction with diagnostics and treatment.**OBJECTIVES:** To build a flexible framework for a disease model, that simulates cancer progression to obtain clinical, patient and economic outcomes, while taking diagnostics treatment pathways and surveillance schedules into account . **METHODS:** The modeling framework discerns two levels to describe disease progression, the level of the patient and the tumor. At the patient level, an individual is characterized by clinical states; "primary tumor only", "local recurrence", "regional recurrence", "distant metastasis, stable", "distant metastasis, progressing" and "death". The clinical state is derived from disease development at the tumor level. Seven tumor growth states are defined: "absent tumor", "dormant tumor", "micro tumor", "small macro tumor", "medium macro tumor", "large macro tumor", "symptomatic tumor". Melanoma progression was used as a case study. The model simulates, in parallel, 11 possible tumor sites, ranging from "local" to "regional" and "distant metastatic" locations. Sites were chosen because they are associated with different treatment and prognosis. The disease model is complemented with a treatment and surveillance module. In this module, treatment choices in each of the clinical states are specified. Treatment choice may depend on patient and tumor features, and subsequently influences rate of transitioning between tumor growth states. For surveillance, timing of surveillance visits, techniques used and their detection rate(s) are specified. **CONCLUSIONS:** The proposed framework provides a flexible and widely applicable cancer modeling design.

PRM233

HOLISTIC DATA GENERATION AND SYNTHESIS FOR HTA ASSESSMENT: BRINGING TOGETHER COMPARATIVE EFFECTIVENESS RESEARCH, PERSONALISED MEDICINE AND PATIENT-CENTRED OUTCOMES RESEARCH

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Defining value and generating innovation in health care relies increasingly on real world evidence. Consequently, there is an ongoing evolution in the data needs for health technology assessment (HTA). Three key elements of data generation are comparative effectiveness, personalised medicine and patient-centred outcomes. Integrating these three to support synthesis via systematic reviews, meta-analyses and modeling is necessary to maximise value and drive innovation. Effectiveness is not just about reduced morbidity and mortality. It now covers quality of life, patient satisfaction, intermediate endpoints, and screening/diagnosis/monitoring. Additionally, there is a shift away from effectiveness versus placebo to comparative effectiveness versus other technologies or standards of care in the real world, focusing on the effect on health outcomes in defined patient populations based on ethnicity, comorbidities or age. Personalised medicine signals another shift of focus away from broad, homogenous patient populations to small, more-or-less defined patient subgroups. For example, in oncology, markers such as KRAS, HER-2/neu and BRCA 1,2 are used for prognosis and to direct treatment. To reflect this evolution, comparative effectiveness research programme designs and analytical methods must be able to detect important treatment effects and outcomes for specific patient subgroups. The emergence of patient-centered care adds further complexity to HTA data requirements. The systematic collection of patient-reported outcomes (PROs) and their application to medicine is far from standard in clinical practice, although many clinical trial programmes now include the collection of PROs. For products in development, data generation plans must reflect ongoing changes and evolving complexities. We will review the growing range of methods employed in clinical effectiveness research, and show how personalised medicine and patient outcome programmes can strengthen HTA data packages.

PRM234

AN ANALYSIS OF HOW NOT TO USE COST-EFFECTIVENESS ANALYSIS FOR PRICE-SETTING

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OBJECTIVES: Cost-effectiveness Analysis (CEA) and the calculation of the Incremental Cost-Effectiveness Ratio (ICER) together with its comparison with a threshold such as Gross Domestic Product (GDP)/capita, have long been used to assess the value for money of a new intervention compared with a comparator that this new intervention precisely seeks to displace. In this paper we show the paradoxical increase in cost-effective price using data from middle, low and very low income settings. **METHODS:** Using the introduction of rotavirus vaccination compared with no-vaccination as the example. We create a theoretical framework for calculating the ICER by gradually decreasing the investment for treatment of rotavirus related disease (the 'no-vaccination comparator') representing different countries with different GDP levels and decreasing levels of existing health care investment. We compare these results with an analysis of cost-effectiveness using real data from 9 countries representing a range of different GDP levels. **RESULTS:** The theoretical framework works well in situations where the GDP/capita exceeds $10,000 – as expected the cost-effective price decreases with a decrease in the GDP/capita. Below this the scant investment in health care infrastructure, thereby reducing potential cost-offsets, coupled with the significant increase in the potential effect gain, results in a much wider margin between a cost-neutral and cost-effective price that could effectively be set using this approach. **CONCLUSIONS:** Although Cost-Effectiveness Analysis is widely used to assess the value for money of a new intervention for a particular price, we would argue that where investment in health care is low and disease burden is high, the use of CEA leads to paradoxes in price-setting.

PRM235

RE-ENGINEERING OF THE DISTRIBUTION OF DRUGS IN THE HOSPITAL. TOC APPLICATION AND TRZ

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OBJECTIVES: Presents a reengineering process of the distribution of drugs into the hospital, analyzing all the options available in the market, and looking for alternative solutions that may be more cost-effective. **METHOD:** The processes and subprocesses in the cycle from prescribing, distribution, and drug administration, are defined and discussed based on studies of medication errors (ME). The differential analysis is performed on the subprocesses. As technique for finding creative solutions (new cost-effective alternatives) apply the Theory of Constraints (TOC), and the TRIZ methodology. **RESULTS:** Since patient safety can distinguish four processes: prescription (about 40% of ME), transcription, distribution (about 10% each), and administration (about 40% of ME). In the administration, avoided ME before they reach the patient are minimal (only 2%). In the prescription/transcription there are 4 options: manual prescription, preprinted sheets, electronic prescription, and assisted prescription. In the distribution has 3 options: clasical SUD, filling carts using automated carousels, and automated dispensing systems (ADS). For administration there are other 3 options: manual record, electronic registration, and registration across the barcode. The most expensive option would be the introduction of ADS in all plants (1.4 million€ for a hospital of 280 beds). But these teams only reduces errors about 10% of all ME. Applying the TOC and TRIZ, investment in electronic prescribing, and administration with barcodes is the most cost-effective. Dose-day (sending medication for one day but not rated by patient) could be the most efficient system by simplifying processes. The error difference between Dose-day, and SDU can be annulled by the advantages of the assisted prescription, and administration with barcode **CONCLUSIONS:** It is surprising to invest large sums in improving distribution processes (ADS) - where the fewest mistakes occurs - instead of prescribing and administration. The dose-day with barcode administration would be the most cost-effective theoretical-model.

PRM236

HOW CAN HEALTH ECONOMIC ASSESSMENT METHODS HELP DECISION MAKING IN PORTFOLIO DEVELOPMENT

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OBJECTIVES: The R&D costs of a new drug approximate $1.3 billion and are increasing due partly to regulatory hurdles and development costs. There is a need for smarter investments, which consider the requirements of regulatory bodies, increasing the chances of securing market access and high return on investment. We describe how health economic methods could support capital investment decisions in funding, valuing and bringing new pharmaceuticals to market. **METHODS:** A literature review was performed on health economic and capital investment methods. The different analyses were mapped to the commercial roadmap and R&D pipeline

of a biopharmaceutical company. An approach based on real options valuation model was proposed to support investment and market decisions and to predict the potential net present value (NPV) of a drug. The conceptual structure of the model was face-validated by health economic and valuation experts. **RESULTS:** A decision-tree based valuation method, populated partially by information from health economic tools, was adopted to analyse and clearly communicate R&D investment opportunities, to capture management flexibility and to improve strategic thinking. A feedback loop can be built into the model to analyse resiliency to assumption changes. In early phases, headroom and multi-criteria decision analyses indicate the likelihood of an investment being cost-effective. Phase I and II trials provide early evidence on drug efficacy and tolerability and initial cost estimates. Based on value of information, cost-effectiveness and budget impact models, only drugs deemed to meet authority requirements would be selected. Market intelligence and uncertainties and clinical success probability further enable identification of the optimal portfolio containing drug candidates that maximize NPV for given risk levels. **CONCLUSIONS:** Health economic methods are commonly applied during late stage development, but if implemented alongside capital investment tools from earliest R&D stages they could increase the likelihood of selecting the right products to compose an effective investment portfolio.

PRM237

MULTIVARIATE NETWORK META-ANALYSIS OF PROGRESSION FREE SURVIVAL AND OVERALL SURVIVAL

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Cancer treatment effectiveness is often quantified by analyzing time from treatment initiation to the occurrence of a particular event. Very commonly studies report data on overall survival (OS), where the event is death from any cause, and on progression-free survival (PFS), where the event is death from any cause or disease progression, whichever occurred first. Both OS and PFS can inform decision making. Separate meta-analyses of OS and of PFS data ignore the correlation between the outcomes. We introduce a method for the joint meta-analysis of OS and PFS that is based on a tri-state transition model with time-varying hazard rates modeled with fractional polynomials. In English, we assume that, at any time, patients can be in one of three health states: "alive but not progressed", "alive and progressed", and "dead". PFS corresponds to time spent in the first state, and OS to time spent in the two alive states. The proposed approach allows the joint network meta-analysis of OS and PFS, relaxes the proportional hazards assumption, extends to a network of more than two treatments, and simplifies the parameterization of decision and cost-effectiveness analyses. The data needed to run these analyses can be extracted directly from published survival curves. We demonstrate use by applying the methodology to a network of trials for the treatment of non-small cell lung cancer.

PRM238

USING LOWER COST, LOWER EFFICACY INTERVENTIONS CAN IMPROVE POPULATION HEALTH OUTCOMES UNDER BUDGET CONSTRAINTS

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BACKGROUND: The global economic crisis imposes severe restrictions on budgets allocated to health care. Innovative technologies in medicine may improve patient outcomes but such improvements come at a substantial cost, thus limiting the number of patients that may benefit from them. According to current cost-effectiveness analyses (CEA), most innovative interventions are associated with a higher efficacy and higher costs compared with the standard of care. These analyses do not account for the budget impact associated with implementing the interventions on all eligible patients. Even when a new intervention is highly cost-effective, health care systems may not be able to adopt it due to substantial budgetary impacts. Implementing a substantially lower-cost intervention to a substantially wider population, accepting inferior per-patient outcomes, may improve overall health outcomes under a restricted budget. **OBJECTIVES:** Develop an innovative health technology assessment (HTA) model that combines CEA and budget-impact analyses, thus enabling to compare the impact of intervention alternatives on the entire intended use population, under a pre-specified budget constraint. **METHODS:** We identified the following steps to be included in the model formulation: 1) Define the intended use and the target population. 2) Define two or more interventions, one of them at higher cost and better per-patient outcome, and the second with lower cost and inferior per-patient outcome. 3) Forecast the diffusion of the alternatives into the entire intended use population, under a pre-defined budget, in order to estimate the treated and untreated populations. 4) Calculate the clinical impact of each alternative on the treated population. 5) Calculate the clinical impact of no therapy on the untreated population 6) Compare the aggregated clinical impact of each alternative on the entire intended use population – both treated and untreated. Using the proposed population-based model may result in improved health care outcomes, especially in times of economic downturn and austerity.

PRM239

EVIDENCE-BASED METHODS IN FOOD SCIENCES AND NUTRITION

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Evidence-based medicine has emerged as the bottom line of Health Technology Assessments for drug evaluations. Over the last decade, evidence-based assessment of food and nutritional products has accelerated. Specific quantitative tools to synthetize evidence have been increasingly developed, and used for decision support. This work aims at highlighting the critical role of systematic reviews and model-based evidence synthesis in the field of food sciences and nutrition, especially with the view of safety assessment. To first set the scene of food assessment in Europe, the latest Guidelines on Systematic Reviews published by the European Food Safety Authority (EFSA) (EFSA, 2010) are described with the approach on how to handle observational data on the general population. Specific examples of large systematic reviews conducted for estimating food safety accounting for population variability and interactions between food contaminants and drugs are also presented. Details on the model-based meta-analyses of such safety data are described and discussed for the purpose of regulator's decision making. Systematic reviews have been to the context of food and nutritional epidemiology requiring more stringent quality assessment and more advanced management of variability. This resulted in a Bayesian random effect model accounting for population variability. Metabolic interactions between food and drugs were evidenced and variability metrics could be explicated in terms of "uncertainty factors" to be used by the food regulators to assess safety limits for food ingredients, contaminants or drugs and their combined use. Food regulator in EU is aligning and even sometimes anticipating drug regulators in terms of evidence-based safety assessment in the real life. Common tools for model-based evidence synthesis can be applied to quantify safety signals and interaction in the general population.

PRM240

COMPARATIVE EFFICIENCY RESEARCH: META-ANALYSIS OF COST-EFFECTIVENESS STUDIES

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OBJECTIVES: Cost-effectiveness analyses (CEA) have become widely used in several pathologies. Currently, new CEA studies comparing active vs control treatment have been incorporated each year. For this reason, the combination of CEA studies could give a more consistent and accurate estimate of an intervention's efficiency than one study alone. The aim of study was to develop a new method to do comparative efficiency research (COMER) based in individual patient data. **METHODS:** After, adjusted the marginal distribution and copula distribution of a hypothetical cohort, we stated the parameters and distribution estimated like our unknown theoretical distribution. We conducted an iterative analysis of a random Frank Copula distribution with a different range of sample size. We performed a comparison between samples and theoretical distribution in terms of incremental cost-effectiveness ratio (ICER), incremental monetary benefit(IMB) fixed a threshold (k= 20.000 monetary units) and goodness of fit for Frank copula, assuming a tolerance. **RESULTS:** The Theoretical distribution fixed, showed a cost of 604.34 monetary units for active and 516.12 monetary units for control, and a utilities of 0.529 for active and 0.492 for control. ICER for theoretical cohort was 2,380 monetary units per quality-adjusted life year gained and IMB was 653. With a tolerance of 500 monetary units for ICER and 50 monetary units for IMB, only 15.52% of simulations were near the theoretical ICER and only 6.12% of IMB. The amount of individual patients simulated was more than 500 patients per treatment to fit Frank Copula. **CONCLUSIONS:** Preliminary results showed that COMER based in individual patients' data could allow decision maker to know real add-value of a new intervention.

PRM241

EVALUATING THE ECONOMIC IMPACT OF TECHNOLOGICAL ADVANCES IN DIAGNOSTICS: THE CASE OF HIGH THROUGHPUT SEQUENCING FOR HEREDITARY BREAST CANCER

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Benefits of diagnostics tests generally centre on test accuracy measures. However, additional benefits of diagnostics may include: reduced laboratory time, reduced time to results and increases in the capacity of a laboratory to deliver more tests. New technological developments, such as high throughput sequencing (HTS) are challenging the current methods used in establishing the case for the introduction into clinical practice terms of economic impact. This is evident in the case study developed here examining *BRCA1/2* genetic testing in providing information on the risk of development of breast cancer. Current *BRCA1/2* testing technologies are limited by long (up to one-year) turnaround times, which together with limited resources to increase the volume of tests and associated genetic counselling, has driven the use of a 'risk threshold' to target women eligible for testing. HTS offers the opportunity of decreased turnaround time and increased volume of *BRCA1/2* tests, which will impact on the benefits and costs associated with the diagnostic service. Systematic reviews have identified Markov-type models as the dominant modeling methodology for the assessment of genetic testing. We propose that discrete event simulation (DES) is the appropriate model type to quantify the economic impact of HTS *BRCA1/2* testing as it allows evaluation of the impact of capacity constraints and increased turnaround time on the costs and benefits of this new diagnostic technology. Importantly, DES also allows for the assessment of structural uncertainty by considering changes in patient pathways when using a new diagnostic technology. While DES may be the most appropriate modeling methodology in assessing the economic impact of novel genetic tests; typically the type of data and information required to popuate these models in lacking. We conclude by highlighting the type of data required to both population appropriate models and to adequately assess the economic impact of these novel genetic tests.

PRM242

THE IMPORTANCE OF SENSITIVITY ANALYSES IN HEALTH TECHNOLOGY ASSESSMENTS

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In this paper, we critically evaulated analytical design of health technology assessment methodologies, particularly related to sensitivity analyses and willingness-to-pay thresholds. To this end, we have used two studies: the first one analyzing cost-effectiveness of a human papillomavirus vaccination of boys at age 12 against oropharyngeal carcinoma and anogenital warts and the second one examining cost-effectiveness of a universal programme of vaccinating children against pneumococcal disease. We have shown – as expected – that the impact of variation of parameters can be substantial, however, outcomes of sensitivity analyses are often understated both by marketing authorization holders and authorities. Few would

disagree that innovation in health care is worthwhile; the tremendous technological success in pharmacological treatment of HIV patients is a case in point. On the other hand, a relatively large number of "me-too" entries in the pharmaceutical market and the diminishing productivity of R&D sector call for robust methodologies, which could distinguish high-value, breakthrough products. Sensitivity analyses of cost-effectiveness studies should be made pivotal in decision-making process in order to ensure efficient diffusion of innovation.

PRM243
SURVEY DESIGN IN THE ASSESSMENT OF THE IMPLEMENTATION OF RISK MINIMISATION MEASURES FOR MEDICINAL PRODUCTS
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The introduction of the risk management plan (RMP) has ensured greater proactivity to the pharmacovigilance and post-authorisation benefit risk assessment of human medicines. An RMP may include risk minimisation measures (RMM), public health interventions intended to prevent the occurrence, or reduce the impact of adverse drug reactions associated with the exposure to a drug. The new EU legislation on pharmacovigilance explicitly requires the active monitoring of the outcome of RMM, placing obligations on regulators and industry for this purpose. In this respect, the European Medicines Agency's good pharmacovigilance practices module dedicated to the practical implementation of the legislation on the evaluation of the effectiveness of RMM foresees a dual evidence approach. This approach builds on the assessment of two distinct levels of evidence: the actual implementation of the RMM, and the attainment of its final objective(s). The approach requires research encompassing analysis of implementation (process indicators), and traditional epidemiological research addressing the attainment (final outcome indicators) of RMM. Surveys are usually involved in the assessment of process indicators, in particular when RMM imply the provision of educational information to health care professionals (HCP) and the surveys are intended to measure what the HCP have learned. This paper aims to conceptualise the construction of surveys designed for the analysis of implementation of RMM. Such surveys should be developed following the principles of content validation. This requires a body of relevant questions (items), the sample population to which it will be administered, and a test plan. The test plan includes the type of items to be used, the number of items, the length of administration, how it is to be administered, and how it is to be scored and analysed in terms of item difficulty and discrimination. The paper concludes with a checklist to assist stakeholders in designing surveys for RMM assessment purposes.

DISEASE-SPECIFIC STUDIES

NEUROLOGICAL DISORDERS – Clinical Outcomes Studies

PND1
DISEASE BURDEN IN EPILEPSY ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX: SYSTEMATIC REVIEW
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OBJECTIVES: To summarize literature on the burden of epilepsy in tuberous sclerosis complex (TSC); TSC is a genetic disease characterized by behavioral disorders, benign tumors in multiple organs, and neurological manifestations including epilepsy. **METHODS:** A systematic search of keywords for TSC and burden of illness was conducted in MEDLINE- and EMBASE-indexed publications from 5/2000-1/2013, and non-indexed materials. **RESULTS:** In total, 83 articles on TSC-associated epilepsy were included. Up to 93% of TSC patients have epilepsy, with severe forms more common than in non-TSC epilepsy patients (infantile spasms, 35-57% vs. 9%; generalized tonic-clonic or grand mal seizures, 37% vs. 7%; complex focal seizures, 87% vs. 33%). Seizure onset is early (median age: 7 months, 82% by age 3). TSC2 gene mutations and cortical tubers, common brain malformations in TSC, are risk factors for early onset and greater severity of seizures. TSC-epilepsy patients have significant disabilities, including high rates of autism spectrum disorders (13-30%) and cognitive impairment/delay (62-80%). Although data are not available on long-term outcomes, early seizure control may reduce cognitive impairment and autism symptoms. Vigabatrin is a first-line treatment option for TSC-associated infantile spasms and focal seizures in infants, but poses a risk of serious retinal toxicity. Other anti-epileptic drugs are available as second-line options; most patients still require polytherapy, and 62% have refractory epilepsy that can necessitate surgery. With high rates of medication use, hospitalizations, and surgeries, TSC-epilepsy patients may consume substantial health care resources, particularly during the first 5 years post-diagnosis. Longitudinal trends in resource use, direct and indirect costs, and treatment patterns for TSC-epilepsy are largely absent from the literature. **CONCLUSIONS:** TSC-epilepsy is common and may be severe, with presentation early in childhood and long-term morbidity. True disease burden to patients, caregivers, and payers remains unknown given substantial data gaps in longitudinal clinical outcomes, treatment patterns, and costs.

PND2
POTENTIAL PREDICTORS OF ALZHEIMER'S DISEASE: AN ANALYSIS WITH THE QUEBEC PROVINCIAL DRUG REIMBURSEMENT PROGRAM DATABASE
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OBJECTIVES: To identify potential determinants of Alzheimer's disease (AD) by analyzing past medical history in terms of previous diseases or treatment exposures of patients with AD compared to patients without the disease, using the Quebec provincial drug reimbursement program database (RAMQ). **METHODS:** This retrospective study included patients covered by the RAMQ who had at least one diagnosis of AD (ICD-9 code 3310) or have received at least one script for an AD medication (donepezil, rivastigmine, galantamine or memantine) from January, 1985 to December, 2011. A control group of patients without AD was created on a 1:1 ratio and matched for age, gender and geographic location. The index date was defined as the date of the first AD diagnosis or the first script for AD medication whichever comes first. Prevalence of diseases and treatment exposures in the years preceding the index date were analyzed according to the occurrence of diseases (ICD-9 codes) and medication utilization (AHFS codification) between AD patients and the control group. **RESULTS:** Data were obtained for a random sample of 34,086 AD patients (mean age of 78.5 years [SD=8.0], 65.2% females). A higher proportion of patients had a diagnosis of organic psychotic conditions (49.6% vs. 9.2%, p<0.001), other psychoses (21.9% vs. 8.6%, p<0.001) and neurotic disorders, personality disorders and other nonpsychotic mental disorders (69.1% vs. 55.4%, p<0.001) in the AD group compared to the control group. Furthermore, a greater number of patients used psychotropic drugs (53.5% vs. 35.9%, p<0.001) and anxiolytics, sedatives and hypnotics (70.3% vs. 65.9%, p<0.001) in the AD group than in the control group. **CONCLUSIONS:** Comorbidities' frequency was higher in AD patients for several diseases and treatments, particularly for mental disorders-related diagnoses and medications.

PND3
EFFICACY OF FINGOLIMOD IN DELAYING CONFIRMED DISABILITY PROGRESSION IN PATIENTS FAILING PRIOR TREATMENT: A MARKOV MODEL APPLICATION TO ESTIMATE TIME TO DISABILITY HEALTH STATES
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OBJECTIVES: To estimate the efficacy of fingolimod versus placebo on confirmed disability progression (CDP) and on time to severe disability health states in patients with relapsing–remitting multiple sclerosis (RRMS) failing prior treatment. **METHODS:** Patients failing prior treatment were defined as: 1) ≥1 relapse in the previous year and either ≥1 gadolinium-enhancing T1 lesion or a T2 lesion count ≥9 at baseline, or 2) equal or more relapses in the year prior to baseline compared with the previous year. Hazard ratios (HR) for 3-month and 6-month CDP, measured using Expanded Disability Status Scale (EDSS) scores, were estimated using Cox proportional hazards models. Both per-protocol definitions of CDP and revised definitions used in other trials were analysed. Time from EDSS score 0 to scores of 4 or 6 and to conversion to secondary progressive MS (SPMS) were estimated by fitting a multi-state Markov Transition model to individual patient data from the pooled FREEDOMS placebo groups (HRs accounted for treatment effects) and the London Ontario cohort (SPMS and RRMS–SPMS transitions). **RESULTS:** Using both definitions of treatment failure, fingolimod reduced the risk of 3-month CDP (per-protocol) by 35% (definition 1: HR: 0.65; p<0.05) and 34% (definition 2: HR: 0.66; p<0.05) versus placebo. The corresponding HRs for 6-month CDP were 0.61 (p=0.06) and 0.60 (p<0.05). HRs were generally lower using the revised CDP definition. The Markov Transition model, assuming a 40% reduction, estimated that fingolimod delays the median time to EDSS 4 (2.2 years, 61% increase), EDSS 6 (3.3 years, 52% increase) and SPMS (4.5 years, 62% increase) compared with placebo. **CONCLUSIONS:** Fingolimod is highly efficacious in delaying CDP in patients failing prior treatment, and our modeling approach suggests that this translates into a meaningful delay in time to severe disability health states.

PND4
COMPARING THE EFFICACY OF FIRST AND SECOND GENERATION DISEASE-MODIFYING THERAPIES FOR RELAPSING-REMITTING MULTIPLE SCLEROSIS: A NETWORK META-ANALYSIS
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OBJECTIVES: As the number of available disease-modifying therapies (DMT) for relapsing-remitting multiple sclerosis (RRMS) expands, consideration of all evidence on comparative efficacy of newer second generation therapies with established first generation therapies is required to inform clinical care and health policy. This network meta-analysis (NMA) estimates the relative efficacy of DMT in reducing relapses and slowing short-term progression of disability in RRMS. **METHODS:** A systematic review of RCTs of interferon-beta, glatiramer acetate (first generation DMTs), natalizumab, alemtuzumab, fingolimod, teriflunomide, laquinimod, and BG-12 (second generation DMTs) compared with each other or with placebo for the treatment of RRMS, identified 20 eligible RCTs (n=14610). A random-effects NMA model was used to calculate relative annualized relapse rate (ARR) and hazard ratio (HR) of short-term disability progression. **RESULTS:** Statistically significant reductions in ARR versus placebo, between 24% - 69% for second generation DMTs and 16% - 33% for first generation DMTs were found. Alemtuzumab, natalizumab, fingolimod, and BG-12 were significantly more efficacious than other DMTs in reducing ARR. There was greater uncertainty associated with DMT efficacy in reducing short-term disability progression. Significant improvements over placebo in reducing short-term disability progression were restricted to second generation DMTs alemtuzumab, natalizumab, fingolimod, laquinimod, BG-12, and teriflunomide 14mg (HR 0.27 - 0.54). No statistically significant improvements in short-term disability progression were exhibited by first generation DMTs and teriflunomide 7mg. **CONCLUSIONS:** The growing number of innovative second generation DMTs offers the potential of therapeutic advances in reducing relapse rates in RRMS, with less certain benefits on short-term disability progression. Despite these potential advantages, the relative position of second generation DMTs on the RRMS treatment landscape remains to be defined, due to potentially serious side effects, limited long-term safety data and their high cost.

PND5
EFFECTIVENESS OF THE EARLY PSYCHOSOCIAL INTERVENTION ON INSTITUTIONALIZATION OF PATIENTS WITH MILD ALZHEIMER'S DISEASE AND CAREGIVERS' QUALITY OF LIFE – AN ALSOVA STUDY
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OBJECTIVES: To assess the effects of early psychosocial intervention on delaying the institutionalization of patients with mild Alzheimer's disease (AD) and on caregivers' health-related quality of life (HRQOL). **METHODS:** Totally, 240 patient-caregiver dyads were recruited to a pragmatic, controlled, and randomized (1:2) clinical trial in 3 hospital districts in Finland between 2002-2006. A primary outcome measure was the intervention's impact on cumulative risk of institutionalization over 36 months of follow up. In the analysis of the primary outcome, Fine & Gray's (1999) proportional subhazards (sHR) model was applied to adjust the impact of competing risk (i.e., death). Main secondary outcome measures were caregivers' global burden (measured by Global Health Questionnaire GHQ) and HRQOL measured by the 15D. The secondary outcomes were analyzed using generalized linear mixed models (GLMM) with hierarchical structure to account for repeated measures and possible clustering by the hospital district. **RESULTS:** After 36 months of follow up, cumulative competing risk adjusted incidence of institutionalization rates (95% CI) were 21.2% (12.5% – 29.9%) and 16.1% (10.3% - 21.9%) in the intervention and usual care groups, respectively. Age and sex adjusted sHR was 1.37 (95%CI 0.75 – 2.52). No statistical significant differences in the secondary outcomes were found. **CONCLUSIONS:** The early psychosocial intervention for patients with mild AD and their caregivers did not delay time to nursing home placement. The results of the present study are consistent with a recently published study (Waldorff et al. 2012 BMJ) reporting no effect of semi-tailored intervention for patients with mild AD and their caregivers. Even if the present study did not manage to show differences between the study groups, it provides the valuable longitudinal dataset for studying long-term disease progression (in terms of correlated cognitive, behavioral, and functional disabilities) and its economic and quality of life consequences for patients with AD and their caregivers.

PND6

MODELING THE IMPACT OF DISEASE MODIFYING TREATMENT ON TIME TO DISABILITY HEALTH STATES IN MULTIPLE SCLEROSIS: AN EVALUATION OF ORAL THERAPIES THROUGH INDIRECT COMPARISONS OF 6-MONTH CONFIRMED DISABILITY PROGRESSION

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OBJECTIVES: To estimate the comparative efficacy of oral therapies (fingolimod, dimethyl fumarate [DMF] and teriflunomide) in delaying progression to disability health states in patients with relapsing–remitting multiple sclerosis (RRMS). **METHODS:** Cox proportional hazards regression models were used to analyse 6-month confirmed disability progression (CDP; based on Expanded Disability Status Scale [EDSS] scores) in the pooled fingolimod FREEDOMS trials. Initial models were constructed with eight baseline covariates as main and treatment-interaction effects and final models with the most predictive covariates were selected using a stepwise algorithm. Models predicted hazard ratios (HRs) for 6-month CDP for fingolimod 0.5mg versus placebo for average TEMSO (teriflunomide trial) and pooled DEFINE/CONFIRM (DMF trials) patients. Time from EDSS score 0 to scores of 4 or 6 and to conversion to secondary progressive multiple sclerosis (SPMS) were estimated by fitting a multi-state Markov Transition model to individual patient data from the pooled FREEDOMS placebo groups (HRs accounted for treatment effects) and the London Ontario cohort (SPMS and RRMS–SPMS transitions). **RESULTS:** Without covariate adjustment, the HR for CDP for fingolimod versus placebo in the pooled FREEDOMS trials was numerically lower (i.e. fingolimod more efficacious) than that for DMF twice daily versus placebo in DEFINE/CONFIRM (0.62 vs. 0.71). In adjusted comparisons, the predicted HR for fingolimod versus placebo in the DEFINE/CONFIRM population was lower than in the FREEDOMS population (initial model, 0.51; final model, 0.60). Fingolimod increased median time to disability health states (EDSS 4, 1.0 years; EDSS 6, 1.5 years) and SPMS (1.9 years) compared with DMF. Comparisons with teriflunomide also showed fingolimod increased times to disability health states. **CONCLUSIONS:** Fingolimod is the only oral treatment that has demonstrated a significant effect on 6-month CDP in a clinical trial and our modeling approach suggests that progression to severe disability health states is delayed by fingolimod.

PND7

EFFICACY OF INHALED ANTIBIOTICS IN CF PATIENTS WITH CHRONIC P. AERUGINOSA INFECTION: A NETWORK META-ANALYSIS

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OBJECTIVES: To compare the efficacy of tobramycin powder for inhalation (TIP) relative to tobramycin inhalation solution containing 300 mg/5ml of tobramycin (TIS-T) and 300mg/4ml of tobramycin (TIS-B), aztreonam lysine inhalation solution (AZLI), colistimethate sodium solution (colistin) and colistin inhalation powder (colistin-P) for cystic fibrosis (CF) patients with chronic Pseudomonas aeruginosainfection, by updating a systematic literature review (SLR) and network meta-analysis (NMA) with recently published evidence. **METHODS:** The updated SLR was conducted in Medline, Medline in Process, Embase and the Cochrane Library up to 2012. Individual study results were synthesized and indirectly compared with a Bayesian NMA. As some trials included naïve patients (previously not exposed to the treatment) in one arm, and previously exposed patients to the treatment in the other arm, the naïve and exposed arms were considered separate treatment-by-population groups in the network. **RESULTS:** Three new trials were identified and analysed with eleven trials identified in the previous SLR. In naïve populations, TIP is expected to have similar efficacy as TIS-T, TIS-B, and AZLI (difference in % change in FEV1 predicted at week 4 respectively -1.97 (95% Credible Interval -11.84, 8.03), -2.38 (-12.71, 7.98), and 1.53 (-7.04, 10.00)). Compared to colistin-P, TIP is expected to have similar efficacy, however the point estimate is in favour of TIP (11.36 (-1.75, 24.31)). In exposed populations, TIP is expected to have similar efficacy as TIS-T, TIS-B and colistin (respectively -0.78 (-7.65, 5.99), 0.01 (-10.42, 10.46), and -5.75 (-21.23, 9.89)). No data on naïve and exposed populations was available for colistin and colistin-P, respectively. **CONCLUSIONS:** By conducting an alternative approach where the naïve and exposed arms were considered separate treatment-by-population groups, the full evidence base could be evaluated, including the data for the dry-powder colistimethate sodium inhaler. This will provide relevant information to support clinical decision making in CF.

PND8

CLINICAL EFFECTIVENESS OF LACOSAMIDE AND ITS IMPACT ON CONCOMITANT ANTIEPILEPTIC DRUGS CONSUMPTION IN THE CZECH REPUBLIC

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OBJECTIVES: To gather data on clinical effectiveness of lacosamide add-on therapy to standard antiepileptic drugs (AEDs) in the Czech Republic. These data were intended as inputs for a cost-effectiveness analysis. **METHODS:** A retrospective multicenter (n=40) data collection of patients with epilepsy treated with lacosamide for 6 months in clinical practice was performed. Information on the number of seizures and concomitant AEDs before and after lacosamide treatment was observed. In this analysis patients reporting at least a 50% reduction in seizure number 3 months after lacosamide treatment were considered responders. Adverse events reported after initiating lacosamide treatment were collected. **RESULTS:** In total, data from 409 patients were collected, 403 had complete data that were analyzed. Mean (SD) age was 40.4 (±14.2) years and the mean (SD) time since diagnosis 18.7 (±12.8) years. In 91% of patients lacosamide treatment was initiated because of resistance to previous AEDs. Most patients suffered from partial (44.2%), secondary generalized (20.1%) or both (34.0%) types of seizures, or other (1.7%). Following lacosamide administration the mean (median) number of seizures decreased from baseline of 40.3 (12.0) to 25.9 (7.0) (per 3 months). Median (mean) number of seizure reduction was equal to 41% (30%), and 45% were responders. Adverse events occurred in 79 pts (19.6%), with somnolence (6.2%) and dizziness (5.5%) most frequently reported. During lacosamide administration, a decrease in concomitant AEDs number was observed. The mean number per patient decreased from 2.2 to 1.7, as did concomitant AEDs used before and after lacosamide administration: levetiracetam (39% vs. 33%), lamotrigine (38% vs. 32%), carbamazepine (34% vs. 29%), valproate (33% vs. 28%) and zonisamide (17% vs. 8%). **CONCLUSIONS:** Results confirm the effectiveness of lacosamide in the reduction of seizure frequency in clinical practice. In addition, findings suggest that adding lacosamide may lead to a reduced use of other concomitant AEDs.

PND9

COST ANALYSIS OF ANTI-MIGRAINE PRESCRIBING USING A CLAIMS DATABASE

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OBJECTIVES: To analyse the cost of different anti-migraine products to determine price differences and the impact of generic prescribing. **METHODS:** A retrospective drug utilisation study was conducted on South African medical insurance claims data for 2011. No clinical information was available. **RESULTS:** A total of 797 patients received 1583 anti-migraine products during 2011. The majority of patients (70.14%) were females and 47.05% of patients were between 30 and 49 years old. Only 13.96% of patients claimed their anti-migraine products from the chronic plan of their medical insurance schemes. The average age of patients was 41.61 (SD=14.91) years, with females on average slightly older than males (41.89 years vs. 40.96 years). Clonidine was the most frequently prescribed active ingredient (accounting for 49.21% of the number of prescriptions, yet only for 25.70% of the amount claimed for anti-migraine products). Triptans (selective serotonin ($5\text{-}HT_{1B/1D}$)-receptor agonists) accounted for 27.98% of all anti-migraine prescriptions, but accounted for 45.92% of cost. Five different triptans were prescribed. The average cost per sumatriptan prescription was the lowest (R177.64) of all the triptans. Sumatriptan was the only triptan with generic equivalents. Rizatriptan was the most often prescribed triptan, accounting for 18.51% of prescribing frequency and 29.15% of the amount claimed. Tablets and wafers were the preferred dosage forms. Only 0.32% of prescriptions were for triptan nasal sprays and they were on average the most expensive dosage form prescribed (R428.82 per prescription). **CONCLUSIONS:** The results of this study were in agreement with the findings of previous South African studies. The cost saving implications of generic prescribing were clear in this study. Migraine is an expensive condition to treat and is also affecting the economically active sector of the population. Studies investigating the economic impact of migraine will therefore yield valuable results.

PND10

PRACTICE OF CEREBROPROTECTORS CONSUMPTION IN UKRAINE

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OBJECTIVES: Despite the lack of evidence-based efficacy of cerebroprotective drugs, one-third of Europe's population uses of these drugs (WHO statistics). The purpose of the study - to research the dynamics of cerebroprotectors consumption in Ukraine. **METHODS:** Determination of cerebroprotectors consumption by means of frequency analysis, ATC/DDD-methodology during 6 months in 2012 in Ukraine. The consumption of cerebroprotective drugs in money term does not give a true picture about the volume of pharmacotherapy using these drugs, that is why ATC/DDD-methodology was used. As a unit of consumption DDD and PDD were used. **RESULTS:** A comparison of outpatient and inpatient cerebroprotective drugs consumption during 6 months in a neurological hospital and in a drugstore in Kharkov, it was found, that 58 trade names (TN) of drugs in the amount of $ 28218 (the rate of $ 1: 8,16 UAH on 1.10.12), in the hospital 17 TNs were used in the amount of $1518. It is shown, that the inpatient consumption of cerebroprotectors is much higher, than outpatient consumption, for example, vincamine - 2,32 DDDs/100 patients and 1,66 DDDs/100 bed–days; piracetam - 2,59 DDDs /100 patients and 0, 15 DDDs/100 bed-

days, respectively. By frequency of outpatient appointments a combined generic drug fezam (234 appointments, prise $ 5.1), and outpatient cavinton (19 appointments, prise $ 17.27) were used often. **CONCLUSIONS:** In Ukraine, outpatient cerebroprotective drugs consumption is greater than their consumption in hospital due to the lack of prescriptions control.

PND11

UTILIZATION OF ANTI SPASTICITY DRUGS IN MULTIPLE SCLEROSIS: ANALYSIS FROM AN ITALIAN ADMINISTRATIVE DATABASE

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OBJECTIVES: Spasticity is a common condition among patients with progressive and/or relapsing forms of multiple sclerosis (MS). Current therapies seem to partially control spasticity symptoms, and patients often receive multiple treatments or switch to new treatments to achieve a better control. The objective of this analysis was to assess the current usage of spasticity drugs and relative patterns of utilization among patients with MS, through administrative database analysis. **METHODS:** Using DENALI datawarehouse, we detected MS patients who, during the period January 2000 – December 2009, had at least one disease modifying agent (DMA) prescription Then the usage of drugs commonly used in spasticity (muscle relaxant drugs, baclofen, tizanidine, clonidine, dantrolene) was evaluated in this cohort of patients, in terms of number of subjects receiving at least one prescription, and number of DDD (defined daily doses) per patient per year. **RESULTS:** From 2000 to 2009, the annual number of patients with MS, receiving DMA treatment raised from 10,746 to 12,594. Concomitantly, the annual number of patients receiving at least one muscle relaxant prescription raised from 5.87% (n=631) to 9.42% (n=1,186). The most prescribed drug was baclofen with few patients receiving other drugs commonly indicated in spasticity (dantrolene, tizanidine and clonidine). A relevant number of patients using muscle relaxants also received other drugs for the central nervous system, although its usage achieved a peak in 2005 (8% of MS patients). The analysis of DDD per patient/year suggested that the usage of muscle relaxant might be almost chronic in these patients (in 2009, 303 DDD per patients per year). **CONCLUSIONS:** Only 10% of patients with MS currently receive active pharmacological treatment, although this condition seems affecting more than 20% of MS patients in Europe. Also, there are not relevant alternatives or second line options to baclofen, which is the most commonly prescribed drug in this condition.

PND12

USE OF THE FRENCH CLAIMS AND HOSPITALISATIONS DATABASE TO ESTIMATE THE PREVALENCE AND INCIDENCE OF PARKINSON'S DISEASE IN FRANCE

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OBJECTIVES: Few studies have assessed the prevalence and incidence of Parkinson's disease (PD) in France. The objectives of this study were to estimate the prevalence and incidence of PD between 2005 and 2010 using a claims and hospitalisations database. **METHODS:** The EGB database is a 1/97 permanent random sample of the French health care insurance system database linked to the national hospital discharge summary database. Data for all adults with full insurance coverage for PD, or hospitalised with main, related, or associated PD diagnosis, or with at least 3 antiparkinson agent reimbursements over a one-year period were extracted for the years 2004 to 2010. A specific and a sensitive PD criterion were defined: i) patients with a medical diagnosis of PD from full insurance coverage or hospitalisation; ii) same patients plus those without a PD medical diagnosis in the database but a drug pattern compatible with this diagnosis (a second set of at least 3 antiparkinson agent reimbursements over another one-year period and no co-medication with extrapyramidal side effects, as well as no antiparkinson agent pattern specific of another indication). EGB estimations were applied to the French population with age and gender standardization to estimate the prevalence and incidence in France. **RESULTS:** Prevalence of PD increased from 0.27% in 2005 to 0.33% in 2010 using the specific definition of disease, and from 0.38% to 0.46% using the sensitive definition. The incidence rate per year was 0.03-0.04% using the specific definition of disease, and 0.05-0.06% using the sensitive definition. Estimated population size was between 180,000 and 255,000 persons in 2010 with approximately 22,000 to 32,000 new patients per year. **CONCLUSIONS:** The prevalence and incidence of PD in France are likely to be within the range of estimations found in the EGB database using the specific and sensitive definitions of disease; results are consistent with that reported internationally.

NEUROLOGICAL DISORDERS – Cost Studies

PND13

BUDGET IMPACT ANALYSIS OF BOTULINUM TOXIN A THERAPY FOR UPPER LIMB SPASTICITY IN THE UNITED KINGDOM

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OBJECTIVES: Upper limb spasticity (ULS) secondary to upper motor neurone lesions has a considerable patient and caregiver burden, particularly with regards to pain, activities of daily living and personal care. BotulinumtoxinA (BoNT-A) injections are effective in treating ULS. We developed a budget impact model (BIM) to assess different BoNT-A treatments available in the UK for reducing ULS. We also assessed annual costs of treating each ULS patient with BoNT-A or best supportive care (BSC). **METHODS:** The BIM was developed from the UK NHS (National Health Service) and Personal and Social Services (PSS) perspective. The status quo scenario assumed the three BoNT-As, Dysport® (abobotulinumtoxinA), Botox® (onabotulinumtoxinA), or Xeomin® (incobotulinumtoxinA), are used in 33%, 52% and 15%, respectively, of patients with ULS receiving BoNT-A in the UK. The new market share scenario assumed an increased proportional use of abobotulinumtoxinA (to 73% in year 5) compared to other interventions. The patients were modelled over a 5-year horizon. Epidemiologic data inputs were from published sources. Unit costs for BoNT-As, other health care costs and non-medical costs came from the *British National Formulary*and PSS. Resource-use inputs were obtained from UK clinicians. One-way sensitivity analyses for model inputs were conducted. **RESULTS:** Total care costs were decreased by between £425,765 in year 2 and £1,854,601 in year 5 by shifting market share to abobotulinumtoxinA. In the base-case scenario, BSC (no BoNT-A treatment) or with incobotulinumtoxinA or onabotulinumtoxinA cost more per patient per year than abobotulinumtoxinA. Sensitivity analyses showed that number of patients treated with BoNT-As, time-to-re-injection, and dose per injection of abobotulinumtoxinA and onabotulinumtoxinA were the most influential parameters on budget impact, impacting both drug acquisition costs and physician visits. **CONCLUSIONS:** Study findings suggest that increased use of abobotulinumtoxinA compared with incobotulinumtoxinA and onabotulinumtoxinA for ULS in the UK could potentially reduce total treatment costs.

PND14

THE BUDGET IMPACT OF INTRODUCING BG-12 (DIMETHYL FUMARATE) FOR TREATMENT OF RELAPSE-REMITTING MULTIPLE SCLEROSIS (RRMS) IN CANADA

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OBJECTIVES: Multiple sclerosis causes significant disability and mortality globally and is especially prevalent in Canada and across Europe. BG-12 is an orally administered disease modifying treatment for relapsing-remitting MS (RRMS) patients currently on the market in the United States and Canada and under review in Europe. A budget impact model (BIM) was developed to assess the financial consequences of introducing BG-12 for the treatment of RRMS in Canada. **METHODS:** A BIM calculated the financial consequences of introducing BG-12 in Canada over three years based on RRMS prevalence, treatment market share, and clinical effects. RRMS prevalence in Canada was derived from published literature and natural relapse rates and disease state distribution from clinical trial data. It was conservatively assumed that 100% of RRMS patients were treated with a disease modifying treatment. BG-12 was assumed to absorb market share proportionally from the following current treatments: interferon beta-1a IM, interferon beta-1a SC, interferon beta-1b, glatiramer acetate, natalizumab, and fingolimod. Treatment efficacy, in terms of reductions in relapse rate, and treatment discontinuation rates were determined from a mixed treatment comparison. Treatment costs (including costs of acquisition, monitoring, and administration) and the cost of relapse were considered. Deterministic one-way sensitivity analyses were conducted to assess the most sensitive input parameters. **RESULTS:** Over three years, the introduction of BG-12 resulted in an average annual increase of CAD279 per treated patient per year, with reductions in costs associated with relapses (CAD192/patient/year) partially offsetting increased drug acquisition costs (CAD471/patient/year). On a population level, the average annual cost increase was CAD16,494,850. The main drivers of budget impact were cost of BG-12, drop-out rates, proportion of RRMS patients treated, and market share assumptions. **CONCLUSIONS:** The acquisition costs of BG-12 for treatment of RRMS are predicted to be partially offset by reduced costs of relapses in the Canadian health care system.

PND15

BUDGET IMPACT OF EVEROLIMUS FOR TUBEROUS SCLEROSIS COMPLEX (TSC) RELATED ANGIOMYOLIPOMA (AML): UNITED KINGDOM PERSPECTIVE

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OBJECTIVES: AMLs are benign tumors common in patients with TSC, associated with high morbidity (aneurysm, hemorrhage, chronic kidney disease), and can result in death. Complication risk may correlate with increased AML volume. Historically, AMLs were treated surgically with embolization or tissue-sparing resection. In the EXIST-2 trial, everolimus significantly reduced AML volume in TSC patients. This analysis estimates the cost of reimbursing everolimus for TSC-related AML to the UK health care system. **METHODS:** A Markov model was built to analyze budget impact over five years. The treated population is estimated using TSC and AML prevalence. Adult patients with growing AML ≥3 cm are assumed eligible for everolimus. Treatment reference costs are from the UK, resource utilization data from The Netherlands, efficacy and safety assumptions from EXIST-2. The model assumed one-year treatment duration. Responding patients (≥30% AML volume reduction) may restart everolimus upon AML regrowth. Costs are discounted at 3.5% per annum. Sensitivity analyses were conducted. **RESULTS:** Up to 1,474 adults in the UK have TSC-related AML; 30% are assumed eligible for everolimus. On average, 165 patients are estimated to be treated annually with everolimus (Year 1: 88; Year 5: 233) at an average cost of £4,600,000 (Year 1: £2,700,000; Year 5: £6,200,000). Over five years, AML-related medical spending decreased £54,000. Annual per patient treatment cost with everolimus is £31,000. Results were most sensitive to patient prevalence, percent eligible for everolimus, and the percent experiencing ≥30% AML volume reduction. **CONCLUSIONS:** TSC is a relatively rare genetic disease for which everolimus is the only non-surgical treatment that has demonstrated efficacy in reducing AML volume. Reducing AML volume may prevent long-term complications and avoid surgeries, resulting in decreased AML-related medical costs. Further long-term studies are needed to better understand the benefits of everolimus in preventing AML-related morbidity and the associated costs.

PND16

NATALIZUMAB FOR RAPIDLY EVOLVING SEVERE RELAPSING-REMITTING MULTIPLE SCLEROSIS (RESRRMS) PATIENTS: 5-YEAR BUDGET IMPACT ANALYSIS (BIA) FROM THE BRAZILIAN PUBLIC PAYER PERSPECTIVE

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OBJECTIVES: Multiple sclerosis (MS) is a neurodegenerative disease associated with long-term disability and significant economic impact. With the addition of new agents for the treatment of MS (e.g. natalizumab), there is a need to evaluate the relative value of newer therapies in terms of cost, given health care resource constraints in Brazil. This analysis considered just the indication for rapidly evolving severe relapsing-remitting multiple sclerosis (RESRRMS) patients (≥2 disabling relapses per year, and ≥1 gadolinium-enhancing lesions on brain magnetic resonance imaging or a significant increase in T2 lesion load). Brazilian reimbursement guidelines recommend natalizumab only as 3rd line treatment for MS. A budget impact analysis (BIA) has been created to analyze the impact of introducing natalizumab in RESRRMS treatment in Brazilian Public Healthcare System (SUS). **METHODS:** BIA was based on a Markov model with monthly cycles and 5-year time horizon with MS epidemiological data obtained from Brazilian public database (DATASUS). The model compared current MS treatment options reimbursed by the Brazilian government – interferons-betas, glatiramer acetate and natalizumab (3rd line) with an alternative scenario with 1st line natalizumab. **RESULTS:** The number of Brazilian patients eligible for REHARRMS treatment was estimated to be 1,574, 532 and 110 patients for 1st, 2nd and 3rd line treatment, respectively, in the first year. Compared to the current scenario, the inclusion of natalizumab in the reimbursement protocol for 1st line shows potential savings of USD 729.1K, 524.6K, 360.3K, 200.6K and 83.6K for 5 consecutive years. **CONCLUSIONS:** The inclusion of natalizumab as RESRRMS treatment option is estimated to yield savings of USD 1.9 M in five years for MS treatment in SUS.

PND17

BUDGET IMPACT OF SWITCHING PRAMIPEXOLE IMMEDIATE RELEASE TO PRAMIPEXOLE EXTENDED RELEASE IN TREATMENT OF PARKINSON'S DISEASE; PERSPECTIVE OF THE SOCIAL SECURITY INSTITUTION

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OBJECTIVES: Budget impact analysis of switching Pramipexole Immediate Release (IR) to Pramipexole Extended Release (ER) in treatment of Parkinson's Disease in the Turkish health care setting from a Social Security Institution's (SSI) perspective. **METHODS:** Based upon a literature review demonstrating that, Pramipexole ER is similar to Pramipexole IR in efficacy and safety in treatment of Parkinson's Disease (non-inferiority), budget impact analyses were performed using Microsoft Excel (2007). **RESULTS:** The switch from IR to ER was analyzed for the following formulations 0.75MG /1.50MG /3.00MG /4.50MG per day and patient. The daily pill burden per patient was reduced from 3 to 1 and 6 to 1 for 0,75MG /1,5MG /3,0MG and 4,5MG respectively. The total annual treatment cost per patient was reduced by 2.91%, 6.25%, 1.74% and 3.30% for 0.75MG, 1.50MG, 3.00MG and 4.50MG respectively. **CONCLUSIONS:** The findings of this study indicate that, switching Parkinson's Patients from Pramipexole IR to ER will not result in an additional budget impact for the Turkish health care system from a SSI perspective. However, further research needs to be conducted in order to explore the potential implications of compliance benefits and if they can be translated into long-term savings. No local effectiveness data was available at the time this analysis was performed. Potential benefits in patients' adherence were not considered.

PND18

HEALTH CARE RESOURCE UTILIZATION AND COST AMONG NATALIZUMAB INITIATORS WITH MULTIPLE SCLEROSIS IN THE UNITED STATES

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OBJECTIVES: To evaluate MS-related health care resource utilization and costs prior to and after initiating natalizumab in the US. **METHODS:** A retrospective administrative claims analysis was conducted using the Truven Health MarketScan Commercial and Medicare supplemental databases to identify adults diagnosed with MS (ICD-9-CM 340) who initiated natalizumab between January 1, 2007 and December 31, 2010 (first claim is the index date). Patients had ≥24 months of continuous enrollment (12 months before [pre-period] and 12 months after [post-period] the index date) and remained on natalizumab for the 12 month post-period. Patients with and without other disease modifying treatment (DMT) during the pre-period were examined. Patient characteristics, MS-related inpatient stays and corticosteroid use were described in the pre- and post-periods. **RESULTS:** The 1458 patients in this study had a mean age of 45.2 years (standard deviation 10.5) and 74% were female. The majority (70.1%) used a DMT during the pre-period. After initiating natalizumab, there was a significant reduction in percentage of patients with MS-related inpatient stays (7.6% vs. 2.4%, p<0.001), MS-related inpatient costs (median $12,078 vs. $9,784, p<0.001) and length of stay (7.12 days vs. 6.26 days, p=0.005). Reduction in percentage of patients with MS-related inpatient stays and costs were numerically higher for patients without DMTs in the pre-period (-6.2% and -$1,496 respectively) compared with those with a DMT in the pre-period (-4.8% and -$1,262, respectively). Compared to the pre-period, there were significant reductions in IV and oral corticosteroid use for natalizumab initiators (-60.1% and -52.9%, respectively, p<0.001 for both). These reductions correspond to a mean corticosteroid cost per patient reduction of $101 across all natalizumab users (p<0.001). **CONCLUSIONS:** The initiation of natalizumab was associated with significant decreases in MS-related inpatient stays and corticosteroid use with corresponding decreases in length of stay and costs among natalizumab users with and without DMTs in the prior year.

PND19

HEALTH CARE RESOURCE USE AND DIRECT COSTS ASSOCIATED WITH FRAGILE X SYNDROME (FXS) IN THE UNITED STATES

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OBJECTIVES: FXS is the most common inherited form of intellectual disability and is associated with comorbidities that impair functioning and adaptive behavior. This study is aimed at evaluating the incremental direct health care costs and resource utilization associated with FXS using administrative health care claims data. **METHODS:** Using the Optum Health Reporting and Insights Employer database covering 1999-2012, subjects <65 years old with ≥1 FXS diagnosis (ICD-9-CM: 759.83) and ≥6 months of continuous enrollment prior to the first observed FXS diagnosis were matched with up to 5 non-FXS controls using high-dimensional propensity score matching. Individuals were followed until the end of continuous enrollment in the health plan. All-cause and FXS-related costs and resource utilization stratified by hospitalizations, emergency room (ER), outpatient, and home care visits were examined. **RESULTS:** 590 FXS individuals (mean[median] age: 25.7[27]; female: 54.1%; employee: 32%) and 2,950 non-FXS controls (mean[median] age: 25.7[27]; female: 52.1%; employee: 32%) were identified. Significant differences were observed between FXS and non-FXS in the all-cause per-patient per-year (PPPY) incidence of hospitalizations (0.414 vs. 0.237; incidence rate ratio [IRR] [95% CI]: 1.75[1.51-2.02]), outpatient visits (14.345 vs. 9.078; IRR: 1.58[1.54-1.62]), and home care visits (1.817 vs. 0.348; IRR: 5.22[4.80-5.69]). Similar results were found for FXS-related hospitalizations (0.206 vs. 0.092; IRR: 2.23[1.80-2.77]), outpatient visits (4.929 vs. 1.976; IRR: 2.49[2.39-2.61]), and home care visits (0.341 vs. 0.029; IRR: 11.70[9.09-15.06]). FXS subjects were also associated with significantly higher PPPY all-cause health care costs (total[SD]: $14,674[47,163] vs. $5,110[18,378]; hospitalization: $4,507[18,141] vs. $1,328[10,203]; outpatient: $4,730[12,538] vs. $2,394[10,515]; drugs: $2,331[6,226] vs. $844[2,244]; p<.01 for all) and FXS-related costs (total: $5,890[16,541] vs. $1,744[10,149]; hospitalization: $2,730[13,628] vs. $788[9,506]; outpatient: $1,799[4,243] vs. $555[1,510]; drugs: $1,008[2,999] vs. $197[1,030]; p<.01 for all), compared to non-FXS controls. **CONCLUSIONS:** The economic burden associated with FXS is significant and underscores the need to improve outcomes of individuals with FXS.

PND20

DIRECT AND INDIRECT COSTS OF MS IN IRELAND

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OBJECTIVES: Multiple Sclerosis (MS) has significant financial consequences for health care systems, individual patients and households, and the society in general. This study examines the distribution of MS costs and resource utilisation across cost categories and from various perspectives, as MS disability increases. **METHODS:** A total of 214 patients with MS were recruited from a specialised MS outpatient clinic in Dublin, Ireland, to participate in an interview-based study on MS-related resource consumption and costs. Mean annual direct medical, direct non-medical and indirect costs per patient were calculated, stratified by MS disability: mild (n=114), moderate (n=72) and severe (n=27). **RESULTS:** Participants were 66% female; mean (sd) age 47.6(12.75) years; mean (sd) EDSS score 3.6(2.6); 53% relapsing-remitting MS. Mean annual direct costs increased as MS disability increased from ~€10,000 in mild disease, more than five fold to ~€56,000 in severe MS. Direct costs exceed indirect costs in mild and severe MS, driven by costly disease-modifying therapies and professional home-help respectively. In contrast, indirect costs dominate in moderate MS (~€32,000 indirect vs. ~€13,000 direct) due primarily to early retirement. Disease-modifying therapies account for 76% of total direct costs in mild MS. A total of 74%-96% of all direct costs are borne by the health care payer in Ireland. Remaining costs are incurred by patients, their families or other non-health care organisations predominantly relating to non-medical resources such as living-aids, home-modifications and home-help. **CONCLUSIONS:** MS is associated with high levels of health care resource consumption and costs, which increase with disability. The majority of direct costs in our study are borne by the health care payer. However out-of-pocket spending at the individual patient level and the contribution of other organisations can be significant, particularly in severe disease. There is potential to significantly reduce the economic burden of MS through interventions which prevent progression to severe disability, support independent living at home and maintain labour force participation.

PND21

THE ANNUAL TREATMENT AND REHABILLITATION COSTS OF PATIENTS WITH PARAPLEGIA IN THE PRIVATE HEALTH CARE SETTING IN GREECE

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OBJECTIVES: To examine the annual resource use and related treatment costs for patients with paraplegia in Greece in 2011. **METHODS:** This was a prospective study, which recorded data from all inpatient and outpatient visits to Olympion Hospital, a private rehabilitation center in Patras, during 2011. Patient files, which recorded the patients' demographic, clinical and economic/ cost data, were created. Direct costs included medical and pharmaceutical costs, lab tests and direct non-medical costs, which were retrieved through the Center's IT system. Indirect cost data consisted of the loss of individual and family income and were elicited via face-to-face or telephone interviews with the patients or their relatives. Each patient participating in the study signed an informed consent. **RESULTS:** A total of 300 patients were treated in the rehabilitation center in 2011, of which 36 (12%) suffered from paraplegia. Of these, 20 were treated in the inpatient setting and 16 in the outpatient setting. The total average annual cost of treating patients with paraplegia was estimated at €101,228; the average costs of the inpatient and outpatient settings were €86,699 (€74,296 direct cost + €12,403 indirect cost) and €14,529 (€9,445 direct cost and €5,084 indirect cost) respectively. The mean number of hospitalization days for inpatients

were 178. The key cost driver for inpatients was daycare (hospitalization, medical and nursing care, therapies). **CONCLUSIONS:** The annual cost of treating patients with paraplegia in the private health care sector in Greece is high. This study is the first cost study in this disease area and additional studies should be undertaken in order to acquire a more complete picture of the cost of managing disease, in both the private and public health care sectors.

PND22

BURDEN OF L-DOPA-INDUCED DYSKINESIA IN PARKINSON'S DISEASE PATIENTS (PD-LID) IN FRANCE – THE LIDIA STUDY ECONOMIC ANALYSIS (LEVODOPA INDUCED DYSKINESIA IMPACT EVALUATION)

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OBJECTIVES: PD-LID, a complication of L-Dopa treatment, is associated with inability to perform daily living activities, reduction in quality of life and increase in health care costs. Limited data are currently available on the burden of this disease. LIDIA describes medical and non-medical resource utilization and economic impact of PD-LID patients from payer and society perspective according to LID severity: mild (mAIMS score<8), moderate (mAIMS [8-12]) and severe (mAIMS>12) patients. **METHODS:** This observational, prospective, longitudinal, multicentre 6 month-study was conducted by French neurologists specialized in Parkinson's disease (PD). PD patients taking L-dopa for at least 3 years were included, with PD-LID present for more than 3 months and for more than 25% of the time. **RESULTS:** Thirty-three neurologists included 186 patients (mean 68 years old, 52% women) with mean mAIMS score at 10. PD-LID patients were mainly followed by their neurologists (96%) and general practitioner (GP) (84%) with more non-medical follow-up for severe patients. Almost 60% had at least one biological or radiological examination, only 31% required transport. All patients received L-Dopa (including 32% long-acting), and 69% dopaminergic agonists. Only 21% had at least one hospitalization and over 40% needed home layout and mobility equipment. Most patients (70%) were assisted by a caregiver (24h/week), 43% required external assistance (6h/week), 22% received an invalidity allowance. Total costs represent 35117€, 33640€ and 43739€ in respectively mild, moderate and severe patients (on average per patient/year). Non-medical costs (transportations, paid external help, caregivers time, mobility equipment, home layout) are the major cost drivers (80%), including caregiver help (70%), followed by medical (consultations, treatments, hospitalizations)(15%) and indirect costs (allowances and work stoppages)(5%). **CONCLUSIONS:** The LIDIA study confirms that in this disabling disease, the economic burden is mainly supported by the patient family, with the payer part being 23%. Economic burden is greater in patients with severe dyskinesia.

PND23

HERPES ZOSTER IN EUROPE: A REVIEW OF EVIDENCE DOCUMENTING HUMANISTIC, ECONOMIC AND SOCIETAL BURDEN

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OBJECTIVES: Herpes zoster (HZ) and its most common complication post-herpetic neuralgia (PHN: pain persisting months after the rash onset) are associated with substantial burden of disease. There is a sharp increase in incidence from the age of 50, impacting individuals, their relatives and society. The objective of our work was to conduct a critical review documenting the Humanistic, Economic and Societal Burden of HZ in Europe. **METHODS:** Systematic searches were conducted in Medline, EMBASE, PSYCHINFO, EconLit, HEED and CRD databases, using a combination of search terms in title and abstracts. Articles, published from 2000 onwards, were selected for full review by two independent researchers in accordance with predefined eligibility criteria. **RESULTS:** From a review of 1448 abstracts, 42 eligible articles, were identified which reported data concerning health care resource use (n=26), direct costs (n=21), indirect costs (n=14), impact on health-related quality of life (HRQoL) (n=21) and impact on caregivers (n=3). Findings across studies highlight that levels of pain severity and the presence of PHN are associated with greater impairments in HRQoL and higher costs of management. At least 50% of employed patients missed work due to the disease. While the incidence of HZ and PHN increase with age, age was not a key driver of overall costs for HZ and PHN. Specifically, while direct costs (e.g. GP, specialists, medications, hospitalisations) tend to be higher for older patients, indirect costs (e.g. work time missed) are higher for younger patients. **CONCLUSIONS:** Available evidence highlights that HZ and PHN result in significant humanistic and economic burden for patients, health care systems and wider societies. There is a tendency to focus upon health care resource use and the direct costs of management which may result in an underestimation of the true burden of HZ and PHN, which is also expected to grow with the ageing European population.

PND24

SIDE-EFFECTS OF ANTIEPILEPTIC DRUGS: THE ECONOMIC BURDEN

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OBJECTIVES: Epilepsy is a brain disorder which is characterized by recurrent unprovoked seizures. The outward effect of seizures can be as dramatic as a wild trashing movement or as mild as a brief loss of awareness. To reduce frequency and severity of seizures, antiepileptic drugs are potentially an effective treatment for patients with epilepsy. However, side-effects are common. The negative consequences of side-effects can lead to treatment ranging from minor care to very expensive hospitalization. This cost analysis has been conducted to provide insight into the costs of side-effects due to antiepileptic drugs in The Netherlands from a societal perspective. **METHODS:** Health care, patient and family and other use of resources for five different categories of side-effects were measured by means of a questionnaire. Respondents were patients with epilepsy who experienced at least one side-effect due to antiepileptic treatment in the last 12 months. **RESULTS:** Based on data from 203 chronic epilepsy patients, the overall societal costs of common side-effects in 2012 are estimated to be €20,751 (CI: 15,049-27,196) per patient per year in the base case analysis. These societal costs exist of: mean health care costs (€4,458), mean patient and family costs (i.e. informal care and out of pocket expenses) (€10,526) and mean other costs (i.e. productivity and daily routine losses) (€5,761). Examining the different categories of side-effects separately, ranging from the most to the least expensive category, the cost estimates were as follows: other side-effects (€13,228), behavioral side-effects (€9,689), general health side-effects (€7,454), cognitive side-effects (€7,285) and cosmetic side-effects (€2,845) per patient per year. Subgroup analyses showed significant differences in costs between patients using monotherapy and those using polytherapy when looking at cognitive and cosmetic side-effects. **CONCLUSIONS:** These estimates should be considered in the overall assessment of the economic impact of a pharmacotherapy.

PND25

HEALTH CARE RESOURCES UTILIZATION IN ALZHEIMER'S DISEASE: AN ANALYSIS WITH THE QUEBEC PROVINCIAL DRUG REIMBURSEMENT PROGRAM DATABASE

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OBJECTIVES: To assess resource utilization before and after the development of Alzheimer's disease (AD), using the Quebec provincial drug reimbursement program database (RAMQ). **METHODS:** This study included patients covered by the RAMQ who had at least one diagnosis of AD (ICD-9 code 3310) or have received at least one script for an AD medication (donepezil, rivastigmine, galantamine or memantine) from January, 1985 to December, 2011. A control group of patients without AD was created on a 1:1 ratio and matched for age, gender and geographic location. The index date was defined as the date of the first AD diagnosis or the first script for AD medication whichever comes first. Health care resource costs were analyzed in terms of emergency room, outpatient clinic, intensive care unit and physician's visits, hospitalizations and long-term care, plus AD medications and other medications costs. Annual health care costs were reported for the 5-years before and the 5-years after the index date. **RESULTS:** Data were obtained for a random sample of 34,086 AD patients (mean age of 78.5 years [SD=8.0], 65.2% females). Before the index date, health care costs were similar between AD patients and the control group, except for the year preceding AD. Indeed, cost per patient for this year increased from CDN$5,126 to CDN$8,839 for the AD group and from CDN$4,466 to CDN$5,212 for the control group (72.4% vs. 16.7% increase respectively). For the 5-year period after the index date, costs were significantly higher for AD patients with an average cost per patient per year of CDN$9,364 vs. CDN$5,864 for the control group (mean difference of CDN$3,500,p<0.001). **CONCLUSIONS:** AD significantly increases health care resource costs, including medical resources and medications. Costs generated by AD patients cumulate over time leading to a major difference in long-term costs compared to non-AD patients.

PND26

COST EFFECTIVENESS OF APOMORPHINE IN THE TREATMENT OF ADVANCED PARKINSON DISEASE IN THE UK AND GERMANY: RESULTS FROM A MULTICOUNTY DECISION ANALYTIC MODEL

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OBJECTIVES: Parkinson Disease (PD) is the second commonest cause of neurological disability and affected approximately 5.2 million men and women worldwide. Continuous subcutaneous apomorphine (CSAI) represents an alternative treatment option of advanced PD with motor fluctuation. The purpose of this analysis was to estimate the cost-effectiveness of CSAI compared with Levodopa/carbidopa intestinal gel (LCIG), Deep-Brain-Stimulation (DBS) and Standard-of-care (SOC). **METHODS:** We developed a multicounty Markov-Model to simulate the long-term consequences, disease progression (Hoehn&Yahr-stages 3-5, percentage of waking-time in the OFF-state), complications and adverse-events. Complications are different for the alternatives (e.g. pump problems in case of LCIG, temporary/permanent complications in case of DBS). We include moderate and severe adverse-events and death. Monte-Carlo-simulation accounted for uncertainty. The model includes 25 health-states. Probabilities were derived from RCT and open-label studies; direct costs (2012) from published sources from the payer's perspective (NHS and German health care systems). QALYs, life-years (LYs) and costs were projected over a life-time horizon and discounted according the national guidelines. **RESULTS:** UK life-time costs associated with CSAI amounts to 70,258 £ and generates 2.85 QALYs and 6.28 LYs (106,530 €, 2.92 QALYs and 6.49 LYs for Germany). Costs associated with LCIG are 117,121 £, achieves 3.06 QALYs and 6.93 LYs (178,405 €, 3.18 QALYs and 7.18 LYs for Germany). The incremental-cost per QALY gained (ICER) was 223,052 £ (281,089 €). Costs for DBS are 88,361.61 £, associated with 2.75 QALYs and 6.38 LYs (121,988 €, 2.85 QALYs and 6.61 LYs for Germany). CSAI dominates DBS. SOC associated UK costs are 68,082.92 £; 2.62 QALYs and 5.76 LYs were reached (91,588 €, 2.73QALYs and 6 LYs for Germany). **CONCLUSIONS:** CSAI is a cost-effective treatment alternative, reducing OFF-time and improving quality-of-life and is associated with a cost-advantage.

PND27

COST-EFFECTIVENESS OF SOMATROPIN ADMINISTRATION WITH INCREASED ADHERENCE DUE TO MONITORING COMPARED TO NON-MONITORED ADMINISTRATION IN PATIENTS WITH GROWTH HORMONE DEFICIENCY

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OBJECTIVES: All recombinant human growth hormones (rhGH) have the same molecular structure, therefore providing equal efficacy and safety, and are granted the same reimbursement in the Czech Republic (CR). All rhGH are currently administered subcutaneously once a day, differing only in applicators. Easypod is the only applicator that enables monitoring the dose, time and date of each injection and allows feedback control by doctors. The objective was to assess the cost-effectiveness of monitored rhGH treatment administered by Easypod with an increase in reimbursement of 10% compared to the standard non-monitored rhGH administration in CR. **METHODS:** The interim results (n=596) of an ongoing multicenter, non-comparative, observational, longitudinal study (ECOS) were used to populate deterministic cohort model. The model simulated long-term costs and benefits development of rhGH treatment. Evaluation was developed primarily on evidence-based connection (from ECOS) between the monitoring of treatment and patient adherence to the treatment. Increased adherence of monitored patients was transferred to the increased effectiveness of the treatment, based on published study. Model further transformed the long-term treatment benefits to the increased quality of life, using QALY as the target parameter using empirical transformation. Costs were expressed from the payer's perspective. **RESULTS:** Due to an increased adherence in monitored patients, the hypothetical cohort of 10,000 boys generated 9,517 incremental QALY and CZK1.6 billion incremental costs in a lifetime horizon. A hypothetical cohort of 10,000 girls generated 11,504 incremental QALY and CZK1.35 billion incremental costs. The average cost per 1 QALY (ICER) is approximately CZK157,000 for the patient with GHD. **CONCLUSIONS:** Monitoring of the treatment may lead to an increased adherence and more effective treatment at relatively low cost, hence being considered cost-effective. Sensitivity analysis showed that ICER did not exceed CZK500,000 upon the considered uncertainty.

PND28

THE COST EFFECTIVENESS OF BG-12 (DIMETHYL FUMARATE) FOR THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS IN CANADA

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OBJECTIVES: Multiple sclerosis (MS) causes significant disability and diminished quality of life globally. BG-12 is a new oral treatment for relapsing forms of MS that is currently approved in the US and Canada and is under regulatory review in Europe. A cost-effectiveness model was developed to compare the health economic impact of BG-12 against other disease-modifying therapies (DMTs) as first-line treatment for relapsing-remitting MS (RRMS) from a Ministry of Health perspective in Canada. **METHODS:** A cohort-based Markov model was developed to simulate patients' progression through a series of health states, based on the Kurtzke Extended Disability Status Scale (EDSS) over a lime-time horizon. Patients entered the model based on a distribution of baseline EDSS scores, from which they could either progress/regress to higher/lower EDSS state, or remain in the same state. Relapses could occur at any EDSS score. Results from a mixed-treatment comparison were used to inform model inputs for disease progression and relapse rates per treatment. In addition to the overall discontinuation rates reported in trials, patients discontinued treatment on conversion to secondary-progressive MS or reaching EDSS 7. Costs included direct medical costs stratified by EDSS score, along with relapse, adverse events (AEs), and treatment-related costs. Utilities were accrued based on time spent in each EDSS state, adjusted for disutilities associated with AEs and caregiver burden. A 5% discount rate was applied. **RESULTS:** Compared with glatiramer acetate, BG-12 yielded 0.396 incremental quality adjusted life years (QALYs) at an incremental cost of CAD22,437, resulting in an ICER of CAD56,649. Compared with Rebif 44µg, BG-12 resulted in an ICER of CAD10,669. Results were consistent across a wide range of one-way and probabilistic sensitivity analyses. **CONCLUSIONS:** Based on traditional cost-effectiveness thresholds in Canada, BG-12 can be considered a cost-effective option compared to other first line DMTs.

PND29

COST-EFFECTIVENESS OF GLATIRAMER ACETATE AND INTERFERON BETA-1A FOR RELAPSING-REMITTING MULTIPLE SCLEROSIS, BASED ON THE COMBIRX STUDY

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OBJECTIVES: To assess the cost-effectiveness of the Disease Modifying Treatments (DMT), Glatiramer Acetate (GA) and Interferon beta-1a (IFN) in monotherapy alone and in combination for the prevention of relapses with established Relapsing–Remitting Multiple Sclerosis (RRMS) among Spanish patients aged between 18 and 60 years old. **METHODS:** A Markov model was developed to represent the transition of a cohort of patients over a 10 year period using the perspective of the Spanish National Health Service (NHS). The model considered five different health states with one-year cycles including without relapse, patients with suspect, non-protocol defined and protocol defined exacerbations, as well as the category information lost. Efficacy data was obtained from the 3-year CombiRx Study. Costs were reported in 2013 Euros and a 3%discount rate was applied for health and benefits. Deterministic results were presented as the annual treatment cost for the number of relapses. A probabilistic sensitivity analysis was performed to test the robustness of the model. **RESULTS:** Deterministic results showed that the expected cost per patient was lower when treated with GA (€13,843) compared with IFN (€15,589) and the combined treatment with IFN+GA (€21,539). The number of relapses were lower in the GA cohort with 3.81 versus 4.08 in the IFN cohort and 4.18 in the cohort treated with IFN+GA. Results from probabilistic sensitivity analysis showed that GA has a higher probability of being cost-effective than the treatment with IFN or IFN+GA for threshold values from €28,000 onwards, independent of the maximum that the Spanish NHS is willing to pay for avoiding relapses. **CONCLUSIONS:** GA showed to be a cost-effective treatment option for the prevention of relapses in Spanish patients diagnosed with RRMS. When GA in monotherapy is compared with INF in monotherapy and IFN+GA combined, it may be concluded that the first is a dominant strategy.

PND30

ECONOMIC EVALUATION OF THE TREATMENT COMPLIANCE IN PATIENTS WITH PARKINSON'S DISEASE RECEIVED DIFFERENT PREPARATIONS OF LEVODOPA

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OBJECTIVES: To assess the cost-effectiveness of two conventional combinations of levodopa and decarboxylase inhibitors (benserazide or carbidopa) in the treatment of Russian patients with Parkinson's disease. **METHODS:** The pharmacoeconomic model was developed based on the data from multicentre randomized controlled triple-blind trial (H. Pakkenberg et al., 1976) on the efficacy and tolerance of levodopa+benserazide and levodopa+carbidopa in the treatment of patients with Parkinson's disease previously not treated with levodopa. A six-month time horizon was adopted in the model. The cost analysis included costs of the original preparation of levodopa+benserazide and costs of the available in Russia generic preparations of levodopa+carbidopa and considered on-demand antiemetic treatment with domperidone to reduce the incidence of gastrointestinal side effects of levodopa. The efficacy of treatment was defined as proportion of patients with full compliance to the treatment protocol and proportion of patients without side effects (nausea and vomiting, hyperkinesia). **RESULTS:** Treatment with levodopa+benserazide was associated with significantly lower incidence of patient non-compliance (43% as compared to 76% in the levodopa+carbidopa group). Less patients in levodopa+benserazide group experienced side effects of levodopa. The expenses for antiemetic treatment was 8.7-fold lower in patients treated with levodopa+benserazide as compared to those received levodopa+carbidopa. Total costs in levodopa+benserazide group were 912,264.90 RUB per 100 patients and varied from 682,154.60 RUB to 1,255,226.00 RUB in levodopa+carbidopa groups. The cost-effectiveness ratios (CERs) were 15,692.02 RUB and 21,988.11 – 45,866.08 RUB per one patient with full compliance to the protocol in the levodopa+benserazide and levodopa+carbidopa groups, respectively. The similar results were observed for the CERs estimated per one patient without side effects of levodopa. **CONCLUSIONS:** The present study has demonstrated that administration of levodopa+benserazide is an economically effective strategy in the treatment of Russian patients with Parkinson's disease.

PND31

PHARMACOECONOMIC ANALYSIS OF DIFERENT ANTI-PARKINSONIAN DRUGS USED IN MONOPHERAPY DURING EARLY STAGES OF PARKINSON DISEASE

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OBJECTIVES: To evaluate the cost-effectiveness ratio of antiparkinsonian medication taken as monotherapy in patients with Parkinson's disease (PD). **METHODS:** A cost-effectiveness analysis (CEA) of therapies including pramipexole ER, pramipexole, ropinirole, piribedil and rasagiline has been performed. Direct medical costs including costs of medications and treatment of adverse drug effects for 1-year therapy of PD have been considered. The clinical effect of selected antiparkinsonian medication was assessed in percentage of patients responding to treatment, and also by means of the UPDRS II-III scale. All calculations were done in RUR prices of 2013 (nominal exchange rate RUR/USD = 30/1). **RESULTS:** Pramipexole ER has the lowest cost-effectiveness ratio (CER) of RUR 57,572 per patient/year responding to antiparkinsonian therapy. Hence, pramipexole ER was the most effective antiparkinsonian preparation studied in pharmacoeconomic terms. Based on cost-effectiveness ratio, the medications evaluated can be arranged in the following order: pramipexole ER (RUR 57,572), pramipexole (RUR 59,548), piribedil (RUR 70,921), ropinirole (RUR 71,887), and rasagiline (RUR 91,112). The model results were robust to deterministic sensitivity analysis with variable drug costs. Limitations: Absence of direct comparative evidence from randomized, double-blind, controlled studies makes interpretation of the data difficult. Only short-term studies (up to 24 months) were available and hence do not allow to evaluate the influence of pharmacotherapy on motor fluctuations as well as other longterm factors. **CONCLUSIONS:** The results of the present pharmacoeconomic analysis indicate that pramipexole ER is cost-effective as first line therapy for the treatment of early stages of Parkinson's disease from a Russian health care perspective. All five formulations evaluated, are well below the conditional "willingness to pay ratio" (equal to RUR 1,308607 in 2012). Hence, these preparations would qualify for application in the Russian system of public reimbursement.

PND32

COST-EFFECTIVENESS ANALYSIS OF LACOSAMIDE COMPARED WITH STANDARD OF ANTIEPILEPTIC CARE BASED ON CLINICAL PRACTICE DATA

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OBJECTIVES: To perform a cost-utility analysis of lacosamide as add-on therapy to standard antiepileptic drugs (AEDs) compared to standard AEDs alone based on individual patients data derived from actual clinical practice in the Czech Republic. **METHODS:** Based on retrospective data collection of 409 patients with epilepsy treated with lacosamide for 6 months in actual clinical practice, we developed a cost-utility Markov cohort model. The model has 4 basic health states defined by number of seizures within 3 months plus 1 state represented by occurrence of severe side effects and 1 absorption state; death. Each health state was described by utility levels derived from literature. Transition probabilities for the first cycle were derived from observational study data and subsequently published literature. The model time-horizon was 20 years, 1 cycle length covered 3 months, and a 3% discount rate was used for costs and outcomes (Quality adjusted life years (QALYs)). Only costs attributed to drug acquisition were calculated, dosing of each AED was derived from the retrospective study. We performed probabilistic sensitivity analysis (PSA) with 3000 iterations using a willingness to pay (WTP) threshold equal to 3

times GDP per capita (43,000 EUR) in the Czech Republic. **RESULTS:** Over a 20 year time-horizon, add-on lacosamide generated 11.47 QALYs and costs 33,439 EUR (per patient), whereas standard AEDs alone provided 11.09 QALYs and costs 22,916 EUR (per patient), respectively. The base-case ICER was calculated as 27,692 EUR/QALY. Based on the PSA and its cost-effectiveness acceptability curve (CEAC) we calculated that add-on lacosamide has a probability of cost-effectiveness at 43,000 EUR per QALY gained of 80.2% compared to standard AEDs alone. **CONCLUSIONS:** Based on data from clinical practice lacosamide as add-on treatment in patients with partial-onset seizures is cost-effective under the WTP threshold implicitly applied in the Czech Republic.

PND33

COST EFFECTIVENESS OF PHARMACOGENETIC SCREENING PRIOR TO INITIATION OF CARBAMAZEPINE TREATMENT FOR EPILEPSY

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OBJECTIVES: Carbamazepine (CBZ) is a widely-used, first-line treatment in epilepsy. However, CBZ is associated with hypersensitivity adverse drug reactions (ADRs) ranging from mild rash such as maculopapular exanthema, to hypersensitivity syndrome, Steven-Johnson syndrome and toxic epidermal necrolysis (TEN). TEN is associated with a mortality rate of up to 30%. The presence of the *HLA-A*3101* allele is associated with an increased risk of CBZ-induced hypersensitivity reactions [OR 9.1, 95% CI, 4.0 to 20.7]. *HLA-A*3101* is present in 2% - 5% of populations of Northern European descent. We aim to investigate the cost effectiveness of pharmacogenetic testing for *HLA-A*3101*prior to initiation of CBZ treatment in patient with epilepsy. Patients testing positive for the allele are prescribed an alternative antiepileptic drug, lamotrigine. **METHODS:** A decision analytic model was developed to represent the first three months post initiation of anti-epileptic drug, to cover the period when the majority of severe ADRs manifest. A Markov model (cycle length 1 year) was used to simulate costs (from the perspective of the NHS in the UK) and utilities incurred in subsequent years. This enables modelling of costs and disutilities from long term sequelae of severe ADRs as well as the effectiveness of treatment in terms of remission of seizures. Transition probabilities, costs and utilities were sourced from patient level data from the SANAD trial [Lancet 369(9566):1000-15] and relevant literature. **RESULTS:** Compared with no pharmacogenetic testing, and prescribing CBZ for all patients, the test results in an incremental cost effectiveness ratio of £26,684 per QALY gained. The probability that testing is cost-effective at a threshold of £30,000 per QALY is 0.55, and the cost of preventing a single ADR is £35962. **CONCLUSIONS:** Pharmacogenetic testing for *HLA-A*3101* prior to treatment with CBZ might be cost-effective for populations of North European descent.

PND34

COST-MINIMIZATION ANALYSIS OF TREATMENT OF SPASTICITY WITH BOTULINUM TOXIN TYPE A

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OBJECTIVES: Botulinum toxin type A (BoNT-A) is considered one of the treatments of dynamic equinus foot deformity due to spasticity in paediatric cerebral palsy (CP) patients, two years of age or older by decreasing hyperactivity and increasing muscle tone in patients. The aim was to compare the cost of Botox® (Allergan) and Dysport® (Ipsen), considering the administered dose per weight (U/kg) in child patients with equinus foot CP related. **METHODS:** We performed an observational, longitudinal and retrospective study with data from clinical records from December 1995 to October 2012. Records included patients younger than 18 years old with spasticity treated with BoNT-A at the Pediatric Neurology Service of the Hospital of La Paz (Madrid), with recorded birth and visit dates, weight and dose by muscle. Cost analysis only evaluated four muscle groups (pronator teres, adductor, semitendinosus and triceps surae) including only direct costs (drug and visit costs). We used bootstrap as sensitivity analysis to assess the robustness of results. Costs were in euros 2013. **RESULTS:** A total of 895 patients treated with BoNT-A for spasticity (543 treated with Botox®, 292 with Dysport® and 60 with both) were included. Baseline characteristics and follow-up were similar in both groups. Patients had an average dose infiltrated per visit of 5.44 U/kg (SD 2.17) for Botox® and 14.73 U/kg (SD 5.26) for Dysport®, and average yearly visits of 3.71 for Botox® and 3.46 for Dysport®. The annual total cost per patient was 850 € for Botox® and 636 € for Dysport®. Of these total costs, annual visit costs of 362 € for Botox® and 347 € for Dysport®, and annual drug costs were 488 € for Botox® and 289 € for Dysport®. **CONCLUSIONS:** Based on the real-world management of pediatric spasticity patients with BoNT-A observed in our study, Dysport® could reduce annual total costs per patient.

PND35

COST-UTILITY ANALYSIS OF DISEASE-MODIFYING DRUGS IN RELAPSING-REMITTING MULTIPLE SCLEROSIS IN IRAN

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OBJECTIVES: Disease-modifying drugs (DMDs) are a significant expenditure for treating multiple sclerosis. However, assessment of the cost-utility of DMDs compared with symptom management in the presence of long-term data has been limited. To assess the lifetime cost-utility from the Iranian health care perspectives of 4 disease-modifying drugs relative to symptom management alone in patients with relapsing-remitting multiple sclerosis using evidence from long-term published studies. **METHODS:** A Markov model was developed with patients transitioning through health states based on Kurtzke expanded disability status scale (EDSS). Patient costs included drug costs, other medical and lost worker productivity costs. Patient quality of life was considered in the form of utilities. Costs were valued in 2011 USD, and costs were discounted at 7.2%per annum. Various parameters and assumptions were tested in sensitivity analyses. **RESULTS:** Total costs per patient over the time horizon of a patient's lifetime were estimated at 20285, 144194, 299279, 251255 and 69796 USD for symptom management, Avonex, Betaferon, Rebif and CinnoVex, respectively. As a result, the incremental cost per QALY for patients receiving Avonex, Betaferon, Rebif and CinnoVex was 607397, 1374355, 1166515 and 1010429 USD, respectively, when compared with symptom management. The results were sensitive to changes in time horizon, disease progression and drug costs. **CONCLUSIONS:** DMDs in RRMS patients is associated with increased benefits compared with symptom management, albeit at higher costs. Because patients receiving Avonex incurred slightly higher QALYs than patients receiving other DMDs, treatment with Avonex dominate other DMDs in Iran.

PND36

COST-UTILITY ANALYSES OF NATALIZUMAB VERSUS INTERFERON BETA-1A 44 MCG FOR RAPIDLY EVOLVING SEVERE RELAPSING-REMITTING MULTIPLE SCLEROSIS (RESRRMS) PATIENTS IN BRAZIL

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OBJECTIVES: Multiple sclerosis (MS) is a neurologic disease that can dramatically affect patients' quality of life. The aim of this study is to conduct a cost-utility analysis of natalizumab (Tysabri®) versus interferon beta-1a 44 mcg (Rebif®) – a commonly prescribed 1st line disease modifying therapy – in rapidly evolving severe relapsing-remitting MS patients from the Brazilian Public Healthcare System (SUS) perspective. **METHODS:** A Markov model with 20-year time horizon with health states based on Expanded Disability Status Scale (EDSS) and disease relapses was developed. Since there are no published data evaluating long-term course specifically in RESRRMS, it was assumed transition probabilities on EDSS states were based on natural history studies in unselected RRMS patients, and relapse probabilities based on a *post-hoc* analysis of the placebo patients on pivotal natalizumab AFFIRM trial. In each monthly cycle, patients can discontinue treatment, remain stable, progress to higher EDSS state, experience progressive multifocal leukoencephalopathy (PML) or die. For natalizumab, we assumed efficacy data on disability progression and relapse from AFFIRM trial and for interferon beta-1a 44 mcg we assumed efficacy data on disability progression and relapse from pivotal trial PRISMS. Patients with EDSS score $\geq$ 7.5 receive best supportive care. Resource use and costs were validated by an expert panel and valued using Brazilian public official lists (DATASUS and BPS). Costs and outcomes were discounted (5%). Probabilistic sensitivity analyses covered variability in efficacy and costs. **RESULTS:** The use of natalizumab was associated with slower EDSS progression and reduced relapse burden. The quality-adjusted life years obtained with natalizumab and interferon beta-1a 44 mcg were 9.27 and 8.75, and costs were USD119,977 and USD132,446, respectively. In the base-case, natalizumab was dominant versus interferon beta-1a 44 mcg. **CONCLUSIONS:** For a patient with HARRMS, the model shows that natalizumab was dominant when compared to interferon beta-1a 44 mcg in the Brazilian Public Healthcare System.

PND37

COSTS ASSOCIATED WITH THE IMPACT OF PROGRESSIVE MULTIPLE SCLEROSIS: INSIGHTS FROM A THREE YEAR CLINICAL TRIAL (THE CUPID TRIAL)

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OBJECTIVES: To estimate the costs associated with health and social care resource use in a UK cohort of people with progressive multiple sclerosis (MS). **METHODS:** Health and social care resource use data were collected prospectively over 33 months from a cohort of 458 patients with progressive MS enrolled in a UK clinical trial (the CUPID Trial). Resource use data are used in combination with unit costs (2011 costs) from published UK national sources, and estimates of costs/prices where required. Costs for informal (unpaid) care are estimated using equivalent hourly home care rates for UK NHS and social care services. Data are presented over the 33-month period of follow, and also to allow comparison with other studies, against an estimated 6-monthly cost. Regression analyses were used to explore the impact on cost estimates from explanatory variables. **RESULTS:** The main component of resource us and costs was informal care provided by friends and family, accounting for over 84% of the estimated costs over time. Excluding informal care, the most important cost items, within the remaining sub-total of costs, were social care (52%), health care services (23%), medications (10%), adaptations (8%), and hospitalisations (6%). From a Payer perspective, the estimated mean six-monthly costs of health and social care were £927, but from a broader perspective the estimated six-monthly cost was £10,737, when private and patient costs were included. Regression analyses identified disease severity, as characterised by the EDSS, as the main explanatory driver of cost estimates. **CONCLUSIONS:** This study presents new information to inform on the impact of progressive multiple sclerosis to add to the currently sparse evidence base. Data suggest that costs are considerable and fall mainly on patients and carers. The findings also confirm the central role of disability status in predicting overall costs associated with the impact of progressive MS.

NEUROLOGICAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PND38

TREATMENT ADHERENCE AND COSTS IN MULTIPLE SCLEROSIS: A NARRATIVE REVIEW OF THE LITERATURE

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OBJECTIVES: To appraise the literature relating adherence and other patients' reported outcomes (PROs) to Multiple Sclerosis (MS) costs. **METHODS:** Electronic databases [MedLine/PubMed, Google Scholar, Congress proceedings] were searched to identify publications analyzing MS costs related to adherence, persistence, sat-

isfaction and preferences for MS treatments. Bibliographic references were hand searched. English or Spanish studies published between January 2007 and January 2013 were selected. **RESULTS:** A total of 398 citations were identified; 12 studies accomplished the inclusion criteria. Six referred to PROs and treatment costs; 4 analyzed satisfaction with disease-modifying therapies (DMTs) and 2 assessed preferences for treatment attributes. An increased adherence and persistence on DMTs was associated to higher pharmacy costs and to better clinical outcomes [lower relapse risk (OR=0.71 CI 95%, 0.59-0.85); decreased MS hospitalizations (OR=0.63, CI 95%, 0.47 – 0.83)] leading to a cost reduction of up to 22% patient/year. DMT adherent patients had a significantly lower rate of severe relapses (12.5% vs. 19.5%; *p=0.0200*), lower MS-related or all-causes medical (7.6% vs. 12.5%; *p=0.0447* and 11.2% vs. 20.0%; *p=0.0027*) and emergency visits (8.9% vs. 15.0%; *p=0.0215* and 34.6% vs. 43.5%; *p=0.0305*) than non-adherent. MS-related and all-cause inpatient costs (354.77±2.485.03 vs. 853.13±3,635.48; *p=0.0270* and 648.71±3,753.74 vs. 62.51±265.23; *p=0.0018*) as well as emergency visit costs (46.46±255.94 vs. 1,740.88±6,127.27; *p=0.0076* and 147.82±430.79 vs. 242.42±592.96; *p=0.0044*) were significantly lower in adherent patients. Self-injection [Visual Analogue Scale (VAS) mean 6.9; range 0-10] render higher treatment satisfaction. Slower disability progression (efficacy) was the most preferred attribute (*p<0,001*). Newly developed electronic devices that allow adjusting injection settings as well as adherence objective monitoring appeal more to patients (VAS mean 7.7; range 0-10) than more traditional methods of administration. **CONCLUSIONS:** MS studies assessing adherence and costs are scarce. Treatments and devices better tailored to patients' needs improve adherence, enhance clinical outcomes and procure a reduction on MS costs.

PND39

HEALTH STATE (QALY) VALUES FOR MULTIPLE SCLEROSIS: A REPORT USING DATA FROM THE UNITED KINGDOM SOUTH WEST IMPACT OF MULTIPLE SCLEROSIS (SWIMS) STUDY

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OBJECTIVES: To present health state values (QALY weights) for multiple sclerosis (MS) health states using data from a prospective, longitudinal, cohort study. **METHODS:** Data from a large UK cohort study for MS, the South West Impact of MS (SWIMS) Study, were used for analysis. SWIMS data comprise six-monthly self-report assessments, including EQ-5D and SF-36 health status measures, and data on relapse frequency/severity. Self-report data is supplemented with data from clinician assessment of disability using the EDSS. Health state valuation data are sourced from published UK tariffs (EQ-5D and SF-6D) to present values for MS against EDSS, relapse characteristics, and against other disease related characteristics. **RESULTS:** Analyses of SWIMS data included 1,441 respondents, over an average of 8 time-points. Findings on health state values show a health profile that worsens by disease progression, against EDSS stages, using both the EQ-5D and SF-6D methods. Health state values estimated from EQ-5D data range from 0.76 at EDSS stage 1.0 to 0.03 at EDSS stage 8, with lower values seen for progressive MS. Values estimated from SF-36 data reflect the narrower range of values possible on the SF6D tariffs, with values from 0.7 to 0.53 across EDSS stages 1.0 to 8. Findings demonstrate impact on health state values due to relapse events, with this impact reported at 0.08 using the EQ-5D and at 0.05 using the SF-6D. The impact of relapse frequency, severity and endurance on health has also been assessed. **CONCLUSIONS:** This study presents health state valuation data derived from a high quality longitudinal cohort study, including values (QALY weights) for features/characteristics of relapse events in people with MS. This data can support improvements in the conduct of cost-effectiveness analyses of treatments for MS, and can be helpful in a general health policy context.

PND40

CAREGIVER BURDEN IN FRAGILE X SYNDROME AS A FUNCTION OF A HEALTH STATE UTILITY INDEX IN THE UNITED STATES

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OBJECTIVES: To assess the association between burden experienced by caregivers of patients with fragile X syndrome (FXS) in the United States and a health state utilities index derived from the Aberrant Behavior Checklist-Community (ABC-C). **METHODS:** A total of 340 US caregivers of children with FXS completed a questionnaire that captured information on FXS-related burden (i.e., specialist visits, medical tests, medications, financial burden, employment status, paid and unpaid caregiving, caregiver injuries, and mental health). Using the ABC-Utility Index (ABC-UI), an estimate of health-related quality-of-life derived from the ABC-C, five utility index categories were created: very low (0.00–0.33); low (0.34–0.66); moderate (0.67–0.77); high (0.78–0.89); and very high (0.90–1.00). After controlling for sex, age, overall ability level, and income, multivariable regression models documented the association between utility score and the nine burden-related outcomes. **RESULTS:** Respondents (283 with FXS male child; 57 with FXS female child) were mostly female (91%), Caucasian (92%), and married (84%), with mean age of 50 years. Approximately 2% of individuals with FXS were in the very low utility category, 30.6% low, 27.1% moderate, 37.6% high, and 2.6% very high. The mean utility score was 0.71. Females with FXS and adults ≥18 years had higher health utilities. Results from regression models indicate that increasing utility values reduced the likelihood of ≥5 (vs. <5) specialist visits (b=-4.583; p<0.001) and ≥2 (vs. 0 or 1) prescription medications used (b=-4.517; p<.001). Similarly, increasing utility score was associated with a decreased likelihood of ≥8 (vs. <8) hours of unpaid caregiving (b=-2.723; p=0.003), ≥1 (vs. 0 or 1) caregiver injuries (b=-7.540; p<0.001), and ≥1 (vs. 0) mental health provider visits (b=-2.613; p=0.002). **CONCLUSIONS:** The ABC-UI appears to function well as a health-related quality-of-life indicator in individuals with FXS. Among caregivers of patients with FXS in the US, significant differences in burden exist across health state utilities.

PND41

DYNAMICS OF QUALITY OF LIFE IN CHILDREN WITH CYSTIC FIBROSIS AGED 5-16 YEARS

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OBJECTIVES: For improvement of aiding effectiveness both for clinicians and specialists in the field of health care system one should know quality of patient's life in different time period rating of the disease. **METHODS:** 70 cystic fibrosis (CF) children from Russia and CIS countries 5-16 years were interviewed using HUI version 15Q, while children over 12 years responded on their own (self assessment), information about children younger 12 years was obtained from parents (proxy assessment) .Version was translated into russian language and adapted. HUI currently consists of two systems: HUI Mark 2 and HUI Mark 3. Each HUI2 and HUI3 classification system consists of attributes (domains) of health and 3 to 6 levels of functional ability/disability within each attribute and is very responsive to changes and to highlight avenues of additional study. Single-attribute utility scores and multi-attribute utility scores evaluated corresponding to each system, ranges from 0 to 1. **RESULTS:** Mean Mark 2 has a tendency to increase from 0,85 in children 5 years to 0,95 in children 15 years with reduction in 6 years (0,80), 12 years (0,85) and 16 years (0,85). Same tendency was observed in Mark 3: 6 years- 0,75; 12 years- 0,75; 16 years- 0,77 **CONCLUSIONS:** Decrease of quality of life in above mentioned ages is a result of unadequate treatment in children living in some regions of CIS and severe complications of CF in older children also.

PND42

HEALTH RELATED QUALITY OF LIFE (HRQL) IN PARKINSON'S DISEASE: THE IMPACT OF 'ON' AND 'OFF' TIME

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OBJECTIVES: Diurnal variation in symptoms and functioning is a feature of Parkinson's disease, referred to as 'on' and 'off time'. Typically patient reported outcomes (PROs) don't capture this variability or its value, instead requesting participants report over the last day or week. This study evaluated the impact and value of 'on' and 'off time' for people with Parkinson's (PwP) by assessing their HRQL and strength of preference. **METHODS:** PwP from UK, Spain, France and Italy (n=305), experiencing ≥ 2 hours 'off time' daily, completed EQ-5D-5L assessments for 'on' and 'off time' that day, followed by a discrete choice experiment (DCE) evaluating 5 treatment attributes: duration of 'on time'; quality of 'off time'; predictability of 'off time'; feelings of anxiety/depression, and dosing frequency. The DCE was informed by qualitative work with patients (n=20), carers (n=6) and health professionals (n=6) in UK and Spain and employed an orthogonal, factorial, fold-over design. Analysis used the mixed-logit model and effects coding of categorical levels (predictability of off-time attribute). **RESULTS:** Mean EQ-5D utility values were significantly lower for 'off time' (0.37, 95%CI: 0.33-0.40) than 'on time' (0.60, 95%CI: 0.57-0.62). All attributes were significant drivers of treatment choice. PwP valued increased duration of 'on time' (per hour per day: OR=1.40, 95%CI 1.31-1.45) and predictability of 'off time' most highly (predictability to within 30 minutes of symptoms returning: OR=1.42, 95%CI 1.15-1.57). High disutility was reported for substantial unpredictablility of 'off time' (OR=0.67, 95%CI 0.49-0.91). **CONCLUSIONS:** Important differences in quality of life between 'on' and 'off time' were found which could be missed by standard PRO assessment, including the relative value that PwP placed on increased duration of 'on time' and predictability of 'off time'. Assessments and interpretation of outcomes in Parkinson's should consider diurnal variation. Capturing this variation and its value may require modifications to PRO design. [Study HO-11-802]

PND43

CULTURAL ADAPTATION AND VALIDATION TO SPANISH OF THE "MS TREATMENT CONCERNS QUESTIONNAIRE-MSTCQ"

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OBJECTIVES: Albeit effectiveness of subcutaneous treatments for Multiple Sclerosis (MS) has been demonstrated, adverse reactions and pain may entail problems regarding treatment satisfaction and continuity. This study aims to adapt and validate the Spanish version of the "Multiple Sclerosis Treatment Concerns Questionnaire-MSTCQ", which evaluates satisfaction with the injection device (ID) in 4 dimensions: Injection system (A), Side-effects (B) (flu-like symptoms, reactions, and satisfaction), Treatment experience (C) and Benefits (D). **METHODS:** Two Stages: 1) Cultural adaptation: Forward-backward translation and expert (n=6) and patient (n=30) panels; 2) Validation: Observational, cross-sectional, multicenter study. A total of 143 adult patients suffering from MS and using an ID were evaluated. Tools employed: MSTCQ, *Patient-Reported Indices for Multiple Sclerosis* (PRIMUS), *Treatment Satisfaction Questionnaire for Medication (*TSQM), Morisky Green and Patient Injection Site Reaction (ISR) and Injection Site Pain (ISP). Psychometric properties: Feasibility (% valid cases and ground/ceiling effects); Reliability (Cronbach α) and test-retest (41 patients, Intraclass Correlation Coefficient, ICC); as well as construct (Factorial analysis of dimensions A and B, FA) and convergent (Spearman MSTCQ vs. TSQM) validity. **RESULTS:** Mean age(SD) in cases was 41,94(10,47) years, 63% female, 88,11% suffering from Relapsing-Remitting MS. MSTCQ feasibility was adequate (missing 0%-2,80%). High internal consistency, total score (A+B) α =0, 89, by dimensions α (A, B and C): 0,76, 0,89 and 0,92, respectively. Furthermore, a concordance was found between total (ICC= 0, 98) and by dimensions ICC (A, B and C) scores: 0,82, 0,97 and 0,89, respectively. The FA confirms dimensions A and B from the original questionnaire. Lastly, the association between total and by dimensions scores, from MSTCQ and TSQM was, overall, moderately strong (Rho between-0, 74, y 0, 42) and significant

(p<0,05; p<0,01). **CONCLUSIONS:** The Spanish version of the MSTCQ questionnaire is a feasible, reliable and valid tool for the evaluation of satisfaction with the injection device in the treatment of MS.

PND44

ELICITING PATIENTS' PREFERENCES FOR EPILEPSY DIAGNOSTICS: A DISCRETE CHOICE EXPERIMENT

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OBJECTIVES: Diagnosing epilepsy is a lengthy and burdensome process for patients and their family. Although the need for a more patient-centered approach in clinical practice is widely acknowledged, empirical evidence regarding patient preferences for diagnostic modalities in epilepsy is missing. The objectives of this study are 1) to identify to what extent important attributes of diagnostic procedures in epilepsy affect preferences for a procedure; 2) to determine the relative importance of these attributes; and 3) to calculate overall utility scores for routine electroencephalography (EEG) and magnetoencephalography (MEG) registrations. **METHODS:** A discrete choice experiment was performed to determine patients' preferences, which involved presentation of pair-wise choice tasks regarding hypothetical scenarios. Scenarios varied along six attributes: "Way of measuring brain activity"; "Duration"; "Freedom of movement"; "Travel time"; "Type of additional examination"; and "Chance of additional examination". Choice tasks were constructed using a statistically efficient design and the questionnaire contained 15 unique unlabeled choice tasks. Mixed multinomial logistic regression was used to estimate patients' preferences. **RESULTS:** A total of 289 questionnaires were included in the analysis. McFadden's pseudo R^2 showed a model fit of 0.28 and all attributes were statistically significant. Heterogeneity in preferences was present for all attributes. "Freedom of movement" and "Chance of additional examination" were perceived as the most important attributes. Overall utility scores marginally differ between MEG and routine EEG. **CONCLUSIONS:** Our study suggests that the identified attributes are important in determining patients' preference for epilepsy diagnostics. It can be concluded that MEG is not necessarily more patient-friendly than a routine EEG in primary diagnostics and, regarding additional diagnostics, patients have a strong preference for long-term 24h EEG over EEG after sleep deprivation. Furthermore, barring substantial heterogeneity within the parameters in mind, our study suggests that it is important to take individual preferences into account in clinical decision-making.

PND45

QUALITY OF LIFE OUTCOMES IN MULTIPLE SCLEROSIS: A REVIEW OF THE LITERATURE

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OBJECTIVES: Multiple sclerosis (MS) is a chronic neurodegenerative disease affecting the central nervous system. There are a variety of symptoms and activity limitations associated with MS including mobility problems, muscle spasticity, fatigue and mental health problems. In order to gain an accurate insight into the impact of MS on patients it is important for accurate patient-reported outcome (PRO) instruments to be applied. The purpose of this review was to evaluate the available MS-specific PRO measures. **METHODS:** The online literature databases PubMed, Psychinfo and Web of Science were used for the search. The search identified all studies that used a PRO measure in the study design and was restricted to publications from the last fifteen years. Only measures used in at least three clinical trial studies were included. The measures identified were evaluated in terms of; source of items, item reduction methods, unidimensionality, practicality, responsiveness, reliability, internal consistency and face, content and construct validity. **RESULTS:** The search yielded 2317 articles, of which 1066 were duplicates and removed. The review of the remaining articles identified six measures that met the review criteria: MSIS-29, LMSQoL, MSQoL-54, HAQUAMS, MSQLI and PRIMUS. In addition, the MUSIQoL was reviewed because of recent development activity. Most of the measures exhibited some weaknesses. Only the PRIMUS performed well on all the review criteria. It was the only measure to apply a clear theoretical framework and meet the strict measurement requirements of the Rasch model. **CONCLUSIONS:** The PRIMUS is recommended for use in clinical trials. The review suggests that many clinical trials are using PROs that have not benefitted from the use of Item Response Theory and modern psychometric approaches.

PND46

PATIENT-CENTERED OUTCOMES IN UPPER LIMB SPASTICITY: RESULTS FROM A LARGE INTERNATIONAL COHORT STUDY (ULIS-2)

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Muscle spasticity following stroke may interfere with motor and activity performance, cause pain, and lead to secondary complications. Goals of spasticity management include improving function (active and passive) and body image, and facilitating concomitant treatments. The efficacy of BoNT-A in upper limb spasticity (ULS) patients focusing on reduction of muscle tone and pain is well established. However, there are no specific ULS patient-reported outcome measures (PROs) available. As patients with ULS are highly heterogeneous, there is a need to develop measures to capture realistic, patient-specific treatment goals. **OBJECTIVES:** To assess effectiveness of BoNTA on ULS considering patient-specific experience. **METHODS:** A prospective multinational, multicenter (84 centers in 22 countries), observational, post-marketing, longitudinal study (ULIS-2), investigating routine use of BoNT-A for treating post-stroke ULS. Primary outcome: achievement of the patient's primary goal for treatment using Goal Attainment Scaling (GAS). Goals were set together by physicians and patients/caregivers. Patients were able to rate goals for importance. Secondary outcome: global assessment of benefits by both physician and patients/caregiver. **RESULTS:** Among the 456 adults with post-stroke ULS presenting for treatment with BoNT-A, the most commonly selected primary treatment goals were passive function (132 (28.9%)), active function (104 (22.8%)), pain (61 (13.4%), and impairment (105 (23%)). Patients rated 404/456 primary goals (88.6 %) as "important" (395/456 (86.6%) as "very" or "moderately" important), indicating high patient involvement in goal-setting. Overall, 363 (79.6%) (95% CI 75.6% to 83.2%) patients achieved (or overachieved) their primary goal. GAS T-scores were strongly correlated with rating of global benefit and other standard measures (correlations of 0.38 and 0.63, respectively; p<0.001). **CONCLUSIONS:** Patient-centered goal setting and evaluation using GAS to calculate changes of health-related status is a feasible way to capture changes in ULS patient experience. GAS as primary outcome measure in ULIS-2 is a step closer to a PRO in ULS patients.

PND47

PATIENT PREFERENCES AND PRIORITIES FOR ANTI-EPILEPTIC DRUG TREATMENT

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OBJECTIVES: Clinical trials in epilepsy may not routinely prioritise patient-oriented outcomes that consider the harms of treatments in addition to their benefits. To date, no systematic empirical research has been undertaken to assess the views of people with epilepsy about treatment outcomes. The aim was to identify which outcomes of drug treatment are considered important to three groups of adults with epilepsy: (i) recently diagnosed, (ii) established diagnosis, (iii) women of childbearing age. **METHODS:** Semi-structured individual interviews containing ranking exercise were used to explore views and interpretations of benefits, harms, and potential life-impacts of anti-epileptic drug treatments (n=41); the feasibility of these findings were evaluated in focus groups of health care professionals responsible for prescribing anti-epileptic drugs (n=8) . Outcomes ranked 1-4 were scored 4-1. For each group, scores were summed and divided by the number of participants. **RESULTS:** Ten recently diagnosed men (mean age 45.9), 13 established (mean age 39.3, 92% male), and 18 women of childbearing age (mean age 34.5) participated. Reduction in seizure frequency was the most highly ranked outcome of drug treatment across all three subgroups (women of childbearing age [score]=2.5, recent=2.4, established=2.23). Adults recently diagnosed were most concerned about feelings of aggression (1.6), depression (1.0) and ability to work (0.9). Adults with established epilepsy were most concerned with ability to work (1.15) negative impacts on relationships (1.0), memory problems (0.69), and social-life (0.69). Women of childbearing age were concerned about memory (1.22), reduced independence (0.78), feeling in control (0.56) and foetal abnormality (0.5). Clinicians considered life-impacts (eg work, relationships, independence) as consequences of benefits and harms of treatment. **CONCLUSIONS:** The importance of remission from seizure was consistent. However, patients' rankings of unfavourable outcomes of drug-treatment varied by subgroup. Selection of outcome measures in clinical trials in epilepsy must consider relevant patient-oriented outcomes which differ by population.

PND48

EVALUATING FATIGUE IN FIBROMYALGIA: DEVELOPMENT AND VALIDATION OF THE DAILY DIARY OF FATIGUE SYMPTOMS IN FIBROMYALGIA (DFS-FIBRO)

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OBJECTIVES: Despite being recognised as an important symptom in Fibromyalgia (FM), existing measures of fatigue are unlikely to meet regulatory standards for clinical trial endpoints. We therefore describe the development and validation of a new, electronically administered patient reported outcome (ePRO) measure of fatigue in FM - the Daily Diary of Fatigue Symptoms-Fibromyalgia (DFS-Fibro). This was developed in accordance with the FDA regulatory guidance and ISPOR good practice recommendations for the development and validation of PROs. **METHODS:** Initial item generation was based on concept elicitation interviews with 40 FM patients (from the US, Germany and France), and clinical relevance of the findings was confirmed by expert clinician review. The draft tool was pilot tested with 20 FM patients for 5-9 days, followed by cognitive debriefing interviews. A methodology study with 145 FM patients then followed, providing data to conduct the psychometric validation of the measure. Both the qualitative and quantitative findings were used to finalise the DFS-Fibro. **RESULTS:** Twenty-three items were generated from concept elicitation interviews, including items focussed on the physical and cognitive impacts of fatigue as well as fatigue 'symptom' items. Some minor wording revisions were made following pilot testing and cognitive debriefing, but none were deleted. All patients found the measure easy to understand and use. Initial psychometric analyses supported removing items previously identified as candidates for deletion in the qualitative work, resulting in a 5-item measure focussed on the core symptom of FM fatigue. The psychometric analyses were then repeated on the final 5-item measure, which had very high internal consistency (alpha = 0.99), strong test-retest reliability (r > 0.84), and met a priori criteria for convergent and known groups validity. **CONCLUSIONS:** The DFS-Fibro development followed accepted guidelines and demonstrates strong psychometric properties and content validity as a measure of the symptom of fatigue in FM.

PND49

EVALUATING PATIENT ADHERENCE RATES TO APPROVED DISEASE MODIFYING THERAPIES (DMT) FOR RELAPSING-REMITTING MS (RRMS): OPERATIONAL SETUP FOR A MULTI-COUNTRY, MULTI-CENTER STUDY

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OBJECTIVES: DMTs constitute an important backbone of MS treatment. To investigate Health Related Quality of Life (HRQOL) and patient adherence rates to the approved DMTs for RRMS among geographically and culturally diverse patient populations, a multinational study was to be implemented. Operational and scientific outcomes are presented. **METHODS:** The study was designed as an observational, multicenter, multinational post marketing study. Patients and physicians received paper questionnaires evaluating adherence to DMTs approved at the time of the study. HRQOL (MusiQol) and a Neuropsychological Questionnaire (MSNQ) also were applied. **RESULTS:** The study was implemented in 22 countries. Special challenges: cross-cultural CRF design, country-specific recruitment procedures for sites and patients, country/site specific contractual arrangements. Ethical approval was collected from 70 local and 15 central institutions. Patient recruitment was performed via 176 neurologists (hospital and office based). In total, 2.566 patients were enrolled within 6 months. Average treatment duration / observational period covered 31 months. The study findings revealed that 75% of the patients were adherent (i.e. not missing an injection or changing dose). 12.6% of all patients forgot to administer injections compared to 50% of non-adherent patients. Compared to non-adherent patients, adherent patients showed shorter disease duration (adherent: median 6.0 yrs; non-adherent: Median 7.0 yrs.), significant shorter treatment time (30.0 months vs. 36.0 months; p<0,001) and a better MSNQ score (18.0 vs. 22.0; p<0,001). **CONCLUSIONS:** For implementing a global multicenter center important issues include: linguistic specifics for CRF development, availability of medical centers for site recruitment, country specific legal and ethical requirements, careful organization and sharing of responsibilities between the study coordination center and local affiliates. Non-adherence to DMT in RRMS was demonstrated to be mainly caused by injection problems; adherent patients showed better clinical and HRQOL outcomes.

PND50

WELLBEING, LIFE SATISFACTION AND PROGRESSION IN ALZHEIMER'S DISEASE – AN ALSOVA FOLLOW-UP STUDY

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OBJECTIVES: To examine the quality of life (QoL) of the Alzheimer's Disease (AD) patients in relation to disease progression during the five-year ALSOVA follow-up study. **METHODS:** The baseline sample consisted of 240 subjects with very mild or mild AD, 65 years or older, from three Finnish hospital districts. The subjects were recruited between 2002 and 2006, and were followed-up for five years. Three separate patient-reported wellbeing and life satisfaction instruments were used as proxy variables for QoL: a generic, preference-based health-related quality-of-life instrument, 15D; an AD -specific wellbeing measure, AD-QOL; and a VAS-based life satisfaction scale. AD progression was evaluated with the Clinical Dementia Rating (CDR). Both CDR Sum-of-Boxes (CDR-SOB) and global rating were used in the analysis. Generalized linear mixed models with hierarchical structure were applied to account for repeated measures and possible clustering by the hospital district. Data were adjusted for age, sex and years of education. **RESULTS:** On average, none of the three outcome measures demonstrated statistically significant changes over time during the five year follow-up. However, when the outcomes were examined in relation to AD progression, both CDR-SOB and CDR global rating demonstrated statistically significant association between the severity of AD and lower QoL on all three outcome measures. However, when using CDR global rating to define disease progression, we observed meaningful impairments in QoL variables only in the patients with severe AD (CDR 3). **CONCLUSIONS:** Severe AD has a considerable impact on patients' QOL through substantial impairments in wellbeing and life satisfaction. Evidence suggest that CDR-SOB is a potential continuous measure of AD severity. While CDR-SOB is strongly associated with decrease QoL measures, our observations indicate that it is unlikely to be linearly correlated with QoL. Thus, the use of CDR-SOB as a determinant of QoL needs to be examined further.

PND51

LONG-TERM PROLONGED-RELEASE FAMPRIDINE TREATMENT AND HEALTH-RELATED QUALITY OF LIFE OUTCOMES: INTERIM RESULTS OF THE ENABLE STUDY

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OBJECTIVES: Prolonged-release (PR) fampridine tablets (dalfampridine extended release in US) improve walking in some patients with multiple sclerosis (MS). The ENABLE study assessed the effect of long-term PR-fampridine treatment on health-related quality of life (HRQoL) in MS patients with walking impairment. **METHODS:** ENABLE is an open-label, 48-week study to evaluate the effect of PR-fampridine 10 mg twice daily on HRQoL in MS patients. Patients completed the Timed 25-Foot Walk (T25FW) at baseline and Weeks 2 and 4, and the 12-item MS Walking Scale (MSWS-12) at baseline and Week 4. Patients with any improvement in T25FW speed at both Weeks 2 and 4, and any improvement in MSWS-12 score at Week 4 remained on treatment. HRQoL measures are assessed at baseline and Weeks 12, 24, 36, and 48, and include the Short-Form Health Survey (SF-36), Multiple Sclerosis Impact Scale (MSIS-29), and the Patient Reported Indices for MS Activity Limitations Scale (PRIMUS ALS). The primary endpoint is the change from baseline in the SF-36 physical component summary (PCS) score at each visit in patients on treatment. **RESULTS:** At Week 4, 704 patients (78.1% of total enrollment [N=901]) met the criteria to remain on treatment. Interim results at 36 weeks in patients on treatment show improvement from baseline (mean change [95% CI]) in MSIS-29 Physical scores to Week 12 (-12.99 [-14.24, -11.74; P<0.0001], n=672) and Week 36 (-9.50 [-10.97, -8.04; P<0.0001], n=584). PRIMUS ALS scores also improved from baseline (mean change [95% CI]) to Week 12 (-2.47 [-2.83, -2.11; P<0.0001], n=501) and Week 36 (-1.53 [-1.96, -1.10; P<0.0001], n=437) in patients on treatment. Results for the change from baseline to Week 48 for outcomes, including the SF-36 PCS, in patients on treatment will be presented. **CONCLUSIONS:** PR-fampridine, which improves walking in MS, shows benefits on HRQoL through 36 weeks of treatment.

PND52

QUALITY OF LIFE IN PATIENTS WITH MULTIPLE SCLEROSIS IN SLOVAKIA

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OBJECTIVES: The current prevalence of Multiple Sclerosis (MS) in Slovakia ranges from 100 till 150 cases per 100 000 population Being a typical chronic disease with tendency of progression, MS can have a great impact on quality of life (QoL). The objective of this paper was to find out the level of QoL in patients with MS in Slovakia. **METHODS:** The primary method used for the analysis of QoL was the presence of disability period and combined questionnaire consisting of 4 parts: A. Demography and socioeconomics (13 items), B. Generic questionnaire (SF-36), C. Visual scale (4 items), D. Complementary (information and habits, 13 items). There were 2 groups of patients. Group A: 41 (29 women, 12 men) patients were treated by conventional therapy. Group B: the 41 (32 women, 9 men) patients were treated by moderns disease modifying treatment and biological therapy (Betaferon, Avonex, Rebif, Tysabri, Gilenya, Copaxone). The average age in the group A was 50.59 vs 41.82 years in the group B. **RESULTS:** Disability was 9,39 months per one patient per year in group A vs 5,02 in group B, loss of income was 123 vs 165 € per person, the expectations of the future was 2,39 vs 2,41 (in the five degrees scale). Present level of QoL was identified as 5.29 vs 4,34 on the scale of 10, while in the time of the MS diagnosis it was 3,29 vs 2,15. QoL was 8.68 vs 8,17 in the time without SM and 9,24 vs 8,29 in the total optimal state of health. **CONCLUSIONS:** The treatment of MS by conventional or disease modifying therapy (DMT) had a significant impact on QoL. The modern DMT had the higher statistical influence as on physical health (45,65 vs 28,23) so on mental health (51,65 vs 33,01) in comparison with the patients treated by conventional therapy.

PND53

CORRELATION BETWEEN MONTGOMERY-ASBERG DEPRESSION RATING SCALE (MADRS) AND THE BECK DEPRESSION INVENTORY II (BDI-II) IN PATIENTS WITH FOCAL EPILEPSY

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OBJECTIVES: To determine the correlation between the Montgomery-Asberg Depression Rating Scale (MADRS) and the Beck Depression Inventory II (BDI-II) scores in patients with drug-resistant focal epilepsy (DRE) in comparison with patients with controlled focal epilepsy (CFE). **METHODS:** Observational, cross-sectional study performed in patients with focal epilepsy (FE) with and without DRE, ≥18 years. Presence and severity of depression were measured using validated Spanish versions of the Montgomery-Asberg Depression Rating Scale (MADRS) and the Beck Depression Inventory (BDI-II). In order to know the correlation between MADRS and BDI-II, two different criteria were used; degree of association obtained on prevalence of depression and correlation between scores from both scales, using Pearson correlation coefficient. **RESULTS:** 515 patients (DRE=248) were included. Using the MADRS scale, prevalence of depression in the DRE group was almost double than in the CFE group (59.3% vs. 30.3% using unadjusted data and 62.1% vs. 32.6% using adjusted data; p<0.001). Similar results were seen with the BDI, with an overall depression rate of 48.1% using the ≥10 point threshold, and considerably higher rates of depression in the DRE group compared to CFE patients (61.9 % vs. 35.3% using unadjusted data, and 64.8% vs. 37.2% using adjusted data; p<0.001). Correlation between MADRS and BDI-II was 24,4 % (65/266) in CFE and 51,0% (126/247) in DRE patients, according to the degree of association; while the Pearson correlation coefficient between the two scales was high, at r=0.80. **CONCLUSIONS:** MADRS and BDI-II showed a positive correlation; the score increment of one scale is directly proportional to the increase of the other scale. In both cases, the strongest contributor to higher MADRS and BDI-II scores was having a previous clinical diagnosis of depression but being untreated for the condition.

NEUROLOGICAL DISORDERS – Health Care Use & Policy Studies

PND54

ADDITIONAL CLINICAL BENEFIT FOR PATIENT RELEVANT ENDPOINTS: INVESTMENT DISINCENTIVES BY AMNOG IN THE EXAMPLE OF PARKINSON'S DISEASE

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OBJECTIVES: After the introduction of the new German law AMNOG a statistically significant and clinically meaningful difference in patient relevant endpoints are required in order to achieve a (significant) clinical benefit for a new (drug) therapy. The question remains if such an incentive is sufficient in all disease areas for positive investment decisions for the pharmaceutical industry. **METHODS:** In Parkinson's disease motor fluctuations and dyskinesias are two major patient relevant outcomes. Different target profiles for a clinical development programme of a theoretical new treatment were developed including scenarios following the regulatory guidelines only, an efficacy-driven programme and one including the above mentioned key patient relevant endpoints. An investment decision model was developed based on these profiles with respect to additional clinical benefit by the joint federal committee and premium pricing in Germany were assessed. **RESULTS:** Positive investment decisions were possible for the regulatory and efficacy-driven

scenarios even though that the additional clinical benefit profile was uncertain and pricing not optimal. When developing potential budget estimates based on sample size and complexity of a clinical trial for motor fluctuations or dyskinesias as primary endpoint a significant clinical benefit was highly likely and premium pricing possible. However, a positive investment decision was uncertain due to the high development cost. **CONCLUSIONS:** Even though there are incentives to add patient relevant endpoints in the development programmes the return on investment could potentially not be high enough for a positive investment decision. Target profiling including market access and pricing outcomes could optimize investment decisions.

PND55

DISEASE BURDEN AMONG PATIENTS WITH MULTIPLE SCLEROSIS NOT RECEIVING DISEASE MODIFYING TREATMENTS IN EUROPE AND THE UNITED STATES

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OBJECTIVES: To assess clinical characteristics of MS patients not on any DMTs in key countries in European Union (EU) and the U.S. **METHODS:** A multi-country multi-center medical chart-review study of MS patients was conducted in 4Q2012 among Health care providers (HCPs; >85% neurologists) in hospitals and private practices to collect de-identified data. HCPs from UK, Germany, France, Italy and Spain (5EU) and the US were screened for duration of practice (>=3yrs) and patient volume (>=15 MS patients/month) and recruited from a large panel to be geographically representative in each country. Medical charts of next 10 consecutive MS patients were completed by each physician. HCPs abstracted patient diagnosis, treatment patterns and patient symptomatology/disease status. MS patients not on any DMTs were analyzed. **RESULTS:** A total of 967 eligible MS patients were included in the analysis (5EU:749; US:218). Mean age (yrs) – 5EU:39.0yrs, US:42.2yrs; Female – 5EU:69%; US:67%. Key reasons for not receiving DMTs were (5EU/US): mild/early-MS (35%/36%), patient refusal (26%/44%), progressive/severe/advanced-MS (20%/17%), lack of efficacy of current treatment options (10%/14%), side-effects/tolerance/co-morbidities (6%/12%), waiting for DMTs to become available (5%/12%) and funding/authorization/guidelines (4%/7%). Among patients who refused DMTs, more than half were not convinced of therapy benefits. Distribution of MS type was (5EU/US): Clinically Isolated Syndrome (CIS)-26%/25%, Relapse Remitting MS (RRMS)-44%/49% and Secondary Progressive MS (SPMS)-30%/26%. Patients with moderate/severe disease and those with active/highly active disease (both, per physician judgment) were (5EU/US): CIS:10%/11%, RRMS:25%/40%, SPMS:95%/86%, and CIS:31%/44%, RRMS:39%/37%, SPMS:36%/32% respectively. Mean Expanded Disability Status Scale score were (5EU/US): CIS:0.8/0.7, RRMS:1.8/2.2, SPMS:6.5/5.6); % patients currently suffering a relapse were (5EU/US): CIS:20%/29%, RRMS:21%/15%, SPMS:6%/16%; % patients with >=1 relapses in last 12months were (5EU/US): CIS:69%/69%, RRMS:52%/58%, SPMS:18%/32%. **CONCLUSIONS:** Among MS patients not on any DMTs, disease burden seems substantial. Further research is warranted to scrutinize the observed patient management practices to alleviate patient burden.

PND56

DISEASE BURDEN AMONG PATIENTS WITH SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS CURRENTLY USING DISEASE MODIFYING TREATMENTS IN EUROPE UNION AND THE UNITED STATES

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OBJECTIVES: To assess disease burden of SPMS patients treated with DMTs in EU and the U.S. **METHODS:** A multi-country chart-review study of SPMS patients was conducted among neurologists in hospitals/private practices to collect de-identified data. Neurologists from UK/Germany/France/Italy/Spain (5EU) and US were screened for practice-duration (>=3yrs) and patient-volume (>=15MS patients/month) and recruited from a large panel to be geographically representative in each country. Charts of next 2 consecutive SPMS patients were selected by each neurologist. Neurologists abstracted patient diagnosis, treatment patterns and patient symptomatology/disease status. SPMS patients on DMTs were analyzed. **RESULTS:** In 4Q2012, 360 Neurologists (5EU:259; US:101) abstracted 699 eligible SPMS patient charts (5EU:497; US:202); 420 (5EU:274; US:146) patients were managed with DMTs. Mean age – 5EU:46.5yrs, US:49.2yrs; Female – 5EU:58%; US:66%. Mean time-to-1st DMT initiation (5EU/US; months) from diagnosis was 21/27; current DMT patterns (5EU/US) were: 1st line (25%/34%), 2nd line (39%/38%) & 3rd+ line (36%/28%). Interferon beta-1b (5EU) and glatiramer acetate (US) were predominantly observed in 1st/2nd line; fingolimod and natalizumab use was observed in 2nd-line but they dominated later lines. Mean time-to-1stDMT initiation (5EU/US: months) from diagnosis (1st:45/35, 2nd:13/30, 3rd+:12/10) and mean treatment time (5EU/US: months) on current 1st (85/91), 2nd (38/35; prior 1st line: 57/48) and 3rd+ line (19/24; prior 2nd line: 35/46) differed. Patients with severe disease and those with active/highly active disease (both, per physician judgment) were (5EU/US): 1st:15%/20%, 2nd:20%/18%, 3rd+:35%/37% and 1st:45%/61%, 2nd:63%/73%, 3rd+:57%/68% respectively; mean Expanded Disability Status Scale scores also differed (5EU/US): 1st:5.1/5.0, 2nd:5.6/5.5, 3rd+:5.8/6.1. **CONCLUSIONS:** Among SPMS patients currently managed with DMTs, the disease burden increased as the line of treatment increased, both in 5EU and the US. Patients in 2nd/3rd+line of treatments had progressed through earlier line(s) of treatment quickly. Further research is warranted to scrutinize the effectiveness of therapeutic options and sequencing strategies to alleviate patient burden.

PND57

PATTERNS OF USE OF TESTS TO DIAGNOSE AND ASSESS DISEASE PROGRESSION IN MULTIPLE SCLEROSIS (MS): A MULTICOUNTRY COMPARISON

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OBJECTIVES: To assess the patterns of use of tests to diagnose and assess disease progression/activity in MS in the European Union and United States (US). **METHODS:** A multi-center retrospective chart-review study of MS patients conducted in United Kingdom (UK), France (FR), Germany (DE), Italy (IT), Spain (SP) and US to collect de-identified data on diagnosis, clinical status and DM approaches. Health care providers (HCPs; 95% neurologists) were screened for duration of practice (>=3yrs) and patient volume (>=15 MS patients/month) and recruited from a large panel to be geographically representative in each country. Medical charts of next 10 consecutive MS patients were selected by each physician. **RESULTS:** A total of 3490 eligible MS patient charts were abstracted by 360 HCPs (mean age:47yrs; female: 31%; mean practice duration:18yrs; mean # of patients seen per month:63; % working in specialty MS clinic:45%). Patient mean age: 39yrs; female: 66%; top-5 comorbidities: depression (14%), anxiety (10%), hypertension (8%), obesity (7%), migraine/headache (6%). Tests used by physicians to diagnose MS varied between the countries (UK/FR/DE/IT/SP/US: %): History/Neurological exam – 79/88/99/95/97/88, Gadolinium MRI – 56/93/66/93/96/89, T1 MRI – 49/89/80/84/93/74, T2 MRI – 65/89/66/91/94/82, CSF analysis – 51/82/71/3/90/56, Evoked potentials – 34/48/65/77/80/29. Patients with moderate/severe disease and currently on disease modifying treatments (DMTs) varied (UK/FR/DE/IT/SP/US: %): 50/45/37/58/50/47 & 52/71/75/77/73/78; correspondingly, tests used by physicians to assess MS disease progression/activity also varied between the countries (UK/FR/DE/IT/SP/US: %): EDSS–63/83/84/91/92/40, Neurological exam–81/91/88/89/84/86, Gadolinium MRI–33/69/36/90/68/70, T1 MRI–21/53/53/76/54/54, T2 MRI–29/62/41/89/63/65, Ambulation index–9/13/9/24/16/19, Brain atrophy–4/14/6/23/15/18, Nine hole peg test–6/3/10/5/3/1 and PASAT–1/0/12/5/4/1. **CONCLUSIONS:** UK physicians appear to under-utilize the tests to diagnose/manage MS patients, whereas physicians in Spain often used them more frequently. Observed trends were not correlated to the patient disease severity observed in these settings, warranting further scrutiny of observed patterns to optimize MS management.

PND58

WITHDRAWN

PND59

DRUG COMPLIANCE AND PERSISTENCE IN PATIENTS WITH PARKINSON'S DISEASE TREATED IN PRIMARY CARE IN THE UNITED KINGDOM: A CPRD-BASED STUDY

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OBJECTIVES: Differences in compliance and persistence between Parkinson's disease (PD) drugs were found in a previous US claim database analysis. The objective was to apply the same methodology in another setting using the Clinical Practice Research Datalink (CPRD) in the UK. **METHODS:** A retrospective analysis of patients starting a new PD drug (rasagiline, selegiline, pramipexole, ropinirole, entacapone, tolcapone, levodopa) between January 2009 and January 2012 was conducted using CPRD. Patients were categorized as naive to PD therapy (NT) or having prior PD therapy (PT), depending on the prescription of other PD drugs within a 12-month look-back period. The observation period was 12 months. Compliance was measured using the medication possession ratio (MPR) and non-compliance was defined as an MPR≤80%. Persistence was measured as the duration (days) of uninterrupted therapy without gap higher than 45 days. **RESULTS:** Of the 4,784 patients included in the compliance analysis, 3,675 patients (76.8%) had compliance rates >80%. Mean MPRs were generally comparable across PD products (range:84%-90%, all pairwise p=NS). Percentage of patients with MPR>80% was significantly greater with rasagiline (85.6%, all p<0.05 except vs. ropinirole p=NS). Of the 5,266 patients included in the persistence analysis, the highest mean number of persistent days of treatment was reported for rasagiline (284 days; all p<0.05 vs others, except vs. ropinirole p=0.14 and levodopa p=0.06). Patient persistence at 12 months was significantly greater with rasagiline compared with others in NT patients (66.5%, all p<0.05)

and with levodopa in PT patients (72.7%, all p<0.05). **CONCLUSIONS:** A high and comparable level of compliance was observed across PD drugs. Persistence was significantly higher than other drugs with rasagiline in treatment-naïve patients and with levodopa in previously treated patients.

PND60

DISEASE-MODIFYING THERAPIES (DMT) FOR MULTIPLE SCLEROSIS (MS): ANALYSIS OF ITS EVOLUTION IN SPAIN BETWEEN 2004 AND 2012

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OBJECTIVES: To analyze determinants of recent evolution of DMT consumption for MS in Spain. **METHODS:** Available DMT market data comprised monthly figures for the period 2004-2012. Monthly and annual evolution of consumption, treated patients and annual cost of treatment were calculated for each DMT. This analysis was replicated for first-line (intramuscular and subcutaneous interferon (IFN) β-1a, subcutaneous IFN β-1b, and glatiramer acetate) and second-line therapies (natalizumab and fingolimod). Evolution of these variables was analyzed for both the whole period 2004-2012 and since 2007 (when second-line therapies become available in Spain). **RESULTS:** DMT expenditure in Spain increased by 147% in 2004-2012 (from €115.5M to €284.9M, 11.95% annually). This evolution can be decomposed into: the growth in the figure treated patients (126%; 10.70% annually) and the increase in the average annual cost per patient (9%, from €11,739 to €12,839; 1.13% annually). For 2007-2012 subperiod, DMT spending increased by 73% (11.57% annually) is attributable to 59% more treated patients (9.73% annually) and an increase of 9% (1.68%) in annual cost per patient. Cost per patient in second-line is 70% higher (average 2007-2012) than average cost per treated patient (€ 21,074 vs. € 12,372) and 82% higher than annual cost of first-line therapy (€ 21,074 vs. € 11,549). Between 2007 and 2012, second-line therapies accounted 32% of new treatments and 48% of incremental cost per patient. By omitting year 2007 from analysis (68 second-line treatments and €1.44M associated consumption), second-line therapies account for 38% of new treatments and 55% of incremental cost per patient. By 2012 second-line therapies already represent 50% of new treatments and 67% of DMT cost increase. **CONCLUSIONS:** The increase of patients treated with DMT in Spain (10.70% annually in 2004-2012), more costly new therapies incorporation and its growing consumption are crucial factors in handling hospital pharmacy budgets for prevalent diseases such as MS.

PND61

ASSOCIATION BETWEEN NON-MOTOR SYMPTOMS AND HEALTH CARE UTILIZATION AMONG PATIENTS WITH PARKINSON'S DISEASE IN THE UNITED STATES

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OBJECTIVES: To investigate the characteristics and extent of health care utilization among patients with Parkinson's disease (PD) with and without non-motor symptoms (NMS). **METHODS:** Data were obtained from a US administrative claims database (SDI/IMS). Index date was 1 June 2010, and study duration was 12 months. Patients were required to have at least two PD diagnoses before the index date. They were subsequently matched 1:1 to control patients (no PD diagnoses) based on propensity scores derived from age and pre-index Charlson comorbidity index for each gender. **RESULTS:** In total, 127,630 patients with PD were matched to controls. Patients with PD had higher annual mean numbers of primary care (16.4 vs 12.3; p ≤0.0001) and neurologist visits (6.7 vs 0.4; p ≤0.0001) compared with matched controls. In the PD group, 48,823 patients (38.3%) had a diagnosis for at least one NMS, of whom 15,242 (31.2 %) were also treated for at least one NMS. Most frequently reported NMS were pain (27.2%), mood disturbance (depression, anxiety or nervousness; 12.7%) and sleep disorder (7.4%). Patients with pain, mood and sleep disorders (n=1,159), had higher total annual primary care and neurologist visits than patients with no NMS (50.7 vs. 17.2). Patients who received treatment for pain, mood and sleep disorders (n=118), had a higher total number of annual primary care and neurologist visits (66.6) compared with patients treated only for mood (26.0; n=3,233) only for pain (35.6; n=9,432), or only for sleep (30.6; n=676). **CONCLUSIONS:** Results of the study demonstrate that treatment of NMS increases health care utilization – patients with PD suffering from NMS had a substantially greater number of health care visits than those with no NMS. Results also indicate that there are substantial levels of undertreatment of NMS among patients with PD, with less than a third being treated.

PND62

NATALIZUMAB TREATMENT IS ASSOCIATED WITH REDUCED NEUROLOGY OUTPATIENT APPOINTMENTS, UNPLANNED HOSPITAL ADMISSIONS AND LENGTH OF STAY

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OBJECTIVES: Global wellbeing of patients is an important outcome in research and clinical practice. Multiple Sclerosis (MS) is a degenerative, neurological condition, characterised by progressive disability, affecting approximately 110 per 100,000 people in England and Wales. Natalizumab is a humanised monoclonal antibody, licensed for use in highly active relapsing-remitting MS and administered as an IV infusion every 28 days. The purpose of this study was to explore the impact of natalizumab on both patients and use of health service resource in clinical practice in England. **METHODS:** Health Episode Statistics (HES) data were used to perform a retrospective cohort study. A structured coding search elucidated a comprehensive list of natalizumab users by hospital trust. Analysis of health service usage, including outpatient appointments and admissions, was undertaken. Comparison of use during the year before and after treatment initiation was conducted. **RESULTS:** A total of 2,196 patients with at least 1 year of available HES data after treatment initiation were identified. In this cohort, natalizumab treatment was associated with 38% fewer unplanned admissions (981 vs. 604, X_1^2 = 89.2, p<0.001) and 58% fewer unplanned bed nights (8,817 vs. 3,681, X_1^2 = 2109.8, p<0.001) in the year following treatment initiation compared with the year before. A 14% reduction in all outpatient appointments was also observed, due principally to a 25% reduction in neurological outpatient appointments (from 7,826 to 5,901, X_1^2 = 269.7, p<0.001). Evidence from this study indicates that duration of treatment is a significant factor in this response; patients receiving between 12 and 14 doses (n=1,122) experienced 70% reduction in unplanned admissions and 90% reduction in unplanned bed nights. **CONCLUSIONS:** Our data support the notion that natalizumab treatment significantly reduces unplanned hospital treatment and outpatient attendance.

PND63

PRESCRIBING PATTERNS OF PARKINSON'S DISEASE

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OBJECTIVES: Parkinson's disease has the second largest number of patients among 56 designated diseases/syndrome of the Specified Disease Treatment Research Programme for rare and intractable disease programme. The purpose of this study were to investigate prescribing patterns of Parkinson's disease and its pharmaceutical expenditures. **METHODS:** We analysed the Social Health Insurance (SHI) claims data processed from February to April 2011 provided by the Planning, Review and Research Institute for Social Insurance and Medical Program. **RESULTS:** During the three months, 52,851 patients in Social Health Insurance programme received medical treatments that cost 9,391,451,520 JPY. Average costs for inpatient care without meal expense and for outpatient care were 263,782 JPY and 33,209 JPY respectively. Except the cases that fell into Diagnosis Procedure Combination (DPC), 37% of the total cost, 3,515,091,420 JPY was for pharmaceutical expenditure including dispensing fee. Only 7,437,873 (23.5%) of 31,699,153 dispensed drugs were generics on a volume basis. If all the pharmaceutical that have generics had been substituted, estimated 899,586,280 JPY would have been saved in the study period by simple arithmetic. Generic usage is fewer in the elderly than in the younger generation in all therapeutic categories. **CONCLUSIONS:** Percentage of pharmaceutical expenditure in total health expenditure for Parkinson's disease is high. Our study find that generic substitution rate is low in general and even lower in the elderly. This might be partly related to the medical expense subsidy under the Specified Disease Treatment Research Programme, which exempts eligible patients from co-payment according to their income. There seems to be a room for prescribing pattern change for cost optimization and further study is expected.

PND64

COSTS OF FORMAL AND INFORMAL HOME CARE AND QUALITY OF LIFE OF PATIENTS WITH MULTIPLE SCLEROSIS IN SWEDEN

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OBJECTIVES: To describe and to estimate costs of formal and informal home care and quality of life related to multiple sclerosis. **METHODS:** A random sample of 1500 members of the Swedish organization for patients with neurological diseases (NHR), specifically MS, were mailed a questionnaire between February-March 2012. Collected data included number of hours per month of home care received, type of help, productivity losses, quality of life (EQ-5D) and disease characteristics. The recall period was one month. Using published Swedish unit cost data, the costs for home care were estimated in 2012 euros. A semi-logarithmic linear regression evaluated other factors that may influence the likelihood of getting home care. **RESULTS:** Of 839 respondents, 65.5% had progressive MS, 24.5% had RRMS and 10% had no information. Formal care was given to 27% of respondents at an average of 238.7 hrs/month at a mean cost of €2873 per person with MS per month. Informal care was received by 49% of respondents at an average of 47.3 hrs/month at a mean cost of €389 per person with MS per month. Based on disease severity, the mean total home care costs/patient/month were: mild (EDSS 0-3) = €63, moderate (EDSS 4-6) = €461 and severe (EDSS > 6.5) = €8446. Total home care costs were three-fold higher in persons with moderate MS and seven-fold higher in persons with severe MS versus mild MS. Total home care costs of patients cohabiting with another person were nearly 70% higher compared to people living alone. The reported average utility was 0.513 (sd 0.307). Utilities across disease severity: mild MS=0.709 (sd 0.233), moderate MS=0.562 (sd 0.232) and severe MS=0.284(sd 0.283). **CONCLUSIONS:** Total home care costs, of which formal care costs accounted for a large proportion, increased with increasing disease severity. Informal caregiving contributes significantly to MS home care and is an important complement to formal home care in Sweden.

PND65

A COMPARISON OF DEMOGRAPHIC AND CLINICAL VARIABLES OF DOWN SYNDROME PATIENTS IN UTAH AND THE UNITED STATES

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OBJECTIVES: To explore the demographics, comorbidities and medication exposure of Down Syndrome (DS) patients in Utah compared to a national cohort. **METHODS:** National and local data on adult patients with DS were extracted from the General Electric Healthcare National Clinical Data Services Warehouse and the University of Utah Healthcare System Enterprise Data, respectively. The ICD-9 code for Down Syndrome (758.0) was used to identify patients, alive through 2012, and their associated comorbidities and prescribed medications. We used descriptive statistics, *t*-test, test of proportion and Fisher's exact test to examine relationships between demographics, comorbidities and pharmacotherapies and compared results between local and national cohorts. **RESULTS:** Data was extracted on 513 patients in Utah and 11,736 nationally, 98% and 64% of patients are adults in cohorts, respectively. Through 2012, adult DS patients in Utah were younger (37 vs. 39, p<0.005), more likely to be female (54.08% vs. 50.47%, p<0.05)

and more likely to be Caucasian (64.61% vs. 41.53%, p<0.001) than national cohort patients. DS patients in Utah suffered significantly more comorbidities: autism (6.43% vs. 1.12%, p<0.001), heart problems (2.53% vs. 0.57%, p<0.001), blood and blood-forming problems (14.81% vs. 10.05%, p<0.001), epilepsy (7.02% vs. 2.23%, p<0.001) and arthritis (28.46% vs. 10.68%, p<0.001). Higher proportions of Utah patients used ulcer drugs (21.64% vs. 16.83%, p<0.005), majority PPIs (85.6%); antidepressants, (17.93% vs. 11.55%, p<0.001), majority SSRIs (79.3%); analgesics-NSAIDs (15.59 % vs. 11.13%, p<0.005), majority NSAIDs (98.8%); multivitamins (16.18% vs. 9.02%, p<0.001), and fluoroquinolones (10.53% vs. 7.45%, p<0.01) than the national cohort. **CONCLUSIONS:** The Utah DS population differs from the comparative U.S. Cohort in demographics, comorbidities and medications. These results will be incorporated into the development of a Quality of Life scale to value new treatments in Down Syndrome.

PND66

TREATMENT PATTERNS FOR PARKINSON'S DISEASE: REAL-WORLD EVIDENCE FROM THE EU5 (FRANCE, GERMANY, ITALY, SPAIN, AND THE UNITED KINGDOM)

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OBJECTIVES: To assess the distribution of initial Parkinson's Disease (PD) treatment, along with time to and reasons for changes in therapy. **METHODS:** Adelphi Real-World Disease-Specific-Programme (DSP) cross-sectional PD data from January 2011 to February 2012 were analyzed. The DSP surveyed 299 physicians in the EU5 who completed PD patient reviews (≥10 each). Kaplan-Meier estimation was used to evaluate times from initial monotherapy to follow-up therapy by treatment. Reasons for adding or switching drug classes were documented as efficacy-related, levodopa-related (dyskinesia or on-off fluctuations), due to side-effects, and/or other reasons. **RESULTS:** Of the 3,351 patients included, 60% were male; mean age at treatment initiation was 65 years; 55% had mild Hoehn & Yahr severity scores (≤2.5); and 59% initiated treatment on monotherapy. Overall, Dopamine Agonists (DA) were the most common first-line monotherapy (45%; mean age 62 years), followed by Levodopa (39%; 71 years), Monoamine-oxidase-B Inhibitors (MAOB) (14%; 62 years), and Other (2%; 64 years). The median time to change from DA monotherapy was 36 months. Levodopa was the first choice add-on (16%) and switch from (5%) DA monotherapy. Reasons for change to Levodopa were efficacy-related (92% add-on; 70% switch patients). The median time to change from Levodopa monotherapy was 54 months. DA was the first choice add-on (13%) and switch from (1.4%) Levodopa monotherapy. Reasons for change to DA were efficacy-related (86% add-on; 82% switch patients). The median time to change from MAOB monotherapy was 12 months. DA was the first choice add-on (32%) and switch from (6%) MAOB monotherapy. Reasons for change to DA were efficacy-related (95% add-on; 94% switch patients). **CONCLUSIONS:** This EU5 sample represents a levodopa-sparing treatment strategy, favoring initiation with DA for younger patients. Initial treatment with Levodopa monotherapy was of longer duration than that with DA or MAOB. Physicians predominantly reported efficacy-related reasons for treatment changes.

URINARY/KIDNEY DISORDERS – Clinical Outcomes Studies

PUK1

ANALYSIS COST EFFECTIVENESS OF PHARMACOLOGICAL PROPHYLAXIS OF CONTRAST-INDUCED NEPHROPATHY

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OBJECTIVES: Analyze the cost-effectiveness of the prophylaxis (n-acetylcysteine 1200mg 4 oral-doses+1/6M bicarbonate 500ml IV) of the contrast-induced nephropathy (CIN) at risk patients. The CIN is usually reversible, but may affect 50% of patients with some risk factors (diabetes, age...) and may favor the progressive renal damage. **METHODS:** Retrospective observational study. The population were patients candidates at prophylaxis protocol CIN in a university hospital during 2012 (5142 patients). We calculated a sample size of 115 patients for a confidence level of 90%, an error of 7.5% and a frequency of CIN equal 40% . CIN was considered as the relative elevation of serum creatinine greater than or equal to 25% during the 48 hours after the test. For the economic analysis were used acquisition-costs of drugs, and the hemodialysis costs described by Lorenzo et al (Nephrology2010,30(4):404-412). We consider, according to literature that at least 35% of risk patients affected by NIC would require a hemodialysis session. **RESULTS:** Of the patients who received prophylaxis, 3 had CIN and 93 no. Of those who received no prophylaxis 5 had CIN, and 14 no. We did a Fisher Test being the difference in favor of the protective effect of the protocol statistically significant (p <0.01). The prophylaxis would have prevented 25.26 CIN. The prophylaxis costs per patient were € 2.29 . The cost of a hemodialysis sessions was € 423. Then € 220.42 has been invested to avoid a minimum of € 3739.74 on hemodialysis. (16.9 € savings per euro spent on prophylaxis. Each avoided NIC had cost € 8.73.) **CONCLUSIONS:** The economic analysis is difficult because of the diversity of data about CIN. We chose a cost-minimization model, considering minor treatment needs found in the literature. In any case this prophylaxis is highly cost-effective and should be considered before introducing other methods.

PUK2

COST EFFECTIVE USE OF URINE SAMPLING AND DIPSTICK TESTING TO DIAGNOSE URINARY TRACT INFECTIONS IN PRE-SCHOOL CHILDREN PRESENTING TO PRIMARY CARE

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OBJECTIVES: Diagnosis of urinary tract infection (UTI) in young children is difficult. Prompt treatment could alleviate short-term symptoms and prevent serious long-term sequelae, but over-treatment will increase antibiotic resistance. We evaluated the cost-effectiveness of a UTI risk score based on signs, symptoms and dipstick test findings compared to clinical judgement in guiding urine sampling and antibiotic treatment. **METHODS:** We developed a risk score based on urine samples collected (by clean catch or nappy pad) in a multicentre diagnostic cohort study (DUTY) of 7,163 children <5 years presenting to primary care. The diagnostic value of symptoms, signs and dipstick test results were evaluated against a reference standard of urine culture results from a research laboratory. We constructed decision-analytical models comparing the cost-effectiveness of 3 DUTY risk score thresholds (high sensitivity, high specificity or intermediate) versus clinical judgement in younger (nappy pad) and older (clean catch) children. We explored the role of the dipstick in guiding diagnosis. We considered health service costs and patient utilities during the initial diagnosis, acute illness and long-term sequelae. **RESULTS:** The 'high specificity' DUTY threshold resulted in fewer urine samples than clinical judgement (4.8% vs. 9.2%) with similar sensitivity (58.6% vs. 57.1%) and higher specificity (96.1% vs. 91.4%). The difference in short-term net benefits between DUTY thresholds was small (range £1088 'high sensitivity' to £1091 'high specificity'). In younger children (nappy pads) the distinction in cost-effectiveness between the DUTY risk score and clinical judgement was not clear-cut. Dipstick tests could potentially expedite therapy in higher risk children. **CONCLUSIONS:** Clinicians can reduce prescriptions and provide more cost effective care by using the DUTY risk score. Clean catch samples should be obtained whenever practical. Low UTI prevalence, imperfect NHS laboratory tests and an uncertain link between UTI and long-term sequelae mean that conservative sampling strategies may be most appropriate.

PUK3

COMPARISONS OF THE CLINICAL EFFECTIVENESS OF TREATMENTS FOR THE SYMPTOMS ASSOCIATED WITH OVERACTIVE BLADDER (OAB)

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OBJECTIVES: This research was carried out during a review of the manufacturer's submission (MS) to the NICE Single Technology Appraisal programme for the selective beta$_3$-adrenoceptor agonist, mirabegron. Antimuscarinics are the mainstay of treatment for the symptoms of OAB. They may be used at different doses and in different formulations (immediate release [IR] or extended release [ER]). However, there is limited evidence on their comparative clinical effectiveness with each other. This research evaluated the available evidence for mirabegron, antimuscarinics, and placebo. **METHODS:** Randomised controlled trials (RCTs) for inclusion were identified using the MS for mirabegron. RCTs were assessed for comparability based on diagnosis, patient population, treatment regimen, and with outcomes reported at 12 weeks. Mixed treatment comparison (MTC) using Bayesian Markov Chain Monte Carlo simulation was used to perform a meta-analysis of a network of RCTs. Summary statistics used were mean difference (MD) for continuous outcomes and odds ratio (OR) for dichotomous outcomes. **RESULTS:** Of the 40 RCTs identified in the MS, 22 met the criteria for inclusion in the analysis. No statistically significant differences in frequency of micturition were identified between any of the active treatments. Compared with mirabegron 50mg, statistically significant differences in the remaining outcomes assessed, were: fewer incontinence episodes, MD (solifenacin 5mg -0.39, 95%CI: -0.72 to -0.06; solifenacin 10mg -0.38, 95%CI: -0.69 to -0.07); increased risk of constipation , OR (fesoterodine 8mg 2.12, 95%CI: 1.13 to 3.64; solifenacin 5mg 2.11, 95%CI: 1.16 to 3.59; solifenacin 10mg 4.52, 95%CI: 2.60 to 7.47; trospium 60mg 7.63, 95%CI: 2.12 to 22.95); increased risk of discontinuation, OR (oxybutynin 15mg IR 2.67, 95%CI: 1.60 to 4.22). Mirabegron was associated with significantly lower risk of dry mouth than all other active treatments. **CONCLUSIONS:** None of the treatments assessed for OAB have a consistently superior efficacy with a reduced risk of adverse events.

PUK4

CONTINUOS RENAL REPLACEMENT THERAPY VERSUS INTERMITTENT HEMODIALYSIS: SYSTEMATIC REVIEW ON PATIENT-ORIENTED OUTCOMES

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OBJECTIVES: Acute renal failure is responsible for about 1% of hospital admissions, and occurs in up to 7% of hospitalized patients and up to 20% of patients admitted to intensive care units (ICU's). When it is severe enough to require dialysis, in-hospital mortality rate ranges from 50% to 75% and is also increases risk for chronic and terminal kidney diseases. Continuous Renal Replacement Therapy (CRRT) in its various forms has theoretical advantages over conventionally done Intermittent Hemodialysis (IHD) at significantly higher costs, but these advantages attributed to CRRT have not yet been consistently proven in terms of clinical outcomes in controlled trials. **METHODS:** We have made a literature search in PubMed to identify systematic reviews and randomized controlled trials that studied patient-oriented outcomes (mortality and renal recovery). **RESULTS:** We have found five systematic reviews published in 2007 and 2008 and conducted our own metanalysis on six trials published from 2001 to 2009 (no clinical outcomes oriented trial has been published since them). None of the reviews that directly compared CRRT to IHD have shown statistically significant advantages of any of them regarding in-hospital or ICU mortality or renal function recovery We have analyzed six randomized no-blinded clinical trials that met eligibility criteria of evaluating patient-oriented outcomes including 1151 patients. Five of them had high to moderate GRADE scores. None have shown absolute risk reduction of in hospital, ICU or at 60 days mortality or statistically significant renal recovery rates. Overall mortality relative risk of CRRT over IHD was 1,01 (95%CI: 0,92 – 1,11). We found moderate heterogeneity and no publication bias. **CONCLUSIONS:** Clinical trials published until October 2012 have shown no difference in patient-oriented outcomes between the uses of CRRT and IHD techniques in adult patients admitted to intensive care units with acute renal failure and requiring renal replacement therapy.

URINARY/KIDNEY DISORDERS – Cost Studies

PUK5

THE FINANCIAL IMPACT OF INCREASING HOME-BASED HIGH DOSE HAEMODIALYSIS AND PERITONEAL DIALYSIS

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OBJECTIVES: The increasing prevalence of end-stage kidney disease in the UK has resulted in a heavy economic burden. The National Institute of Health and Care Excellence reported that patients receiving dialysis at home have better health outcomes and lower health care resource use. This study aims to assess the financial impact of increasing the use of home-based dialyses vs. UK current practice. **METHODS:** A Markov model was constructed to estimate the financial impact of different dialysis scenarios from the UK payer perspective. We modelled prevalent and incident dialysis patient population over 5 years. The current UK dialysis modality distribution of 15% prevalent and 20% incident peritoneal dialysis (PD), 82% prevalent and 79% incident in-centre haemodialysis (ICHD), 3% prevalent and 1% incident conventional home HD (HHD), and 0% high dose HHD was compared to 3 scenarios: 1) Increase high dose HHD to 10% among prevalent patients; 2) Increase high dose HHD to 10% and PD to 20% among prevalent patients and increase PD to 25% among incident patients; 3) Increase high dose HHD to 10% and PD to 25% among prevalent patients and increase PD to 30% among incident patients. In each scenario, the proportion of patients on ICHD changes accordingly, while conventional HHD is kept constant. Model inputs were from published sources. **RESULTS:** The base case results show that all 3 scenarios result in lower costs versus current UK practice. A prevalent population size of 22,654 patients was modelled, accounting for an annual incident population size of 5,393 in England. Scenario 1 saves £25 million (£559 per patient). Scenario 2 saves £67 million (£1,526 per patient). Scenario 3 saves £110 million (£2,493 per patient). Sensitivity analyses demonstrate consistent results. **CONCLUSIONS:** Under the current UK national tariff, increasing the proportion of patients on home-based dialyses is associated with lower total health care costs.

PUK6

BUDGET IMPACT OF SWITCHING FROM AN IMMEDIATE-RELEASE TO A PROLONGED-RELEASE FORMULATION OF TACROLIMUS IN RENAL TRANSPLANT RECIPIENTS IN THE UK BASED ON DIFFERENCES IN ADHERENCE

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OBJECTIVES: Advagraf® is a once-daily prolonged-release formulation of tacrolimus with proven non-inferiority to Prograf®, a twice-daily immediate-release formulation of tacrolimus, in biopsy-proven acute rejection in renal transplant recipients. Advagraf is associated with improved adherence compared with Prograf, which may ultimately improve long-term outcomes. The present study assessed the budget impact of switching patients from Prograf to Advagraf in the UK. **METHODS:** A budget impact model was constructed based on published data on acute rejection, graft failure and mortality in the UK setting. Patients were assumed to convert from Prograf to Advagraf on a 1:1 mg:mg basis. In a study comparing the adherence rates between once-daily versus twice-daily formulations of tacrolimus, the proportion of patients taking the prescribed number of daily doses was 88.2% in Advagraf patients and 78.8% in Prograf patients. The model applied a relative risk of graft failure of 3.47 to non-adherent patients based on data from a 2004 meta-analysis. Cost data were taken from the British National Formulary and 2012–13 NHS tariff information. The analysis was performed over a 5-year time horizon and future costs were not discounted, in line with International Society for Pharmacoeconomic and Outcomes Research guidelines. **RESULTS:** Over a 5-year time horizon, the mean cost per patient (including tacrolimus, concomitant immunosuppressive medications, dialysis after graft failure, and treatment for acute rejection) was GBP 29,290 for Advagraf versus GBP 33,032 for Prograf. The total cost saving of GBP 3,742 was driven by reduced Advagraf pharmacy costs and lower dialysis costs arising from the lower risk of graft failure in the larger proportion of adherent patients in the Advagraf arm. **CONCLUSIONS:** Conversion of renal transplant recipients from Prograf to Advagraf was associated with lower pharmacy and dialysis costs, with the reduction in dialysis costs being driven by improved adherence to Advagraf regimen and the consequent improvement in graft survival.

PUK8

AN ANALYSIS OF THE COST OF SWITCHING RENAL TRANSPLANT PATIENTS FROM AN IMMEDIATE-RELEASE TO A PROLONGED-RELEASE FORMULATION OF TACROLIMUS BASED ON DIFFERENCES IN TROUGH CONCENTRATION VARIABILITY IN THE UNITED KINGDOM

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OBJECTIVES: Randomized controlled trials have shown that Advagraf®, a once-daily prolonged-release tacrolimus formulation, is non-inferior to Prograf®, a twice-daily immediate-release tacrolimus formulation, in terms of biopsy-proven acute rejection in renal transplant recipients. However, relative to Prograf, Advagraf exhibits reduced variability in tacrolimus trough concentration, which has been associated with reduced graft failure. Based on these data, the present study evaluated the cost of switching UK renal transplant patients from Prograf to Advagraf. **METHODS:** UK-specific data on acute rejection, graft failure and mortality were used to construct a budget impact model to assess the costs of switching from Prograf to Advagraf on a 1:1 mg:mg basis. The model assumed that 3.1% of patients on Advagraf had high tacrolimus trough concentration variability compared with 17.4% on Prograf, based on a study comparing Advagraf and Prograf pharmacokinetics. The model applied a relative risk of graft failure of 2.38 to high variability patients based on data from a tacrolimus variability study. Cost data were taken primarily from the British National Formulary and 2012–13 NHS tariff information and the analysis was performed over a 5-year time horizon. **RESULTS:** The mean cost per patient (including tacrolimus, concomitant immunosuppressive medications, dialysis after graft failure, and treatment for acute rejection) was GBP 26,958 with Advagraf versus GBP 30,379 for Prograf over a 5-year period. The total cost saving (GBP 3,421) was driven by reduced Advagraf pharmacy costs and lower dialysis costs resulting from the lower proportion of patients with high variability in tacrolimus trough concentrations in the Advagraf arm, leading to lower risk of graft failure. **CONCLUSIONS:** Converting renal transplant recipients from Prograf to Advagraf was associated with lower pharmacy and dialysis costs, with the reduction in dialysis costs being driven by the lower proportion of Advagraf patients with high tacrolimus trough concentration variability and the resultant improvement in graft survival.

PUK9

ECONOMIC EVALUATION OF EPOETIN ALFA HEXAL (BINOCRIT) COMPARED TO DARBEPOETIN ALFA (ARANESP) IN THE TREATMENT OF CHRONIC HAEMODIALYSIS (CKD5) PATIENTS IN GERMANY

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OBJECTIVES: To compare the CKD5 budget requirements of utilizing epoetin alfa Hexal vs. darbepoetin alfa in the German health care system. **METHODS:** Chronic kidney disease (CKD) is a condition that is prevalent worldwide, and the number of patients affected continues to increase. ESAs and iron are the mainstays of treatment for haemodialysis patients. The purpose of this pharmacoeconomic analysis was to evaluate the cost-effectiveness of the short-acting biosimilar ESA epoetin-alfa Hexal (EA) 6,000-8,000 IU per week (TIW) vs. long-acting erythropoiesis-stimulating agent (ESA) darbepoetin alfa (DA) 30-40 mcg weekly (QW), for treating chronic haemodialysis patients. A budget impact model was constructed employing a payer perspective, per patient with 5 year time horizon. The treatment period considered was based on 52 weeks and was aligned with real world clinical experience data from germany[1]. Model inputs included: medical treatment, outcomes, and health care service utilization from published clinical studies[2]and summary of product characteristics recommendation. Effectiveness of therapeutic alternatives was determined by comparing haemoglobin maintenance rates. Costs presented reflect 2013 prices. The analysis was performed from the perspective of the German health care system. **RESULTS:** The average expected pharmaceutical costs per patient were €3791 to €5002 for DA QW (30-40mcg weekly) versus €2690 to €3520 for EA TIW (6,000-8,000IU weekly). Cost-savings associated with utilizing EA TIW was 41-42% for comparable DA doses. Previous German research has demonstrated that ESA consumption of patients on chronic haemodialysis based on DDD is similar for biosimilar and originator ESAs[1]. **CONCLUSIONS:** In the treatment of chronic haemodialysis patients in Germany, epoetin alfa Hexal is projected to provide substantial savings for the health care system when compared to darbepoetin alfa. German stakeholders could consider the extent that darbepoetin alfa is utilized in haemodialysis patients. [1] Horbrand et al. Eur J Clin Pharmacol 10/2012. [2] Horl et al. Clin. Nephrology 1/2012.

PUK10

ECONOMICS OF DIALYSIS DEPENDENCE FOLLOWING ACUTE KIDNEY INJURY (AKI) IN THE INTENSIVE CARE UNIT (ICU)

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OBJECTIVES: AKI is common in the ICU and often necessitates the provision of renal replacement therapy (RRT). Two main modalities exist: continuous (CRRT) or intermittent (IRRT) therapy. Neither modality has been found superior in terms of survival. However, dialysis dependence among survivors remains a significant medical and economic issue. A recent meta-analysis showed initial IRRT might be associated with higher rates of dialysis dependence than initial CRRT. We performed a preliminary cost-utility analysis comparing both modalities based on these recent data. **METHODS:** We assumed a pool of patients who would potentially be eligible for either modality and modeled LYG, QALYs gains and costs comparing initial CRRT vs. initial IRRT, all else being the same. Using the US perspective, we designed a 1-year Markov model with daily cycle and 2 health states (dialysis independence/dependence). Survival for both modalities was fitted from published estimates (Weibull regression). The proportion of dialysis independent survivors was fitted from published estimates for CRRT (Weibull regression). IRRT dialysis independence estimates were obtained by applying the meta-analysis risk-ratio to the fitted CRRT estimates. Sensitivity analysis was conducted on the daily implementation cost difference between CRRT and IRRT (from $250 to $1,000; basecase: $500) and the risk-ratio for dialysis dependence for IRRT as compared to CRRT (from 1.20 to 3.00; basecase: 1.99). **RESULTS:** The QALYs gain was slightly better for CRRT as compared to IRRT (0.301 vs. 0.292 respectively). Despite higher hospitalization costs for CRRT ($86,397 vs. $83,309 for IRRT), the one-year cumulative total cost including the cost of dialysis dependence was similar between the two modalities ($94,286 for CRRT vs. $94,118 for IRRT). In the basecase analysis, the ICER of CRRT vs. IRRT was $17,562/QALY. **CONCLUSIONS:** Initial CRRT may actually be cost-effective as compared to initial IRRT by reducing the rate of dialysis dependence among AKI survivors.

PUK11

IN-PATIENT HOSPITALIZATIONS FOR CHRONIC KIDNEY DISEASE IN THE UNITED STATES

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OBJECTIVES: To understand the trends in rate and cost of hospitalizations due to Chronic Kidney Disease (CKD) in the U.S. **METHODS:** We analyzed the last five years

of hospitalizations with ICD-9 diagnosis codes of CKD and End Stage Renal Disease (ESRD). The annual number of hospitalizations for specific diagnosis was obtained from AHRQ's National In-patient Sample (NIS) databases of 2005-2009. Data was also analyzed for length of stay (LOS), charges and cost of hospitalization. **RESULTS:** During the last five years the number of hospitalizations with diagnosis of CKD and ESRD has increased 4.1 and 4.6 fold, respectively. In 2009, an estimated 1,634,422 and 931,641 hospitalizations were with diagnosis of CKD and ESRD respectively. The mean LOS for patients with CKD increased from 4.9 to 5.5 days between2005-2009. The mean LOS for patients with ESRD has remained steady at ~6 days between 2005-2009. The cost of hospitalization with diagnosis of CKD has increased 31% between 2005-2009. The cost of hospitalization with diagnosis of ESRD has increased 21% between 2005-2009. In 2009, the mean cost of hospitalization for patients with CKD and ESRD was $11,209 and $21,358, respectively. **CONCLUSIONS:** Hospitalizations due to CKD and ESRD have significantly increased during the last five years. There is a need for prevention, treatment, and disease management programs to lower the medical and socioeconomic burden of this disease.

PUK12

ASSESSING THE ECONOMIC BURDEN AND HEALTH CARE UTILIZATIONS OF VETERAN PATIENTS DIAGNOSED WITH CHRONIC KIDNEY DISEASE IN THE UNITED STATES

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OBJECTIVES: To examine the economic burden and health care utilizations of patients diagnosed with chronic kidney disease (CKD) in the U.S. veteran population. **METHODS:** A retrospective database analysis was performed using the Veterans Health Administration (VHA) Medical SAS datasets (01OCT2008-30SEP2012). Patients diagnosed with CKD were identified using International Classification of Disease 9th Revision Clinical Modification (ICD-9-CM) diagnosis codes 585.xx, 250.4xx, 791.0x, 583.xx, and 403.xx. The first diagnosis date was designated as the index date. A group of non-CKD patients of the same age, region, gender and index year were identified and matched on baseline Charlson Comorbidity Index (CCI) as the comparison group with a randomly chosen index date to minimize selection bias. Patients in both groups were required to be at least 18 years old, and have continuous health plan benefits 1 year before and 1 year after the index date. One-to-one propensity score matching was used to compare the health care costs and utilizations during the follow-up period between the CKD and comparison groups, adjusted for baseline demographic and clinical characteristics. **RESULTS:** A total of 477,078 patients were identified for the CKD cohort and the comparison cohort. After 1:1 matching, 155,324 of patients were matched from each group, and the baseline characteristics were well-balanced. CKD Patients incurred higher health care utilizations in inpatient (17.00% vs. 2.84%, p<0.01), emergency room (17.81% vs. 6.64%, p<0.01), physician office (99.28% vs. 67.92%, p<0.01), outpatient (99.36% vs. 68.69%, p<0.01), and pharmacy visits (91.16% vs. 72.61%, p<0.01). The CKD group also had higher patient expenditures in inpatient ($6,228 vs. $802, p<0.01), emergency room ($194 vs. $62, p<0.01), physician office ($3,287 vs. $1,516, p<0.01), outpatient ($3,788 vs. $1,715) and pharmacy ($848 vs. $490, p<0.01) than patients in the comparison group. **CONCLUSIONS:** CKD patients had a significantly higher burden of illness compared to a similar comparison group of non-CKD patients.

PUK13

ECONOMIC IMPACT OF PRURITUS AMONG END-STAGE RENAL DISEASE PATIENTS RECEIVING HEMODIALYSIS

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OBJECTIVES: Itchy and dry skin, symptoms of pruritus, are commonly reported by patients with end-stage renal disease (ESRD). Previous analyses of a large dialysis organization (LDO) suggested that these symptoms are associated with decreased quality of life and poorer health outcomes. As a result, these patients may represent a higher economic burden to payers. This retrospective cohort study compared direct health care resource utilization (HRU) and costs associated with varying degrees of self-reported itchiness/dryness skin severity. **METHODS:** Adult patient data (≥ 18 years old) from the 2009 United States Renal Disease System (USRDS) dataset were combined with corresponding Kidney Disease Quality of Life (KDQOL) survey data obtained between January to September 2009, at an LDO. Patients were included if they had answered KDQOL itchiness/dryness questions, had KDQOL assessments ≥ 3 months after starting dialysis, and had Medicare as their primary payer. Patients were grouped by their itchiness/dryness severity. All HRU and cost outcomes were described over a 3-6 month follow-up period post-KDQOL survey. Patients were censored for death, transplant, change in treatment modality, discontinued treatment, or loss of observation during the follow-up period. **RESULTS:** Study population included 1,387 patients. HRU analyses of itchiness showed increased rate of hospitalizations (42.5% vs. 28.4%) for patients who were extremely bothered versus not bothered by itch. Similar results were observed for dryness (34.3% vs. 27.5%) and combined itchiness and dryness (34.2% vs. 28.0%). Extremely bothered patients had higher overall health care costs: $33,755 vs. $26,933 for itchiness; $29,801 versus $26,321 for dryness; and $29,249 vs. $26,736 for combined itchiness and dryness. Dialysis and hospitalization costs contributed the most toward overall health care costs. **CONCLUSIONS:** These results suggest an association between increased skin itchiness/dryness and increased hospitalizations and health care costs. Additional research, adjusting for patient characteristics, is needed to provide more evidence for the burden of skin itchiness/dryness in ESRD patients.

PUK14

COST OF TREATMENT AFTER RENAL TRANSPLANTATION IN IRAN: SHOULD GOVERNMENT CONTINUE PAYING FOR NEW EXPENSIVE IMMUNOSUPPRESSIVE DRUGS?

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OBJECTIVES: The primary aim of the study was to estimate costs of treatment for the first year after renal transplantation from the perspective of health insurance organizations in Iran. **METHODS:** An Excel-based and a Monte Carlo model were developed to determine the treatment costs of current clinical practice in renal transplantation therapy (RTT). Inputs were derived from Ministry of Health and insurance organizations' database, hospital and pharmacy records, clinical trials and local and international literature. According to the model, there were almost 17,000 patients receiving RTT in Iran, out of which about 2,200 patients underwent the operation within the study year (2011- 2012; n= 2200). **RESULTS:** The estimated first year total treatment cost after renal transplantation was almost $14,000,000. These costs corresponded to annual total cost per patient of almost $6500 for the payers. **CONCLUSIONS:** Renal transplantation therapy is almost fully reimbursed by government in Iran. However, regarding new expensive medicines, cost of medical expenditure is rapidly growing and becoming quite unaffordable for the government; therefore, out-of-pocket (OOP) payments are dramatically increasing over time. In order to improve reimbursement policy making under pressure of current budget constraints, the present study is providing decision makers with practical tools make them possible to easily compare budgetary impact of the current therapy strategy with the future financial consequences of purchasing newly proposed medicines. In other words having estimation of the current budget spending on RTT would help policy makers in making efficient resource allocation and decrease quite high OOP expenditures.

PUK15

A NON-INTERVENTIONAL RETROSPECTIVE EVALUATION OF RESOURCES CONSUMED DURING THE PROVISION OF CARE FOR OVERACTIVE BLADDER SYNDROME: A REAL WORLD EVALUATION: GERMAN PERSPECTIVE (THE REDUCE STUDY)

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OBJECTIVES: To evaluate resource utilisation for subjects with overactive bladder (OAB) syndrome who are managed with the commonly prescribed oral medications: solifenacin succinate, tolterodine tartrate, or trospium chloride from the payer perspective. **METHODS:** Data were abstracted from medical records for qualified subjects who were ≥ 18 years, with a diagnosis for OAB (at least one of the following: urgency, frequency with or without urgency incontinence) on or before December 31, 2010. Subjects must have been on one of the study medications for at least 3 months and have at least 12 months of medical records available. The study was approved by local ethics committees and all data provided was anonymised. Medication costs for Germany are reported for 2013 €. **RESULTS:** A total of 136 of 229 subjects were included for the German analysis. The remaining subjects were from the Czech Republic to be reported elsewhere. Top 3 reasons for exclusion from Germany include: primary diagnosis of urinary tract infection, urologic surgery within 6 months of the data collection, and diabetic neuropathy. The annual overall mean cost for office visits, specialist visits, investigations, other treatments, medications and incontinence pad use with solifenacin (5,10mg/day) (N=60), trospium (IR and ER maximum dose of 60mg/day) (N=51), and tolterodine (IR 2, 4mg/day and ER 4mg/day) (N=25), were €1,059.31, €1,247.76, and €1,626.01, respectively. Incontinence pad use for weekly frequency with solifenacin, trospium, and tolterodine was, 17.34, 19.51 and 20.35, respectively. Overall satisfaction with medication as perceived by the clinician (very satisfied, satisfied, neutral, dissatisfied, very dissatisfied) for very satisfied and satisfied was 97%, 86%, 100%, for solifenacin, trospium, tolterodine, respectively. **CONCLUSIONS:** Solifenacin had the lowest annual cost-in-use compared to other study drug annual cost. This was corroborated in part by the lowest incontinence pad use for solifenacin compared to trospium and tolterodine and the high treatment satisfaction.

PUK16

COST AND COST-EFFECTIVENESS OF TREATING URGENCY STRESS INCONTINENCE-RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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OBJECTIVES: Urgency urinary incontinence (UUI) has a substantial impact on patients' QOL and well-being, and may pose a substantial economic burden on patients and health insurers. We assessed the cost and cost-effectiveness of four conservative treatment modalities for UUI in Israel. **METHODS:** A total of 164 women were randomly allocated to one of four interventions: drug therapy (DT), bladder training (BT), pelvic floor muscle-training (PFMT), and combined pelvic floor rehabilitation (CPFR) and were followed over a period of 12-months. Resource utilization including physician encounters, dispensed prescriptions, physical therapist treatment and any other medical services was estimated for each study participant. We also estimated the women's self-reported utilizations of pads, laundry and new underwear. Total costs were calculated by multiplying the volumes of resource utilization by the corresponding unit-prices. We used the bootstrap method to report bias-corrected confidence-intervals of cost estimates. Utility weights were elicited using the EQ-5D questionnaire at baseline, 3-months and 12-months of follow-up. **RESULTS:** Women in all four treatment groups showed improvements in QOL from baseline to 12-months (DT:0.87 - 0.93, BT:0.85 to 0.89, PFMT:0.82 - 0.84, CPFR: 0.82 to 0.86). Changes in QOL summary scores from study enrollment and end of follow-up were estimated after correction for potential baseline differences, and were not statistically different among study groups. The mean total cost was somewhat lower for the DT group participants ($1,460), as compared with the three other interventions (range: $1,760-$1,990). These differences, however, were not statistically significant. The mean monthly personal costs were significantly reduced from baseline to 12-months of follow-up in all treatment groups. **CONCLUSIONS:** The four treatment modalities for treating UUI were equally effective and associated

with comparable costs. Therefore, an incremental cost-effectiveness ratio was calculated. Due to the possibility of declining adherence to drug therapy over time, pelvic floor physical therapy can be considered as the first line treatment for UUI.

PUK17

THE COST IMPLICATIONS OF RENAL DENERVATION THERAPY AT THE HOSPITAL LEVEL IN THE UNITED KINGDOM

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OBJECTIVES: Hypertension is a chronic medical condition and an important risk factor in several fatal and debilitating diseases. NICE estimates the cost of pharmacologic intervention in the UK for hypertension at £409.8 million. Resistant hypertension arises when blood pressure remains uncontrolled despite antihypertensive treatment. Renal denervation is a new procedure aimed at reducing blood pressure in resistant hypertension patients by decreasing efferent sympathetic signalling to the kidneys. The objective of this research was to review the evidence on the cost of renal denervation and to provide a costing model for the procedure. **METHODS:** A targeted review of costing data was performed and information gathered from renal denervation experts to establish relevant procedure costs. Once specific health care resource use (HRU) and equipment costs were identified, an Excel™ costing model was constructed. A further search of NHS costing documents, academic literature, and expert consultation provided GBP figures for each cost and identified those that were time dependent (e.g. hourly staff costs). **RESULTS:** The required in-patient HRU was identified as staff costs per hour including surgeon costs, nurse costs, technician costs and anaesthesiologist costs, all of which vary with procedure time depending on the device used (ranging from 20-60 minutes). Catheter lab overhead costs per hour and recovery costs (bed days) were also identified. Total HRU costs vary between £923.02 and £991.62 (for 20 and 60 minute procedure times respectively). An additional in-hospital recovery day adds £680. Equipment costs were for 12 items including from syringes to catheters to valves, totaling £281.70 plus the cost of the renal denervation therapy device. **CONCLUSIONS:** It is essential the cost of the procedure is estimated to fully inform payers and health care providers. HRU costs are dependent on procedure time and length of recovery in hospital, thus devices that reduce these factors are best for cost savings.

PUK18

LONG-TERM COSTS AND SURVIVAL ASSOCIATED WITH IMMUNOSUPPRESSANT FOLLOWING LIVER TRANSPLANTATION: A MARKOV MODEL

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OBJECTIVES: Despite significant improvements in survival and quality of life (QoL) of liver transplant (LTx) recipients, patients remain at risk from complications related to disease recurrence and long-term use of immunosuppressant (IS). The objective was to assess cost, survival, and QoL outcomes of LTx recipients and the impact of renal dysfunction on LTx outcomes. **METHODS:** A *de novo* cohort Markov model was developed to predict long-term outcomes post LTx along two independent pathways: 1) liver-related (acute rejection, hepatocellular carcinoma, hepatitis C (HCV) recurrence, graft loss), 2) kidney-related (chronic kidney disease, dialysis, renal transplantation) and death. All patients, stratified by liver diagnosis, entered the model at time of LTx and followed both pathways, allowing for multiple combinations of liver and kidney health states. Costs and utilities were assigned to each health renal and liver state. Renal complications costs and utility decrements were added to those accrued in the liver pathway. The lifetime model used an annual cycle length except for the 1st year post LTx (quarterly). Choice of immunosuppressant strategy could impact the risk of acute rejection, change in renal function and HCV fibrosis progression. A 3% discount rate was applied to costs and outcomes. **RESULTS:** On average, life expectancy post LTx was 13.3 years with 10.2 QALYs. Lifetime cost of managing post LTx recipients was USD 550,000 (excluding LTx procedure): >50% was related to IS regimen, monitoring and adverse events; around 40% to renal complications and 2-7% to liver complications. Patients developing renal dysfunction lost 5.2 life-years and 1.5 QALYs. **CONCLUSIONS:** To our knowledge, this is the first Markov model simulating lifetime costs and outcomes post-LTx and the impact of change in renal function on patient survival. A health care intervention that could improve or maintain renal function would have significant impact on survival and costs.

PUK19

COST-EFFECTIVENESS OF FESOTERODINE AND TOLTERODINE FOR THE TREATMENT OF OVERACTIVE BLADDER WITH URGE URINARY INCONTINENCE IN SPAIN AND FINLAND

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OBJECTIVES: To assess the economic value of fesoterodine compared to tolterodine for the treatment of overactive bladder (OAB) with urgency urinary incontinence (UUI) in Spain and Finland. **METHODS:** A decision-tree economic model estimated the 52-week costs and quality-adjusted life years (QALYs) of OAB/UUI patients initiating treatment with fesoterodine 4mg/day or extended-release (ER) tolterodine. Treatment response (UUI <1 episode/day) and persistence were evaluated at weeks 4, 12, and 24. Titration from fesoterodine 4mg/day to 8mg/day was permitted at week 4. At week 12, non-responders discontinued treatment permanently. Efficacy, discontinuation, and utility data were derived from four clinical trials of fesoterodine. OAB-related costs including physician visits, laboratory tests, incontinence pads, and comorbidities (fracture, skin infection, urinary tract infections, depression, and nursing home) were also included. The perspective was that of the National Health Systems (2012€). Uncertainty surrounding the model parameters was assessed by univariate and probabilistic sensitivity analysis (PSA). **RESULTS:** A total of 19.5% and 18.0% of fesoterodine and ER tolterodine patients remained on treatment until week 52, respectively. QALYs were higher with fesoterodine than tolterodine (0.762 vs. 0.760). In Spain, fesoterodine treatment had higher costs than (generic) ER tolterodine (€6 697 vs. €6 597), resulting in a cost of €15 600/QALY gained. In Finland, fesoterodine was cost-saving relative to (non-generic) ER tolterodine (€7 885 vs. €8 024). Sensitivity analysis confirmed these findings were robust to the expected price decrease for generic ER tolterodine in Finland. In the PSA, fesoterodine was consistently the preferred therapy in Finland regardless of the value of a QALY and in Spain for QALY valuations greater than €15 000. **CONCLUSIONS:** Fesoterodine is cost-effective or cost-saving relative to ER tolterodine for the treatment of OAB with UUI in two European countries. Payers and prescribers should consider a broad scope of costs in order to make informed cost-conscious choices of antimuscarinic treatment.

PUK20

ECONOMIC EVALUATION OF PHARMACOLOGICAL TREATMENTS FOR OVERACTIVE BLADDER

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OBJECTIVES: Overactive bladder (OAB) is a chronic condition which affects quality of life through the main symptoms of urinary urgency, urinary frequency, and urinary incontinence. Treatments include behavioural therapy, antimuscarinics (AM), β_3-adrenoceptor agonsits (mirabegron), botulinum toxin (botox) and sacral nerve stimulation (SNS). The aim of this analysis was to evaluate the costs and outcomes associated with different sequences of oral treatments (AM and mirabegron). **METHODS:** A Markov model with monthly cycle length and a time horizon up to 3 years compared two different sequences of up to three lines of oral treatments. Patients who discontinue one oral medication may switch to another oral medication, or may discontinue treatment. Patients whose symptoms are not improved are considered for botox or SNS. Outcomes are measured by (a) number of patients with improved symptoms (< 2 incontinence episodes and < 8 micturitions per 24-hours); (b) patients with < 2 incontinence episodes per 24-hours; and (c) patients with < 8 micturitions per 24-hours. **RESULTS:** Including a third-line oral medication before considering other treatment options improved all patient outcomes, irrespective of the particular drugs used. A three-line sequence including two generics (oxybutynin (1st line), and tolterodine ER (2nd line)), and one branded drug (solifenacin 5mg (3rd line)) resulted in inferior patient outcomes and higher cost compared with a sequence of branded drugs (mirabegron (1st line), solifenacin 5mg (2nd line), solifenacin 10mg (3rd line)): improved patients (70/1000 vs. 92/1000); patients with < 2 incontinence episodes (181/1000 vs. 217/1000); patients with < 8 micturitions (248/1000 vs. 299/1000). Annual treatment costs were higher in the generic sequence (£2659 per patient vs. £2479). **CONCLUSIONS:** Low-cost generic treatments are not necessarily more cost-effective than branded drugs. The main reason is that a better efficacy and tolerability balance improves symptoms and quality of life, leading to better persistence and lower overall treatment costs.

PUK21

COST-EFFECTIVENESS OF MIRABEGRON COMPARED WITH TOLTERODINE ER 4MG FOR THE TREATMENT OF PATIENTS WITH OVERACTIVE BLADDER IN THE UNITED KINGDOM: RESULTS FROM A TRIAL-BASED MODEL

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OBJECTIVES: Mirabegron is a first-in-class beta-3 adrenoceptor agonist for the treatment of overactive bladder (OAB) that demonstrated superior efficacy compared to placebo in OAB. The cost-effectiveness of mirabegron 50 mg (MGN) was assessed in comparison with tolterodine ER 4 mg (TOL) in the UK. **METHODS:** A Markov model was developed to simulate the therapeutic management, the changes in symptoms (micturitions and incontinence), and complications in OAB patients. The model was used to predict costs and QALYs over 5 years in cohorts initially treated with MGN or TOL, followed by antimuscarinics in case of lack of efficacy or adverse events. Transition probabilities and EQ-5D utilities were obtained from regression models, estimated from a P3 randomized controlled trial of mirabegron. Costs were evaluated from the UK National Health Service (NHS) perspective and included drug acquisition, physician visits, pads and botulinum toxin injections. Subgroup analyses were performed for previously treated, treatment naïve, incontinent, female and elderly patients. **RESULTS:** The MGN strategy was more expensive compared to TOL, with a difference of £37.88 per patient, and produced more QALYs (+0.009 per patient). The incremental cost-effectiveness ratio (ICER) was estimated at £4,386/QALY gained. Results of one-way sensitivity analyses showed that in all scenarios, except one (the transition probabilities between symptom levels of micturition for mirabegron), MGN remained cost-effective or was dominant compared to TOL. Key cost-effectiveness drivers included parameters related to efficacy and treatment discontinuation. Based on the probabilistic sensitivity analysis, the probability of MGN being cost-effective against TOL was 89.4% at a threshold of £20,000 per QALY gained. ICERs in subgroups ranged from £3,091 (female subgroup) to £5,736 (elderly subgroup). **CONCLUSIONS:** Treatment with mirabegron 50 mg appears to be a cost-effective strategy compared with tolterodine ER 4 mg for the general OAB population and the specified subgroups, from a UK NHS perspective.

PUK22

COST-EFFECTIVENESS OF MIRABEGRON COMPARED WITH ANTIMUSCARINICS FOR THE TREATMENT OF PATIENTS WITH OVERACTIVE BLADDER IN THE UNITED KINGDOM

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OBJECTIVES: Mirabegron is a first-in-class beta-3 adrenoceptor agonist for the treatment of overactive bladder (OAB) that demonstrated superior efficacy compared to placebo by reducing OAB symptoms and improving HRQoL. We sought to assess the cost-effectiveness of mirabegron 50 mg in comparison with current antimuscarinics for the treatment of patients with OAB in the UK. **METHODS:** A Markov model was developed to simulate the therapeutic management, the changes in symptoms (micturitions and incontinence), and complications in hypothetical cohorts of OAB patients. The model was used to predict costs and QALYs over 5 years in cohorts initially treated with antimuscarinics or mirabegron 50mg. Effectiveness and safety data were based on the results from a mixed treatment comparison (MTC). A calibration approach was used to derive transition probabilities from mean changes in frequency of micturitions and incontinence episodes. Other input data were obtained from several sources, including scientific literature and expert opinions. Costs were evaluated from the UK National Health Service (NHS) perspective and included costs of drug acquisition, GP visits, specialist visit, incontinence pad use and botox injections. Utilities were obtained from equations predicting EQ-5D index scores according to symptom severity, estimated from a clinical trial of Mirabegron. **RESULTS:** The Mirabegron strategy was slightly more expensive and associated with a greater number of QALYs, as a result of improved persistence, related to a lower risk of adverse event compared to each antimuscarinic. Mirabegron 50mg was found to be cost-effective compared to each antimuscarinic, with an ICER of £340 vs. solifenacin 10mg, £3,607 versus fesoterodine 4mg, £3,715 vs. tolterodine ER 4mg, £3,878 vs. oxybutynin ER 10mg, £8,881 versus trospium chloride MR 60 mg, £12,493 versus solifenacin 5mg, and £14,234 oxybutynin IR 10mg. **CONCLUSIONS:** Treatment with mirabegron appears to be a cost-effective strategy compared with antimuscarinics from a UK NHS perspective.

PUK23

COST-MINIMIZATION ANALYSIS OF FERUMOXYTOL IN THE MANAGEMENT OF ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE IN BELGIUM

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OBJECTIVES: Intravenous (IV) irons are second line treatments for iron deficiencies in severe chronic kidney disease (CKD) patients with iron deficiency anaemia. Aim of this study was to compare ferumoxytol, a new agent, against IV ferric carboxymaltose (FC) and IV iron sucrose (IS), from a Belgian health care payer (BP) and hospital perspective (HP). **METHODS:** The CKD patients were categorized in haemodialysis (HD), peritoneal dialysis (PD), non-dialysis (post-renal transplant and non-dialysis) and all patients combined. The available IV irons have a similar efficacy. Adverse events were not included due to missing comparative data and low rates. However, the administration time and number of administrations differ among treatments. So a cost-minimization analysis was conducted (time horizon: 1 year). The average annual need of IV Iron is 3,500 mg in HD, 2,500 mg in PD and 1,500 mg in non-dialysis patients. The hospital perspective was modelled by deducting the nurse time cost from the hospital fee per administration (HP). For the health care payer the administration cost (hospital fee) and the drug costs are included (BP). Other costs were excluded because they did not affect the incremental cost of treatment. **RESULTS:** The total cost (euro 2012) for all patients was € 676.57, € 819.82 and € 617.34 for ferumoxytol, FC and IS, respectively (BP). In the renal transplant and non-dialysis subgroups, ferumoxytol is less costly than FC and IS (BP). In the HD subgroup (86.77% of all eligible patients), IS is the least costly option (BP). The hospital cost in all patients is higher with IS due to more nurse time (€ 101.31, € 7.58 and € 144.19 for ferumoxytol, FC and IS) (HP). **CONCLUSIONS:** Hospitals benefit from lower administration costs with ferumoxytol and FC (HP). From a Belgian payer perspective, ferumoxytol is less costly than FC and more costly than IS.

PUK24

HEALTH CARE RESOURCE UTILIZATION COSTS RELATED TO ANAEMIA MANAGEMENT IN CHRONIC KIDNEY DISEASE NON-DIALYSED PATIENTS: A RETROSPECTIVE CLINICAL AND ADMINISTRATIVE DATABASE ANALYSIS

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OBJECTIVES: Anaemia is a frequent complication among patients with Chronic Kidney Disease (CKD) and is associated with poor outcomes. European data on the patterns of treatment of anaemia in non-dialysed (ND) CKD patients are scarce. The aim of this study was to describe the anaemia-associated Health Resource Utilization (HRU) in an Italian cohort of ND-CKD patients. **METHODS:** The administrative data and clinical laboratory files of 5 Italian Local Health Units from 2006 to 2011 were used to identify ND patients with CKD (stage3b, 4, 5) and anemia. Anaemia-related HRU and associated costs were investigated. **RESULTS:** A total of 1175 patients were included; 790 in CKD stage 3b; 331 in stage 4; 54 in stage 5. Anaemia-related medications were prescribed to 31.9% of patients and the percentage increased along the CKD stages from 28.9% for stage 3b to 42.6% for stage 5. Among the drug-treated patients Erythropoiesis-stimulating agents were prescribed to 82.6% of CKD stage 5 patients whereas CKD stage 3b patients received mostly oral iron (59.6%). Patients receiving any anaemia-related medications had lower per patient-per year cost for almost all studied resources compared to patients not receiving any medications. For anaemia-related outpatient services [drug-treated and not drug-treated]: stage 3b costs per patient year were €62.12 and €62.32 respectively; stage 4 costs were €52.23 and €72.76; stage 5 costs were €55.83 and €83.08. For general visits: stage 3b costs were €168.51 and €170.28; stage 4 costs were €124.17 and €173.79; stage 5 costs were €134.49 and €343.63. For CV hospitalizations: stage 3b costs were €1378.63 and €1828.60; stage 4 costs were €1185.17 and €2155.82; stage 5 costs were €521.61 and €514.63. **CONCLUSIONS:** Among ND CKD patients drug treatment may help control anaemia-related outpatient services and contain CV hospitalization costs and represents an opportunity for health care improvement.

URINARY/KIDNEY DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PUK25

IMPLICATIONS OF NON-ADHERENCE TO PHOSPHATE BINDERS ON PATIENTS' PHOSPHATE LEVELS

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OBJECTIVES: Elevated serum phosphate (hyperphosphataemia) usually accompanies end-stage renal disease and results from the inability of damaged kidneys to effectively regulate phosphate levels. Failure to maintain adequate phosphate balance has important clinical consequences, with an increased morbidity and risk of mortality. When dietary phosphate restriction is inadequate for control, administration of phosphate binders may be required. A number of phosphate binders are currently available; however, these often require high doses to control serum phosphate levels and this may result in lowered patient compliance. The objectives of this research were to assess the pill burden associated with phosphate binders and highlight any links between pill burden, patient adherence and outcomes in terms of serum phosphate levels. **METHODS:** A literature review was performed using the PubMed database using the search term "phosphate binders AND adherence". Twenty six articles were identified in total, with ten relevant articles. **RESULTS:** Six of the ten relevant articles (60%) found that low patient adherence or high pill burden were associated with higher mean serum phosphate level, whereas only one article (10%) concluded that no link existed. Seven articles reported dose increases with phosphate binder treatment or an increased number of pills per patient per day over the treatment course, with two reporting that the actual dose of phosphate binders in clinical practice was higher than those recommended in clinical guidelines. A high pill burden was found to lead to low adherence by three of the articles identified (30%), whereas only one of the papers identified did not support this hypothesis (10%). **CONCLUSIONS:** This research indicates that there is a high pill burden associated with phosphate binders, as well as a requirement in clinical practice for high dosages. There is a suggestion that these factors are linked to low patient adherence and poorer control of serum phosphate levels.

PUK26

IMPACT OF MAJOR CLINICAL EVENTS ON UTILITIES IN THE CONTEXT OF SECONDARY HYPERPARATHYROIDISM (SHPT) AND CHRONIC KIDNEY DISEASE (CKD) TREATED WITH DIALYSIS

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OBJECTIVES: Health economic evaluations of therapeutic interventions in patients with CKD and SHPT requiring dialysis (CKD-SHPT) should incorporate the impact of major clinical events related to their disease. However, little is known about the disutility (i.e, utility decrease) associated with cardiovascular (CV) and fracture events in the context of CKD-SHPT. The purpose of this study was to estimate, via preference-based valuation completed by general population respondents, the added disutility of these events beyond the impact of CKD-SHPT. **METHODS:** One-year health states were developed describing CKD-SHPT and related CV/fracture acute events/procedures. Events with long-term effects (post one year) were also captured in chronic health states. General population participants in Canada completed time trade-off (TTO) interviews to assess health state utilities. Respondents initially rated the CKD-SHPT health state. Then, events and procedures were added to this health state: myocardial infarction (MI); unstable angina (UA); heart failure exacerbation; peripheral vascular disease (PVD) ± amputation; stable angina (SA); stroke; hip/arm fractures; parathyroidectomy; kidney transplant. Each participant was randomly-assigned 11 of 16 health states to rate. **RESULTS:** A total of 199 participants (54.8% female; mean age = 46.3 years) completed interviews. Each health state had ≥130 valuations. CKD-SHPT had a mean utility of 0.60 (SD=0.34). For acute events, mean utility decrements additional to CKD-SHPT were: MI, -0.06; UA, -0.05; PVD with amputation, -0.33; PVD without amputation, -0.11; heart failure, -0.14; stroke -0.30; hip fracture, -0.14; arm fracture, -0.04; parathyroidectomy, +0.02; kidney transplant, +0.06. Disutilities for chronic effects were: SA, -0.09; stroke -0.27; PVD with amputation -0.30; PVD without amputation, -0.12; heart failure, -0.14. **CONCLUSIONS:** Valuation of health states representing CKD-SHPT plus major clinical events was feasible using TTO with a one-year time horizon. These data will assist investigators in applying appropriate disutilities to clinical events in economic evaluations of treatments for patients with CKD-SHPT requiring dialysis.

PUK27

THE IMPACT OF SACRAL NEUROMODULATION ON EQ-5D INDEX SCORES AND COSTS TO MANAGE OVERACTIVE BLADDER

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OBJECTIVES: To determine the impact of sacral neuromodulation (SNM) on EQ-5D index scores and OAB management costs using an Economic Impact Questionnaire (EIQ) in patients who failed at least one anticholinergic medication enrolled in the InSite study, an ongoing, prospective, multicenter trial of SNM. **METHODS:** EQ-5D and EIQ were administered at baseline, 3-, 6- and 12-months post-implant. OAB-related expenses included durable and disposable medical supplies and health service utilization (emergency room, hospitalizations and outpatient). A total of 340

patients completed the SNM pre-implant evaluation; data from 265 subjects were included in EQ-5D or EIQ analyses. Matched paired t-tests compared EQ-5D scores and costs from baseline to each follow-up. **RESULTS:** Baseline mean EQ-5D index score (n=265) was 0.777. Index scores significantly improved (p<0.05) from baseline at each follow-up period [3-months (n=247)=0.850, 6-months (n=246)=0.828, and 12-months (n=232)=0.839]; the largest improvement in scores (0.073) was at 3 months. The proportion of patients reporting no problems on the EQ-5D dimensions of Usual Activities, Anxiety/Depression and Pain/Discomfort and Self-Care increased from 61.2% (baseline) to 72.0% (12 months); 57.3% to 69.4%; 40.9% to 50.9%, and 93.1% to 95.3%, respectively; the Mobility dimension had a non-significant decline (68.5% to 66.4%). At baseline, study subjects reported a 3-month average expenditure of $228 (US) for durable and disposable medical supplies and health service utilization; 74% of the expenditure was attributed to ER, hospitalization and outpatient health services use. Expenditures significantly declined (p<0.05) by an average of $163 per 3-month period post-implant. **CONCLUSIONS:** After receiving SNM implant, EQ-5D index scores were significantly improved and self-reported durable and disposable medical supplies and health service expenses to manage OAB were significantly reduced.

PUK28

THE MINIMAL IMPORTANT DECREASE OF HEALTH UTILITY IN LIVING KIDNEY DONORS

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OBJECTIVES: 1) To determine what is the utility change for kidney donors from before to 3 months after donation; 2) To determine the minimal important difference (MID) of a decrease (MIDe) in utility for kidney donors. **METHODS:** We used data from a prospective multicenter observational study, measuring the Health Related Quality of Life (HRQoL) of kidney donors before and three months after transplantation. Utility scores were estimated using the SF-6D and EQ5D. Two methods were used to estimate the MIDe: i) the anchor-based method by the Global Rating of Change (GRoC) for donors rating their global health "somewhat worse" 3 months after donation; ii) the distribution-based method by the standard error of measurement (SEM). **RESULTS:** In total, 211 donors for the EQ-5D and 192 for the SF-6D completed the questionnaire. Results showed a significant (p<.0001) decrease in utility score at three months. The mean (SD) utility score before transplantation was 0.932 (±0.091) with the EQ5D, and 0.834 (±0.085) using the SF-6D, and 0.882 (±0.151) and 0.757 (±0.118) respectively at three months with a significant decrease (<.0001). Half of donors (53.9%) rated their global health "about the same" and 35 (15.4%) "somewhat worse" at follow up. Using the GRoC method, the MIDe was -0.113 units for the EQ-5D and -0.128 units for the SF-6D. By the SEM method, MIDe was -0.076 for the EQ5D and -0.073 for the SF6D. More than third of patient rechead the MIDe using the SEM method. **CONCLUSIONS:** This study showed a significant descrease in utility score three months after donation in most donors while reporting their global health "about the same". The MIDe can be used by clinician as a threshold to identify donors with a meaningful decrease in utility score in a short run after donation.

PUK29

FREQUENCY OF LOWER URINARY TRACT SYMPTOMS IN MEN AND WOMEN IN HUNGARY – RESULTS OF AN OPEN LABEL QUESTIONNAIRE STUDY FROM 2012

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OBJECTIVES: Urinary incontinence (UI) is a public health issue with a considerable social and economic impact. It affects temporarily or permanently about 400 000-500 000 adults in Hungary. The purpose of our study was to estimate the prevalence, consultation rates and treatment behaviour of the adult population. **METHODS:** In 2012 a 15-item questionnaire survey was performed as a part of a mobile health unit screening "The comprehensive health test program of Hungary 2010-2020". **RESULTS:** Altogether 13 355 respondents (60.4% female) completed the questionnaire, the mean age was 40.2 years (SD 12.2). The prevalence rate of UI was 9.7% (n=786) of women and 3.8% (n=200) of men. Consultation rates were 22.9% (n=180) for women and 32.5% (n=65) for men. Seventy-three women (40.6%) consulted a gynaecologist, 37 (20.5%) a GP, 46 (25.6%) an urologist and 24 (13.3%) consulted more than one physicians. Five men (7.7%) consulted a GP, 44 (67.7%) an urologist and 16 (24.6%) didn't answer. Among those who consulted a physician 52.2% (n=94) of women and 66.2% (n=43) of men found solution for their urinary symptoms. In the group of respondents who consulted a doctor (n=245) the most common therapies were medications, surgical treatment, absorbent pads or any combination of the foregoing. In the group who self-managed their symptoms without consulting a doctor (n=741) absorbent products and/or pelvic muscle training were the most frequently applied therapies. **CONCLUSIONS:** Our prevalence results are in line with the international UI screenings. We found low medical consulting rates and the majority of the respondents having symptoms used self-management techniques for UI.

PUK30

ELICITATION OF HEALTH-RELATED QUALITY OF LIFE CONCEPTS ASSOCIATED WITH OVERACTIVE BLADDER

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OBJECTIVES: To review and identify HRQL dimensions in dry and wet OAB patients through literature review and patient interviews. **METHODS:** A literature review on OAB HRQL was performed using the EMBASE database. Specialized forums were also searched for relevant HRQL issues reported by OAB patients. A trained psychologist conducted semi-structured individual interviews with 2 clinical experts and 30 patients in the UK recruited through general practitioners. Clinical experts were asked to identify key concepts attributable to the overactive bladder (symptoms). Patients were asked to describe their symptoms and impact on HRQL and rate them. All patient responses were coded using code frequency and bother ratings. **RESULTS:** Seven men, 23 women were interviewed; the majority of patients were older than 65 years. 50% of the patients were incontinent. Preliminary analysis suggests that OAB affects the patient's quality of life on several aspect of their life: psychological (embarrassment and worry), occupational limitations, domestic (usual activities) and limitations in leisure activities. All patients reported that feeling the need to go "too often" to the bathroom (urgency and frequency) led to significant limitations such as avoidance of any unplanned activities. HRQL concepts were similar across the different age group. As expected, patients suffering from urgency incontinence reported this symptom as being the most impactful, especially in terms of embarrassment and worry. **CONCLUSIONS:** Although the impact of all OAB symptoms was found to be significant and similar across all patients regardless of their age, the greatest impact or burden of OAB was felt and reported by wet patients compared to dry patients.

PUK31

HEALTH RELATED QUALITY OF LIFE OF PATIENTS WITH BLADDER CANCER IN HUNGARY

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OBJECTIVES: Bladder cancer (BC) is the fourth most common malignancies among men and it has high medical costs per-patient from diagnosis until death. Generally little is known about the burden BC imposes on patients' health-related quality of life (HRQL) and the literature lacks detailed utility data for economic evaluations in BC. The authors' goal was to assess the HRQL and health status utility of BC patients. **METHODS:** A cross sectional survey was performed in three hospital based urology centres. Adult patients with BC attending routine care were invited to participate in the study. Data on demographics, disease history and co-morbidities were obtained, validated versions of the EQ-5D and SF-36 generic questionnaires were applied. The UK tarrifs were used to calculate EQ-5D score and the SF-36 was converted to SF-6D utilities. Disease-specific HRQL was assessed by the FACT-BL questionnaire. **RESULTS:** Altogether 98 patients (males 63.3%) were involved with mean age of 66.4 (SD=8.6) and disease duration of 3.4 (SD=3.0) years. The SF-36 physical and mental health summary measures were 62 (SD=24), 65 (SD=24), respectively, the scores of the 8 domains were comparable to the >65 years old general population's results. The average SF-6D, EQ-5D and EQ VAS utility scores were 0.705 (SD=0.145), 0.772 (SD=0.252) and 68.8 (SD=19.0). The difference of EQ-5D score compared to the age-matched population norm was not significant (p=0.65). The FACT-BL physical, social, emotional and functional well-being scores were mean 23.1 (SD=5.4), 20.6 (SD=5.7), 18.1 (SD=5.1) and 19.0 (SD=6.7), the total score was 114.0 (SD=23.5). **CONCLUSIONS:** According to our knowledge this study is the first to assess BC patients' HRQL using diverse preference based measures. Further studies involving larger samples might increase our knowledge on the performance of these questionnaires in BC subgroups by disease stage, type of treatment and urinary diversion.

PUK32

THE BURDEN OF UNTREATED PATIENTS EXPERIENCING SYMPTOMS OF OVERACTIVE BLADDER

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OBJECTIVES: The reluctance of those with overactive bladder OAB to seek medical advice can leave a considerable part of the population untreated, with significant costs for society. The present study investigates the burden of individuals who experience symptoms of OAB but are not treated. **METHODS:** Data were taken from the 5EU (France, Germany, Italy, Spain, and UK) 2013 National Health and Wellness Survey (NHWS), a cross-sectional survey representative of the total adult populations in each 5EU market. 62,000 respondents self-reported physician diagnosis of various health conditions, including 1,347 who reported symptoms compatible with OAB. These respondents were compared to those who didn't report symptoms of OAB. Variables of interest were demographics (age, gender, marital status, education, income and employment status), BMI, alcohol and smoke behaviour, health-related quality of life (HR-QoL), work productivity and activity impairment (WPAI). **RESULTS:** The OAB group, compared to the controls, was older (57 vs. 47 years), with a lower education level (49.14% went to college vs. 54.49%), less were in a relationship (26.43% vs. 31.82%), less were employed (35.04% vs. 58.15%), more were obese (31.11% vs. 17.22%), they had lower HR-QoL (SF-36v2, PCS: 42.09 vs. 51.36; MCS: 42.55 vs. 46.25; Utility: 0.62 vs. 0.73), had lower work productivity (overall work impairment of 34.46 vs. 20.03) and higher activity impairment (46.07 vs. 24.35). All differences were significant (p<0.001). **CONCLUSIONS:** Respondents reporting symptoms compatible with OAB but are not treated and would not be captured by clinical studies, are significantly worse-off than the rest of the population, e.g. in their quality of life, income and work productivity. It is likely that undergoing treatment would benefit them and decrease health care costs.

URINARY/KIDNEY DISORDERS – Health Care Use & Policy Studies

PUK33

ANTIBIOTIC UTILIZATION IN COMPLICATED URINARY TRACT INFECTION IN A TERTIARY CARE TEACHING HOSPITAL IN SOUTH INDIA

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OBJECTIVES: To identify and analyze the sensitivity pattern of microorganisms isolated and to study the antibiotic utilization pattern in complicated urinary tract infection (cUTI) and the outcome of the therapy. **METHODS:** Retrospective, observational study conducted in the medicine units of a tertiary care teaching hospital from January 2011 to December 2011. Patients who met the inclusion criteria were include in the study and patient details like demography, clinical diagnosis, microbiological data, antibiotic regimen used and patient outcome were recorded from the medical records. Data were analyzed using SPSS 20.0 **RESULTS:** Out of 297 patients included in the study, majority of them were in the age group of 48-59 years. ESBL E. coli (61.4%) was the most common causative microorganism isolated, followed by *E.coli* (23.9%). The antibiotic sensitivity profile of microorganisms causing cUTI showed that E coli was sensitive to majority of the antibiotics and ESBL producing *E. coli* was most sensitive to cefoperazone-sulbactum followed by amikacin and carbapenems. Dual drug regimen was the most preferred choice for the treatment of cUTI compared to single or triple or more drug regimens. Among the different category of antibiotics used, cephalosporins was the most commonly prescribed while macrolides were the least preferred antibiotics. **CONCLUSIONS:** The treatment of ESBL E. coli with dual drug regimen showed maximum improvement in outcome (97.2%) followed by single drug regimen (89.7%). The organisms isolated were found to be more sensitive to cephalosporins, amikacin and carbapenems. Cephalosporins were the most effective antibiotic for the treatment of cUTI. The broader outcome of this study would be the potential utility of this data in designing strategies both at the level of physicians and the administrators for rational prescribing and policy decisions respectively.

PUK34

DIFFERENCE IN INTERDIALYTIC INTERVALS LEADING TO HOSPITAL ADMISSION AND MORTALITY IN HEMODIALYSIS PATIENTS

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OBJECTIVES: To determine the importance of long and short interdialytic interval leading to hospital readmission and mortality in hemodialysis patients. **METHODS:** Reviewed data of 240 patients with 182 male and 58 female patients receiving maintenance hemodialysis (HD) twice weekly on a Mon/Thu, Tue/Fri, Wed/Sat schedule with prevalent adult's HD patients on period from 2010 through2012. Eligible patients were actively recruited who were on chronic HD fulfilling the inclusion criteria. Analyzed the patients getting frequent hospitalized for Infectious and cardiovascular (CV) admissions were determined by principal ICD-9-CM diagnosis codes. **RESULTS:** A total of 240 patients with End-stage renal disease (ESRD) on long term hemodialysis were included the study cohort. The mean age was 50.4±13.6 years; 24.2% were women with a mean year of patients on hemodialysis of 4.2±2.6. Hypertension was the leading cause of end-stage renal disease in 28.8% of the patients, 27.1% of patients with hypertension and diabetes, 12% with diabetes and rest were due to Glomerulonephritis, *Interstitial nephritis*, Cystic kidney disease. Over the study period, mortality was 39.6% (95) , Cardiac cause 19.2 (46) were high on the day after 3 day interdialytic interval (31 death vs. 15), Vascular cause 2.5% (6), Infection 7.5% (18), other cause 10.4% (25) and readmission was more both on the day after long interdialytic interval and day after short interdialytic interval for IHD, stroke, infection. **CONCLUSIONS:** Interdialytic interval does not influence mortality and readmission rates for all cause cardiovascular and infectious causes.

PUK35

TIME SAVINGS WITH ONCE-MONTHLY C.E.R.A.: A TIME AND MOTION STUDY CONDUCTED IN 13 HEMODIALYSIS CENTRES IN ITALY

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OBJECTIVES: A major challenge for haemodialysis (HD) centres is to maximise efficiency in care provision while maintaining high standards of care. Our objective was to document health care professional (HCP) time for renal anaemia management for both shorter-acting erythropoiesis-stimulating agents (ESA) and Mircera, a continuous erythropoiesis receptor activator (C.E.R.A.) once monthly (Q4W), and model time savings with the use of Q4W C.E.R.A. **METHODS:** This descriptive multi-centre Time and Motion (T&M) study was conducted in 13 centres in Italy. The time spent on frequent anaemia management-related tasks (preparation, distribution, and injection) was recorded for both ESA and C.E.R.A. groups in each centre by trained observers. Time/patient/session was used to calculate time/patient/year, time/centre/year and modelling of potential time savings of a 100% uptake of C.E.R.A. A Random intercept generalized linear mixed effect model assuming gamma distribution with log link function to account for the centre clustering effect was fitted for each task separately. **RESULTS:** In all centres, more than 80% of an average 86 ESRD patients received ESA treatment. The average number of ESA injections/patient/year, weighted by type of ESA, frequency and route of administration, was 89 (range: 33-150). The average uptake of C.E.R.A. was 26% (range 11-41%). The mean annual reduction in the number of ESA administrations following conversion to C.E.R.A. was 77 (21-138). Average time per patient HD session was 1.54 minutes for ESA (95% CI: 1.17-1.90) vs. 1.64 minutes for C.E.R.A. (95% CI: 1.57-2.02). Estimated time/patient/year was 137 min (range: 65-277) for ESA and 20 min for C.E.R.A. (range: 5-51). Assuming a 100% uptake of Q4W C.E.R.A. maintenance therapy, annual time savings/centre for frequent anaemia management tasks would be 86% (range: 62-95%). **CONCLUSIONS:** Substantial annual time savings on frequent anaemia management-related tasks were found in HD centres in Italy with 100% uptake of Q4W C.E.R.A. maintenance therapy.

PUK36

EVALUATION OF A PROCESS OF CARE MODEL FOR OPEN INTRAVESICAL URETERAL REIMPLANTATION FROM A CONTEMPORARY HEALTH CARE PERSPECTIVE

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OBJECTIVES: The surgical management of vesicoureteral reflux consists of open and minimally invasive approaches. Open approaches are associated with post-operative hospitalization rates of stay typically 2 to 3 days, varying with the type of procedure. We evaluated the impact of a "one night cost-saving stay process of care" model for open surgical correction of vesicoureteral reflux on quality of care, as defined by return to emergency room or office and/or readmission to the hospital within 2 days of discharge. **METHODS:** An IRB-approved chart review of all open uncomplicated ureteral reimplantations for vesicoureteral reflux from the January 2009 through January 2013 was performed. Length of postoperative stay, emergency room records, hospitalizations and office records were reviewed to assess for presentation to the emergency room/office and/or readmission to the hospital within 2 days of discharge from the ureteral reimplantation. **RESULTS:** Ninety-five children (17 males, 78 females) underwent open ureteral reimplantation. Eighty-four (88.4%) were discharged POD #1 , 8 (8.4%) on POD #2 and 3 (3.2%) on the POD #3. Two patients presented to the ER within 2 days of discharge, one in the one night stay group and one in the three night stay group. No child required readmission within 2 days of discharge. Transient ureteral obstruction requiring stent placement occurred in 1 patient (1.05%) 3 days after discharge. Presentation to the ER > 2 days post-discharge was more frequent in those discharged from home POD #1. **CONCLUSIONS:** A process of care model decreased the length of stay to one night in 84 of the 95 patients (88.4%) and did not appear to increase the risk of early (within 2 days of discharge) presentation to the ER/office or readmission. ER/office presentations > 2 days after discharge were increased in the POD #1 group.

RESEARCH POSTER PRESENTATIONS – SESSION I

DISEASE-SPECIFIC STUDIES
Individual's Health – Cost Studies

PIH16

COSTS OF MANAGEMENT OF PREGNANCY IN OBESE WOMEN ACROSS EUROPE: THE DALI EXPERIENCE

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OBJECTIVES: To assess resource use and costs in the usual clinical management of pregnant obese women, considered at high risk for developing GDM. **METHODS:** Information was collected in the framework of the DALI project by means of a structured survey about usual clinical practice in the management of obese women from week 12 of pregnancy until delivery and a second survey about unit costs of related tests and interventions including analytics, imaging tests, follow-up visits and delivery. 9 centers in 8 EU countries were included (Austria, Belgium, Denmark, Ireland, Italy, The Netherlands, Spain, UK) Unit costs were inflated, using consumer price index when needed to 2012 prices and exchanged to US$ using power purchase parities. **RESULTS:** According to the reported data, resource utilization according to usual practice in management of obese women differed across countries: number of ultrasound scans ranged 2-6, OGTT 0-3, obstetrician visits 2-10, GP visits 0-6, nurse/midwife visits 0-12. Follow-up involved different professionals depending on the country (GPs, obstetricians, nurses, midwives, diabetes educators and endocrinologists). Mean costs were 4,624 US$ (SD 2,034), ranging from 2,571 US$ in Belgium to 7,682 US$ in Denmark. The main drivers for costs were delivery, health care professionals' follow-up visits and ultrasound scans. When delivery costs were excluded mean costs dropped to 722 US$ (SD 226), ranging from 340 US$ in the UK to 1052 US$ in Spain. **CONCLUSIONS:** A high heterogeneity in the management of obese women during pregnancy and in the unitary costs reported, are observed among the centers included in the study, associated with a threefold difference in costs across hospitals.

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RESEARCH PRESENTATIONS FINANCIAL DISCLOSURE STATEMENTS

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PCN23	Novartis Pharmaceuticals UK, Camberley, UK
PCN24	Boehringer Ingelheim International, Binger Str. 173, Germany
PCN25	Hungarian Academy of Sciences (HAS) Bolyai János Research Fellowship, Budapest, Hungary; University of Pécs, Faculty of Health Sciences, Pécs, Hungary
PCN26	Hungarian Academy of Sciences (HAS) Bolyai János Research Fellowship, Budapest, Hungary; University of Pécs, Faculty of Health Sciences, Pécs, Hungary
PCN27	National Cancer Institute - Cancer Health Disparities Training Program (Grant # 5T32CA128582-043), Bethesda, MD, USA
PCN28	None
PCN29	Boehringer INgelheim, Bingen, Germany
PCN30	Janssen-Cilag Ltd., High Wycombe, UK
PCN31	Janssen-Cilag, Neuss, Germany
PCN32	None
PCN33	Sanofi, Cambridge, MA, USA; Regeneron, Tarrytown, NY, USA
PCN34	Health Reserach Board, Dublin, Ireland
PCN35	Bristol Myers Squibb, Uxbridge, UK
PCN36	None
PCN37	None
PCN38	Teva, Frazer, PA, USA
PCN39	Amgen, Inc., Thousand Oaks, CA, USA
PCN40	None
PCN41	Sandoz International GmBH, Holzkirchen, Germany
PCN42	Novartis Pharmaceuticals UK Ltd., Surrey, UK
PCN43	Sanofi, Cambridge, MA, USA
PCN44	Basque Government Health Department, Vitoria-Gasteiz, Spain
PCN45	Bayer Healthcare Pharmaceuticals, Wayne, NJ, USA
PCN46	Roche Pharmaceuticals, São Paulo, Brazil
PCN47	None
PCN48	TEVA PHARMA, MADRID, Spain
PCN49	Amgen, Inc., Thousand Oaks, CA, USA
PCN50	F. Hoffmann - La Roche Ltd.., Basle, Switzerland
PCN51	Takeda, Moscow, Russia
PCN52	Teva Europe, Utrecht, The Netherlands
PCN54	F. Hoffmann - La Roche AG, Basel, Switzerland
PCN55	National Cancer Institute (INCa) , Boulogne Billancourt, France
PCN56	Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
PCN57	TEVA Pharma, Madrid, Spain
PCN58	Bristol-Myers Squibb, Bogotá, Colombia
PCN59	None
PCN60	Novartis Pharmaceuticals Canada Inc., Dorval, QC, Canada
PCN61	Bristol-Myers Squibb de México, Mexico City, Mexico
PCN62	NIH, Bethesda, MD, USA
PCN63	Bristol-Myers Squibb, Princeton, NJ, USA
PCN64	Janssen-Cilag Farmaceutica, Sao Paulo, Brazil
PCN65	None
PCN66	None
PCN67	LEO-PHARMA HELLAS, Athens, Greece
PCN68	None
PCN69	Pfizer, Berlin, Germany
PCN70	None
PCN71	None
PCN72	Novartis, SP, Brazil
PCN73	Merck Sharp Dohme, Istanbul, Turkey
PCN74	Novartis, São Paulo, Brazil
PCN75	GSK, Marly le Roi, France
PCN77	Amgen, Zug, Switzerland
PCN78	Amgen (Europe) GmbH, Zug, Switzerland
PCN79	Amgen, Inc, Thousand Oaks, CA, USA
PCN80	Sanofi Pasteur MSD, Maidenhead, UK
PCN81	Amgen Inc, Thousand Oaks, CA, USA
PCN82	The German Federal Ministry of Education and Research (BMBF), Berlin, Germany
PCN83	None
PCN84	AMGEN S.A.S, Neuilly sur Seine, France
PCN85	Ministry of Health, Prague, Czech Republic
PCN86	Janssen-Cilag Farmaceutica, São Paulo, Brazil
PCN87	ÖGHO Austrian Society of Haematology and Oncology, Vienna, Austria
PCN88	Fresenius Biotech GmbH, Munich, Germany
PCN89	Zilico Ltd., Manchester, UK
PCN90	Sanofi Pasteur MSD, Madrid, Spain
PCN91	Sanofi Pasteur MSD, Madrid, Spain
PCN92	PHAROS REGISTRY, Amsterdam, The Netherlands
PCN93	Endo Pharmaceutical, Philadelphia, PA, USA
PCN94	Janssen, Mexico City, Mexico
PCN95	Ipsen Pharma SAS, Boulogne-Billancourt, France
PCN96	COMET Center ONCOTYROL, Innsbruck, Austria
PCN97	None
PCN98	Sirtex Medical Ltd., North Sydney, Australia
PCN99	Janssen, Mexico City, Mexico
PCN100	Janssen Pharmaceutica N.V., Beerse, Belgium
PCN101	Eli Lilly and Company, Windlesham, Surrey, UK
PCN102	Bayer Pharma AG, Montville, NJ, USA
PCN103	Roche Molecular Diagnostics, Pleasanton, CA, USA
PCN104	None
PCN105	None
PCN106	COMET Center ONCOTYROL, Innsbruck, Austria
PCN107	University of Sheffield, Sheffield, UK
PCN108	Janssen Global Services, Raritan, NJ, USA
PCN109	None
PCN110	Janssen, Mexico City, Mexico
PCN111	Pfizer, Bucharest, Romania
PCN112	F. Hoffmann - La Roche Ltd.., Basle, Switzerland
PCN113	None

Reference Code	Financial Support
PCN114	Cancer Research UK, London, UK
PCN115	None
PCN116	None
PCN117	Sirtex Medical Ltd., North Sydney, Australia
PCN118	None
PCN119	Janssen, Mexico City, Mexico
PCN120	Sanofi Aventis Ilaclari Ltd..Sti., Istanbul, Turkey
PCN121	NIHR HTA, Southampton, UK
PCN122	None
PCN123	AstraZeneca Nordic-Baltic, Södertälje, Sweden
PCN124	Cancer Research UK, London, UK
PCN125	CTMM, Eindhoven, The Netherlands
PCN126	National Institute for Health Research (NIHR), London, UK
PCN127	Given Imaging K.K., Tokyo, Japan
PCN128	F. Hoffmann-La Roche Ltd., Basel, Switzerland
PCN129	GAZPROM Germania GmbH, Berlin, Germany
PCN130	Ewopharma AG Representative Office, Budapest, Hungary
PCN131	Napp Pharmaceuticals Limited, Cambridge, UK
PCN132	Amgen BV, Breda, The Netherlands
PCN133	None
PCN134	National Evidence-based Collaboration Agency, Seoul, South Korea
PCN135	None
PCN136	GAZPROM Germania GmbH, Berlin, Germany
PCN137	Novartis Pharmaceuticals UK Ltd., Surrey, UK
PCN138	None
PCN139	Ferrer Internacional, Barcelona, Spain
PCN140	Center for Translational Molecular Medicine, Eindhoven, The Netherlands
PCN141	Federal Ministry for Education and Research, support code: 01KQ0902V, Berlin, Germany
PCN142	None
PCN143	Amgen, Inc, Thousand Oaks, CA, USA
PCN144	None
PCN145	Roche (HK) Ltd., Hong Kong, Hong Kong
PCN146	Health Research Board, Dublin, Ireland
PCN147	Roche Farmacêutica Quimica, Amadora, Portugal
PCN148	Boehringer Ingelheim, Bratislava, Slovak Republic
PCN149	Bayer, Pine Brook, NJ, USA
PCN150	None
PCN151	Boehringer Ingelheim France, Paris, France
PCN152	Millennium: The Takeda Oncology Company, Cambridge, MA, USA
PCN153	Bayer HealthCare, Montville, NJ, USA
PCN154	Irish Cancer Society, Dublin, Ireland
PCN155	GlaxoSmithKline, Uxbridge, UK
PCN156	The University of Hong Kong, Hong Kong, Hong Kong; Food and Health Bureau, Hong Kong Government, Hong Kong, Hong Kong
PCN157	Sanofi, Cambridge, MA, USA
PCN158	None
PCN159	Amgen Inc., Thousand Oaks, CA, USA
PCN160	None
PCN161	None
PCN162	None
PCN163	None
PCN164	None
PCN165	None
PCN166	Convatec Polska Sp. z o.o., Warsaw, Poland
PCN167	ISCIII, Madrid, Spain; Kronikgune, Bilbao, Spain
PCN168	None
PCN169	Amgen (Europe) GmbH, Zug, Switzerland
PCN170	Bristol-Myers Squibb, Rueil-Malmaison, France
PCN171	GAZPROM Germania GmbH, Berlin, Germany
PCN172	None
PCN173	None
PCN174	Truven Health Analytics, Ann Arbor, MI, USA
PCN175	None
PCN176	GfK Bridgehead, Melton Mowbray, UK
PCN177	COMET Center ONCOTYROL, Innsbruck, Austria
PCN178	Pfizer, New York, NY, USA
PCN179	None
PCN180	European Union, Brussels, Belgium
PCN181	None
PCN182	German Ministry of Research and Education, Berlin, Germany
PCN183	None
PCN184	Janssen, São Paulo, Brazil
PCN185	GLAXOSMITHKLINE, MARLY LE ROI, France
PCN186	None
PCN187	Janssen, São Paulo, Brazil
PCN188	GLAXOSMITHKLINE, MARLY LE ROI, France
PCN189	CTMM DeCoDe, Eindhoven, The Netherlands
PCN190	Ontario Institute for Cancer Research/Cancer Care Ontario, Toronto, ON, Canada
PCN191	None
PCN192	Public Health Research Consortium, London, UK
PCN194	None
PCN195	Dutch Cancer Society, Amsterdam, The Netherlands; Dutch Research Council, The Hague, The Netherlands; GlaxoSmithKline, Zeist, The Netherlands
PCN196	None
PCN197	Sandoz International GmBH, Holzkirchen, Germany
PCN198	Celgene, Summit, NJ, USA
PCN199	None
PCN200	None
PCN201	Sanofi U.S. LLC, Bridgewater, NJ, USA
PCN202	None
PCN203	None
PCN204	None
PCN205	Context Matters Inc., New York, NY, USA
PCN206	Agency for Health Technology Assessment in Poland (AHTAPol), Warsaw, Poland
PCN207	Costello Medical Consulting, Cambridge, UK
PCN208	None
PCN209	NIHR, Leeds, UK
PCN210	None
PCN211	None
PCN214	Pfizer Deutschland GmbH, Berlin, Germany
PCN215	None
PCN216	Ontario Institute for Cancer Research, Toronto, ON, Canada
PCN217	Roche, São Paulo, Brazil
PCN218	Amgen (Europe) GmbH, Zug, Switzerland
PCN219	Amgen Inc., Thousand Oaks, CA, USA
PCN220	Amgen Inc., Thousand Oaks, CA, USA
PCN221	None
PCV1	None
PCV2	Pharmaceutical Company, Madrid, Spain
PCV3	Janssen Scientific Affairs, LLC, Raritan, NJ, USA; National Institutes of Health, Bethesda, MD, USA
PCV4	None
PCV5	None
PCV6	AstraZeneca, Wilmington, DE, USA
PCV7	Bayer Pharma AG, Berlin, Germany
PCV8	None
PCV9	Sanofi, Paris, France; Regeneron, Tarrytown, NY, USA
PCV10	None
PCV12	Chinese University of Hong Kong, Hong Kong, Hong Kong
PCV13	Merck, Sharp & Dohme Corp., Whitehouse Station, NJ, USA
PCV14	None
PCV15	Novartis Pharma AG, Basel, Switzerland
PCV16	Pfizer and BMS, New York, NY, USA
PCV17	None
PCV18	None
PCV19	Servier, Belarussian brunch, Minsk, Belarus
PCV20	Health Information and Quality Authority, Dublin, Ireland
PCV21	None
PCV22	Pfizer and BMS, New York, NY, USA
PCV23	Bristol-Myers Squibb, New York, NY, USA; Pfizer Pharmaceutical, New York, NY, USA
PCV24	Bristol-Myers Squibb, New York, NY, USA; Pfizer Ltd., New York, NY, USA
PCV25	Bristol-Myers Squibb, New York, NY, USA; Pfizer Ltd., New York, NY, USA
PCV26	NRF, Pretoria, South Africa
PCV27	None
PCV28	None
PCV29	None
PCV30	LEO PHARMA HELLAS, Athens, Greece
PCV31	Sanofi, Paris, France
PCV32	Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany
PCV33	None
PCV34	FAPESP, Sao Paulo, Brazil
PCV35	EUSA Pharma, Oxford, UK
PCV36	Novartis, Barcelona, Spain
PCV37	None
PCV38	None
PCV40	None
PCV41	Bayer, Milano, Italy
PCV42	Boehringer Ingelheim, Berkshire, UK
PCV43	Boehringer Ingelheim, Berkshire, UK
PCV44	Pfizer Inc., New York, NY, USA
PCV45	Takeda, Moscow, Russia
PCV46	Takeda, Moscow, Russia
PCV48	Boston Scientific Corp, Natick, MA, USA
PCV49	None
PCV50	None
PCV51	Department of Health via NIHR comprehensive Biomedical Research Centre award at Guy's & St Thomas' NHS Foundation, London, UK
PCV52	Department of Health via the NIHR comprehensive Biomedical Research Centre award at Guy's & St Thomas' NHS Foundation Trust, London, UK
PCV53	Boston Scientific, Maple Grove, MN, USA
PCV54	Novartis Farmaceutica S.A., Barcelona, Spain

Reference Code	Financial Support
PCV55	Bayer HealthCare, Wayne, NJ, USA
PCV56	Bayer HealthCare, Wayne, NJ, USA
PCV57	Novartis Pharma AG, Basel, Switzerland
PCV58	Boehringer Ingelheim, Barcelona, Spain
PCV59	The Medicines Company, Parsippany, NJ, USA
PCV60	Amgen, Thousand Oaks, CA, USA
PCV61	Boehringer Ingelheim, Barcelona, Spain
PCV62	None
PCV63	Edwards Lifesciences, Nyon, Switzerland
PCV64	Bristol-Myers Squibb Brazil/Pfizer Brazil, São Paulo, Brazil
PCV65	Novartis Pharma AG, Basel, Switzerland
PCV66	Bristol-Myers Squibb, Madrid, Spain; Pfizer, Madrid, Spain
PCV67	Bristol-Myers Squibb, Rueil-Malmaison, France
PCV68	Research Grant "Fonds Nuts Ohra zorgsubsidies" 0702086, Amsterdam, The Netherlands
PCV69	Bristol-Myers Squibb, Madrid, Spain; Pfizer, Madrid, Spain
PCV70	None
PCV71	SBHCl, São Paulo, Brazil
PCV72	SERVIER HELLAS Pharmaceuticals Ltd., Athens, Greece
PCV73	Bayer Pharma AG, Berlin, Germany
PCV74	Pfizer S.A. de C.V., Mexico City, Mexico; Bristol-Myers Squibb S.A. de C.V., Mexico City, Mexico
PCV75	Pfizer Hellas, Athens, Greece; BMS Hellas, Athens, Greece
PCV76	Boston Scientific, Mascot, Australia; Boston Scientific, Milan, Italy
PCV77	Pfizer Hellas, Athens, Greece; BMS Hellas, Athens, Greece
PCV78	None
PCV79	Boston Scientific, Natick, MA, USA
PCV80	Bayer, Milan, Italy
PCV81	Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany
PCV82	Abbott Laboratories, Allschwil, Switzerland
PCV83	None
PCV84	None
PCV85	Center for Translational Molecular Medicine, Eindhoven, The Netherlands
PCV86	Boehringer Ingelheim Pty Limited, Sydney, Australia
PCV87	None
PCV88	ZonMw, The The Netherlands Organisation for Health Research and Development, The Hague, The Netherlands
PCV89	None
PCV90	NIHR HTA, Southampton, UK
PCV91	Servier Laboratories (Ireland) Ltd. , Dun Laoghaire, Ireland
PCV92	MEDTRONIC INC. , Brussels, Belgium
PCV93	None
PCV94	Research Grants Council, Hong Kong, Hong Kong
PCV95	None
PCV96	KNMP, Den Haag, The Netherlands
PCV97	Servier Poland, Warsaw, Poland
PCV98	None
PCV99	Danish Heart Foundation, Copenhagen, Denmark; Biosense Webster, Diegem, Belgium
PCV100	INFARMED – National Authority of Medicines and Health Products, IP, Lisbon, Portugal
PCV101	UCB, Mexico, Mexico
PCV102	Brstol-Myers Squibb, Dublin, Ireland; Pfizer, Dublin, Ireland
PCV103	Bristol-Myers Squibb, Woerden, The Netherlands; Pfizer bv, Capelle aan den Ijssel, The Netherlands
PCV104	None
PCV105	NIHR HTA, Southampton, UK
PCV106	Sorin Group, Milano, Italy
PCV107	Pfizer China, Beijing, China
PCV108	None
PCV109	None
PCV110	Sorin Group, Milano, Italy
PCV111	None
PCV112	Servier, Belarusian branch, Minsk, Belarus
PCV113	Sorin Group, Milano, Italy
PCV114	None
PCV115	Edwards Lifescience, Newbury, UK
PCV116	European Union's Seventh Framework Programme, Brussels, Belgium
PCV117	None
PCV118	None
PCV119	None
PCV120	None
PCV121	Daiichi Sankyo, Munich, Germany
PCV122	Pfizer Inc, New York, NY, USA
PCV123	Servier Laboratories Ltd., Slough, UK
PCV124	ASTELLAS PHARMA S.A., Madrid, Spain
PCV125	The Israel National Institute for Health Services Research, Tel Hashomer, Israel
PCV126	None
PCV127	None
PCV128	Welsh Assembly Government, Wales, UK
PCV129	AstraZeneca GmbH, Wedel, Germany
PCV130	None
PCV131	Novatis, Seoul, South Korea
PCV132	Medtronic, Meerbusch, Germany; Federal Ministry of Education and Research, Berlin, Germany
PCV133	Pfizer S.L.U, Madrir, Spain
PCV134	ISCIII, Madrid, Spain; Departamento Sanidad. Gobierno Vasco, Vitoria-Gasteiz, Spain; Kronikgune, Bilbao, Spain
PCV135	None
PCV136	None
PCV137	Institute of Cardiology, Warsaw, Poland
PCV138	Boehringer Ingelheim, Barcelona, Spain
PCV140	Daiichi Sankyo, Munich, Germany
PCV141	Novartis Hellas, Athens, Greece
PCV143	Pfizer Deutschland GmbH, Berlin, Germany
PCV144	Bristol-Myers Squibb Brazil/Pfizer Brazil, Sao Paulo, Brazil
PCV145	Laboratorios Esteve, Barcelona, Spain
PCV146	None
PCV147	None
PCV148	None
PCV149	National Association of Pharmacies (ANF), Lisboa, Portugal
PCV150	None
PCV151	University of South Florida, Tampa, FL, USA
PCV152	None
PCV153	LEO Pharma GmbH, Neu-Isenburg, Germany
PCV154	None
PCV155	Bayer HealthCare Pharmaceuticals, Loos, France
PCV156	CADTH, Ottawa, ON, Canada
PCV157	BMS, Lisbon, Portugal
PCV158	Novartis International AG, Basel, Switzerland
PCV159	Eli Lilly & Co, Windlesham, Surrey, UK
PCV160	None
PCV161	Dr. Werner-Jackstaedt Foundation, Wuppertal, Germany
PCV162	Fondazione CARIPLO, Milano, Italy
PCV163	Merck, Sharp & Dohme, Oeiras, Portugal
PCV164	HVB, Vienna, Austria; GÖG, Vienna, Austria
PCV165	Main Association of Austrian Social Security Organisations, Vienna, Austria
PCV166	None
PCV167	None
PCV168	None
PDB1	None
PDB2	Janssen, Copenhaguen, Denmark
PDB3	Novo Nordisk A/S, Søborg, Denmark
PDB4	Bristol-Myers-Squibb, Princeton, NJ, USA
PDB5	Bayer HealthCare, Barcelona, Spain
PDB6	AstraZeneca, Wilmington, DE, USA
PDB7	Bristol-Myers Squibb, Princeton, NJ, USA
PDB8	Bristol-Myers Squibb, Rueil-Malmaison, France; AstraZeneca, Brussels, Belgium
PDB9	Novo Nordisk, Zurich, Switzerland
PDB10	None
PDB11	Novartis Pharma AG, Istanbul, Turkey
PDB12	Janssen, Copenhaguen, Denmark
PDB13	Novartis, Rueil Malmaison, France
PDB14	None
PDB15	Viropharma SPRL, Maidenhead, UK
PDB16	Bristol-Myers Squibb, Rueil-Malmaison, France
PDB17	None
PDB18	None
PDB19	ViroPharma LTD., Maidenhead, UK
PDB20	None
PDB21	European Commission, Brussels, Belgium
PDB22	Eli Lilly and Company, Indianapolis, IN, USA
PDB23	None
PDB24	None
PDB25	Sanofi, Berlin, Germany
PDB26	None
PDB27	Novo-Nordisk, La Defense, France
PDB28	Novartis Hellas, Metamorphosis, Greece
PDB29	Novartis, Athens, Greece
PDB30	Viropharma LTD., Maidenhead, UK
PDB31	Johnson & Johnson, S.A., Madrid, Spain; Sociedad Española de Diabetes, Madrid, Spain; Fundación Andaluza para la I+D, Sevilla, Spain; CIBERDEM, Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas, Barcelona, Spain; Instituto de Salud Carlos III , Madrid, Spain
PDB32	Eli Lilly and Company, Indianapolis, IN, USA
PDB33	None
PDB34	None
PDB35	NovoNordisk, Sofia, Bulgaria
PDB36	None
PDB37	Roche, Mannheim, Germany
PDB38	None
PDB39	Ipsen, Warsaw, Poland
PDB40	Ipsen, Warsaw, Poland
PDB41	Merck, S.L, Madrid, Spain
PDB42	None

Reference Code	Financial Support
PDB43	Novo Nordisk Inc., Plainsboro, NJ, USA
PDB44	Medtronic, Tolochenaz, Switzerland
PDB45	AstraZeneca, Mölndal, Sweden; Bristol Myers Squibb, Princeton, NJ, USA
PDB47	Brsitol-Myers Squibb, Madrid, Spain; Astra-Zeneca, Madrid, Spain; Oblikue Consulting, Barcelona, Spain
PDB48	Johnson&Johnson, LifeScan EMEA, Zug, Switzerland
PDB49	Novo Nordisk, Madrid, Spain
PDB50	Medtronic, Tolochenaz, Switzerland
PDB51	BC Pharma B.V., Moscow, Russia
PDB52	Berlin-Chemie AG/Menarini Group, Moscow, Russia
PDB53	Janssen, High Wycombe, UK
PDB54	Bristol-Myers Squibb , Rueil-Malmaison, France; Bristol-Myers Squibb, Uxbridge, UK; AstraZeneca UK Ltd., Luton, UK
PDB55	Janssen, High Wycombe, UK
PDB56	Bristol-Myers Squibb , Rueil-Malmaison, France; Bristol-Myers Squibb , Uxbridge, UK; AstraZeneca UK Ltd., Luton, UK
PDB57	AstraZeneca and Bristol-Myers Squibb, Zoetermeer/Woerden, The Netherlands
PDB58	Bristol-Myers Squibb , Rueil-Malmaison, France; Bristol-Myers Squibb, Uxbridge, UK; AstraZeneca UK Ltd., Luton, UK
PDB59	Janssen, High Wycombe, UK
PDB60	Janssen, High Wycombe, UK
PDB61	Novo Nordisk Pharma, Warsaw, Poland
PDB62	Novo Nordisk, Copenhaguen, Denmark
PDB63	Abbott Laboratories, Allschwil, Switzerland
PDB64	Novo Nordisk Ltd., Copenhagen, Denmark
PDB65	Novo Nordisk Ltd., Copenhagen, Denmark
PDB66	sa Novo Nordisk Pharma nv, Brussels, Belgium
PDB67	Novo Nordisk, Moscow, Russia
PDB68	Hangzhou MSD Pharmaceutical Company Limited, Hangzhou, China
PDB69	The National Science Centre, Cracow, Poland
PDB70	Sanofi, Lysaker, Norway
PDB71	IMS Health, Basel, Switzerland
PDB72	BC Pharma B.V., Moscow, Russia
PDB73	None
PDB74	None
PDB75	Novo Nordisk A/S, Copenhagen, Denmark
PDB76	Novo Nordisk A/S, Copenhagen, Denmark
PDB77	None
PDB78	None
PDB80	None
PDB81	Novo Nordisk A/S, Søborg, Denmark
PDB82	None
PDB83	Janssen, High Wycombe, UK
PDB84	The National Science Centre, Cracow, Poland
PDB85	None
PDB86	AstraZeneca GmbH, Wedel, Germany; Bristol-Myers Squibb GmbH & Co. KGaA, Munich, Germany
PDB87	Forest Research Institute, Jersey City, NJ, USA
PDB88	NovoNordisk, Moscow, Russia
PDB89	None
PDB90	None
PDB91	None
PDB92	IPSEN, Boulogne Billancourt, France
PDB93	Merck Serono, London, UK
PDB94	Janssen Global Services, LLC, Raritan, NJ, USA
PDB95	Janssen Global Services, LLC, Raritan, NJ, USA
PDB96	None
PDB97	None
PDB98	Medtronic Australasia Pty Ltd., North Ryde, NSW, Australia
PDB100	Bayer, Barcelona, Spain
PDB101	Novo Nordisk International Operations, Zurich, Switzerland
PDB102	Pfizer Inc., New York, NY, USA
PDB103	Novo Nordisk International Operations, Zurich, Switzerland
PDB105	None
PDB106	Boehringer Ingelheim France, PARIS, France
PDB107	Novo Nordisk A/S, Copenhagen, Denmark
PDB108	Ipsen Pharma, Boulogne-Billancourt, France
PDB109	MSD, Hoddesdon, UK
PDB110	Roche Diagnostics GmbH, Mannheim, IN, Germany
PDB111	Sanofi, Berlin, Germany
PDB112	None
PDB113	None
PDB114	None
PDB115	AstraZeneca, Södertälje, Sweden
PDB116	None
PDB117	None
PDB118	None
PDB119	None
PDB120	Novartis, Each Hanover, NJ, USA
PDB121	Sanofi, Berlin, Germany
PDB122	Novartis, Each Hanover, NJ, USA
PDB123	Independant Sickness Funds, Brussels, Belgium
PDB124	None
PDB125	Bristol-Myers Squibb, Princeton, NJ, USA
PDB126	Abbott Diabetes Care, Alameda, CA, USA; Animas Corporation, a Johnson & Johnson Company, West Chester, PA, USA; Bayer HealthCare, Diabetes Care, Tarrytown, NY, USA; DexCom, Inc, San Diego, CA, USA; Johnson and Johnson, New Brunswick, NJ, USA; LifeScan, Inc., a Johnson & Johnson Company, Milpitas, CA, USA; Medtronic Diabetes, Northridge, CA, USA; Roche Diagnostics, Indianapolis, IN, USA; Sanofi-Aventis, Bridgewater, NJ, USA
PDB127	Eli Lilly, Windlesham, Surrey, UK
PDB128	Bristol-Myers Squibb, Princeton, NJ, USA
PGI1	None
PGI2	Thermo Fisher Scientific, Uppsala, Sweden
PGI3	Abbott Laboratories S.A., Madrid, Spain
PGI4	None
PGI5	Merck & co., Inc., Whitehouse Station, NJ, USA
PGI6	Almirall S.A., Barcelona, Spain
PGI7	AstraZeneca R&D, Molndal, Sweden
PGI8	None
PGI9	Ethicon, Somerville, NJ, USA
PGI10	None
PGI11	None
PGI12	Merck, Rome, Italy
PGI13	Danone, São Paulo, Brazil
PGI14	None
PGI15	None
PGI16	MSD TAIWAN, Taipei, Taiwan
PGI17	Takeda SpA, Roma, Italy
PGI18	None
PGI19	Ontario Neurotrauma Foundation, Toronto, ON, Canada
PGI20	MSD Hellas, Athens, Greece
PGI21	Nestlé Health Science, Vevey, Switzerland
PGI22	Novartis, East Hanover, NJ, USA
PGI23	WL Gore & Associates Ltd., Livingstone, UK
PGI24	WL Gore & Associates Ltd., Livingstone, UK
PGI25	Roche (Hellas), Athens, Greece
PGI26	Janssen Pharmaceutica, Beerse, Belgium
PGI27	Almirall S.A, Barcelona, Spain
PGI28	Janssen Pharmaceutica, Beerse, Belgium
PGI29	None
PGI31	None
PGI32	MSD, Moscow, Russia
PGI33	Almirall, Vilvoorde, Belgium
PGI34	Given Imaging, North Ryde, Australia
PGI35	Astellas, Brussels, Belgium
PGI36	National Institute for Health Research Health Technology Assessment (NIHR HTA) Programme, London, UK
PGI37	None
PGI38	Almirall, Vilvoorde, Belgium
PGI39	Forest Research Institute, Jersey City, NJ, USA
PGI40	None
PGI41	Crohn's and Colitis UK (NACC), Manchester, UK
PGI42	Forest Laboratories, Inc., New York, NY, USA; Ironwood Pharmaceuticals, Inc., Cambridge, MA, USA
PGI43	FADE, Milan, Italy
PGI44	Laboratorios Almirall, Barcelona, Spain
PGI45	Gilead Sciences, Foster City, CA, USA
PGI46	F. Hoffmann-La Roche Ltd., Basel, Switzerland
PGI47	None
PGI48	None
PGI49	None
PGI50	None
PGI51	Takeda SpA, Roma, Italy
PHP1	None
PHP2	German Federal Ministry of Education and Research (BMBF), Berlin, Germany
PHP3	None
PHP4	None
PHP5	None
PHP6	None
PHP8	Center for Innovation in Regulatory Science, London, UK
PHP9	None
PHP10	Becton, Dickinson UK Limited, Oxford, UK
PHP12	LEEM, PARIS, France
PHP13	None
PHP14	None
PHP16	None
PHP17	None
PHP18	ANF, Lisbon, Portugal
PHP19	None
PHP20	Biotest AG, Dreieich, Germany
PHP21	None
PHP22	None

Reference Code	Financial Support
PHP23	None
PHP24	None
PHP25	None
PHP26	Ministry of Science and Higher Education, Warsaw, Poland
PHP27	IMS HEALTH, Frankfurt/Main, Germany
PHP28	Abbott, Allschwill, Switzerland
PHP29	None
PHP30	None
PHP31	IMS Consulting Group, London, UK
PHP32	Macquarie University, Sydney, Australia
PHP33	GlaxoSmithKline, Dublin, Ireland
PHP34	None
PHP35	None
PHP36	None
PHP37	RTI-HS, Durham, NC, USA
PHP38	None
PHP39	None
PHP40	None
PHP41	None
PHP42	None
PHP44	Institue for Health Economics and Polucy, Tokyo, Japan
PHP45	None
PHP46	None
PHP47	Department of Health, London, UK
PHP48	Health Research Board, Dublin, Ireland
PHP49	Swiss Medical Association, Bern, Switzerland; Santésuisse, Solothurn, Switzerland
PHP50	The Islamia University of Bahawalpur, Bahawalpur, Pakistan
PHP51	co-funded by Greece and the European Union, Athens, Greece
PHP52	None
PHP53	Novartis, Athens, Greece
PHP54	None
PHP55	Double Helix Consulting, London, UK
PHP56	the 7th Framework Programme (FP7) , Brussel, Belgium
PHP57	the 7th Framework Programme (FP7), Brussel, Belgium
PHP58	the 7th Framework Programme (FP7), Brussel, Belgium
PHP59	Co funded by Greek and EU funds, Athens, Greece
PHP60	European Union, Brussels, Belgium
PHP61	None
PHP62	EuroQol Group, Rotterdam, The Netherlands
PHP63	None
PHP64	Roche, Mississauga, ON, Canada
PHP65	None
PHP66	None
PHP68	Health Research Board, Dublin, Ireland
PHP69	None
PHP70	None
PHP71	None
PHP72	None
PHP73	None
PHP74	None
PHP75	None
PHP76	None
PHP77	Medical Research Council Network of Hubs for Trial Methodology Research, London, UK
PHP78	University of the Witwatersrand, Johannesburg, South Africa
PHP79	None
PHP80	NOVARTIS Hellas, METAMORFOSI, Greece
PHP81	IHS, London, UK
PHP82	None
PHP83	None
PHP84	Takeda, Zurich, Switzerland
PHP85	None
PHP87	Covidien (Mallinckrodt), Moscow, Russia
PHP88	GE Healthcare, Milan, Italy
PHP89	None
PHP90	None
PHP91	Nestlé Health Science, Vevey, Switzerland
PHP92	None
PHP93	None
PHP94	None
PHP95	None
PHP96	Novartis Hellas, Athens, Greece
PHP97	None
PHP98	None
PHP99	None
PHP100	Novartis Hellas, Athens, Greece
PHP101	None
PHP103	National Institute for Health Research, London, UK
PHP104	Merck & Co., Inc, Whitehouse Station, NJ, USA
PHP105	University of Technology, Sydney, Sydney, Australia
PHP106	Nestlé Health Science, Vevey, Switzerland
PHP107	None
PHP108	None
PHP110	None
PHP111	King Abdullah international medical research center, Riyadh, Saudi Arabia
PHP112	GIRP, Brussels, Belgium
PHP113	None
PHP114	GIRP, Brussels, Belgium
PHP115	PAREXEL International, Waltham, MA, USA
PHP116	None
PHP118	None
PHP120	Institute for Quality and Efficiency in Health Care, Cologne, Germany
PHP122	None
PHP123	GlaxoSmithKline Biologicals SA, Rixensart, Belgium
PHP124	Institute for Quality and Efficiency in Health Care, Cologne, Germany
PHP125	Roche Diagnostics International Ltd.., Rotkreuz, Switzerland
PHP126	Top Institute Pharma, Leiden, The Netherlands
PHP127	None
PHP128	None
PHP129	Pharma.be, Brussels, Belgium
PHP130	None
PHP131	None
PHP132	Roche Diagnostics International Ltd.., Rotkreuz, Switzerland
PHP133	GSK, Ireland, Dublin 16, Ireland
PHP134	None
PHP135	None
PHP136	None
PHP137	None
PHP138	Quintiles, Hoofddorp, The Netherlands
PHP139	GSK, Ireland, Dublin, Ireland
PHP140	None
PHP141	None
PHP142	RTI-HS, Research Triangle Park, NC, USA
PHP143	None
PHP144	EFPIA, Brussels, Belgium; EuropaBio, Brussels, Belgium; sbg Healthcare Consulting, Pully, Switzerland; BC Consulting & Solutions Sàrl, Lausanne, Switzerland; Virtuoso, Grand Saconnex, Switzerland
PHP145	None
PHP146	None
PHP147	None
PHP148	None
PHP149	None
PHP150	None
PHP151	None
PHP152	Costello Medical Consulting Ltd.., Cambridge, UK
PHP153	None
PHP154	None
PHP155	PPD, Morrisville, NC, USA
PHP156	Evidera, London, UK
PHP157	None
PHP158	None
PHP159	None
PHP160	HERON Evidence Development Ltd., London, UK
PHP161	None
PHP162	None
PHP163	Novartis, East Hanover, NJ, USA
PHP164	Pfizer, New York, USA
PHP165	None
PHP166	None
PHP167	SmartStep Consulting GmbH, Hamburg, Germany
PHP168	None
PHP169	RTI Health Solutions, Manchester, UK
PHP170	Hoffman La Roche, Mississauga, ON, Canada
PHP171	HERON Evidence Development Ltd., London, UK
PHP172	None
PHP173	None
PHP174	None
PHP175	The Israel National Institute for Health Policy and Health Services Research (NIHP), Tel Aviv, Israel
PHP176	Boehringer Ingelheim, Sant Cugat del Vallès (Barcelona), Spain
PHP177	London School of Economics, London, UK
PHP178	SmartStep Consulting GmbH , Hamburg, Germany
PHP179	None
PHP180	None
PHP181	None
PHP182	None
PHP183	None
PHP184	None
PHP185	None
PHP186	None
PHP187	None
PHP188	Sanofi, Germany, Berlin, Germany
PHP189	None
PHP190	None
PHP191	Health Research Board (HRB), Dublin, Ireland
PHP192	Health Research Board, Dublin, Ireland
PHP193	None

Reference Code	Financial Support
PHP194	None
PHP195	None
PHP197	Ethicon, Somerville, NJ, USA
PHP198	SROP-4.2.2.C-11/1/KONV-2012-0005, Well-being in the Information Society, Budapest, Hungary
PHP199	Abbott Products Operations AG, Basel, Switzerland
PHP200	None
PHP201	Abbott Products Operations AG, Basel, Switzerland
PHP202	Top Insitute Pharma, Leiden, QC, The Netherlands
PHP203	Európai Integrációs Alap, a Belügyminisztérium és a Tullius Kft, Budapest, Hungary
PHP204	None
PHP205	Ministry of Food and Drug Safety, Chungcheongbuk-do, South Korea
PHP206	None
PHP207	None
PHP208	None
PHP209	None
PHP210	None
PHP211	None
PHP212	Fundación Mútua Madrileña, Madrid, Spain; Fondo de Investigación Sanitaria (FIS-ISCIII), Madrid, Spain
PHP213	None
PHP214	IDEX Bordeaux, Bordeaux, France
PHP215	None
PHP216	None
PHP217	German Federal Ministry of Education and Research (BMBF) , Berlin, Germany
PHP218	None
PHP219	None
PHP220	None
PHP221	None
PHP222	None
PHP223	Janssen Pharmaceutica NV, Beerse, Belgium
PHP224	None
PHP225	None
PHP226	None
PHP227	None
PHP228	None
PHP229	None
PHP230	None
PHP231	None
PHP232	None
PHP233	None
PHP235	None
PIH1	Ferring Pharmaceuticals A/S, Copenhagen, Denmark
PIH2	None
PIH3	None
PIH4	None
PIH6	Bayer Schering, Berlin, Germany
PIH7	Roche Diagnostic, Pleasanton, CA, USA
PIH8	Johnson & Johnson, Somerville, NJ, USA
PIH9	Bayer Healthcare Brazil, São Paulo, Brazil
PIH10	GlaxoSmithKline SpA, Verona, Italy
PIH12	None
PIH13	GSK s.r.o., Prague, Czech Republic
PIH14	None
PIH15	None
PIH16	European Commission, Brussels, Belgium
PIH17	None
PIH18	None
PIH19	GlaxoSmithKline, Athens, Greece
PIH20	None
PIH21	Bayer Hispania, S.L., Barcelona, Spain
PIH22	Kolplast Comérico e Indústria LTD.A, São Paulo, Brazil
PIH23	Merck & Co., Inc., West Point, PA, USA
PIH24	Sheffield Teaching Hospitals Charitable Trust, Sheffield, UK
PIH25	None
PIH26	GSK, Utrecht, The Netherlands
PIH27	Bayer HealthCare Pharmaceuticals, Moscow, Russia
PIH28	Bayer Healthcare Brazil, São Paulo, Brazil
PIH29	National Institute for Health Research (NIHR), London, UK
PIH30	Health Research Board, Dublin, Ireland
PIH31	None
PIH32	The Israel National Institute for Health Policy Research, Tel-Aviv, Israel
PIH33	ZonMw, The Hague, The Netherlands
PIH34	None
PIH35	Novo Nordisk, Søborg, Denmark
PIH36	None
PIH37	None
PIH38	None
PIH40	Ministry of Health, Labour and Welfare, Tokyo, Japan
PIH41	None
PIH42	None

Reference Code	Financial Support
PIH43	Roche, Boulogne-Billancourt, France
PIH44	Pfizer Inc, Collegeville, PA, USA
PIH45	None
PIH46	Adelphi Values, Bollington, UK
PIH47	None
PIH48	Pfizer S.L.U, Alcobendas, Spain
PIH49	Abbott Laboratories, Abbott Park, IL, USA; GRIDES, São Paulo, Brazil
PIH50	The Israel National Institute for Health Policy Research, Tel-Hashomer, Israel
PIH51	Abbott Laboratories, Abbott Park, IL, USA; GRIDES, São Paulo, Brazil
PIH52	None
PIH53	Gedeon Richter Plc, Budapest, Hungary
PIH54	European Commission, Brussels, Belgium
PIH55	Merk S.L., Madrid, Spain
PIH56	None
PIH57	None
PIH58	European Medicines Agency, London, UK
PIH59	KVBaWue, Stuttgart, Germany; vdek, Stuttgart, Germany; Janssen, Neuss, Germany; Shire, Wayne, PA, USA
PIH60	Swedish council for working life and social research [Forskningsrådet för arbetsliv och socialvetenskap, FAS], Stockholm, Sweden
PIH62	None
PIN1	None
PIN2	Gilead, Foster City, CA, USA
PIN3	Gilead Sciences, Foster City, CA, USA
PIN4	Janssen Pharmaceutical NV, Beerse, Belgium
PIN5	GAP, Bruxelles, Belgium
PIN6	F. Hoffmann-La Roche Ltd., Moscow, Russia
PIN7	Roche Pharma AG, Grenzach-Wyhlen, Germany
PIN8	Pfizer S.A de C.V, Mexico City, Mexico
PIN9	Janssen Pharmaceutica NV, Beerse, Belgium
PIN10	None
PIN11	Boehringer Ingelheim GmbH, Ingelheim, Germany
PIN12	Merck & Co. Inc., West Point, PA, USA
PIN13	NCDC, Tripoli, Libya
PIN14	Sanofi Pasteur MSD, Lyon, France
PIN15	Sanofi Pasteur MSD, Lyon, France
PIN16	None
PIN17	None
PIN18	Gilead Sciences, Foster City, CA, USA
PIN19	GAP, Bruxelles, Belgium
PIN20	Pfizer Hellas, Athens, Greece
PIN21	Covidien, Ankara, Turkey
PIN22	Roche Spa, Monza, Italy
PIN23	BD, Franklin Lakes, NJ, USA
PIN24	None
PIN25	Sanofi Pasteur MSD, Maidenhead, UK
PIN26	F. Hoffmann-La Roche Ltd., Moscow, Russia
PIN27	Janssen Cilag Farmaceutica, Sao Paulo, Brazil
PIN28	None
PIN29	ViiV Healthcare, Moscow, Russia
PIN30	Cepheid, Maurens-Scopont, France
PIN31	None
PIN32	None
PIN33	GSK Vaccines, Wavre, Belgium
PIN34	None
PIN35	Novartis Vaccines and Diagnostics, Rueil-Malmaison, France
PIN36	None
PIN37	sanofi pasteur MSD, Stockholm, Sweden
PIN38	None
PIN39	GlaxoSmithKline Biologicals SA, Rixensart, Belgium
PIN40	None
PIN41	Novosys Health, Flemington, NJ, USA
PIN42	None
PIN43	GlaxoSmithKline GmbH & Co. KG, Munich, Germany
PIN44	Centre for Public Affairs Studies Foundation, Budapest, Hungary
PIN45	None
PIN46	ViiV Healthcare, Brentford, UK
PIN47	Boehringer Ingelheim GmbH, Ingelheim, Germany
PIN48	None
PIN49	None
PIN50	Astellas Pharma Europe Ltd., chertsey, UK
PIN51	Cubist Pharmaceuticals, Lexington, MA, USA
PIN52	Gilead Sciences Inc, Toronto, ON, Canada
PIN53	Sanofi Pasteur MSD, Maidenhead, UK
PIN54	Merck Sharp & Dohme , Madrid, Spain
PIN55	None
PIN56	The Medicines Company, Parsippany, NJ, USA
PIN57	Gilead Sciences, Foster City, CA, USA
PIN58	The Medicines Company, Parsippany, NJ, USA
PIN59	None
PIN60	None
PIN61	Cepheid, Maurens-Scopont, France

Reference Code	Financial Support
PIN62	Robert Koch Institute, Berlin, Germany
PIN63	Pfizer S.L.U, Alcobendas, Spain
PIN64	Pfizer Central America and the Caribbean, San José, Costa Rica
PIN65	MSD Hellas, Athens, Greece
PIN66	Janssen Cilag Farmaceutica, Sao Paulo, Brazil
PIN67	MSD, Hoddesdon, UK
PIN68	Pfizer , Prague, Czech Republic
PIN69	Astellas Pharma Co Ltd., Dublin, Ireland
PIN70	GlaxoSmithKline, Wavre, Belgium
PIN71	Copper Development Association, Oxfordshire, UK
PIN72	Pfizer Spain, Madrid, Spain
PIN73	None
PIN74	Pfizer Central America and the Caribbean, San José, Costa Rica
PIN75	Janssen Cilag Farmaceutica, Sao Paulo, Brazil
PIN76	None
PIN77	Pfizer Inc., Paris, France
PIN78	MSD Denmark, Ballerup, Denmark
PIN79	JANSSEN-CILAG S.A., MADRID, Spain
PIN80	None
PIN81	None
PIN82	Pfizer Hellas, Athens, Greece
PIN83	Sanofi Pasteur MSD, Maidenhead, UK
PIN84	None
PIN85	None
PIN86	None
PIN87	3M Deutschland GmbH, Neuss, Germany
PIN88	None
PIN89	None
PIN90	None
PIN91	None
PIN92	None
PIN93	None
PIN94	GlaxoSmithKline, Verona, Italy
PIN95	None
PIN96	Gilead Sciences, London, UK
PIN97	None
PIN98	None
PIN99	None
PIN100	None
PIN101	2) Basilea Pharmaceutica International Ltd.., Basel, Switzerland
PIN102	ViiV Healthcare, Moscow, Russia
PIN103	Merck , Whitehouse Station, NJ, USA
PIN104	MSD, Sollentuna, Sweden
PIN105	None
PIN106	Janssen, Issy-les-Moulineaux, France
PIN107	Janssen-Cilag Polska, Warsaw, Poland
PIN108	Pfizer S.A de C.V, Mexico City, Mexico
PIN109	1. Eli Lilly (Suzhou) Pharmaceutical Co., Ltd., Shanghai, China
PIN110	Sanofi Pasteur MSD, Lyon, France
PIN111	Abbott Laboratories, Saint-Petersburg, Russia
PIN112	Sanofi Pasteur MSD, Lyon, France
PIN113	None
PIN114	Gilead Sciences Inc, Toronto, ON, Canada
PIN115	Novartis Pharma AG, Basel, Switzerland
PIN116	Council for Scientific and Humanistic Development Central University of Venezuela, Caracas, Venezuela
PIN117	Gilead Sciences Inc, Toronto, ON, Canada
PIN118	GSK, London, UK; ViiV Healthcare, London, UK
PIN119	National Institute for Public Health and the Envoironment, Bilthoven, The Netherlands
PIN120	Janssen, Beerse, Belgium
PIN121	None
PIN122	None
PIN123	AbbVie, North Chicago, IL, USA
PIN124	AbbVie, Inc, North Chicago, IL, USA
PIN125	AbbVie, Inc., North Chicago, IL, USA
PIN126	Janssen, Beerse, Belgium
PIN127	Sanofi Pasteur MSD, Lyon, France
PIN128	None
PIN129	None
PIN130	Merck & Co., West Point, PA, USA
PIN131	Vaccines Europe, European Federation of Pharmaceutical Industries and Associations, Brussels, Belgium
PIN132	Albutran M, Moscow, Russia
PIN133	Health Research Board, Dublin, Ireland
PIN134	ViiV Healthcare, Research Triangle Park, NC, USA
PIN135	Ministry of Higher Education, Putrajaya, Malaysia
PIN136	GlaxoSmithKline GmbH & Co. KG, Munich, Germany
PIN137	Context Matters, Inc., New York, NY, USA
PIN138	French Society of General Medicine, Issy les Moulineaux, France
PIN139	Context Matters, Inc., New York, NY, USA
PIN140	None
PMH1	Lundbeck SAS, Paris, France
PMH2	None
PMH3	None
PMH4	Eli Lilly and Company, Indianapolis, IN, USA
PMH5	None
PMH6	Forest Research Institute, Jersey City, NJ, USA; Pierre Fabre Médicament, Toulouse, France
PMH7	None
PMH8	None
PMH9	Takeda Pharmaceuticals International GmbH, Zurich, Switzerland
PMH10	Lundbeck SAS, Paris, France
PMH11	None
PMH12	None
PMH13	H.Lundbeck A/S, Valby, Denmark
PMH14	H.Lundbeck A/S, Valby, Denmark
PMH15	Eli Lilly and Company, Indianapolis, IN, USA
PMH16	Eli Lilly and Company, Indianapolis, IN, USA
PMH17	None
PMH18	None
PMH19	Takeda Pharmaceuticals, Deerfield, IL, USA
PMH20	None
PMH21	None
PMH22	None
PMH23	Lilly Suzhou Pharmaceutical Company, Ltd.., Shanghai, China
PMH24	Lilly Suzhou Pharmaceutical Company, Ltd.., Shanghai, China
PMH25	sponsored by Novartis Hellas, Metamorfosi, Greece
PMH26	Roche, Warsaw, Poland
PMH27	KVBaWue, Stuttgart, Germany; vdek, Stuttgart, Germany; Janssen, Neuss, Germany; Shire, Wayne, PA, USA
PMH28	Federal Ministry of Education and Research, Berlin, Germany
PMH29	Richter Gedeon Nyrt., Budapest, Hungary
PMH30	Shire Development, LLC, Wayne, PA, USA
PMH31	Janssen Cilag Ltd., Budapest, Hungary
PMH32	Pfizer S.L.U., Madrid, Spain
PMH33	None
PMH34	Janssen, Neuss, Germany
PMH35	AstraZeneca, Mexico city, Mexico
PMH36	None
PMH37	Janssen EMEA, Beerse, Belgium
PMH38	Ministry of Health, Brasilia, Brazil
PMH39	Takeda , Zurich, Switzerland
PMH40	Lundbeck, Istanbul, Turkey
PMH41	Lundbeck, Istanbul, Turkey
PMH42	Shire Development, LLC, Wayne, PA, USA
PMH43	Lundbeck SAS, Issy les Moulineaux, France
PMH44	Lundbeck Italia SpA, Milan, Italy
PMH45	Janssen-Cilag UK Ltd., High Wycombe, England
PMH46	Federal Ministry of Education and Research, Berlin, Germany
PMH47	Shire Development, LLC, Wayne, PA, USA
PMH48	Takeda Pharmaceuticals International, Inc., Deerfield, IL, USA
PMH49	Takeda Pharmaceuticals International, Inc., Deerfield, IL, USA
PMH50	H Lundbeck A/S, Valby, Denmark; Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA
PMH51	None
PMH52	None
PMH53	None
PMH54	Pfizer S.L.U., Madrid, Spain
PMH55	None
PMH56	None
PMH57	Lundbeck, Issy, France
PMH58	None
PMH59	None
PMH60	None
PMH61	Shire Development, LLC, Wayne, PA, USA
PMH62	Lundbeck, Valby, Denmark; Otsuka Pharmaceutical Development & Commercialization, Princeton, NJ, USA
PMH63	Shire Development, LLC, Wayne, PA, USA
PMH64	Lundbeck, Valby, Denmark; Otsuka Pharmaceutical Development & Commercialization, Inc, Princeton, NJ, USA
PMH65	None
PMH66	Mapi, Lexington, KY, USA
PMH67	Janssen Alzheimer Immunotherapy Research & Development, LLC,, Dublin, Ireland
PMH68	None
PMH69	Restore FX, Austin, TX, USA
PMH70	None
PMH71	None
PMH72	Danish Center for Healthcare Improvement, Aalborg, Denmark; University College of Norther n Denmark, Aalborg, Denmark
PMH73	Lilly Suzhou Pharmaceutical Company, Ltd.., Shanghai, China
PMS1	None
PMS2	None
PMS3	None
PMS4	None
PMS5	Amgen , Uxbridge, UK; GSK, Brentford, UK

Reference Code	Financial Support
PMS6	AbbVie Inc., North Chicago, IL, USA
PMS7	None
PMS8	Sanofi Biosurgery, Cambridge, MA, USA
PMS9	UCB Pharma, Colombes, France
PMS10	Medtronic International, Tolochenaz, Switzerland
PMS11	Egis Pharmaceuticals, Budapest, Hungary
PMS12	Avtelion Pharmaceuticals Australia, Frenchs Forest, Australia
PMS13	NIHR, UK
PMS14	None
PMS15	Pfizer, Collegeville, CT, USA
PMS16	Faculty of Pharmacy, Charles University in Prague, Hradec Kralove, Czech Republic
PMS17	Pfizer Italy, Milan, Italy
PMS18	None
PMS19	None
PMS20	None
PMS21	Egis Pharmaceuticals, Budapest, Hungary
PMS22	Hospira, Royal Leamington Spa, UK
PMS23	Heron, Stockholm, Sweden; Medtronic, Tolochenaz, Switzerland
PMS24	None
PMS25	Bristol-Myers Squibb, Moscow, Russia
PMS26	None
PMS27	Costello Medical Consulting, Cambridge, England
PMS28	Pfizer, Malaga, Spain
PMS29	AbbVie, North Chicago, IL, USA
PMS30	None
PMS31	Novartis Pharma Co., Ltd., Beijing, China
PMS32	Amgen Romania SRL, Bucharest, Romania
PMS33	Pfizer, Istanbul, Turkey
PMS34	None
PMS35	Central and Eastern European Society of Technology Assessment in Health Care, Krakow, Poland
PMS36	Eli Lilly and Company, Indianapolis, IN, USA
PMS37	Eli Lilly and Company, Indianapolis, IN, USA
PMS38	Eli LIlly, Shanghai, China
PMS39	CNPQ, Sao Paulo, Brazil
PMS40	National Science Council, Taiwan, Taiwan
PMS41	Fidia Farmaceutici SpA, Abano Terme, Italy
PMS42	None
PMS43	Fidia Farmaceutici SpA, Abano Terme, Italy
PMS44	UCB Pharma, Colombes, France
PMS45	AbbVie Inc., North Chicago, IL, USA
PMS46	F. Hoffmann-La Roche, Moscow, Russia
PMS47	Products Roche , Bogotá D.C, Colombia
PMS48	Pfizer, Rome, Italy
PMS49	None
PMS50	BMS Hellas, Athens, Greece
PMS51	F. Hoffmann-La Roche, Moscow, Russia
PMS52	GlaxoSmithKline, Verona, Italy
PMS53	F. Hoffman – La Roche, Basel, Swaziland
PMS54	Bristol-Myers Squibb, Madrid, Spain
PMS55	MSD, Moscow, Russia
PMS56	None
PMS57	Bone Index Finland, Kuopio, Finland
PMS58	MSD, Hoddesdon, UK
PMS59	Roche Farma, Madrid, Spain
PMS60	Roche (Hellas) S.A., Athens, Greece
PMS61	National Institute for Health Research, London, UK
PMS62	Roche (Hellas) S.A., Athens, Greece
PMS63	Roche Oy, Espoo, Finland
PMS64	Wyeth/Pfizer, Rome, Italy
PMS65	UCB Pharma, Brussels, Belgium
PMS66	UCB Pharma, Brussels, Belgium
PMS67	Polish Ministry of Science and Higher Education, Warsaw, Poland
PMS68	Polish Ministry of Science and Higher Education, Warsaw, Poland
PMS69	Polish Ministry of Science and Higher Education, Warsaw, Poland
PMS70	None
PMS71	Amgen (Europe) GmbH, Zug, Switzerland
PMS72	Amgen (Europe) GmbH, Zug, Switzerland
PMS73	Amgen (Europe) GmbH, Zug, Switzerland
PMS74	Amgen Ltd., Uxbridge, UK; GSK, Brentford, UK
PMS75	AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany
PMS76	Grant-in-Aid for Young Scientists (B), The Ministry of Education, Culture, Sports, Science and Technology(MEXT), Chiyoda-ku, Tokyo, Japan
PMS77	Pfizer Limited, Taipei, Taiwan
PMS78	Pfizer, Rome, Italy
PMS79	Amgen, Zug, Switzerland
PMS80	UCB Pharma, Brussels, Belgium
PMS81	UCB Pharma, Brussels, Belgium
PMS82	Patient-Reported Outcome Consortium's RA Working Group, Tuscon, AZ, USA
PMS83	Merck, Whitehouse Station, NJ, USA
PMS84	None
PMS85	UCB Pharma, Brussels, Belgium
PMS86	UCB Pharma, Brussels, Belgium
PMS87	UCB Pharma, Brussels, Belgium
PMS88	UCB Pharma, Brussels, Belgium
PMS89	UCB Pharma, Colombes, France
PMS90	MSD, Rome, Italy
PMS91	pfizer health research foundation, Shibuya-ku, Tokyo, Japan
PMS92	None
PMS93	None
PMS94	None
PMS95	None
PMS96	None
PMS97	None
PMS98	None
PMS99	UCB Pharma, Colombes, France
PMS100	None
PMS101	Pfizer, Rome, Italy
PMS102	Pfizer, Collegeville, CT, USA
PMS103	Ipsen Pharma, Paris, France
PMS104	Sandoz International GmBH, Holzkirchen, Germany
PMS105	IOF Invest in Your Bones (IYB), Nyon, Switzerland; Amgen, Thousand Oaks, CA, USA; Eli Lilly, Indianapolis, IN, USA; Medtronic, Fridley, MN, USA; Novartis, Basel, Switzerland; Sanofi-Aventis, Paris, France; Servier, Neuilly-sur-Seine, France; Pfizer, New York City, NY, USA
PMS106	Amgen Switzerland AG, Zug, Switzerland
PMS107	None
PMS108	None
PMS109	None
PND1	Novartis Pharmaceuticals Corporation, Florham Park, NJ, USA
PND2	Pfizer Canada, Kirkland, QC, Canada
PND3	Novartis Pharma AG, Basel, Switzerland
PND4	None
PND5	Yrjö-Jahnsson Foundation, Helsinki, Finland; The Foundation for Municipal Development, Helsinki, Finland; Hospital Neuron, Kuopio, Finland; Kuopio University Hospital (EVO-grant 5220/5772728), Kuopio, Finland; Novartis AG , Basel, Switzerland; the Social Insurance Institute of Finland (Kela), Helsinki, Finland
PND6	Novartis Pharma AG, Basel, Switzerland
PND7	Novartis Pharma AG, Basel, Switzerland
PND8	UCB, s.r.o., Prague, Czech Republic
PND9	NRF, Pretoria, South Africa
PND10	None
PND11	None
PND12	Haute Autorité de Santé, Saint Denis La Plaine, France
PND13	IPSEN Pharma, Boulogne-Billancourt, France
PND14	Biogen Idec, Weston, MA, USA
PND15	Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
PND16	Biogen Idec, São Paulo, Brazil
PND17	None
PND18	Biogen Idec Inc, Weston, MA, USA
PND19	Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
PND20	None
PND21	None
PND22	Novartis Pharma AG, Basel, Switzerland
PND23	Sanofi Pasteur MSD, Lyon, France
PND24	None
PND25	Pfizer Canada, Kirkland, QC, Canada
PND26	EVER Neuro Pharma, Unterach, Austria
PND27	Merck Serono, Prague, Czech Republic
PND28	Biogen Idec, Weston, MA, USA
PND29	TEVA Pharma, Madrid, Spain
PND30	F. Hoffmann-La Roche Ltd., Moscow, Russia
PND31	Boehringer Ingelheim, Moscow, Russia
PND32	UCB s.r.o., Prague, Czech Republic
PND33	None
PND34	Ipsen Pharma, Barcelona, Spain
PND35	None
PND36	Biogen Idec, São Paulo, Brazil
PND37	None
PND38	None
PND39	None
PND40	Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
PND41	None
PND42	GSK, Brentford, UK
PND43	Novartis Farmacéutica, S.A, Barcelona, Spain
PND44	None
PND45	None
PND46	IPSEN Pharma, Boulogne-Billancourt, France
PND47	NNS National Institute for Health Research, London, UK
PND48	Pfizer Ltd., Walton Oaks, UK
PND49	Biogeneldec, Basel, Switzerland
PND50	Yrjö-Jahnsson Foundation, Helsinki, Finland; The Foundation for Municipal Development, Helsinki, Finland; Hospital Neuron, Kuopio, Finland; Kuopio

Reference Code	Financial Support
	University Hospital (EVO-grant 5220/5772728), Kuopio, Finland; Novartis AG , Basel, Switzerland; the Social Insurance Institute of Finland (Kela), Helsinki, Finland
PND51	Biogen Idec, Weston, MA, USA
PND52	None
PND53	Bial Industrial Farmaceutica, Madrid, Spain
PND54	None
PND55	None
PND56	None
PND57	None
PND59	LUNDBECK, ISSY-LES-MOULINEAUX, France
PND60	Merk S.L., Madrid, Spain
PND61	UCB Pharma, Brussels, Belgium
PND62	Biogen Idec Limited, Maidenhead, UK
PND63	Ministry of Health, Labour and Welfare, Tokyo, Japan
PND64	Merck Serono, Stockholm, Sweden; Neurologiskt Handikappades Riksförbund, Stockholm, Sweden
PND65	None
PND66	Merck & Co., Inc., Whitehouse Station, NJ, USA
PP1	None
PP2	EuroQoL, Rotterdam, The Netherlands
PP3	Evidera, London, UK
PP4	Quintiles, Reading, UK
PRM1	None
PRM2	Novartis Pharma AG, Basel, Switzerland
PRM3	None
PRM4	F. Hoffmann-La Roche, Basel, Switzerland
PRM5	None
PRM6	None
PRM7	Sanofi-Aventis Deutschland GmbH, Berlin, Germany
PRM8	GSK Hungary, Budapest, Hungary
PRM9	GSK Hungary, Budapest, Hungary
PRM10	Truven Health Analytics, Ann Arbor, MI, USA
PRM11	Region of Northern Jutland, Aalborg, Denmark
PRM12	None
PRM13	None
PRM14	F. Hoffmann La Roche, Basel, Switzerland
PRM15	None
PRM16	None
PRM17	None
PRM18	Takeda Pharmaceuticals, Deerfield, IL, USA; Lundbeck, Deerfield, IL, USA
PRM19	None
PRM20	Bristol-Myers Squibb pharmaceuticals Ltd., uxbridge, UK
PRM21	National Institute for Health Research, London, UK
PRM22	None
PRM23	Bristol-Myers Squibb, Uxbridge, UK
PRM24	Bristol-Myers Squibb, Uxbridge, UK
PRM25	Boehringer Ingelheim GmbH, Ingelheim, Germany
PRM26	None
PRM27	Health Information and Quality Authority, Dublin, Ireland
PRM28	Medical Research Council, London, UK
PRM30	None
PRM31	NIHR, London, UK
PRM32	NIHR, Sheffield, UK
PRM33	None
PRM34	None
PRM35	Hellenic Association of Pharmaceutical Companies (SFEE), Athens, Greece
PRM36	Amgen, Inc., Thousand Oaks, CA, USA
PRM37	None
PRM38	None
PRM39	Federal Ministry of Education and Research, Berlin, Germany
PRM40	Novartis, East Hanover, NJ, USA
PRM41	Novartis Pharma AG, Basel, Switzerland
PRM42	AstraZeneca, Alderly Park, England; IMS, London, England
PRM43	Novartis Pharma AG, Basel, Switzerland
PRM44	None
PRM45	AstraZeneca Canada Inc, Mississauga, ON, Canada
PRM46	None
PRM47	None
PRM48	Sanofi, Cambridge, MA, USA
PRM49	OptumInsight, Eden Prairie, MN, USA
PRM50	Sanofi, Cambridge, MA, USA
PRM51	AstraZeneca R&D, Mölndal, Sweden
PRM52	None
PRM53	None
PRM54	Bayer Yakuhin Ltd.., Tokyo, Japan
PRM55	None
PRM56	Business & Decision Life Sciences, Brussels, Belgium
PRM57	None
PRM58	None
PRM59	None
PRM60	GlaxoSmithKline, London, UK
PRM61	AstraZeneca, Molndal, Sweden
PRM62	None
PRM63	None
PRM64	Novartis, East Hanover, NJ, USA
PRM65	None
PRM66	None
PRM67	GlaxoSmithKline, Mississauga, ON, Canada
PRM68	GSK, Sofia, Bulgaria
PRM69	IMS Health, Basel, Switzerland
PRM70	TreeAge Software, Inc (2 authors are employees), Williamstown, MA, USA
PRM71	None
PRM72	The The Netherlands Organisation for Health Research and Development, The Hague, The Netherlands
PRM73	IMS Health, Basel, Switzerland
PRM74	Novartis Pharmaceuticals Corp, East Hanover, NJ, USA
PRM75	Center for Translational Molecular Medicine, Utrecht, The Netherlands; Dutch Heart Foundation, Den Haag, The Netherlands
PRM76	Adelphi Values, Boston, MA, USA
PRM77	Boehringer Ingelheim GmbH, Ingelheim, Germany
PRM78	None
PRM79	IMS Health, Basel, Switzerland
PRM80	Danone Research, Palaiseau, France
PRM81	None
PRM82	IMS Health, Alexandria, VA, USA
PRM83	F. Hoffmann - La Roche Ltd.., Basel , Switzerland
PRM84	Myriad Genetics, Inc., Salt Lake City, UT, USA
PRM85	None
PRM86	AstraZeneca, Zoetermeer, The Netherlands
PRM87	None
PRM88	None
PRM89	Novartis AG, Basel, Switzerland
PRM90	Bristol-Myers Squibb, Rueil-Malmaison, France; AstraZeneca, Brussels, Belgium
PRM91	Almirall, Barcelona, Spain
PRM92	Heron , London, England
PRM93	PhRMA Foundation, Washington, DC, DC, USA
PRM94	None
PRM95	Austrian Research Promotion Agency, Vienna, Austria
PRM96	National Institute for Health Research, London, UK
PRM97	None
PRM98	IMS Health, Basel, Switzerland
PRM99	None
PRM100	None
PRM101	None
PRM102	Novartis Pharma AG, Basel, Switzerland
PRM103	Ipsen pharma, Boulogne-Billancourt, France
PRM104	Boehringer Ingelheim GmbH, Ingelheim, Germany
PRM105	Roche, Basel, Switzerland
PRM106	None
PRM107	Bristol-Myers Squibb, Paris, France
PRM108	University of Leicester, Leicester, UK; National Cancer Centre Singapore, Singapore, Singapore
PRM109	None
PRM110	F. Hoffmann - La Roche, Basel, Switzerland
PRM111	None
PRM112	GSK, London, UK
PRM113	None
PRM114	None
PRM115	Bayer Hispania, S.L., Barcelona, Spain
PRM116	None
PRM117	None
PRM118	Biogen Idec GmbH, Ismaning, Germany
PRM119	None
PRM120	Pfizer Ltd., Tadworth, UK
PRM121	None
PRM122	None
PRM124	None
PRM125	None
PRM126	None
PRM127	Pfizer Italia Srl, Latina, Italy
PRM128	Kantar Health, New York, NY, USA
PRM129	None
PRM130	National Science Council, Taipei, Taiwan
PRM131	None
PRM132	Les Laboratoires Servier, Paris, France
PRM133	None
PRM134	Shire, Wayne, PA, USA
PRM135	None
PRM136	None
PRM137	None
PRM138	None
PRM139	None
PRM140	None
PRM141	National Institute of Health, Bethesda, MD, USA
PRM142	Oxford Pharmagenesis Ltd., Tubney, Oxford, UK
PRM143	None

Reference Code	Financial Support
PRM144	None
PRM145	AbbVie Inc, Chicago, IL, USA
PRM146	Novo Nordisk A/S, Søborg, Denmark
PRM147	Exelixis, Inc, South San Francisco, CA, USA
PRM148	None
PRM149	None
PRM150	None
PRM151	UCB Pharma, Brussels, Belgium
PRM152	None
PRM153	None
PRM154	None
PRM155	None
PRM156	National Science Council, Taipei, Taiwan
PRM157	TransPerfect, New York, NY, USA
PRM158	TransPerfect, New York, NY, USA
PRM159	AbbVie Deutschland GmbH & Co. KG, Wiesbaden, Germany
PRM160	National Institute for Public Health and the Envoironment, Bilthoven, The Netherlands
PRM161	ICON PLC, OXFORD, UK
PRM162	Centers for Disease Control, Atlanta, GA, USA; National Institute of Child Health and Human Development, Bethesda, MD, USA
PRM163	Roche, Boulogne-Billancourt, France
PRM164	Pfizer Ltd., Tadworth, Surrey, UK
PRM165	Kantar Health, Epsom, UK
PRM166	Pfizer Ltd., Tadworth, UK; Janssen AI, Neuss, Germany
PRM167	TransPerfect, New York, NY, USA
PRM168	Double Helix Consulting, London, UK
PRM169	None
PRM170	None
PRM171	National Institute for Health Research, London, UK
PRM172	GlaxoSmithKline, Brentford, London, UK
PRM173	European Union (FEDER), Regional Council of Burgundy, General Council, Grand Dijon and the BALI consortium of industrials, Dijon, France
PRM174	None
PRM175	None
PRM176	None
PRM177	None
PRM178	None
PRM179	None
PRM180	None
PRM181	Forest Research Institute, Jersey City, NJ, USA
PRM182	None
PRM183	None
PRM184	None
PRM185	None
PRM186	LA-SER Analytica, Oviedo, Spain; Carenity, Paris, France
PRM187	None
PRM188	Evidera, London, UK
PRM189	LEO Pharma GmbH, Neu-Isenburg, Germany
PRM190	Medical Research Council, London, UK
PRM191	NIHR, Leeds, UK
PRM192	Roche S.p.A., Monza, Italy
PRM193	Janssen, Copenhaguen, Denmark
PRM194	Analysis Group, Inc., Boston, MA, USA
PRM195	None
PRM196	Roche, Basel, Switzerland
PRM197	Boehringer Ingelheim, Ingelheim, Germany
PRM198	None
PRM199	None
PRM200	None
PRM201	NIHR, Leeds, UK
PRM202	MRC funded (MRC Hub for Trial Methodological Research), Liverpool, UK
PRM203	Boehringer Ingelheim, Ingelheim, Germany
PRM204	None
PRM205	None
PRM206	None
PRM207	NIHR, Leeds, UK
PRM208	Center for Translational Molecular Medicine (PREDICCT), Eindhoven, The Netherlands
PRM209	None
PRM210	None
PRM211	PAREXEL International, Uxbridge, UK
PRM212	None
PRM213	None
PRM214	None
PRM215	None
PRM216	None
PRM217	None
PRM218	Ministry of Health, Labour and Welfare, Tokyo, Japan
PRM219	None
PRM220	None
PRM221	None
PRM222	None
PRM223	None
PRM224	None
PRM225	GlaxoSmithKline Biologicals SA, Rixensart, Belgium
PRM226	None
PRM228	Pfizer Inc., New York, NY, USA
PRM229	None
PRM230	NICE, London, UK; University of Sheffield, Sheffield, UK
PRM231	None
PRM232	GlaxoSmithKline, ZEIST, The Netherlands
PRM233	None
PRM234	GlaxoSmithKline Biologicals SA, Rixensart, Belgium
PRM235	None
PRM236	DELOITTE, Diegem, Belgium
PRM237	None
PRM238	None
PRM239	None
PRM240	None
PRM241	European Commission, Brussels, Belgium
PRM242	None
PRM243	None
PRS1	AstraZeneca, Luton, UK
PRS2	None
PRS3	AbbVie Corporation, Montreal, QC, Canada
PRS4	None
PRS5	AbbVie Corporation, Montreal, QC, Canada
PRS6	National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre, Southampton, UK
PRS7	Almirall, Barcelona, Spain
PRS8	MSD France, Courbevoie, France
PRS9	GlaxoSmithKline, Zeist, The Netherlands
PRS10	Pfizer S.A. de C.V., Mexico City, Mexico
PRS11	AbbVie Corporation, Montreal, QC, Canada
PRS12	Mundipharma International Limited, Cambridge, UK
PRS13	Pfizer S.A. de C.V., Mexico City, Mexico
PRS14	Fresenius Kabi AG, Bad Homburg, Germany
PRS15	Chiesi, Barcelona, Spain
PRS16	Almirall S.A., Barcelona, Spain
PRS17	None
PRS18	None
PRS19	AstraZeneca, Waltham, MA, USA
PRS20	None
PRS21	Endo Pharmaceuticals, Malvern, PA, USA
PRS22	Boehringer Ingelheim, Paris, France
PRS23	GlaxoSmithKline, Tres Cantos (Madrid), Spain
PRS24	GlaxoSmithKline, Istanbul, Turkey
PRS25	National Immunisation Advisory Committee, Health Protection Surveillance Centre, Ireland
PRS26	None
PRS27	None
PRS28	Pfizer S.L.U, Madrid, Spain
PRS29	None
PRS30	None
PRS31	AstraZeneca, Italy, Italy
PRS32	Fresenius Kabi AG, Bad Homburg, Germany
PRS33	Novartis, Täby, Sweden
PRS34	None
PRS35	AbbVie, Chicago, IL, USA
PRS36	Novartis, Barcelona, Spain
PRS37	None
PRS38	NIHR Evaluation, Trials and Studies Coordinating Centre, Southampton, UK
PRS39	MSD, Bratislava, Slovak Republic
PRS40	Philips Research Europe, Eindhoven, The Netherlands
PRS41	National Institute for Health Research, London, UK
PRS42	Pfizer S.A de C.V, Mexico City, Mexico
PRS43	Kantar Health, New York, NY, USA
PRS44	Instituto Salud Carlos III., Madrid, Spain
PRS45	Consejeria Salud Junta de Andalucia, Sevilla, Spain
PRS46	Consejeria de Salud. Juntade Andalucía, Sevilla, Spain
PRS47	None
PRS48	GlaxoSmithKline, Madrid, Spain
PRS49	None
PRS50	None
PRS51	None
PRS52	Kantar Health, New York, NY, USA
PRS53	None
PRS54	None
PRS55	National Heart, Lung and Blood Institute, Bethesda, MD, USA
PRS56	None
PRS57	None
PRS58	None
PRS59	AbbVie Inc., Chicago, IL, USA
PRS60	Novartis Pharmaceuticals Company, East Hanover, NJ, USA
PRS61	None

Reference Code	Financial Support
PRS62	None
PRS63	None
PRS64	Novartis Pharmaceuticals Company, East Hanover, NJ, USA
PR1	None
PR2	Abbott Products Operations AG,, Basel, Switzerland
PR3	IMS Consulting Group, Paris, France
PR4	None
PSS1	Egis Pharmaceuticals, Budapest, Hungary
PSS2	Allergan, Inc, Irvine, CA, USA
PSS3	ThromboGenics NV, Leuven, Belgium
PSS4	PFSA, PARIS, France
PSS5	ThromboGenics NV, Leuven, Belgium
PSS6	PFSA, PARIS, France
PSS7	LEO Pharma GmbH, Neu-Isenburg, Germany
PSS8	German Society of Dermatology (DDG, Berlin, Germany; LEO Pharma, Neu-Isenburg, Germany; Assoc.Office-Based Dermatol. BVDD, Berlin, Germany; Almirall-Hermal, Reinbek, Germany
PSS9	Novartis Pharma AG, Basel, Switzerland
PSS10	Novartis, Moscow, Russia
PSS11	SANOFI PASTEUR MSD, LYON, France
PSS12	Alcon Labs, Geneve, Switzerland
PSS13	None
PSS14	Bayer Pharma AG, Berlin, Germany
PSS15	Novartis Pharmaceuticals Corp., East Hanover, NJ, USA
PSS16	Novartis Pharmaceuticals Canada Inc., Dorval, QC, Canada
PSS17	Bayer Pharma AG, Berlin, Germany
PSS18	Celgene Corporation, Warren, NJ, USA
PSS19	None
PSS20	None
PSS21	Bayer Pharma AG, Berlin, Germany
PSS22	Novartis Pharma AG, Basel, Switzerland
PSS23	AbbVie Inc., North Chicago, IL, USA
PSS24	Leo Pharma A/S, Ballerup, Denmark
PSS25	None
PSS26	Pfizer, Lisbon, Portugal
PSS27	Novartis Pharmaceuticals Canada Inc., Dorval, QC, Canada
PSS28	Bayer Pharma Aktiengesellschaft, Berlin, Germany
PSS29	Allergan, Inc, Irvine, CA, USA
PSS30	Bayer Pharma AG, Berlin, Germany
PSS31	None
PSS32	Novartis, Dorval, QC, Canada
PSS33	Novartis Pharma S.A.S., Rueil-Malmaison Cedex, France
PSS34	Janssen-Cilag, Lysaker, Norway
PSS35	None
PSS36	AbbVie Pty Ltd., Sydney, Australia
PSS37	Novartis Pharma AG, Basel, Switzerland
PSS38	AbbVie Ltd., Maidenhead, UK
PSS39	PFSA, Paris, France
PSS40	PFSA, PARIS, France
PSS41	PFD, LAVAUR, France
PSS42	None
PSS43	Novartis Pharma AG, Basel, Switzerland
PSS44	Pfizer, Collegeville, PA, USA
PSS45	Pfizer, Collegeville, PA, USA
PSS46	Bayer Santé S.A.S., LOOS, France
PSS47	None
PSS48	Roche Canada, Mississauga, ON, Canada
PSS49	Novartis Pharmaceuticals Canada Inc., Dorval, QC, Canada
PSS50	Santen Inc., Emeryville, CA, USA
PSS51	LEO Pharma GmbH, Neu-Isenburg, Germany
PSS52	Abbvie, Wiesbaden, Germany; Biogen-Idec, Ismaning, Germany; Medac, Wedel, Germany; Pfizer, Berlin, Germany; Janssen-Cilag, Neuss, Germany; MSD Sharp&Dohme, Haar, Germany
PSS53	Novartis, Basel, Switzerland
PSS54	AbbVie, Wiesbaden, Germany; Biogen Idec, Ismaning, Germany; medac, Wedel, Germany; Pfizer, Berlin, Germany; MSD Sharp & Dohme, München, Germany; Janssen-Cilag, Neuss, Germany
PSS55	None
PSS56	medi GmbH & Co. KG, Bayreuth, Germany
PSS57	Novartis Farmacéutica, S.A., Barcelona, Spain
PSS58	Novartis Pharma AG, Basel, Switzerland
PSY1	None
PSY2	Novartis Poland Sp. z o.o., Warsaw, Poland
PSY3	None
PSY4	Unimed- Federação Rio de Janeiro, Rio de janeiro, Brazil
PSY5	Bayer Pharma AG, Berlin, Germany
PSY6	Janssen-Cilag GmbH, Neuss, Germany
PSY7	Novartis Pharmaceuticals, East Hanover, NJ, USA
PSY8	Astellas Pharma Europe Ltd., Chertsey, UK
PSY9	None
PSY10	MSD, Rome, Italy
PSY11	Novartis Poland Sp. z o.o., Warsaw, Poland
PSY12	None
PSY13	Novo Nordisk Pharma, Copenhaguen, Denmark
PSY14	Takeda, Moscow, Russia
PSY15	Ethicon Biosurgery, Somerville, NJ, USA
PSY16	Baxter, Madrid, Spain
PSY17	Eisai Inc., Woodcliff Lake, NJ, USA
PSY18	Eisai Inc., Woodcliff Lake, NJ, USA
PSY19	Baxter, Opfikon, Switzerland
PSY20	Grunenthal, Aachen, Germany
PSY21	Viropharma, Maidenhead, UK; Adelphi Real World, Bollington, Cheshire, UK
PSY22	ViroPharma SAS, Courbevoie, France
PSY23	Astellas, Leiden, The Netherlands
PSY24	Covidien, Istanbul, Turkey
PSY25	Astellas, Leiden, The Netherlands
PSY26	Pfizer Inc, Walton Oaks, UK
PSY27	Roche, Mississauga, ON, Canada
PSY28	Novartis, East Hanover, NJ, USA
PSY29	Ethicon SAS, Issy les Moulineaux, France
PSY30	Ariad Pharmaceutical europe Sarl, Lausanne, Switzerland
PSY31	Astellas Pharma Europe Ltd.., Staines, UK
PSY32	None
PSY33	Orphan Europe, Paris La Défense, France
PSY34	MSD Ltd., Hoddesdon, UK
PSY35	Sanofi Pasteur-MSD, Lyon, France
PSY36	Mundipharma International Limited, Cambridge, UK
PSY37	The Netherlands organisation for health research and development, The Hague, The Netherlands
PSY38	GlaxoSmithKline, Lisbon, Portugal
PSY39	Genesis Pharma, Athens, Greece
PSY40	Novartis, Moscow, Russia
PSY41	Mundipharma International, Cambridge, England
PSY42	Sanofi-Aventis, Warsaw, Poland
PSY43	GSK Services Sp. z o.o., Warsaw, Poland
PSY44	Novartis Poland Sp. z o.o., Warsaw, Poland
PSY45	None
PSY46	LighterLife, Harlow, UK
PSY47	Kedrion Spa, Castelvecchio Pascoli , Italy
PSY48	GlaxoSmithKline Polska, Warsaw, Poland
PSY49	Pfizer, Inc, Groton, CT, USA
PSY50	ROcheFarmacêutica Química, Lda, Amadora, Portugal
PSY51	Astellas Pharma Europe Ltd.., Staines, UK
PSY52	Plastic Surgery Education Foundation, Arlington Heights, IL, USA
PSY53	Novo Nordisk A/S, Copenhagen, Denmark
PSY54	FDA, Silver Spring, MD, USA
PSY55	Pfizer Inc, New York, NY, USA
PSY56	None
PSY57	None
PSY58	Astellas Pharma Europe Ltd.., Staines, UK
PSY59	None
PSY60	None
PSY61	Grunenthal, Aachen, Germany
PSY62	None
PSY63	MSD, Seoul, South Korea
PSY64	None
PSY65	Kantar Health, New York, NY, USA
PSY66	None
PSY67	None
PSY68	Masaryk University, Brno, Czech Republic
PSY70	NRF, Pretoria, South Africa
PSY71	None
PSY72	Mundipharma GmbH, Limburg (Lahn), Germany
PSY73	Johnson & Johnson Medical, Madrid, Spain
PSY74	None
PSY75	None
PSY76	Roche, Woerden, The Netherlands
PSY77	None
PSY78	Canadian Institutes of Health Research, Ottawa, ON, Canada; Alberta Innovates Health Solutions, Edmonton, AB, Canada
PSY79	Novo Nordisk, Bagsvaerd, Denmark
PSY80	Medical Consensus, London, UK
PSY81	None
PUK1	None
PUK2	NIHR HTA Programme, Southampton, UK
PUK3	National Institute for Health Research, Southampton, UK
PUK4	Unimed, Rio de Janeiro, Brazil
PUK5	Baxter Healthcare Corporation, Deerfield, IL, USA
PUK6	Astellas Pharma Europe Limited, Chertsey, UK
PUK8	Astellas Pharma Europe Limited, Chertsey, UK
PUK9	Sandoz International GmBH, Holzkirchen, Germany
PUK10	Gambro, Lund, Sweden
PUK11	None
PUK12	None
PUK13	Mitsubishi Tanabe Pharma Corporation, Jersey City, NJ, USA
PUK14	None
PUK15	Astellas Pharma Europe Ltd., Chertsey, UK

Reference Code	Financial Support
PUK16	Maccabi Healthcare Services, Tel-Aviv, Israel
PUK17	Covidien AG, Zurich, Switzerland
PUK18	Novartis Pharma AG, Basel, Switzerland
PUK19	Pfizer Ltd., Helsinki, Finland
PUK20	Astellas Pharma Europe Ltd., London, UK
PUK21	Astellas Pharma Europe Ltd., Chertsey, UK
PUK22	Astellas Pharma Europe Ltd.., Chertsey, UK
PUK23	Takeda Belgium SA, Brussels, Belgium
PUK24	Amgen Dompè SpA, Milano, Italy
PUK25	Mitsubishi Pharma Europe, London, UK
PUK26	Amgen, Inc., Thousand Oaks, CA, USA
PUK27	Medtronic Inc, Minneapolis, MN, USA
PUK28	None
PUK29	Astellas Pharma Kft, Budapest, Hungary; Bella - Hungaria Kft, Egerszalók, Hungary
PUK30	Astellas Pharma Europe BV, Leiden, The Netherlands
PUK31	Astellas Pharma Kft, Budapest, Hungary
PUK32	Kantar Health, Epsom, UK
PUK33	None
PUK34	None
PUK35	Roche S.p.A., Monza, Italy
PUK36	None
QL1	None
QL2	German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF), Berlin, Germany
QL3	NHMRC, Canberra, Australia; DKFZ, Heidelberg, Germany
QL4	Lundbeck SAS, Issy-les-Moulineaux, France

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ABSTRACTS

ISPOR 4TH LATIN AMERICA CONFERENCE RESEARCH ABSTRACTS

RESEARCH PODIUM PRESENTATIONS – SESSION I
BUDGET IMPACT STUDIES

BU1

TREATMENT OF TYPE 2 DIABETES WITH SAXAGLIPTIN/METFORMIN EXTENDED-RELEASE (XR): BUDGET IMPACT ANALYSIS IN ARGENTINA

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OBJECTIVES: To estimate the budget impact of adopting the saxagliptin/metformin XR fixed-dose combination, to treat type 2 diabetes (T2DM) in the Social Security System of Argentina, compared to the current standard treatment. **METHODS:** We used an Excel-based budget impact model assuming coverage for one million people. The time horizon was three years from the perspective of a social security organization in Argentina. T2DM prevalence data was obtained from the national risk factor survey conducted by the Ministry of Health. Only pharmaceutical expenditures of oral antidiabetic agents (OAAs) were analyzed. The cost of OAAs was obtained from the prices list adjusted to co-payments, and expressed in 2012 Argentinean pesos. Asset market-share was taken from the QUALIDIAB Database, market studies and data provided by Bristol Myers Squibb. The analysis reported findings in terms of budget impact, per-member per-month (PMPM) and per-patient per-month (PPPM). Probabilistic Sensitivity Analysis (PSA) was performed using Monte-Carlo simulations (10,000 iterations) and included parameters of demographic characteristics, price and market-shares. **RESULTS:** The net budget impact estimated that the introduction of saxagliptin/metformin XR was $32,930 for the first year, $58,768 for the second year and $85,584 for the third year. The cumulative net budget impact was $177,282. PMPM was $0.0027, $0.0049 and $0.0071 for the first, second and third year, respectively. PPPM was $0.107, $ 0.198 and $0.299 each year, respectively. The cumulative impact in the total annual budget for OAAs represented an increase of 0.27%. Monte Carlo simulation showed that cumulative budget impact varied from 0.08 to 0.30%. **CONCLUSIONS:** The introduction of saxagliptin/metformin XR in a social security organization as a treatment option for patients with T2DM, has a minimal budgetary impact.

BU2

ANÁLISE DE IMPACTO ORÇAMENTÁRIO: QUANTO CUSTARIA AO SISTEMA PÚBLICO DE SAÚDE BRASILEIRO INCREMENTAR, POR MEIO DE TRANSPLANTES, O TRATAMENTO DA DOENÇA RENAL CRÔNICA TERMINAL?

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INTRODUÇÃO: O transplante renal é apontado na literatura como a terapia de substituição renal mais custo-efetiva, permitindo reintegração do paciente as atividades cotidianas, aumentando expectativa e qualidade de vida. Entretanto, os sistemas públicos de saúde deparam-se com necessidades infinitas, recursos finitos, imperativo da qualidade na assistência e gasto e adequação das novas tecnologias aos recursos disponíveis. **OBJETIVOS:** Conhecer o impacto orçamentário no Sistema Único de Saúde (SUS)- no âmbito das avaliações de tecnologia em saúde - gerado por uma possível ampliação da utilização de transplantes como tratamento de pacientes portadores de insuficiência renal crônica. **MÉTODOS:** Foram utilizadas informações metodológicas para desenvolvimento de estudos de impacto orçamentário voltados ao SUS disponibilizado pela publicação: DIRETRIZES METODOLÓGICAS - Análise de Impacto Orçamentário: Manual para o Sistema de Saúde do Brasil. **RESULTADOS:** Em análise temporal de cinco anos, considerando-se cenários alternativos que ampliam a utilização de transplante frente a hemodiálise(HD) e diálise peritoneal(DP), dos atuais 3% para 10%; 20%; 30%, com crescimento esperado de utilização que variam de 20% a 100% no período.Considerando a população brasileira, com prevalência da doença de 0,047%, incidência de 32% e taxa de mortalidade de 22% para HD+DP e 4,5% para transplante, temos que: no Cenário01 (10%)haverá uma queda de 1,2% na taxa de mortalidade e em cinco anos um incremento de gasto de R$7bilhões; Cenário02(20%) 2,9% e R$6,5bilhões; Cenário03(30%) 4,7% e R$6bilhões. Nesse cenário a queda na taxa de mortalidade representa a manutenção de 4.374 vidas, mediante um incremento de gasto médio anual da ordem de R$1,2bilhões, já considerando a inflação. **CONCLUSÕES:** O transplante, apesar de ter menor custo que HD e DP, por resultar em redução significativa na mortalidade gera impacto orçamentário em cinco anos de R1,2bilhões. Esse é o preço a se pagar por aumento na sobrevida e na qualidade de vida. Então, quanto vale a vida?

BU3

COSTO E IMPACTO PRESUPUESTAL DEL TRATAMIENTO DE LA ARTRITIS REUMATOIDE MODERADA Y SEVERA CONSIDERANDO EL USO DE TERAPIAS BIOLÓGICAS EN MÉXICO

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OBJECTIVOS: El impacto económico del potencial uso de terapias biológicas (TB) en el tratamiento de la artritis reumatoide moderada y severa (AR-MS) en el Seguro Popular (SP) de México no se ha estimado. Este estudio estuvo enfocado a estimar este impacto. **METODOLOGÍAS:** Con datos de la Community Oriented Program for Control of Rheumatic Diseases (COPCORD) y registros de casos nuevos en la base de datos del Sistema de Información en Salud (Secretaría de Salud), se estimó la prevalencia de AR-MS para el 2012. Se estimó la cantidad de pacientes con AR-MS candidatos a recibir TB. La estimación de los costos de tratamiento de AR-MS se realizó mediante la metodología *bottom-up* y se expresan en US$ de 2013. Un panel de 10 expertos determinó el perfil de uso de recursos: consultas, medicamentos, pruebas de laboratorio y gabinete, rehabilitación y manejo de eventos adversos. Los costos unitarios se extrajeron de fuentes institucionales. Se realizó un análisis de impacto presupuestal en base al Presupuesto de Egresos de la Federación (PEF) para 2012. **RESULTADOS:** Se estimó que en 2012 había 115,827 pacientes con AR-MS con posibilidad de ser tratados con TB en el SP. El costo esperado (anual) de tratamiento con TB fue de US$16,880, mientras que sin TB fue de $10,883 (64.5%). El costo de la TB está determinado por el costo de adquisición del biológico, mientras que el costo de manejo de complicaciones es el rubro más importante en los pacientes sin TB. Si se tratase con TB al 5% (5,791) de los pacientes candidatos, el impacto presupuestal sería del 0.95% del PEF. **CONCLUSIONES:** El tratamiento de AR-MS con terapias no biológicas representa alrededor de dos terceras partes del costo de tratamiento con TB. La introducción progresiva de TB en el SP permitiría controlar el impacto presupuestal acorde a la disponibilidad de recursos.

BU4

BUDGET IMPACT ANALYSIS OF ABIRATERONE ACETATE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS PREVIOUSLY TREATED WITH DOCETAXEL FROM THE PERSPECTIVE OF THE BRAZILIAN PRIVATE HEALTH CARE SYSTEM

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OBJECTIVES: To evaluate the Budget Impact from the perspective of the Brazilian Private Health Care System after the introduction of abiraterone acetate (AA) for the treatment of metastatic castration-resistant prostate cancer (mCRPC) patients previously treated with docetaxel. **METHODS:** An epidemiological model based on reports of Brazilian National Cancer Institute and published literature was developed to estimate the incidence of mCRPC patients in the next three years. Budget impact was simulated comparing current scenario, where all patients undergo treatment with cabazitaxel, and a new scenario with the introduction of AA from the perspectives of the payers (HMOs) and service provider (infusion clinics). Pharmaceutical costs were based on official list price applying reimbursement inflators. Costs with adverse events and drug administration were obtained from published literature. Deterministic sensitivity analysis (DSA) was conducted to determine the impact of parameters on results. **RESULTS:** According to the model, a total of 5,098 patients were eligible for treatment with either cabazitaxel or AA over the three years of analysis. In the base case scenario, from the payers' perspective the introduction of AA decreased total treatment costs of the target population by R$47,516,469. If reinvested on the treatment of mCRPC patients, these economic savings could allow for the treatment of 692 more patients with AA. For the service provider, assuming reimbursement inflator of 10% in cabazitaxel factory price, better financial results per patient are achieved in a scenario where reimbursement inflator of AA is set at 15% of factory price. In DSA, economic savings from the payers perspective ranged from R$12,454,979 (assuming mean duration of treatment with AA of 10 months) and R$118,637,890 (assuming 100% of market share for AA). **CONCLUSIONS:** The introduction of AA may generate economic savings for both HMOs and infusion clinics, possibly allowing treatment of more patients with mCRPC previously treated with docetaxel.

CARDIOVASCULAR DISEASE OUTCOMES RESEARCH

CV1

UTILIDAD DE BIOMARCADORES CARDIACOS (POINT OF CARE TESTING) EN EL AREA DE URGENCIAS Y SU IMPACTO ECONÓMICO

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OBJECTIVOS: El síndrome coronario agudo (SCA) representa alta carga de la enfermedad para México. Los biomarcadores cardiacos Point of Care Testing (POCT) mejoran la oportunidad diagnóstica, permiten acelerar el tratamiento y reducen la mortalidad. El propósito del estudio fue evaluar, desde la perspectiva del proveedor de servicios de salud, su impacto clínico y económico en los servicios de urgencias en México. **METODOLOGÍAS:** Estudio comparativo, en situaciones habituales, del servicio de urgencias del Hospital General de Zona No. 1-A del Instituto Mexicano del Seguro Social (IMSS) en México, D.F. Los grupos de comparación fueron: sin disponibilidad de biomarcadores POCT, que incluyó pacientes adultos, sin distinción de género, que acudieron al hospital por dolor torácico agudo (DTA) entre marzo y abril de 2012; y con disponibilidad de biomarcadores POCT, que incluyó pacientes que acudieron entre junio y septiembre de 2012. Se realizó seguimiento durante la estancia en urgencias. El resultado de interés fue la identificación de pacientes con SCA. Los costos se calcularon con los recursos utilizados durante la estancia en urgencias; se expresaron de dólares norteamericanos (tasa de cambio 12.65 pesos/dólar). **RESULTADOS:** Se incluyeron 336 pacientes, edad promedio 55±18 años, 52% hombres. El grupo sin POCT incluyó 148 pacientes y con POCT 188. Con POCT se identificaron 50 pacientes con SCA (0.27, IC95% 0.20–0.33) vs 21 sin POCT (0.14, IC95% 0.08–0.19), p=0.006. El costo promedio de la atención en urgencias con POCT fue US$178 (IC95% US$161-US$ 340) y sin POCT fue de US$168 (IC95% US$152-US$320), p=0.93. El costo-efectividad promedio para identificar un paciente con SCA sin POCT fue US$1,206 y con POCT fue US$661. **CONCLUSIONES:** La disponibilidad de biomarcadores POCT en urgencias es costo-efectivo, ya que mejora la probabilidad de identificar SCA en pacientes con DTA y no existe diferencia en el costo de su implementación para el IMSS.

CV2

ESTIMATION OF THE COST-EFFECTIVENESS OF APIXABAN IN NON-VALVULAR ATRIAL FIBRILLATION IN ARGENTINA

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OBJECTIVES: Atrial Fibrillation (AF) affects about 2% of the population and increases 5-fold the risk of stroke and systemic embolism. This risk is managed with vitamin K antagonists (VKA) or aspirin for patients according to their suitability to receive oral anticoagulants (OA) but with several limitations. Therefore, novel OAs have become a treatment option. Apixaban is the most recent drug approved for thrombotic prevention in AF. Our aim is to estimate the cost-effectiveness (CE) of apixaban in AF in Argentina. **METHODS:** We conducted a literature review of published epidemiological AF, and stroke data from Argentina. Data about apixaban, warfarin, rivaroxaban, dabigatran and aspirin were obtained from published trials and indirect comparisons. Two Delphi Panels, with local experts representing private, public and social security health subsectors were held and reviewed and validated data collected and provided information on local treatment patterns. Costs, expressed in 2012U$S, were gathered from published reports and a local database. Apixaban was compared with each available AF treatment option allocating them into a simulated cohort of 1,000 patients per treatment group (according with their suitability for OA) over a lifetime horizon using an MS EXCEL based Markov model. We adopted payer's perspective reporting weighted mean costs for QALY gained. CE threshold for Argentina was considered as per WHO-CHOICE and World Bank data (ranging from 9740 to 29220U$S). **RESULTS:** For the suitable population, the cost per QALY gained with apixaban was U$S 9938 and 1131 versus warfarin and dabigatran 150 mg respectively, and dominant compared to dabigatran 110 mg and rivaroxaban. For the unsuitable population, apixaban was dominant compared to available alternatives: aspirin, dabigatran 110 mg, dabigatran 150 mg, and rivaroxaban. **CONCLUSIONS:** on the model using local inputs, apixaban is dominant or cost-effective according to local CE thresholds becoming the treatment choice in Argentina both in the suitable and unsuitable populations

CV3

PULSE PRESSURE AND STROKE RISK: DEVELOPMENT AND VALIDATION OF A STROKE RISK EQUATION

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OBJECTIVES: Previous stroke risk equations identified systolic blood pressure (SBP) as a key predictive factor. Recent evidence suggests that pulse pressure (PP), defined as the difference between SBP and diastolic blood pressure, could be a new risk factor. This project aims at developing and validating a new stroke risk equation incorporating PP as a potential risk factor. **METHODS:** Electronic medical records including laboratory data of a random sample of 97,237 hypertensive patients from a US integrated health delivery system were analyzed (01/2004-05/2012). Patients with ≥1 peripheral PP (PPP) reading and ≥6 months of observation (baseline period) prior to the first evidence of hypertension were randomly split into the development (two-thirds of sample) and validation (one-third of sample) datasets. Stroke events were identified using ICD-9-CM 433.xx-436.xx. Cox proportional hazards models assessed time to first stroke event based on baseline risk factors, including PPP, age, gender, SBP, smoking status, BMI, diabetes, and cardiac comorbidities. The optimal risk equation was selected using the least absolute shrinkage and selection operator (LASSO); performance was evaluated by the c-statistic. **RESULTS:** A total of 30,525 patients without stroke (mean age 58.2, 48% male) and 4,272 patients with stroke (mean age 67.3, 48% male) were selected. Average observation was 3.89 years. PPP was higher among patients who developed stroke (mean [SD] PPP, stroke: 62.0 [15.3] mmHg; non-stroke: 58.1 [14.0] mmHg, p<.001). The best performing risk equation (c-statistic, development: 0.732; validation: 0.722) included PPP (hazard ratio per 10 mmHg increase: 1.0676, p<.001) as a significant risk factor for stroke in addition to age and diabetes, among others. **CONCLUSIONS:** This stroke risk equation shows that greater PP is a significant predictive factor for increased stroke risk, even in the presence of known risk factors, including SBP. PP should be considered by practitioners along with traditional risk factors in treatment strategies to prevent stroke.

CV4

ANÁLISIS DE COSTO-EFECTIVIDAD DEL USO DE ESTATINAS EN LA PREVENCIÓN DE EVENTOS CARDIOVASCULARES EN COLOMBIA

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OBJECTIVOS: Las enfermedades cardiovasculares (ECV) son una de las principales causas de muerte precoz en los países occidentales, los fármacos hipolipemiantes están indicados para disminuir el riesgo cardiovascular V. El objetivo de este análisis es evaluar la costo-efectividad del uso de estatinas en prevención primaria de ECV en Colombia. **METODOLOGÍAS:** Se utilizó un modelo compuesto por un árbol de decisión y un Markov. El horizonte de tiempo fue la expectativa de vida. Los comparadores fueron: atorvastatina (20mg/día) vs. rosuvastatina (20 mg/día). Se simuló una cohorte de 100 pacientes de 62 años con valor inicial de colesterol LDL de 137.28mg/dL y riesgo anual basal de ECV ≤3.5%. Se utilizó una tasa de descuento de 3%. Los datos de utilidad, eficacia y mortalidad por los eventos fueron tomados de la literatura, ajustados por información local. La medida de efectividad empleada fueron los años de vida ganados (AVG), los años de vida ajustados por calidad (AVACs) y los casos de ECV evitados. Los precios de los medicamentos fueron tomados del SISMED y los costos de una EPS de presencia nacional. Se utilizó como umbral de disposición a pagar, el equivalente a 3 PIB per cápita ≈ US$40,000. **RESULTADOS:** En el horizonte de la expectativa de vida, el ahorro total esperado por persona con atorvastatina fue de US$6374 en comparación con rosuvastatina (costos totales: US$8,802 y US$15,176, respectivamente); rosuvastatina obtuvo 0.0108 AVACs, 0.0127 AVG y 0.0023 casos evitados más que atorvastatina por persona; el ICER de rosuvastatina fue de US$507,266/AVAC, US$426,320/AVG y US$2,624,876/casos evitados de ECV. **CONCLUSIONES:** Atorvastatina sería la alternativa de elección en la prevención de ECV. El diferencial de AVG, AVACs y casos de ECV de rosuvastatina es muy bajo para su costo incremental y su ICER se encuentra por encima del umbral definido, por lo que no es una opción costo-efectiva.

HEALTH CARE EXPENDITURE STUDIES

HC1

ADDRESSING CHILDHOOD-OBESITY IN MEXICO: SAVINGS ON HEALTH CARE EXPENDITURES FROM REGULATING FOOD AND BEVERAGE SALES IN BASIC EDUCATION SCHOOLS

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OBJECTIVES: Estimate potential direct savings for the Mexican Healthcare System generated by the operation of the "Technical Guidelines for the Sale or Distribution of Food and Beverages in Establishments of Basic Education". **METHODS:** The microsimulation model "Chronic Disease Prevention (CDP)" developed by OECD-WHO was used for projecting health gains and costs of treatment in a period of 100 years. The model was adjusted to accommodate the range 6-14 years old stated in the Guidelines. Mexican data on incidence, prevalence, mortality, population at risk, annual unit costs and relative risk of selected chronic diseases (diabetes mellitus type 2, hypertension, cardiovascular, hypercholesterolemia) attributable to obesity and the treatment of obesity as disease itself was used. Sensitivity analyses were developed for most variables used in the model. **RESULTS:** Under a base case scenario present value of potential savings in total spending on medical care associated with the implementation of the Guidelines amount to USD$1052.2 million in 2008. Most savings are derived from averted cases of hypertension (32.7%), obesity-overweight (28.6%) and diabetes mellitus type II (17.8%). Results are robust to changes in all parameters analyzed. Amounts obtained are an underestimation of potential savings as neither expensive complications as renal failure nor other chronic diseases attributable to obesity as arthritis, colorectal or breast cancer were included. **CONCLUSIONS:** The Guidelines, —developed by the Ministry of Public Education in coordination with the Ministry of Health—, represent a good example of cooperation among different sectors to solve a complex public health problem. Results shows the importance of implementing preventive interventions aimed at reducing the prevalence of chronic diseases related to poor eating habits, inadequate physical activity and obesity in Mexico. Implementation of the Guidelines involves significant direct savings that can be assigned to other health needs of the Mexican population.

HC2

EFFECT OF HEALTH SPENDING, INCOME INEQUALITY AND MARGINATION INDEX ON THE EFFICIENCY OF THE HEALTH SYSTEM IN MEXICO

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OBJECTIVES: To explore the effect of health spending, income inequality and margination on maternal and child health care in México. **METHODS:** With the 32 Mexican states an ecological multi spatial study was performed. Correlations between maternal and infant mortalities in the total per capita spending (central and state governments from 2000 to 2010), Gini and margination indexes were computed. Conventional and robust multiple linear regressions were used to explore the effects on the technical efficiency of these indicators in the State's health systems. **RESULTS:** Negative correlations with Spearman rho -0.62 and -0.28 near to the margination and Gini indexes respectively (p <0.05), and higher than 0.59 for the margination index (p <0.05) between life expectancy at birth for the first and the last infant mortality. The multiple linear regression models established the relationship between the deprivation and Gini indexes in health indicators. It showed the positive effect of funding from central gov-

ernment in better health system performance, as well as the positive effect of increased public investment in health over the decade in health indicators and process insurance in the last 5 years. **CONCLUSIONS:** The results suggest a positive effect of central government spending on health and a negative effect of income inequality and margination index on maternal and infant mortalities, clearly mediated by socioeconomic factors characteristic of each state. This methodological approach is proposed to evaluate the relationships of the different levels of functioning of a health system and the dynamics with the social determinants of these levels.

HC3

PAYER AND PHYSICIANS EVIDENCE AND DISCOUNT EXPECTATIONS FOR BIOSIMILARS IN SIX LATIN AMERICAN COUNTRIES

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OBJECTIVES: As follow-up to prior work, investigate what evidence is required for reimbursement and prescribing of biosimilar drugs from four key therapy areas in six Latin American countries (Argentina, Brazil, Chile, Colombia, Mexico and Venezuela). Explore how these requirements may correspond to the regulatory pathways across the different countries. **METHODS:** Conduct secondary research to determine any recent changes to biosimilar regulation in the six studied countries. Conduct targeted primary research with payers and physicians in the six counties exploring: 1) The therapy areas that payers and physicians consider most attractive for biosimilars; 2) The baseline evidence (bioequivalence, comparative trial data, extrapolation of indications, etc.) that stakeholders require across the key therapy areas and across countries; 3) The level of discount, below the branded equivalent, that payers and physicians would require to consider biosimilars for access or to prescribe to their patients; 4) The expected access level and prescribing decisions for those biosimilars that meet these evidence and discount criteria; and 5) The degree to which payer and physician evidence expectations for biosimilars map to our understanding of the evolution of biosimilar regulatory environment. **RESULTS:** Public payers across the region see biosimilars as an opportunity to provide broader access to needed medications, although some stakeholders are more receptive than others and have lower requirements to prove comparability. Clinicians in general have concerns about safety and efficacy, however, their willingness to prescribe biosimilars correlates inversely with the degree of access and affordability of the branded agents. **CONCLUSIONS:** The regulatory and access environment for biosimilars in Latin America can be expected to be more favorable than in the US but not too dissimilar from Europe. However there are systematic differences across countries and therapy areas.

HC4

ANÁLISIS DE COSTO-EFECTIVIDAD DE LAS VACUNAS NEUMOCÓCICAS 13-VALENTE Y 23-VALENTE PARA ADULTOS DE ALTO RIESGO EN COLOMBIA

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OBJECTIVOS: El *Streptococcus pneumoniae* causa una importante morbilidad y mortalidad a nivel mundial, tanto en niños como en adultos. El objetivo de este análisis es estimar la costo-efectividad de la vacuna conjugada 13-valente (PCV13) vs la vacuna neumocócica polisacárida 23-valente (PPSV23) y vs no vacunación en los adultos de alto riesgo (inmunocomprometidos) >50 años en Colombia, desde la perspectiva del tercero pagador. **METODOLOGÍAS:** Se adaptó un modelo de Markov con horizonte de tiempo de la expectativa de vida y tasa de descuento 3% anual. Los comparadores fueron PCV13, PPSV23 y no vacunación (NV), cobertura estimada del 70%; revacunación a los 5 años con PPSV23 para >65 años según criterios del CDC. Se utilizó la población >50 años de alto riesgo en Colombia. Las probabilidades de transición, incidencia de enfermedades y efectividades de las vacunas fueron extraídas de la literatura (para PCV13 se utilizaron datos de PCV7 ajustados por inmunosenescencia), los costos médicos fueron proveídos por una EPS de cobertura nacional; los precios de las vacunas fueron tomados de la OPS para 2013. Los costos se presentan en US$ 2013. Las medidas de efectividad fueron número de casos evitados de enfermedad neumocócica invasiva – ENI (meningitis y bacteremia), neumonía invasiva, muertes y años de vida ganados (AVG). **RESULTADOS:** Vacunar con PCV13 vs NV y PPSV23 previene 4.389 y 4.134 casos de ENI; 2594 casos de neumonía invasiva y 550 y 536 muertes respectivamente. PCV13 genera 199 AVG más que PPSV23 y 4.712 AVG más que NV. El ahorro total esperado (vacunación + costos médicos) con PCV13 fue US$18,254,171 vs NV y US$26,204,251 vs PPSV23. **CONCLUSIONES:** Vacunar adultos inmunocomprometidos >50 años con PCV13 en Colombia es una alternativa costo-ahorradora en comparación con NV y con PPSV23 (US$12.57 y US$18.08 ahorrados por paciente respectivamente). Los hallazgos de este estudio soportan una toma de decisión a favor de PCV13.

HEALTH TECHNOLOGY ASSESSMENT STUDIES

HT1

EFFICACY AND SAFETY OF NEW ANTICOAGULANTS IN THE TREATMENT OF ATRIAL FIBRILLATION: A HEALTH TECHNOLOGY ASSESSMENT

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Patients with AF have a 4-5 times larger risk of stroke than age-matched controls. Anticoagulation with warfarin is currently the standard of care but the requirement for routine monitoring and drug and food interactions, makes its use is suboptimal. New anticoagulants were developed to eliminate these barriers and the results are promising. However, the incorporation of these technologies within the Brazilian Unified Health System (SUS) demands proper consideration. **OBJECTIVES:** To evaluate the efficacy and safety of new anticoagulants in the treatment of AF. **METHODS:** Health Technology Assessment of multiple technologies. We searched the electronic databases Cochrane Library, CRD, Pubmed, Embase and Lilacs, to search for the best available evidence assessing the new oral anticoagulants, compared with warfarin in patients with AF. **RESULTS:** Three randomized controlled trials evaluating dabigatran (110mg e 150mg), rivaroxaban 20mg and apixaban 5mg were included, all of them compared with warfarin. In this regard, dabigatran 110mg was associated with similar rates of stroke or systemic embolism and with a 20% relative risk reduction (RRR) of major hemorrhage compared with warfarin. Dabigatran 150mg was associated with a 34% RRR of stroke or systemic embolism and similar rates of major hemorrhage. Rivaroxaban 20mg was associated with similar rates of the primary efficacy and safety outcomes. Finally, apixaban was associated with a 21% RRR of stroke or systemic embolism and with 31% RRR of major bleeding compared with warfarin. **CONCLUSIONS:** There is strong evidence supporting these new technologies, especially regarding safety. Further studies are needed to support decision making, especially with regards to cost-effectiveness issues.

HT2

HEALTH TECHNOLOGY ASSESSMENT REPORT FOR POSITRON EMISSION TOMOGRAPHY IN PATIENTS WITH CANCER

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OBJECTIVES: Positron Emission Tomography (PET) might be useful for cancer staging and follow-up. The objetive was to assess the available evidence on efficacy, safety and coverage policies for use of PET in oncology. **METHODS:** A bibliographic search was carried in PubMed, DARE, NHS EED, in health technology assessment (HTA) agencies and health insurers. Priority was given to systematic reviews; randomized clinical trials (RCTs); HTA; clinical practice guidelines (CPGs) and coverage policies (CPs). **RESULTS:** Thirty-seven systematic reviews, 3 RCTs and 32 observational studies, 51 CPGs, 15 HTAs and 28 CPs were included. Breast Cancer (17 studies):There is no evidence of its use as routine practice. Some CPGs and CPs recommend it for suspicious images that could not be clarified through conventional studies. PET is not recommended for axillary staging or neodadyuvant response prediction. Lung Cancer (44 studies):The accuracy for lung nodule is similar to conventional methods. Most CPGs do not recommend the use of PET for lung cancer staging except in some non-small cell lung cancer with previous negative tests for metastasis. Colorectal Cancer (20 studies): There is no evidence of its use as routine practice. It might be used in patients with suspected recurrence and non-conclusive images. Genitourinary Tumors (70 studies): PET might be associated with changes in diagnosis or therapeutic only in specific cases, such as ovarian cancer with suspected recurrence and normal conventional images, in residual tumors due to seminoma and cervical cancer recurrence eligible for curative treatment. Primary Tumors of the Central Nervous System (15 studies):PET is not recommended as routine practice. CPGs, RCTs and CPs recognize its usefulness for differential diagnosis between relapse and radionecrosis. **CONCLUSIONS:** There is no evidence to support the use of PET in cancer patients as routine practice. At present, its use should be restricted to specific patients.

HT3

FORMULATIONS OF AMPHOTERICIN B FOR THE TREATMENT OF FUNGAL INFECTIONS IN PATIENTS WITH HIV/AIDS

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OBJECTIVES: To evaluate the efficacy, safety and cost-effectiveness data of lipid formulations of amphotericin B to establish which should be used for the treatment of systemic fungal infections in patients with HIV/AIDS in Brazil. **METHODS:** We searched The Cochrane Library, Centre for Reviews and Dissemination, Tripdatabase, Medline and LILACS databases aiming to find systematic reviews (SRs) and economic evaluations (EE) comparing liposomal amphotericin B (L-AmB) or amphotericin B lipid complex (ABLC). Health Technology Assessments (HTA) were searched on agencies websites. Quality of the evidence and strength of recommendation were evaluated using the GRADE system. **RESULTS:** We selected five SRs, in which one evaluated only safety data, and two economic evaluations. Four SRs were classified as poor quality and the strength of recommendation was considered weak in favor of L-AmB in all studies. In general there were no statistically significant differences in terms of survival and response to treatment ($p<0,05$). However, L-AmB was associated with a lower risk of nephrotoxicity and increased serum creatinine. The two economic studies included had conflicting results. In the cost-minimization study there was no difference in total costs of the therapies, but the daily cost of acquisition and concomitant antifungal therapy and adverse events were lower for ABLC (0,002 and 0,027). The incremental cost-effectiveness analysis favored the L-AmB (€41734 *vs.* €51724). Both studies showed important limitations and there were no studies considering the Brazilian context. **CONCLUSIONS:** Considering all the studies found, as well as their limitations, there is a lack of evidence to support the spread use of L-amB in patients with HIV/AIDS affected by fungal infections, unless strictly in cases where patients have abnormal renal function. Also, L-AmB could be used in case of intolerance to conventional amphotericin B.

HT4

EFICÁCIA E SEGURANÇA DE RANIBIZUMABE E BEVACIZUMABE NO TRATAMENTO DE DEGENERAÇÃO MACULAR RELACIONADA A IDADE

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OBJETIVOS: Avaliar e comparar a eficácia e a segurança do ranibizumabe e do bevacizumabe para o tratamento da Degeneração Macular Relacionada a Idade (DMRI). **MÉTODOS:** Realizou-se uma revisão sistemática / *overview* utilizando as bases *The Cochrane Library, Centre for Reviews and Dissemination, Medline* e LILACS com o objetivo de encontrar estudos que comparassem ranibizumabe ou bevacizumabe com qualquer outra opção terapêutica para o tratamento da DMRI. Os estudos de avaliações econômicas foram buscados em sites da Rede Brasileira de Avaliação de Tecnologias e Saúde (REBRATS), no *National Institute for Clinical Excellence and Health, Health Technology Assessment Programme* e*Canadian Agency for Drugs and Technologies in Health*. **RESULTADOS:** Foram identificados 643 títulos e destes, 14 foram incluídos sendo 5 revisões sistemáticas e 9 avaliações econômicas. A síntese dos resultados das revisões sistemáticas mostrou que ambos os medicamentos são eficazes, isso é, evitam a perda progressiva da visão e/ou aumentam a acuidade visual sobretudo quando comparados aos demais tratamentos disponíveis para a DMRI. Não foram encontrados estudos que comparassem diretamente a eficácia do ranibizumabe versus o bevacizumabe o que comprometeu uma possível avaliação da superioridade clínica entre eles. Por outro lado, as avaliações econômicas apontaram que a vantagem de um medicamento em relação ao outro está na diferença dos custos. O ranibizumabe em todos os cenários estudados foi mais caro e para torná-lo custo-efetivo é necessário que seu preço diminua. Já o bevacizumabe, possui eficácia equivalente e um custo inferior que provavelmente está relacionado a sua forma de administração - uma ampola para mais de um paciente - o que tem ocasionado uma discussão quanto à sua utilização *off label* no Brasil. **CONCLUSÕES:** Recomenda-se a utilização do ranibizumabe ou do bevacizumabe para a forma úmida da DMRI em pacientes maiores de 50 anos de idade.

INFECTIOUS DISEASE STUDIES

IN1
ASSESSMENT OF BURDEN OF ILLNESS DUE TO HERPES ZOSTER IN ARGENTINA: A PROSPECTIVE OBSERVATIONAL STUDY

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OBJECTIVES: Herpes zoster (HZ) is caused by the re-activation of latent varicella-zoster virus (VZV) and is characterized by unilateral, vesicular cutaneous eruptions, acute neuritis and post-herpetic neuralgia (PHN). To date, data on HZ associated pain (ZAP) and its impact on quality of life (QoL) in Argentina are scarce. This study assesses the burden of illness associated with HZ in Argentina in a real-life clinical setting. **METHODS:** This was a prospective, observational, single-cohort study. Patients were enrolled at various time points during the course of a zoster episode and were followed for ≤6 months. ZAP was assessed with the Initial Zoster Impact Questionnaire and the Zoster Brief Pain Inventory, while QoL was assessed with the EQ-5D instrument using the Hispanic preference weights. **RESULTS:** A total of 96 HZ patients were enrolled with a mean (SD) age of 70.14 (10.7) years and 64 (66.7%) being females. At baseline, mean (SD) time since rash onset was 15.92 (16.9) days. Prior to rash onset (prodrome phase), a significant proportion (59.4%) of patients experienced a worst pain score of ≥5. ZAP was reported by 92 (95.8%) patients at baseline. Mean (SD) worst pain score decreased from 5.47 (3.1) at baseline to 2.94 (3.0) at 30 days and 0.21 (0.7) at 180 days. PHN (worst pain ≥3 after ≥90 days since rash onset) was experienced by 11 (11.5%) patients. The mean (SD) EQ-5D score significantly decreased (P<0.001) from 0.84 (0.10) before rash onset to 0.63 (0.20) after rash onset, increasing thereafter, showing significant (P<0.05) QoL deterioration up to 60 days of follow-up. **CONCLUSIONS:** HZ pain can significantly reduce QoL and ability to perform daily activities of people living in Argentina highlighting the importance of early intervention or prevention. These findings are consistent with observational studies in other countries.

IN2
COSTO-EFECTIVIDAD DEL USO DE PRUEBAS TREPONÉMICAS RÁPIDAS PARA LA DETECCIÓN Y TRATAMIENTO TEMPRANO DE SÍFILIS GESTACIONAL EN COLOMBIA

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OBJECTIVOS: Evaluar la costo-efectividad del uso de pruebas treponémicas rápidas inmunocromatográficas (PTRI) para el tamizaje de Sífilis gestacional en Colombia. **METODOLOGÍAS:** Se desarrolló un árbol de decisiones en una cohorte hipotética de pacientes gestantes, las alternativas consideradas fueron: manejo convencional usando prueba no treponémica (VDRL) seguida de treponémica (FTA-ABS) frente a una propuesta usando PTRI, Inicio de tratamiento a gestantes positivas y prueba confirmatoria con VDRL. Se consideraron varios escenarios: Gestantes tamizadas antes de las 24 semanas y a contactos (GT1); Gestantes tamizadas antes de las 24 semanas sin contactos (GT2); Gestantes tamizadas antes de las 34 semanas con y sin contactos respectivamente (GT3), (GT4). La perspectiva fue la del tercer pagador y el horizonte temporal 10 meses. Se incluyeron los costos de los medicamentos, la estancia hospitalaria, los eventos adversos secundarios al uso de los medicamentos, las valoraciones médicas y paraclínicos en su seguimiento. Se realizó análisis de sensibilidad determinístico de las variables con mayor incertidumbre. El modelo fue desarrollado por un equipo de profesionales de la salud Epidemiólogos, Ginecólogos, con asesoría de especialistas en Economía de la Salud en el año 2012. **RESULTADOS:** La estrategia propuesta PRTI-VDRL presenta una dominancia absoluta sobre el manejo convencional VDRL-FTABS con una disminución de costos de US 210 y un aumento de efectividad del 0.18 (18% más de casos evitados de sífilis congénita) en el escenario GT1. Esta dominancia absoluta se observó también en los otros escenarios estudiados (GT2, GT3, GT4). El resultado de dominancia se mantuvo al realizar el análisis de sensibilidad en los escenarios incluidos, demostrando robustez de los resultados del modelo planteado. **CONCLUSIONES:** El uso de las PTRI como prueba inicial de tamizaje para detectar y tratar gestantes con sífilis es costo-efectivo en Colombia, evitando casos de sífilis congénita y sus consecuencias.

IN3
ANÁLISIS COSTO-EFECTIVIDAD DE INTERVENCIONES PARA EL MANEJO DEL TRASTORNO DEPRESIVO MAYOR (TDM) EN PACIENTES CON VIRUS DE LA INMUNODEFICIENCIA HUMANA (VIH+) QUE INICIAN TRATAMIENTO ANTIRRETROVIRAL DE GRAN ACTIVIDAD (TARGA)

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INTRODUCCIÓN: El Trastorno Depresivo Mayor (TDM) es la comorbilidad psiquiátrica de mayor prevalencia en personas con VIH y ocasiona menor adherencia al TARGA, lo que a su vez repercute en una mayor progresión de la enfermedad e incrementa los costos de atención para el sistema. **OBJECTIVOS:** Realizar un estudio de costo-efectividad de intervenciones para el manejo TDM en una cohorte hipotética de pacientes mexicanos con VIH bajo TARGA, desde el punto de vista del Sistema de Salud público en México. **METODOLOGÍAS:** Estudio de costo-efectividad mediante un modelo Markov, ciclosmensuales, para estimar la esperanza de vida por alternativa evaluada, la ocurrencia de sucesos y costos asociados, en pacientes que se encuentran por iniciar TARGA. El modelo está compuesto por los siguientes estados de salud: padecer VIH, estar bajo TARGA y presentar TDM; padecer VIH, estar bajo TARGA y no presentar TDM; muerte. Los comparadores incluidos son el uso de antidepresivos, la Terapia Cognitivo Conductual (TCC), combinación de ambas, ninguna intervención. Las probabilidades para la matriz de transición se obtuvieron de la literatura; y los costos médicos directos institucionales que se midieron son: antidepresivos, consultas especialistas, tratamiento de VIH/SIDA. Se corroboró la información con opinión de expertos. El horizonte temporal evaluado es la sobrevida del paciente. La tasa de descuento es 5%. Se realizó un análisis de costo efectividad incremental y un análisis de sensibilidad. **RESULTADOS:** La TCC fue la intervención más costo-efectiva. Las 3 alternativas resultan en un costo por año de vida ganado menor a un PIB per cápita y presentan una ganancia en salud similar (2.77 años). Costos: TCC ($ 22,622.412); antidepresivos ($24,659.7538) y para la combinación de tratamientos ($24,790.722). El análisis de sensibilidad demostró la robustez del modelo. **CONCLUSIONES:** El proporcionar tratamiento contra el TDM en pacientes con VIH bajo TARGA ofrece una ganancia en salud y resulta costo-efectivo para el sistema.

IN4
COSTO-EFECTIVIDAD DE TRES ESTRATEGIAS DIAGNOSTICAS PARA LA IDENTIFICACIÓN DE INFECCIÓN BACTERIANA SEVERA EN LACTANTES FEBRILES SIN FOCO

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OBJECTIVOS: Aun sigue siendo controversial el manejo del lactante febril (LFSF) sin foco entre uno a tres meses. La introducción de la vacunación contra neumococo ha reducido las tasas de bacteriemia oculta y alterado la utilidad de los tests disponibles para detección de infección bacteriana severa (IBS) en LFSF. El objetivo de este estudio fue determinar la costo-efectividad de tres pruebas para la detección de IBS en LFSF. **METODOLOGÍAS:** Se diseñó un modelo de costo-efectividad utilizando la técnica de análisis de decisiones, bajo la perspectiva del financiador (Obra Social) e incorporando los costos directos del tratamiento, hospitalización y diagnóstico; para comparar la razón de costo efectividad incremental entre la procalcitonina, proteína C reactiva y la escala de Rochester en una cohorte hipotética de 10.000 niños entre 1 a 3 meses con diagnóstico de LFSF. **RESULTADOS:** La proteína C reactiva resulta en un costo de AR$5341 por caso correctamente diagnosticado, frente a AR$5376. El costo por cada caso correctamente diagnosticado con la procalcitonina frente a la proteína C reactiva fue de AR$6127. La proteína C reactiva permanece siendo la estrategia más costo efectiva independiente de los valores dentro de los rangos declarados que puedan tomar los costos de internación y costo de la proteína C reactiva; así como los valores dentro del rango establecido de probabilidad de IBS, IBS por neumococo y efectividad vacunal. **CONCLUSIONES:** La proteína C reactiva constituye la estrategia más costo efectiva en la Argentina para la detección de la IBS en lactantes que acuden con SFSF. Sin embargo dado las moderadas proporciones de casos correctamente diagnosticados (<80%) aun existentes; estas pruebas deben ser interpretadas dentro del contexto clínico del paciente y no como método único para la toma de decisiones terapéuticas.

RESEARCH PODIUM PRESENTATIONS – SESSION II
CANCER OUTCOMES RESEARCH

CA1
IMPLICATIONS OF GLOBAL PRICING POLICIES OF PHARMACEUTICALS FOR ACCESS THE INNOVATIVE DRUGS: THE CASE OF TRASTUZUMAB IN SEVEN LATIN AMERICAN COUNTRIES

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OBJECTIVES: Differential pricing (DP) on the basis of countries' purchasing power has been recommended by the WHO to secure more affordably priced medicines. However, in developing counties (DC) many innovative drugs have similar or even higher prices than in high-income countries (HIC). We conducted a cost-effectiveness

(CE) analysis to estimate the impact of this pricing policy on the CE of trastuzumab in Latin-America (LA). **METHODS:** Model structure and a common methodology for identifying costs and resource use were agreed with country teams. A Markov model was designed to evaluate life years (LY), quality adjusted life years (QALYs) and costs from a health care sector perspective. A systematic search on effectiveness, local epidemiology and costs studies was undertaken to populate the model. A base case scenario using transition probabilities from trastuzumab clinical trials, and two alternative scenarios with transition probabilities adjusted to reflect breast cancer epidemiology in each country, were built to better fit local cancer prognosis. **RESULTS:** Incremental discounted benefits and costs of the trastuzumab strategy ranged from 0·87 to 1·00 LY, 0·51 to 0·60 QALY and $24,683 to $60,835 (2012 US dollars). Incremental CE ratios ranged from $42,104 to $110,283 per QALY, equivalent to 3·6 gross domestic products per capita (GDPc) per QALY in Uruguay to up to 35·5 GDPc per QALY in Bolivia. The probabilistic sensitivity analysis showed a 0% probability that trastuzumab is CE if the willingness-to-pay (WTP) threshold is one GDPpc per QALY, and remains 0% at a WTP threshold of three GDPc except in Chile and Uruguay (probability 4·3% and 26·6% respectively). **CONCLUSIONS:** Despite its proven CE in other settings, trastuzumab was not CE in LA at its current price. Better cooperation between the public and private sectors is still needed to make innovative drugs available and affordable in DC.

CA2

NATIONAL SPENDING WITH SCREENING, DIAGNOSIS AND TREATMENT OF CERVICAL CANCER: ESTIMATES BASED ON HEALTH INFORMATION SYSTEMS, BRAZIL, 2006

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OBJECTIVES: To estimate national expenditure with procedures of the National Cervical Cancer Control Program. **METHODS:** A cost description study was conducted to develop estimates of expenditures related to care held under the National Cervical Cancer Control Program in Brazil. Health Information Systems of the Public Health System, SUS (SIH, SIA, APAC, SIAB, and SIGTAP SISCOLO), national survey (PNAD 2008), and guidelines of INCA / MS, and reference systems for payments of the private system were consulted to construct estimates of direct and indirect costs. The estimates were grouped by sets of procedures of the stages of cervical cancer care (screening, diagnosis, treatment of precancerous lesions of the cervix - CIN I and CIN II / III and treatment of cervical cancer). The study was conducted from the perspectives of the health care system and society. **RESULTS:** The total direct cost of SUS in 2006 was estimated at R$ 227,167,515, ambulatory visits were responsible for 27% of spending. Screening represented the highest spending. The estimated total direct spending to the private sector in 2006 was R$ 938,707,221, ambulatory visits were responsible for 68% of spending. The transport costs were estimated at R$ 230,533,910. Lost productivity was based on the human capital approach and was estimated at R$ 1,463,977,777. The final value of the direct and indirect costs estimated and adjusted for the year 2008 was R$ 3,193,335,402. **CONCLUSIONS:** Spending with National Cervical Cancer Control Program is very significant. There is need for more costing studies in the country, alongside a greater structuring of official systems cost data available in order to contribute to the standardization and accuracy of the estimates of national costs.

CA3

ANÁLISIS DE COSTO-EFECTIVIDAD DE ESTRATEGIAS DE PREVENCIÓN PRIMARIA Y SECUNDARIA PARA CÁNCER DE CUELLO UTERINO EN COLOMBIA

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OBJECTIVOS: Evaluar la costo-efectividad de estrategias de prevención primaria (vacunación) y secundaria (tamización) para la prevención del cáncer de cuello uterino en Colombia. **METODOLOGÍAS:** Un modelo de Markov de la historia natural del cáncer de cuello uterino fue desarrollado para evaluar las siguientes estrategias: no tamización, tamización (citología convencional y en base líquida, pruebas ADN VPH, pruebas rápidas de ADN VPH y via vili), vacunación y tamización + vacunación. Las estrategias se evaluaron solas o combinadas, para un total de 32 estrategias evaluadas. Los años de vida ganados (AVG) fueron usados como medida de efectividad. El estudio tuvo la perspectiva del tercero pagador, solo se incluyeron costos directos. Se calcularon razones de costo-efectividad y costo-efectividad incremental, se condujeron análisis de sensibilidad determinísticos y probabilísticos. Se aplicó tasa de descuento del 3% a los costos y resultados en salud. **RESULTADOS:** Las estrategias que quedaron sobre la frontera eficiente fueron: la vacunación, la vacunación más las pruebas rápidas de ADN VPH cada 10 años desde los 35 - 50 años, la vacunación más la prueba de ADN VPH cada 3 años desde los 30-69 años con triage (via vili) y sin triage de las mujeres positivas a la prueba y la vacunación más la citología en base líquida en el esquema 1-1-1-3 desde 25-69 años. El costo por año de vida ganado para las estrategias arriba mencionadas fue de $US 1.288, $US 6.447, $ US 8.875, $US 14.186 y $US 94.503 respectivamente. El análisis probabilístico mostró que para umbrales de disponibilidad a pagar superiores a $US 13.000 la tamización con prueba de ADN-VPH cada 3 años más vacunación es la estrategia más costo-efectiva. **CONCLUSIONES:** La tamización con prueba ADN-VPH cada 3 años más vacunación en mujeres de 12 años sería una alternativa costo-efectiva para Colombia.

CA4

EMERGING CARDIOVASCULAR EVENTS ASSOCIATED WITH TARGETED ANTICANCER DRUGS. PRELIMINARY RESULTS OF A CARE LINE'S PROGRAM BASED ON AUDIT VIGILANCE IN A PRIVATE HEALTH CARE IN BRAZIL

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OBJECTIVES: Retrospective study of oncology patients with cardiovascular event, in order to help an decision. There is evidence regarding the prognosis of cancer patients, which is seen as a carrier of a chronic disease that throughout its evolution may have acute decompensation, as cardiovascular manifestations. Progress in cancer treatment also resulted in increased exposure of patients to cardiovascular risk factors and chemotherapy with potential cardiotoxicity and sure for expenses in terms of adding costs of care. **METHODS:** We analised 68 cases collected and registered by the time of cardiology and oncology audit, in 2012. Outocmes items used: Costs, cardiovascular events associated with cancer. **RESULTS:** Among 68 cases, Breast Cancer is the majority accounting 32 (47%). All of them were seen by cardiologist and the total amount spent were US$15.000,00 . Thirty one patients were caracterized having a cardio - vascular event and the costs were comprise by echocardio, ergo-cardio test, angio tomography and coronary cardiac catheterization. The costs of oncology treatment range from $1.500,00 to $ 6.800,00 USD per cicle, each 21 or 28 days, that means $18.000,00 to $ 120.000,00 USD a year . It means that the provisional budget will range from $ 1.224.000,00 to $ 8.160.000,00 USD a year for the cohort of 68 patients in our institution. So, we will spend 0.18 % to 1.22 % in cardiac vigilance for the oncologic patients describe above. **CONCLUSIONS:** The costs still low, the price of the oncologic cure with an cardiologic event needs more studies, details need for further recomendations.

FORMULARY DEVELOPMENT AND PUBLICATION OF COST STUDIES

FD1

RESULTADOS DE LA ENCUESTA "CHANGE PAIN" LATINOAMERICANA: DIAGNOSTICO Y TRATAMIENTO ACTUAL DE LOS PACIENTES CON DOLOR CRÓNICO

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OBJECTIVOS: La "Change Pain Survey at EFIC 2009- Physian's perception on management of severe chronic non-cancer pain" realizada en países europeos, confirma la falta de conocimiento para el dolor neuropático y las variedades de enfoques del tratamiento del dolor crónico sin utilizar una guía consistentemente. Aplicando la misma encuesta a médicos generales y especialistas en países de América Latina, se exploró la percepción y comprensión de la forma de manejo del dolor crónico en América Latina. **METODOLOGÍAS:** Se realizaron 2130 encuestas vía electrónica de octubre 2012 a marzo 2013, en forma aleatoria a médicos generales y especialistas a través de sociedades médicas, fuerza de ventas o aplicadas en congresos médicos de 15 países de América Latina, poniendo énfasis en la percepción del tipo de dolor para elección del tratamiento. **RESULTADOS:** El porcentaje por especialidad fue: 18% traumatólogos, 12% médicos generales, 12% de rehabilitación, 13% anestesiólogos, 10% algólogos, y otras especialidades menores a 5%. Clasifican el dolor crónico muy heterogéneamente, desde nivel 4 al 9, en una escala del 1-10. Sus objetivos del tratamiento del dolor son reducción del dolor (30%) y calidad de vida (27%). La elección terapéutica para el dolor la deciden por eficacia (19.28%), tolerabilidad (21.83%), eficacia/equilibrio de efectos adversos (24.69), calidad de vida (18.19%) y costo (15.99%). Perciben un conocimiento limitado de las opciones terapéuticas y sobre la diferencia fisiológica entre dolor nociceptivo y dolor neuropático. **CONCLUSIONES:** La encuesta muestra una ausencia de estandarización en el tratamiento de dolor crónico y desconocimiento de las opciones terapéuticas ideales para el dolor crónico. Existe una necesidad de contar con un mejor conocimiento sobre el dolor crónico para lograr un adecuado manejo multimodal para su seguimiento y control.

FD2

ESSENTIAL MEDICINE LIST (CUADRO BÁSICO) IN MÉXICO. IS IT A GUIDELINE FOR DECISION MAKING ON THE CURRENT AND FUTURE HEALTH NEEDS?

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OBJECTIVES: Cuadro Básico is a list of minimum medicines needed for a basic health care system, listing the most efficacious, safety and cost-effective medicines for priority conditions. The importance is to ensure availability of drugs for current and future public health relevant diseases. The objective is to describe the characteristics of National List in Mexico and compare it with the Instituto Mexicano Seguro Social (IMSS) List in order to hypothesize the relevance of the drugs included on both Lists versus current and future health needs in the country. **METHODS:** It was performed a descriptive analysis of the two lists organized by therapeutic area. The description includes number of total codes, and number per therapeutic area. The information was compared to find the gaps on the number of codes between the two Lists. In addition it was identified the top health priorities and prevalence. **RESULTS:** National list has 1631 codes; the therapeutic areas with the majority of codes are infectious diseases (222) and Oncology (150). IMSS List has 1145 codes. The biggest relative difference between the two lists come from codes available for neurology, dermatology and ophthalmology; 57%, 56% and 45% codes are not available at IMSS, respectively. The top mortality causes in Mexico are heart disease, diabetes, cancer, accidents, liver diseases, stroke and COPD. If the analysis is made by disease, it worth mention that COPD only have 3 codes at IMSS and 7 codes at National Listing, while Alzheimer disease do not have any code at IMSS. **CONCLUSIONS:** A more extensive analysis (already available) brings information about the gaps between health needs and the drugs available. Mexico has an increased number of an aging population, which requires access to different drugs. The Essential list of WHO has 315 compounds versus Mexican which has 1631 codes. Is it a good guideline for decision makers?

FD3

¿PUEDE UN CAMBIO DEL 2003 EN EL REGLAMENTO EN EL CUADRO BÁSICO (CBM) EN MÉXICO IMPACTAR LA CANTIDAD DE ESTUDIOS CIENTÍFICOS PUBLICADOS DE EVALUACIÓN ECONÓMICA COMPLETOS DE MEDICAMENTOS (EECM) EN LOS ÚLTIMOS 10 AÑOS?

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OBJECTIVOS: Efectuar una revisión sistemática de los EECM realizados en México de 1983 a 2012 y evaluar el impacto que tuvo con la adición del reglamento del 2003 en CBM. **METODOLOGÍAS:** Se realizó revisión sistemática de artículos publicados entre 1983 a 2012 de EECM que cumpliera los siguientes requisitos: humanos, idioma español e inglés, realizados en México, no se tomó en cuenta resúmenes presentados en congresos. La búsqueda se realizó en Pub Med, CRD, ScienceDirect, Imbiomed, Medigraphics y la BSV (OMS). Los estudios EECM fueron clasificados de acuerdo a Drummond (2005). Se realizó un análisis de estadística descriptivo, por año de publicación, tipo de estudio, fuente de financiamiento, especialidad. Asimismo, se ejecutó un análisis de comparación de tres períodos continuos (1983/1992, 1993/2002, 2003/2012) para mostrar el crecimiento de EECM por el cambio de reglamento del 2003. **RESULTADOS:** Se identificaron un total de 154 artículos, de esos 68 (44,16%) son EECM. El tipo de estudio más publicado fue costo efectividad (80.88%). Los modelos económicos más utilizados fue el árbol de decisiones (36.66%) y markov (35%). Las especialidades donde se publicó más fueron infectología (14.7%), oncología y ginecología (11.8%). En el período de 1983/1992 se publicaron 1 artículo EECM, 1993/2002 6 y 2003/2012 61. La tasa de crecimiento de 2003/2012 con respecto al 1993/2002 fue del 916.66%, mientras el financiamiento de la industria farmacéutica en ese mismo período creció en 3,095%. **CONCLUSIONES:** Debido al cambio del reglamento en el 2003 en el proceso de inclusión de medicamentos al sector público, impacto de forma positiva en el crecimiento de las publicaciones en EECM en México, siendo su principal fuente de financiamiento la industria farmaceútica.

PRICING STUDIES

PR1

ANÁLISIS DEL IMPACTO EN LA DEMANDA DE TECNOLOGÍAS INCLUIDAS EN EL PLAN DE BENEFICIOS COLOMBIANO (POS) POSTERIOR A SU ACTUALIZACIÓN EN 2012

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OBJECTIVOS: Analizar el impacto de la demanda de tecnologías, tras la actualización del plan de beneficios colombiano (Plan Obligatorio de Salud POS) en 2012, como indicador del acceso a los servicios de salud. **METODOLOGÍAS:** De una muestra aleatoria de 20 medicamentos (37% de las tecnologías incluidas), se analizaron las unidades despachadas según el registro del Sistema de Información de Precios de Medicamentos (SISMED) para sus canales comerciales e institucionales (farmacias, y aseguradoras u hospitales, respectivamente) de 2010 a 2012; estimando lo cambios porcentuales anuales. Las tecnologías que estaban previamente cubiertas en el plan, en la misma indicación, fueron incluidas en el análisis. Para el análisis se definieron 5 intervalos según el nivel de cambio: <-25%, -25% a 0%, 0% a 50%, 50% a 100% y >100%. No se realizó análisis de precios porque durante ese periodo cambió la legislación que los regula. **RESULTADOS:** El 60% de las tecnologías incorporadas presentó un aumento del doble o más, en sus unidades despachadas; y el 15% presentó crecimientos entre el 50% y 100%, mayormente en el canal institucional. Los comparadores de uso para patologías específicas, presentaron disminución en su participación de mercado, tanto en el canal comercial como institucional. Por ejemplo, aciclovir, disminuyó su uso en más del 25%, frente al 2010. El 10% presentó disminución de uso con el ingreso al plan. **CONCLUSIONES:** Aunque los usuarios podían acceder a las tecnologías por vías de carácter legal o administrativo, la incorporación de las nuevas tecnologías en 2012 mejoró el acceso a los servicios de salud entendido como un mayor consumo de tecnologías y se reemplazaron tecnologías en uso desde hace más de 10 años. Si bien esto podría ser un efecto del aseguramiento, al ser los medicamentos resultado de una atención médica, este incremento podría entenderse como pacientes efectivos con mayor acceso.

PR2

ECONOMIC EVALUATION OF AN URINE CLOSED COLLECTION SYSTEM VERSUS A TRADITIONAL OPEN DEVICE IN NON-PREGNANT WOMEN

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OBJECTIVES: The study assessed the cost-effectiveness (CE) of a medical device, an urine collection/transportation system containing or not preservative (UCTS) versus the traditional open device (TOD). The evaluated UCTS is used to collect and transport urine specimens, reducing contamination, and providing more accurate test results to establish UTI presence in non-pregnant women from the Mexican Institute of Social Security (IMSS) perspective. **METHODS:** The CE analysis was based in a decision model, considering a time horizon of two weeks after urine samples were collected. The number of correctly diagnosed UTI was the effectiveness measure. Data was obtained from available published studies reporting contamination rates. To calculate the effectiveness measure of the diagnoses process, a hypothetical cohort of 500 patients was simulated and positive/negative predictive values of the laboratory tests involved in the process were considered for adjustment. Direct medical costs were included and obtained from IMSS available data. CER and ICER were calculated to establish the cost-effectiveness of both medical devices. Univariate and multivariate sensitivity analysis, using pricing discounts and effectiveness were performed. **RESULTS:** Costs of UTI diagnosis in the hypothetical cohort using the UCTS were USD1907.40 compared to USD 2163.2 with the TOD. The number of correctly diagnosed UTI for each alternative was 25% and 51% respectively. CER were USD 3742.80/correctly diagnosed UTI and USD 8,597.79/correctly diagnosed UTI with the TOD. ICER analyses suggest that UCTS is a cost effective alternative, saving USD 4854.99 for each correctly diagnosed UTI. The sensitivity analysis confirmed the robustness of the modeled parameter estimates. **CONCLUSIONS:** . The results from the analyses indicates that UCTS (containing or not preservative) provides a highly cost-effective alternative compared with TOD for collecting, transporting and improving the quality of urine specimens in non-pregnant women from the payer perspective in Mexico.

PR3

ANÁLISIS COSTO-EFECTIVIDAD DE LINEZOLID COMPARADO CON VANCOMICINA EN EL MANEJO DE LA NEUMONÍA ASOCIADA A LA VENTILACIÓN MECANICA EN COLOMBIA

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OBJECTIVOS: La neumonía asociada a la ventilación mecánica (NAV) es la causa más frecuente de morbi-mortalidad en las unidades de cuidado intensivo. La incidencia de NAV en Colombia oscila entre 7 y 29 casos por cada 1000 días de intubación orotraqueal. Adicionalmente, la ventilación mecánica aumenta el riesgo de infección por *Staphylococcus aureus resistente a meticilina*(SARM). El objetivo de este trabajo es estimar la costo-efectividad del tratamiento con linezolid versus con vancomicina en el manejo de la NAV causado por SARM en Colombia. **METODOLOGÍAS:** Se construyó un árbol de decisión para determinar la razón de costo-efectividad incremental de linezolid (600 mg IV/12h) comparado con vancomicina (1g IV/12h) en el tratamiento de NAV por SARM. El estudió se llevó a cabo desde la perspectiva del tercer pagador incluyendo solo costos directos. Todas las unidades monetarias se expresan en dólares americanos (1 US$ = 1.785 COP). Se empleó un horizonte temporal de 30 días. La unidad de resultado fueron los años de vida ajustados por calidad (AVAC). Los datos de efectividad, seguridad y utilidad se tomaron de la literatura, los costos de los procedimientos se obtuvieron del manual tarifarios ISS, para medicamentos se utilizó el SISMED y la regulación de precios vigente (circular 04 de 2012). Se realizaron análisis de sensibilidad univariados y probabilísticos. **RESULTADOS:** Los costos totales esperados por paciente fueron: linezolid (US$ 1589), vancomicina (US$ 1461). Los resultados en términos de AVAC para cada alternativa fueron: Linezolid 0,91; vancomicina 0,87. La razón de costo-efectividad incremental de Linezolid comparado con vancomicina fue US$ 3090 por AVAC. **CONCLUSIONES:** Asumiendo como umbral el PIB per cápita para Colombia en 2012 (US$ 7104) linezolid es una estrategia costo-efectiva en el tratamiento de NAV por SARM.

PR4

ESTUDIO TRANSVERSAL DEL PROCESO DE ACTUALIZACIÓN DE MEDICAMENTOS EN EL CUADRO BÁSICO Y CATÁLOGO DE INSUMOS DEL SECTOR SALUD

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OBJECTIVOS: Los altos costos generados por el actual perfil epidemiológico y la introducción de nuevas tecnologías, impactan en los sistemas públicos, panorama que se complica cuando el gasto en salud es bajo, en especial para medicamentos, donde la mayor parte de este gasto es de bolsillo. Ello hace ineludible el diseño de estrategias para solventar los retos, como fué el fortalecimiento del CBCISS. Este estudio describe los resultados del proceso de actualización de medicamentos al CBCISS para garantizar la eficacia, seguridad y eficiencia de insumos utilizados en las instituciones públicas de salud. **METODOLOGÍAS:** Se realizó un corte transversal del proceso de actualización de medicamentos, de septiembre del 2011 a diciembre del 2012, con un análisis descriptivo para cada etapa (valoración, evaluación y dictamen). **RESULTADOS:** De 394 solicitudes recibidas y valoradas, 244 (62%) correspondieron a medicamentos, de ellas, 151 (62%) cumplieron los requisitos para su evaluación (32% fueron modificaciones y 68% inclusiones), se dictaminaron procedentes el 42% (61% de las modificaciones y 33% de las inclusiones). El 73% de las inclusiones procedentes fueron por consenso, 12% condicionadas a baja de precio y 6% por mayoría de votos, esencialmente. Las principales causas de rechazo fueron: falta de evidencia clínica (31%) y problemas metodológicos en la evidencia económica (27%). **CONCLUSIONES:** El fortalecimiento del proceso se realizo con rigor metodológico basado en análisis crítico de evidencia científica, con transparencia y legitimidad bajo un marco legal para favorecer la optimización de recursos. El mayor porcentaje de solicitudes fueron para medicamentos, que constituyen la tecnología terapéutica más utilizada, que requiere una selección adecuada para garantizar mayor beneficio al menor riesgo y costo posible. La evaluación económica fue herramienta de apoyo para considerar además del precio, el valor de la salud determinado por la calidad de la evidencia, estableciendo un PIB como límite de disposición a pagar.

COST, RISK FACTOR & UNIVERSAL COVERAGE STUDIES

RF1

EFECTO DEL SEGURO POPULAR SALUD SOBRE LA DEMANDA DE SERVICIOS PRENATALES EN EL CONTEXTO DE LA COBERTURA UNIVERSAL, MÉXICO 2012

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OBJECTIVOS: La atención prenatal oportuna es una estrategia efectiva para reducir el riesgo de mortalidad materna. En 2003, en México, se creó el Seguro Popular de Salud (SP); uno de sus objetivos es contribuir a reducir el riesgo de mortalidad materna, a través de intervenciones como la atención profesional del embarazo/parto, incentivar el acceso efectivo a servicios de salud y su mayor demanda. Así, el objetivo de este estudio fue analizar el efecto del SP sobre la demanda oportuna (*DO*) de servicios prenatales y la demanda de al menos 4 visitas prenatales durante el último embarazo (*4VP*) del mujeres mexicanas. **METODOLOGÍAS:** Se utilizó la Encuesta Nacional de Salud y Nutrición de México 2012. El efecto del *SP* sobre *DO* y *4VP*se estimó a partir de métodos no experimentales de pareamiento. Se exploraron además posibles fuentes de heterogeneidad de dicho efecto atribuibles a elementos individuales (la escolaridad y el nivel socioeconómico, NSE) y de contexto (nivel de desarrollo del lugar de residencia). **RESULTADOS:** El SP incrementó la DO en mujeres de NSE I (RM=1.88, $p<0.05$) y la posibilidad de demandar *4VP* (RM=1.65, $p<0.01$). No obstante, al incluir la *DO* como predictor de *4VP*, el *SP* perdió importancia en la explicación de este indicador; en este modelo la *DO* incrementó los momios de *4VP* (RM=6.2, $p<0.01$). Tanto la DO como

4VP se incrementaron con la escolaridad de las mujeres. **CONCLUSIONES:** Pese a los resultados favorables en salud materna atribuibles al SP; es importante redoblar el esfuerzo del sistema mexicano de salud por lograr la cobertura efectiva en salud de la población más vulnerable de México. El uso eficiente y equitativo de los recursos será indispensable para consolidar el acceso universal a la salud en México.

RF2

EPIDEMIOLOGICAL AND ECONOMIC IMPACT OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH HYPERTENSION AND DIABETES IN COLOMBIA

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OBJECTIVES: Epidemiologic transition from infectious to noncommunicable diseases (NCDs) in most countries may increase disease and economic burden. Chronic kidney disease (CKD) is a public health problem worldwide. In Colombia, CKD is related to catastrophic health expenses in the overall health care system. The aim of this study is to assess epidemiological and economic impact of CKD in people with risk factors for CKD in Colombia. **METHODS:** A Markov decision model was carried out to estimate the burden of disease of CKD in Colombia. The Markov model have seven states, which followed people with diabetes mellitus (DM) and hypertension from disease onset to 90 years old (in 50 annual cycles). Five states went from CKD stage-1 to CKD stage-5, one transplant state and one absorbing state (death). Parameters were drawn from a literature review. Direct costs were drawn from a sample of patients with end-stage CKD from a large insurer in Colombia between 2009 and 2011. Outcome measures were: cases of CKD, deaths, disability-adjusted life-years (DALYs), and treatment costs. **RESULTS:** In Colombia, of 1,899,572 patients with hypertension and DM (62.9% were women), 1,083,735 (57.1%) developed CKD. Of all cohort deaths, 55% were caused by CKD. 4,413 transplants occurred in the cohort. 6.3 millions DALYs are associated to CKD in women, and 10.9 in men, for a total of 17.3 millions. The mean cost per patient with end-stage CKD is around I$20.6 dollars (PPP adjusted). This burden would represent I$45.8 billions dollars (14.1% of estimated Gross Domestic Product of Colombia) if all cases were attended. **CONCLUSIONS:** Despite limitations, this study shows the increasing economical and disease burden of NCDs in developing countries. This study also highlights the challenge on health systems of increasing aging population and risk factors for NCDs in developing countries such as Colombia.

RF3

FACTORES PREDICTORES DE OBSTRUCCIONES CORONARIAS SIGNIFICATIVAS EN PACIENTES ADULTOS CON CINEANGIOCORONARIOGRAFÍAS REALIZADAS EN URUGUAY FINANCIADAS POR EL FONDO NACIONAL DE RECURSOS

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OBJECTIVOS: La realización de una cineangiocoronariografía (CACG) es el gold Standard para definir la anatomía coronaria. El porcentaje de lesiones coronarias no significativas varía según la magnitud de obstrucción definida; siendo del 9 al 25 % cuando consideramos lesiones menores al 50 %. Existen factores predictores como sexo masculino, edad avanzada, diabetes, dislipemia y tabaquismo. El Fondo Nacional de Recursos (FNR), financia según normativas de cobertura institucionales, prestaciones médicas altamente especializadas en Uruguay, entre ellas las CACG de las cuales reúne un registro único nacional. Objetivos: 1) Conocer el porcentaje de CACG con lesiones coronarias significativas (mayores al 50 %) realizados entre 1/07/2011 y 30/06/2012; 2) Identificar el tratamiento elegido luego de su realización; 3) Describir los factores predictores que permitan identificar pacientes con alto riesgo de tener lesiones coronarias significativas. **METODOLOGÍAS:** Estudio retrospectivo de una cohorte histórica de pacientes consecutivos mayores de 18 años, con CACG realizada en el período establecido . Se excluyeron las solicitadas por enfermedad cardíaca no coronaria. **RESULTADOS:** Se incluyen 6.737 CACG, de los cuales son de sexo masculino 67,2% , con una media de edad de 64,7 años. El total de CACG realizadas con lesiones mayores al 50 % fue 5.737 (85,1%). En 1549 (23 %) se optó por el tratamiento médico. Los factores de riesgo retenidos en el modelo de regresión logística fueron: edad > 50 años, sexo masculino, procedencia geográfica, diabetes, dislipemia, tabaquismo, ausencia de obesidad, oportunidad del procedimiento, y tener un infarto trasmural. **CONCLUSIONES:** El porcentaje de CACG con lesiones significativas se encuentra dentro de lo reportado en la bibliografía internacional lo que traduce un adecuado proceso de toma de decisiones. La identificación de factores de riesgo es de utilidad para este proceso de financiamiento de CACG en aquellos pacientes con mayor riesgo de presentar lesiones coronarias significativas.

RF4

COST-EFFECTIVENESS OF VARIOUS COMBINATIONS OF HUMAN PAPILLOMAVIRUS (HPV)-BASED PRIMARY SCREENING TESTING, INCLUDING GENOTYPING FOR HPV 16/18, FOR CERVICAL CANCER SCREENING IN MEXICO

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OBJECTIVES: To determine the cost-effectiveness of various cervical cancer (CxCa) screening algorithms including the cobas HPV Test in Mexico, which identifies HPV genotypes 16/18 individually while simultaneously detecting the other high-risk HPV types. **METHODS:** A cohort Markov model was developed to compare five CxCa screening strategies: (S1) cytology only, (S2) cytology with reflex HPV; (S3) HPV with reflex cytology, and (S4) cytology and HPV co-testing; (S5) cobas HPV with genotyping and reflex cytology. Screening began at age 30 with a routine screening interval of every 3 years, and was modeled over a time horizon of 40 years. Performance of the overall screening strategies was derived from the ATHENA (Addressing THE Need for Advanced HPV Diagnostics) trial. Trial baseline data were used for the base case, and 1-year follow-up outcomes were estimated for the alternative scenario, assuming all persistent disease is detected in the subsequent visit. The direct costs for screening and treatment of CxCa were estimated using the perspective of Mexican Institute of Social Security (IMSS). Costs were in 2010 US dollars. Costs and quality-adjusted life years (QALYs) were discounted at 3% annually. One-way sensitivity analyses were conducted. **RESULTS:** Using a $20,000/QALY threshold, baseline screening with S5 dominated S3 and S4 by reducing overall cost, annual cancer incidence, and improving QALYs; and was cost-effective compared to S1 and S2. In the 1-year follow-up scenario, S5 was cost-effective compared to all other strategies. Detection of HPV 16/18 with S5 resulted in earlier diagnosis of clinically relevant CIN 2/3 at the initial visit as well as more efficient use of screening tests during follow-up. Sensitivity analyses showed that test sensitivities were the most impactful on model results. **CONCLUSIONS:** Incorporating the cobas HPV test with HPV 16/18 genotyping was cost-effective compared to various CxCa screening strategies, and resulted in improved protection against CxCa.

TRENDS IN HEALTH CARE STUDIES

TR1

SELF-REPORTED HEALTH STATUS AND EQ-5D-3L VALUES OF THE ARGENTINE POPULATION: COMPARING 2005 VERSUS 2009 NATIONAL RISK FACTOR SURVEYS

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OBJECTIVES: To describe and compare general population self-reported health and EuroQol EQ-5D-3L values in 2005 and 2009 Argentina national risk factors survey. **METHODS:** The 2005 and 2009 waves included 41,392 and 34,732 adults, randomly selected from all Argentine provinces with a probabilistic multi-stage sample design. We report general population summary data on health status (EQ-5D-3L and the general health question of SF-36) as well as of different sociodemographics subgroups. Argentine time-trade off (TTO) and visual analog scale (VAS) values (V) weights were used. A descriptive analysis was done. 2005 results were compared to 2009 using Rao-Scott chi-square or regression analysis. **RESULTS:** Good or better self reported health was similar in 2005 and 2009 (80.1 vs. 80.7%). More people reported no limitations in all EQ-5D domains in 2009 vs. 2009 (61 vs. 57%; p<0.001). Mean values in 2005 versus 2009 were: VAS 75.3 vs. 75.9; p=<0.001; TTO 0.89 vs. 0.91; p==<0.001; VAS-V 0.86 vs. 0.88; p=<.001. 63 vs. 66% of males and 52 vs. 56% of females; 71 versuss 77% of 18-24y; and 37 versus 36% of 65+y; 63 versus 69% in the higher education category reported no limitations. VAS; TTO; and VAS-V 2005 versus 2009 in subjects without limitations: 82.4; 1; 1 versus 82.4; 1; 1; while in subjects with any limitation figures were 66.5; 0.76; 0.69 versus 66.2; 0.76; 0.69. **CONCLUSIONS:** In this analysis of the first two waves of Argentina National Risk Factors Survey, we found a small secular trend between 2005 and 2009, showing slightly better self reported health in 2009. There are few population surveys in our region that incorporated health status measures and did it in a periodic basis. These results can serve as a benchmark for future population studies and also as inputs for cost-utility analysis of health technologies in Argentina and Latin America.

TR2

ANÁLISIS BIBLIOMÉTRICO DE LA PRODUCCIÓN CIENTÍFICA EN ECONOMÍA DE LA SALUD EN LATINOAMÉRICA

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OBJETIVO: Analizar el nivel de producción científica en economía de la salud en Latinoamérica aplicando métodos de valoración cuantitativos de recuento y de análisis bibliométrico. **MÉTODO:** La revisión fue hecha a partir de la base de datos Scopus, dada su mayor cobertura de acuerdo a Academic Database Assesment Tool. Los resultados se analizaron a través de indicadores de producción, difusión, colaboración y bibliométricos, en los que se contemplaron tendencias de publicación, autores, tipo de documento, área de trabajo, revistas, país (Latinoamericanos), número de citaciones, factor de impacto, el índice h, y red de difusión. **RESULTADOS:** Se encontraron 860 artículos científicos con autores de afiliación institucional en países latinoamericanos. La función de crecimiento anual presentó una tendencia exponencial en los últimos veinte años. Brasil, México, Argentina, y Chile son los países con mayor impacto y desarrollo en el campo de economía de la salud aportando el 80,6% del total de referencias encontradas. La producción se encuentra vinculada especialmente a instituciones universitarias y grupos de investigación, principalmente la Universidad de Sao Paulo, la Fundación Oswaldo Cruz, Universidad de Chile. Las áreas de mayor presencia son: medicina (64%); ciencias sociales (7,5%); y ciencias biológicas (5,4%). La economía de la salud cuenta con un índice h: 22. **CONCLUSIÓN:** La producción científica en economía de la salud en Latinoamérica muestra un creciente desarrollo y arraigo institucional. Se espera que el entendimiento y posicionamiento de esta materia cuente como herramienta de soporte en la toma de decisiones para los gobiernos de la región y en la asignación de recursos para la salud.

TR3

A MULTI-NATIONAL SURVEY ASSESSING THE RELATIONSHIP BETWEEN PROPHYLAXIS TREATMENT AND HEALTH-RELATED QUALITY OF LIFE AMONG SEVERE HEMOPHILIA A PATIENTS IN LATIN AMERICA

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OBJECTIVES: Research has shown that Hemophilia A patients report lower health-related quality of life (HRQOL) compared to the general healthy population. While a primary prophylaxis (PP) treatment regimen reduces bleed rates, it remains unclear if it is associated with improved HRQOL. The objective of this analysis was to determine if treatment regimen was associated with better HRQOL among hemophilia A patients in Latin America based on patient self-report. **METHODS:** This cross-sec-

tional survey of severe hemophilia A patients ≥ 18 or older, or the parent/caregiver of patients aged 2-17 was administered in Argentina, Chile, Colombia, Mexico and Panama. A centralized ethics review board approved the study. Eligible, consenting patients completed a questionnaire: from October-November 2009 (Argentina), June-August 2011 (Chile, Colombia, Mexico) and September-October 2012 (Panama). HRQOL was measured by the Short Form 12 (SF-12) for adults and the Pediatric Quality of Life Inventory (PedsQL) for children. Treatment characteristics were also assessed. **RESULTS:** A total of 435 severe hemophilia A patients participated in this study, 58% of whom were adults. Overall, 238 (48%) patients were either receiving primary or secondary prophylaxis (SP). An ordinary least squares regression was performed with SF-12 Physical Component Score (PCS) as the dependent variable, and PP, and SP as independent variables. Age and country were included as control variables. On average, the PCS score was 8.64 points higher among PP patients compared to on-demand (OD) patients after adjusting for age and country (p=0.0363). A comparable analysis among children using the PedsQL Physical Summary score revealed a similar trend: on average, the physical HRQOL score was 7.15 points higher among PP patients, compared to OD controlling for age and country, however this was not significant. **CONCLUSIONS:** Results suggest that primary prophylaxis treatment may be associated with improved physical HRQOL.

TR4

LA PROTECCIÓN FINANCIERA Y EL GASTO DE BOLSILLO EN SALUD DE LA POBLACIÓN MEXICANA 2002-2010

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OBJECTIVOS: Analizar distintos aspectos del gasto de bolsillo en salud de los hogares mexicanos para estimar el impacto de la protección financiera del aseguramiento público en salud. **METODOLOGÍAS:** Se estima el porcentaje de hogares con gasto catastrófico o empobrecedor en salud y su relación con ingreso, condición de aseguramiento, tipo de localidad y rubro de gasto en salud, usando la Encuesta Nacional de Ingreso y Gasto de los Hogares 2002-2010 y una adaptación de la metodología de la Organización Mundial de la Salud así como la definición oficial mexicana de línea de pobreza alimentaria, de ingresos y gastos corrientes totales en los años respectivos. **RESULTADOS:** El porcentaje de hogares con gastos catastróficos en salud presentó una tendencia decreciente a partir de 2006. Los hogares con gastos empobrecedores en salud experimentaron una tendencia decreciente durante el período analizado. Los hogares con ambos gastos en salud, concentrados en localidades rurales, presentan una tendencia decreciente a partir del 2006. El gasto de bolsillo en salud por rubro se concentra en los medicamentos sin receta y vitaminas, alcanzando un promedio de 57.4% en el periodo analizado, independientemente de la condición de aseguramiento, nivel de ingreso y tipo de localidad. **CONCLUSIONES:** La reducción del gasto catastrófico puede estar vinculada con el importante incremento en la protección financiera de la población a través del Seguro Popular de Salud. Se requiere analizar a mayor detalle la dinámica del gasto de bolsillo en medicamentos para generar políticas públicas que incidan en su reducción procurando una mayor protección financiera a hogares vulnerables.

RESEARCH POSTER PRESENTATIONS – SESSION I
HEALTH CARE USE & POLICY STUDIES – Consumer Role in Health Care

PHP1

PERFIL DE ADESÃO AOS PLANOS DE BENEFÍCIO EM MEDICAMENTOS

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OBJETIVOS: Analisar o comportamento de consumo após implantação de benefícios farmácia para diferentes clientes com variados percentuais de desconto e reembolso. **MÉTODOS:** Utilizando a base de dados Orizon, que transaciona cerca de 7milhões de medicamentos ano via plano de beneficio medicamentos (PBM), selecionou-se quatro planos com subsídios variados e foram analisados o coeficiente de adesão dos planos mês a mês e definido a média de consumo por plano, após estes dados estudou-se o tempo médio necessário para atingir a atingir adesão linear ao consumo de medicamentos por plano. **RESULTADOS:** Dos quatro planos estudados, o Plano 1 que concede subsídios de 40% e 80% de acordo com o medicamento, alcançou a média de adesão em 6 meses; o Plano 2 que não oferece subsídios aos usuários demorou 13 meses para chegar a média de adesão; os Plano 3 e 4 que fornecem subsídios de 80 a 100% aos usuários alcançaram a marca respectivamente em 5 e 4 meses. **CONCLUSÕES:** Observamos que, desde a implantação até a média de adesão de consumo, o tempo variou de 4 a 13 meses. Um dos fatores que podem explicar esta diferença são os subsídios proporcionados para cada plano, pois o Plano 2 que não oferecia subsídio aos usuários apresentou o maior tempo - 13 meses - e o que apresentava maiores condições aos usuários levaram apenas até 4 meses. Desta forma o subsidio dado aos benefícios faz com que o tratamento seja seguido podendo minimizar os custos com sinistralidade por planos de saúde.

HEALTH CARE USE & POLICY STUDIES – Drug/Device/Diagnostic Use & Policy

PHP2

ARE GENERIC DRUGS DEFINED AND CLASSIFIED CONSISTENTLY AROUND THE WORLD?

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OBJECTIVES: To systematically identify and compare how generic medications, as defined by FDA, WHO, EMA, are classified and defined by regulatory agencies around the world. **METHODS:** We focused on emerging markets and excluded developed countries. For country selection, we identified the 3 most populace countries in each of the WHO regions: Africa, Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific. A systematic review of the published literature was performed through December 2012. Direct information from regulatory agencies and Ministries of Heath for each of the countries was extracted. Additionally, key informant interviews were performed for validation purposes. **RESULTS:** Of the 18 countries selected, only 50% provided an official country level definition for Generic drugs. The other 50% were comprised of those devoid of any definition and those that refer to the WHO definition of generics. Most countries acknowledge some form of Generic Drug Policy following the WHO framework. However, only 65% have specific requirements for Generic drugs. The requirements are often associated with clinically viable therapeutic interchangeability. Most countries with requirements mention Bioequivalence but few require Bioavailability explicitly. At least one third of the countries have other terms in their definitions and processes that could be associated with Generics. In countries with Generic Drug Policies there is reference to patent or protection during the Drug Registration Process. Lack of patent protection enforcement appears to hinder Generic drug production and utilization despite the existence of incentives for the use of Generics. 20% of countries do not mention Good Manufacturing Practices as part of the evaluation process. Countries in Africa and Eastern Mediterranean Regions appear to have a less developed regulatory framework. **CONCLUSIONS:** There is significant variability in the definition and classification of generic drugs in emerging markets. Standardization of the definitions is necessary to make international comparisons viable.

PHP4

AÇÕES DE FARMACOVIGILÂNCIA: RELATO DE NOTIFICAÇÕES DE MEDICAMENTOS À AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA (ANVISA) – BRASIL

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OBJETIVOS: Avaliar e quantificar as notificações de medicamentos registradas no setor Rede Sentinela do Hospital Instituto Cândida Vargas e enviadas à ANVISA (Agência Nacional de Vigilância Sanitária), durante o período de três anos. **MÉTODOS:** Realizou-se um estudo descritivo e retrospectivo do período de setembro/2009 a setembro/2012 das notificações recebidas, tanto de queixas técnicas como de eventos adversos, no setor Rede Sentinela do Hospital Instituto Cândida Vargas em João Pessoa-Paraíba. As notificações foram recebidas de forma espontânea (encaminhadas pelos profissionais de saúde) ou provenientes da busca ativa. Estas notificações foram enviadas via internet, através do Sistema de Notificação em Vigilância Sanitária, denominado de NOTIVISA para a ANVISA. **RESULTADOS:** No total, foram realizadas 20 (vinte) notificações, sendo 5% (01) no ano de 2009, 5%(01) no ano de 2010, 45% (09) no ano de 2011 e 45%(09) até setembro do ano de 2012. Em relação a forma de recebimento destas notificações, 14 (70%) foram recebidas de forma espontânea e 06 (30%) através da busca ativa. 80% (16) foram de queixas técnicas e 20% (04) de eventos adversos em relação ao uso dos medicamentos; o número de queixas técnicas notificados de forma espontânea foram 62,5%(10) e de busca ativa 37,5%(06), já o número de eventos adversos notificados foi 100% e de forma espontânea. **CONCLUSÕES:** Observou-se um crescimento ano a ano do número de notificações, sendo isto uma prática importante e propositiva. A forma de notificação espontânea foi a mais freqüente, demonstrando maior envolvimento, conscientização e comprometimento da equipe de saúde com o programa de farmacovigilância. Houve mais notificações de queixas técnicas do que de eventos adversos, o que já era esperado. Conclui-se ainda que o estímulo ao desenvolvimento de programas de educação continuada no ambiente de trabalho, buscando identificar os efeitos adversos e problemas relacionados aos medicamentos é de fundamental importância.

PHP5

ARGENTINA'S GENERIC DRUG LAW: WAS IT SUCCESSFUL?

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OBJECTIVES: High drug prices present substantial challenges to providing good, affordable health care, especially in resource poor settings. To combat rising drug prices, in 2002, Argentina implemented "The Generic Law" mandating that prescribers write prescriptions with the International Nonproprietary Name instead of brand name to promote generic drug use and lower overall costs. We examined whether this policy was effective in lowering drug prices. **METHODS:** We used IMS price data of 192 drug products from the WHO essential medicines list in Argentina from 1995-2010 along with limited utilization data. The study employed a longitudinal interrupted-time-series analysis of price and drug use before and after The Generic Law was implemented. We estimated a fixed effects regression model both with real price and log of real price as the dependent variable and time, policy, number of drug products on the market, and brand or generic status and brand policy interaction as independent variables, with residual tests for robustness. **RESULTS:** The robust pooled log price trends of 192 drug products show that prices decreased over all years by 1.1% (CI=0.0067-0.0151, p<0.00). We showed a robust interaction effect between policy and brand with the policy causing a 7.9% decrease (CI=-0.1359--0.0221,p=0.006) in generic drugs prices over brand prices (1.5 pesos). The policy by itself did not have a significant effect over all drug prices, nor did density of market share. Brand drugs across all time periods had a 27% increase (CI=0.0895-0.4525,p=0.003) in price (5.13 pesos). Visual inspection of utilization trends indicated that brand utilization decreased while generic use stayed stable or increased. **CONCLUSIONS:** Argentina's generic policy had its intended differential effect between brand and generic prices with generic prices decreasing significantly with respect to brand prices, although this difference was small. These findings provide some evidence supporting implementation of generic drug policies in other countries, but should be validated.

PHP6

UN SEGURO NACIONAL DE ENFERMEDADES CATASTRÓFICAS: FUNDAMENTOS PARA SU IMPLEMENTACIÓN

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OBJECTIVOS: Unas pocas enfermedades que afectan a un número reducido de personas se llevan una parte cada vez mayor de los recursos de los sistemas de salud. Se las denomina enfermedades catastróficas por el impacto económico que generan en quienes las padecen y las financian. En la Argentina coexisten seis modelos diferentes de cobertura y financiación de estas patologías. Sin embargo, constituyen respuestas fragmentadas e inequitativas. La creación de un Seguro Nacional de Enfermedades Catastróficas (SENEC) permitiría alcanzar una cobertura universal y homogeneizar protecciones de calidad a un costo inferior al actual. Esta investigación tiene por objetivo generar evidencia que contribuya a demostrar tanto la viabilidad económica y financiera como la factibilidad técnica del SENEC. **METODOLOGÍAS:** Para eso, se identifican los tipos de cobertura y financiamiento vigentes en el país y se describen algunas experiencias internacionales. Luego se exponen diferentes opciones para resolver la protección frente a estas enfermedades y se justifica por qué el SENEC es la alternativa más adecuada para el contexto argentino. Finalmente, se estiman los costos que conllevaría la creación del seguro y se describen cuatro escenarios alternativos de implementación. **RESULTADOS:** Los resultados del estudio evidencian que a través del SENEC se puede lograr una reducción de hasta el 75% de los costos en cobertura para estas enfermedades. Se demuestra que el SENEC en pleno funcionamiento, es decir brindando una cobertura explícita y de calidad homogénea a toda la población, tendría un costo menor al que hoy deben asumir algunos agentes del seguro (obras sociales nacionales y prepagas). **CONCLUSIONES:** Esta política pública responde a los desafíos de sustentabilidad económica, calidad y equidad que plantea la cobertura de estas patologías al actual sistema sanitario argentino.

PHP7

ANALYSIS OF THE PRICING AND MARKET ACCESS LANDSCAPE OF ORPHAN DRUGS IN LATIN AMERICA

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OBJECTIVES: In Latin America, despite the efforts recently implemented to improve access for rare diseases, funding remains a challenge due to conflicting priorities to ensure sufficient budget for essential medicines. In this research we aim at providing an understanding of the situation in terms of access and funding of orphan drugs in Brazil, Mexico and Argentina as well as defining the drivers for access in the light of an increasing pressure for drug coverage for orphan conditions. **METHODS:** Review approval and funding regulation for orphan drugs in Brazil, Argentina and Mexico. Selection of 8 orphan drugs differing on a pre-defined set of access drivers (Incidence of the disease, severity of the condition, therapeutic alternative, level of innovation, affordability, etc.). Develop case studies based on HTA reviews and level of access. Formulate hypotheses about the main drivers for successful access. Explore and qualitatively validate hypotheses through primary research with local payers. **RESULTS:** 1) Access to orphan drugs is not universal - programs starting to be put in place in some countries but limited to selected conditions; 2) Brazil and Mexico have implemented a policies for orphan drugs expected to facilitate increased access in the future; and 3) Affordability is the main driver of access followed by the severity of the disease, although exceptions to this rule exist. **CONCLUSIONS:** Whereas regulation for orphan drugs is not available in all countries, public funding overall is increasing. Most funding for rare diseases, however, focuses on selective, severe, life-threatening conditions, and affordability remains a major access barrier. In the medium term, proving value will not be enough to obtain access of OD in these markets. Companies seeking access for ODs will need selective programs, designed to improve affordability.

PHP8

VALUE JUDGMENTS IN HEALTH TECHNOLOGY ASSESSMENT PROCESS IN BRAZIL

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OBJECTIVES: To appraise the value judgments in critical decisions involving resource allocation and use of technologies in Brazilian health system, through the view of health managers and professionals. To evaluate the tendencies of the Brazilians' decision makers when managing the important restriction of financial resources. To analyze the influence of health care sectors in the managers and professionals' decisions. **METHODS:** The research has been conducted through a decision-making questionnaire to incorporate health technologies, applied by internet. 193 respondents fully answered the research. There was presented four scenarios that mimicked real world dilemmas regarding the choice of resource allocation in an environment of severe budget constraint. The decisions should be taken regarding the following trade-offs: 1) disease prevalence and reduction/extinction of current health programs; 2) disease prevalence and creation of new taxes; 3) patients age; and 4) decision among prevention and treatment. **RESULTS:** The results have showed a conservative trend. Most answers were related to lower costs options in every scenario, showing the preference in saving resources instead of incorporating the technologies, in despite of the clinical benefits. The comparison between prevention and treatment demonstrates that health managers and professionals are suited to a preventive though that indicates the long-term strategy of health care policies. It was found different tendencies of answers between the health care sectors considered as players of technology assessment process. **CONCLUSIONS:** The Brazilian health managers and professionals are significantly influenced by economic scarcity when deciding about resource allocation. In search of a paradigm for decision-making, most of them have opted for saving resources rather than incorporating the technology. With a restricted budget, only few demands can be satisfied. Against this background, the cost-effectiveness analysis and the establishment of strategic priorities become essential tools for resource allocation, in order to avoid an undesirable technological gap in the country.

PHP9

COMPARATIVE EVALUATION OF THE APPROPRIATENESS OF THE PRESCRIBING IN GERIATRICS INPATIENTS USING BEERS CRITERIA 2012 AND 2003

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OBJECTIVES: To evaluate appropriateness of prescribing medicines using Beers criteria 2003 and 2012 and determining predictors of potentially inappropriate medications (PIMs) prescribing in elderly in-patients. **METHODS:** Cross-sectional study was conducted at public hospital and baseline data were collected. Elderly in-patients from medicine wards (≥60 years) were included. Multivariate logistic regression analysis was used to determine the predictors of PIMs prescribing. **RESULTS:** A total of 500 patients were recruited during I year of study period;60% were males and 66% were between 60-69 years of age with mean (SD) of 68 (7) years. Mean (SD) number of diagnoses and medications were 3 (1) and 9 (4), respectively. 81 (16%) patients were prescribed with at least ≥1 PIMs according to modified AGS updated Beers criteria 2012, compared to 11% according to Beers criteria 2003. On multivariate regression, important predictors for the PIMs prescribing were found to be age ≥80 years (Odds Ratio (OR) 2.46, 95% CI 1.27-3.12; $p = 0.03$), male gender (OR 1.35, 95% CI 1.06-1.84; $p = 0.03$), more than 3 diagnoses (OR 2.47, 95% CI 1.59-3.39; $p = 0.04$), ≥6 medications prescribed (OR 1.16, 95% CI 1.02-1.35; $p = 0.03$) and ≥10 days of hospital stay (OR 1.59, 95% CI 1.09-2.31; $p = 0.02$). **CONCLUSIONS:** Results indicate that PIMs prescribing is common among hospitalized Indian elderly patients. It is feasible to reduce this practice through provision of appropriate unbiased information to health care professionals. Beers criteria is a well established method for evaluating prescribing appropriateness. Results also show the capture of more number of PIMs through the use of Beers criteria 2012 due to the addition of new medications in the list like spironolactone in heart failure and removal of capping of maximum dose of alprazolam, clonazepam and lorazepam from Beers criteria 2003.

HEALTH CARE USE & POLICY STUDIES – Equity and Access

PHP10

ANALYSING THE ACCESS TO PRIORITY HEALTH SERVICES IN THE ADOLESCENT POPULATION IN SIX PROVINCES IN NORTHERN ARGENTINA

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OBJECTIVES: Adolescents present particular issues that may condition their health and life, this turns adolescents' health into a priority. To identify the barriers that hinder the access to health by adolescents in order to contribute to the design, orientation and formulation/reformulation of public policies. **METHODS:** We implemented a self-administered to 5200 secondary public school students in the northern provinces of Argentina, Jujuy, Misiones, Tucumán, Santiago del Estero, Catamarca and Chaco. On the other hand, we developed in-depth interviews to local referents (Ministries of Health, Education, Social Development, etc). Descriptive statistics techniques were then applied, together with econometric analysis and qualitative techniques of interviews analysis. **RESULTS:** We identified differences regarding priorities and policies oriented to the adolescent population in the six provinces. With regard to the teen gaze, 87% of students rate their health as "very good or good", only half of those reporting a health problem consulting the system. Their concerns are linked to arguments and emerging problems of their age. "Having to wait long to be attended" and "difficulty to get an appointment" are the main barriers they face when accessing to the system. **CONCLUSIONS:** The definition of access ceases to be necessarily linked with aspects of physical capacity or clinical care, but with the system's ability to orient the question and channel the concerns of young people with social problems related to health.

PHP11

URBAN HEALTH NETWORKS AND PERINATAL HEALTH RISK IN ARGENTINA

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OBJECTIVES: Urban Health Care Networks become a strong limitation to guarantee efficient and equitable access, especially in developing countries. Lack of formal protocols in referral procedures, insufficient coordination among levels of care and limited coordination in human resources across health care system allows duplication of clinical studies, informality in the decision-making process within the network, and higher-than-expected health risks, affecting existing financial protection mechanisms. In particular, perinatal health care networks involve the analysis not only of clinical performance in hospitals and health care centers, but also the ability to improve mothers' behavior during pregnancy, by applying safe preventive care procedures. This study analyzes two mayor public hospitals in the Province of Buenos Aires, Argentina, searching for quality of referral procedures **METHODS:** The descriptive and logistic analysis identifies three sets of variables: mother's background and risk factors, pregnancy characteristics and supply-side infrastructure. Using an original database on birth attendance at the hospital head-of-network (Perinatal Information System, designed by the World Health Organization) of circa 16,500 births, as well as structured questionnaires distributed among human resources in both hospitals, the study allows to identify hospital ability to manage network risks, failures arising from the health care system and join responsibilities between formal health care system and the family. **RESULTS:** The study allows the definition of two sets of observations based on number of medical controls during pregnancy, offering the chance of additional comparisons of explanatory variables by including test of differences in mean values. **CONCLUSIONS:** Results show the presence of multiple failures in urban health care networks, with specific risk factors teenage pregnancy and distance to formal health services affecting hospitalization rates, newborn risks and counter-reference behavior.

PHP12
¿LOS FORMULARIOS NACIONALES (CUADROS BÁSICOS) PROVOCAN OLIGOPOLIOS E INCENTIVAN A TENER PRECIOS ALTOS?
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OBJECTIVOS: Demostrar en base a un modelo económico de oligopolio que los formularios provoca oligopolios e incentiva a mantener precios altos. **METODOLOGÍAS:** Los formularios son una barrera a la entrada al mercado que desincentiva la competencia. Los medicamentos patentados no son sujetos a competencia directa por precio, por lo tanto son sujetos a competir conforme a un modelo de Cournot. Este modelo se basa en que los competidores pelean el mercado por cantidades. Los productos patentados no son sujetos a licitación si no a adjudicación directa. Se toma como supuesto que hay un "*n*" número de competidores en los formularios nacionales, siendo "N" el número total de competidores, cada una con un producto que vende a un precio "P". Los competidores toman decisiones al mismo tiempo. La demanda del mercado está dada por $P(Q) = a - bQ$, siendo "Q" la sumatoria de todas las producciones. Hay "X" número de competidores que están fuera del formulario nacional. **RESULTADOS:** El precio del productor dependerá, principalmente, de "Q" y de "N". Si incrementa "Q", y "N" constante, entonces se incrementan los precios. Si incrementa "N", y "Q" constante, bajan los precios. Si no existieran los formularios nacionales, no habría barreras a la entrada y la competencia incrementaría en "X" que provocaría un menor precio. Si "N" tiende al infinito, entonces el modelo tiende a la competencia perfecta. En un caso donde solo un producto ha logrado el acceso al formulario nacional formará monopolio. **CONCLUSIONES:** Las barreras a la entrada causada por formularios nacionales mantendrán precios altos hasta que un nuevo competidor sea incorporado al formulario. Entre mayor sea el número de oferentes se incrementará la competencia y menor será el precio. Se recomienda analizar los beneficios de los formularios nacionales y explorar otros métodos de reembolso como pagar por el desenlace en salud y no por el producto en sí.

PHP14
REACHING THE MIDDLE OF THE PYRAMID: IMPLICATIONS FOR THE P&MA OF PHARMACEUTICAL DRUGS WITH THE EXPANDING MIDDLE CLASS IN BRASIL, CHILE AND COLOMBIA
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OBJECTIVES: Sustained economic growth in Latin America in the last decade led to an astonishing 50% increase in the middle class. With the empowerment of an increasingly educated and wealthier population, governments have been under pressure to adapt their health care models to growing expectations for US/EU health quality standards. As a result, health care funding balance between patient Out-Of-Pocket, contributions to private health plans and public via taxation pathways is likely to be subjected to sizable shifts in the near/medium future. This work presents an outlook on the current health care financing and an analysis of potential trends and likely implications in terms of P&MA for new drugs in three case study countries (Brazil, Chile and Colombia). **METHODS:** Literature review on health care financing distribution from 2003 to 2010. Review of political and private initiatives for drug coverage. Hypothesis development on the implications in terms drug's P&MA. Primary research with payers/proxy-payers. Analyze and compare trends across countries. **RESULTS:** 1) Chile saw the lowest growth in overall HC expenditure with a clear transfer in the funding distribution from OOP to public sources (39% for both to 33% vs. 48%); 2) Brazil overall HC expenditure greatly increased (4.99 fold), and since 2005 a moderately sustained transfer from OOP to public funding have been occurring (from 38.6% and 40.1% to 31.6% and 47% in 2010); 3) In Colombia, funding is dominated by public spending (74.6%) but OOP expenditure has seen the highest growth; 4) HTAs are increasingly involved in drug P&R decisions. **CONCLUSIONS:** Latin American countries are likely to further accommodate 'hybrid' systems for health care financing. However, as Governments are required to make decisions for funds allocation, there is increasing need for sophisticated tools for drug evaluation and decision making. Increasingly robust HTA agencies are expected to be created, implying downward pressures on price pressures and increased evidence requirements.

PHP15
INTEGRACIÓN DE UN MARCO CONCEPTUAL PARA LA EVALUACIÓN DE LA CALIDAD DE SERVICIOS FARMACÉUTICOS HOSPITALARIOS ENFOCADOS A LA MEJORA DE LA FARMACOTERAPIA
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OBJECTIVOS: En el contexto de la incorporación del profesional farmacéutico en el ámbito hospitalario del sistema de salud mexicano, el objetivo fue integrar un marco conceptual para la evaluación de la calidad de servicios farmacéuticos hospitalarios enfocados a la mejora de la farmacoterapia (SMF's). **METODOLOGÍAS:** Se utilizó el marco conceptual de Donabedian para la evaluación de la calidad de la atención médica como un marco de referencia para el desarrollo del marco conceptual de evaluación de la calidad de SMF's. Asimismo, se utilizó el marco conceptual para la identificación, denominación y categorización de acontecimientos adversos a los medicamentos (AAM). Dentro de las dimensiones de estructura, proceso y resultado se adicionaron diferentes tópicos y variables importantes relacionadas con estas dimensiones. Adicionalmente, se realizó un estudio piloto utilizando metodología cualitativa para evaluar la calidad de SMF's de algunos hospitales públicos y privados de México, que consistió de entrevistas en profundidad a jefes de unidades de farmacia hospitalaria o clínica de algunos hospitales públicos o privados de México. Las entrevistas se transcribieron y analizaron utilizando una aproximación a la metodología de teoría fundamentada. **RESULTADOS:** Se integró un marco conceptual para la evaluación de calidad de SMF's que puede abordarse desde diferentes perspectivas metodológicas (cuantitativas o cualitativas). El estudio cualitativo piloto permitió utilizar el marco conceptual desarrollado e identificar aspectos importantes de estructura, proceso y resultado relacionados con la calidad de SMF's, como la calidad de las instalaciones e infraestructura, la presencia y calidad de programas de capacitación, el apoyo de las autoridades del hospital, la aceptabilidad de los servicios por otros profesionales de la salud, el clima laboral y la satisfacción de los recursos humanos. **CONCLUSIONES:** El marco conceptual desarrollado permite fundamentar la evaluación de la calidad de SMF's. El abordaje cualitativo realizado permitió identificar aspectos clave en las dimensiones de calidad.

HEALTH CARE USE & POLICY STUDIES – Formulary Development

PHP16
AUDIT OF THE COVERAGE DECISION-MAKING PROCESS IN A GOVERNMENT AGENCY IN URUGUAY: FROM THE GUIDELINES TILL THE PATIENTS
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OBJECTIVES: The National Resources Fund (FNR) is a government agency devoted to provide coverage of high cost technologies in Uruguay. A particular characteristic of the FNR is being involved in the whole process of providing access to these technologies, from its buying to its patient administration. To guide this process the FNR, has some clinical coverage guidelines that are used in the clinical coverage decision with each individual patient. During 2009 and 2012 the FNR did an audit process of these guidelines and asked IECS (a non profit academic organization) from Argentina to implement it. To present the process were 12 of these guidelines were audited (colorectal, kidney, CNS and breast cancer, leukemias, cystic fibrosis, hepatitis C, diabetes, palivizumab and rituximab, rheumatoid arthritis and multiple mieloma) and the coverage decision taken on patients with the corresponding diseases. **METHODS:** Systematic bibliographic searches were performed to audit the guidelines and the clinical record of patients with the corresponding diseases was audited summarizing 200 patients in total. **RESULTS:** Regarding the guidelines it was observed that in general there were adequate in its clinical content and updated with the actual evidence promoting a better clinical decision coverage process. Only some reporting aspects as date of bibliographic searches not reported or not clear specification of authors or methodology followed were mentioned. Regarding the patients audit, in 198 cases the decision was in concordance with the guideline being adequate in almost all the cases. **CONCLUSIONS:** An audit process of the coverage decisions implemented in a government agency by an external organism as the one described in this study allows to identify potential improvements to the process, promotes transparency and at the end a better coverage decision-making process and utilization of health resources.

HEALTH CARE USE & POLICY STUDIES – Health Care Costs & Management

PHP17
DETERMINANTES DE LOS COSTOS DE ACCIDENTES DE TRÁNSITO OCURRIDOS EN MEDELLÍN (COLOMBIA) 2009-2010
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OBJECTIVOS: Estimar los determinantes de los costos hospitalarios, de rehabilitación y del paciente en personas lesionadas en accidentes de tránsito en Medellín entre 2009-2010. **METODOLOGÍAS:** Estudio de corte transversal con 375 pacientes con lesiones moderadas y graves, según el New Injury Severity Score (NISS), a quienes se les aplicó una encuesta en el momento del accidente, 3 y 6 meses después. Para estimar los costos de las lesiones se asumió una perspectiva que consideró los costos médicos, del paciente y pérdidas asociadas a la productividad. Los costos médicos se valoraron por medio de los precios de los medicamentos suministrados y las intervenciones realizadas en hospitales de alta complejidad de la ciudad; y los costos del paciente según el salario reportado por él mismo. Se estimó un modelo lineal generalizado relacionando el costo total con las variables edad, sexo, tipo de vehículo, presencia de alcohol, utilización de elementos de seguridad, localización de la lesión, rapidez en la atención y condición del accidentado, identificadas en la revisión de la literatura y clasificadas en determinantes estructurales y próximos. **RESULTADOS:** El 80% de los pacientes eran hombres y de éstos el 71% tenían entre 21 y 40 años. El costo promedio de atención por paciente fue de USD 8.509. El costo de los materiales e insumos representa el 33% del total, seguido por los costos de los medicamentos con 20% y el de hospitalización con 18%. El costo asociado al uso de motocicleta representó el 80% de los costos totales. **CONCLUSIONES:** La edad, el sexo, el tipo de vehículo y la condición del accidentado se encontraron como determinantes fundamentales del costo de atención. La presencia de alcohol y la utilización de elementos de seguridad no representaron la carga esperada debido, tal vez, al sesgo en la información suministrada por los entrevistados.

PHP18
FATORES ASSOCIADOS À COMPRA DE MEDICAMENTOS EM BRASÍLIA: UMA ANÁLISE ECONOMÉTRICA COM DADOS TRANSVERSAIS DE BASE POPULACIONAL
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OBJETIVOS: Investigar os fatores associados à compra de medicamentos pela população adulta de Brasília. **MÉTODOS:** Estudo transversal com aplicação de questionário em pessoas entre 18 a 65 anos, selecionadas por meio de amostragem probabilística em dois estágios, com cotas por sexo e idade, para obter representatividade para o Distrito Federal. Calculou-se tamanho amostral considerando nível de confiança de 95%, margem de erro de 2,5% e frequência de utilização de medicamentos em 50%. Foram entrevistadas 1852 pessoas no primeiro semestre de 2012, sendo obtidos dados sociais,

demográficos e econômicos, presença de doenças crônicas, qualidade de vida e a forma de aquisição de medicamentos nos últimos sete dias. Um total de 20% das entrevistas foram auditadas por telefone quanto a sua autenticidade. O projeto foi aprovado pelo Comitê de Ética em Pesquisa da Universidade de Brasília. Para identificar e avaliar os determinantes da compra de medicamentos utilizou-se três métodos distintos, Logit, Probit e Probabilidade Linear, para elevar a robustez dos resultados. Realizaram-se as análises econométricas através dos programas Gretl e R. **RESULTADOS:** Um total de 1.820 entrevistas válidas, dos quais 59,8% eram mulheres. Foram identificados os potenciais determinantes do consumo de medicamento no DF: classe social, qualidade de vida, doenças crônicas, sexo, idade, plano de saúde e consultas médicas. **CONCLUSÕES:** Ter doenças crônicas, ser do sexo feminino, ser mais velho, possuir plano de saúde e ter se consultado elevam as chances de comprar medicamentos. Por outro lado, pertencer às classes sociais mais baixas e ter melhor qualidade de vida reduz essa chance. Os resultados foram qualitativamente equivalentes nos três métodos, além de apresentarem significância estatística próximos de 5%. É possível que os achados estejam influenciados pelo viés de suscetibilidade dos sujeitos de pesquisa e de prevalência/incidência da compra de medicamentos. Entretanto, como diversas características não são influenciadas pelo tempo, a validade da informação não é afetada.

PHP19

ANÁLISIS DEL GASTO SANITARIO ESPAÑOL 1980-2010

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OBJECTIVOS: Ilustrar una metodología de distribución del presupuesto sanitario público entre las 17 categorías CIE-9-MC (Clasificación Internacional de Enfermedades, novena revisión, modificación clínica) y su evolución en el tiempo. **METODOLOGÍAS:** La metodología consta de dos fases: una primera fase en la que se realiza una distribución del presupuesto global por tipo de atención sanitaria (atención hospitalaria, ambulatoria o farmacológica), y una segunda fase en que se distribuye el gasto por tipo de atención entre las categorías CIE-9-MC. Para esta distribución se utilizan, en la primera fase, informaciones que permitan asignar las diferentes partidas del presupuesto a los distintos tipos de atención. Por lo que respecta a la distribución por categorías, se utilizan diferentes elementos según el tipo de atención: la estancia hospitalaria, la visita ambulatoria o el consumo farmacéutico por subgrupo terapéutico. Se utilizan los datos del gasto sanitario en España con propósitos ilustrativos. **RESULTADOS:** El análisis del gasto sanitario español entre 1980 y 2010 muestra que la posición relativa en cada ámbito no varía demasiado, dominando la atención hospitalaria (58%) en el ámbito público y la atención ambulatoria (33%) en el privado. La asistencia farmacéutica incrementa su posición relativa tanto en el ámbito privado como en el público, 2,5 puntos porcentuales en los dos casos. De análisis de las 17 categorías CIE-9-MC, cabe destacar el crecimiento continuo e importante de la categoría VII (enf. del aparato circulatorio, de 10% en 1980 al 17,7% del gasto en 2010) y el decremento de la categoría VIII (enf. Respiratorias, del 17,4% al 10,5%). En un segundo término también cabe destacar el crecimiento de la categoría II (tumores, del 4,2% al 9,1%) y de la categoría I (infecciosas, del 5,2% al 2,31%). **CONCLUSIONES:** La distribución del presupuesto aporta un punto de referencia para la planificación y la gestión sanitarias.

PHP20

IS HOSPITALIZED MULTI-MORBIDITY IN ADULTS DETERMINING COSTS OF RE-ADMISSION? EVIDENCE FROM A MULTICENTRIC CROSS SECTIONAL STUDY IN ARGENTINA

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OBJECTIVES: Multi-morbidity (MM) and readmissions in less than 30 days (ReH) require standarized data, diffficult for Argentina. To measure the economic implications, we evaluated if MM determined direct medical costs of ReH. **METHODS:** In cross sectional study of 1 year hospital discharges (*Value in Health;14 (2011):A18*), of patients ≥19 yrs old, primary diagnosis (Dx1) and secondary diagnosis (Dx2), total costs (CT$) mean and median per discharge cost ($, 25P-75P-percentiles), in international dollars PPP, (UN Data: 1Arg$ = 1.608 I$ PPP, 2008) were obtained. To measure of multi-morbidity (MM) we used chronic conditions table in (CC+) counts as positive (CC+) per 2Dx. The 30day readmissions (ReH<30) defined as: 1) any readmission within 30 days and 2) the number of stays with at least one subsequent hospital stay within 30 days(strict definition) (ReH_s). **RESULTS:** In a universe of 45466 discharges, we found 7286 ReH <30 d among adults (≥19 yrs old). Total cost of ReH TC$ 68 145 431I$; mean cost per discharge ($) was 9629 I$ (SD I$ 23 344); Median cost per discharge 4211 I$; (Q1: 1755 -Q3:9291 I$), taken as baseline values for ReH (ReH_s is N= 6018; with I$ of 10 600 -SD I$ 25271) . Stratified against MM as 2Dx1, N=3357, mean discharge cost was I$ 10823 (SD I$ 24005); 1,12 times the value of all ReH. MM at 2Dx5, N=718, I$ 16538 (SD I$ 36839); 1,72; and when MM was in 2Dx8, N=137, I$ 18785 (SD I$ 34764); 1,95 times baseline (*p trend <0.01*). ReH_s reduce total number of readmissions and produce slightly higher costs (full data not shown), e.g. in MM of 2Dx8, ReH_s is N=130, mean discharge cost I$ 19 052 (SD I$ 35591); 1,80 times baseline. **CONCLUSIONS:** This first estimate of ReH<30 costs, sensible duration, and demonstrates impact of multi-morbidity (MM) with the method used.

PHP22

ANÁLISIS DE MINIMIZACIÓN DE COSTOS DE IOBITRIDOL VERSUS OTROS MEDIOS DE CONTRASTE IODADOS ISO E HIPO-OSMOLALES EN POBLACIÓN GENERAL

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OBJECTIVOS: Desarrollar una evaluación económica del uso de iobitridol en la toma de imágenes diagnósticas versus otros medios de contraste iodados similares (seguridad y tolerancia). **METODOLOGÍAS:** Dada la no superioridad ni inferioridad, encontrada en la literatura, de los medios de contraste iodados iso e hipo-osmolales, se realizó una evaluación económica de iobitridol mediante un análisis de minimización de costos, que incluye costos de insumos y recursos utilizados en la realización de urografía, angiografía y escanografía. Para el desarrollo de la evaluación se utilizaron los siguientes medios de contraste: iodixanol, iobitridol, iopamidol, iohexol, ioversol e iopromide, en todas las concentraciones de yodo disponibles en el mercado en Colombia. Los resultados se analizaron para pacientes con peso entre 5-110 kg tomando como referencia de uso la dosis promedio de Yodo para cada uno de los tres exámenes analizados. Se realizó un análisis de sensibilidad univariado de +/- 20%, en los costos de las tecnologías. **RESULTADOS:** Para urografía, en el 64% de los casos analizados resultó ahorrativo el uso de iobitridol 300 mg/ml, presentando un ahorro de COP$ 4.121 por examen per cápita. Para angiografía, el uso de iopamidol de 370 mg/ml es ahorrativo en el 55% de los pesos (kg), frente al 45% con iobitridol de 300 mg/ml, con un ahorro de 3,44% por examen. Finalmente para escanografía, iobitridol de 300 mg/ml se presenta como la tecnología con más frecuencia de ahorro en los pesos (kg) de los pacientes, mostrando un ahorro de 2,87% por examen. El análisis de sensibilidad muestra consistencia del ahorro del uso de iobitridol 300 mg/ml e iopamidol 370 mg/ml. **CONCLUSIONES:** El análisis de minimización de costos muestra a iobitridol e iopamidol como tecnologías que generan ahorro en urografía, angiografía y escanografía, en concentraciones de 300 mg/ml y 370 mg/ml respectivamente, dependiendo del peso del paciente.

PHP23

DRUG DISTRIBUTION STRATEGIES COST IN BRAZIL

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OBJECTIVES: This research aims to verify the total costs of the medicines that are dispensed by pharmacies of the Brazilian Public Health System (SUS) and that are also part of the *Aqui tem Farmácia Popular* program (PAFP). This program is characterized by the powerful link between the government and the private pharmacies which provide medicines for free or by co-payment for the population. This work also seeks to draft a comparative analysis between the two distribution forms of the drugs. **METHODS:** The direct cost was obtained from the amounts showed on the county purchase invoices. The indirect cost was identified as a result of a field survey. The sampling selection of visited counties was based on a - non- probabilistic - scenario analysis approach from quality criteria and distributed in each of the five country's regions. Collection was performed by completing a semi-structured spreadsheet, by documentary analysis and by participant observation. Data collected correspond to the expenses incurred during 2011. **RESULTS:** The value of the medicines bought by a private pharmacy it is significantly higher than the one paid by the SUS pharmacy. It is considered as possible explanations of differential of the direct cost between two purchases origins some additional elements that elevate the cost of the private pharmacy regarding the one from SUS: purchases volume, purchase frequency, presentation, additional costs as logistics, type of packing, costs related to the certification of good production practices. **CONCLUSIONS:** From the comparative analysis of the SUS pharmacy total cost with the value funded by the Ministry of Health for PAFP medicines, it was possible drawing a comparative with the analyses provided in the National Accounts Tribunal (TCU) audit report. It was observed that the variance shown in the TCU audit report indicates a significant difference between the assessed results in this demonstrative.

PHP24

ECONOMIC BURDEN OF INPATIENT POST-ADMISSION DEHYDRATION – RETROSPECTIVE DATABASE ANALYSIS IN US

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OBJECTIVES: To compare costs and resource utilization of patients experiencing post-admission dehydration (PAD) to those who do not experience PAD. **METHODS:** All adult inpatient discharges excluding those with suspected dehydration present on admission (ICD-9-CM codes for dehydration: 276.0, 276.1, 276.5X present on admission) were identified from the Premier database(CY2011). Patients with missing information on important variables were excluded. PAD patients were identified using ICD-9-CM codes. PAD and no PAD(NPAD) groups were matched on propensity score adjusting for demographics (age, gender, race, medical, elective patients), patient severity (APR-DRG severity scores) and hospital characteristics (geographic location, bed-size, teaching and urban hospital). Costs (total and departmental), days of stay in hospital(LOS), incidence of mortality and Catheter-Associated Urinary Tract Infection(CAUTI) were compared between groups using t-test for continuous variables and chi-squared test for categorical variable. Sub-groups of medical and surgical population were also matched and analyzed separately. **RESULTS:** Total of 86,398(2.1%) of all the selected patients experienced PAD. Post-matching mean total cost were significantly higher for the PAD group compared to NPAD group($33,945 vs. $22,380, p<0.0001). Mean costs associated with room & board, central supply, surgery, pharmacy and other miscellaneous departments were also significantly higher for PAD group(all p<0.0001). Compared to NPAD group, PAD group had higher mean LOS days(12.9 vs. 8.2) and also had a higher incidence of CAUTI(0.6 vs. 0.5%) and in-hospital mortality(8.6% vs. 7.8%) (all p<0.05). The results for sub-group analysis were also significant for total costs(Medical patients: $22,065 vs. 15,700; Surgical patients: $45,728 vs. $32,091) and LOS days(Medical patients: 11.4 vs. 8.3; Surgical patients: 17.8 vs. 11.4) (all p<0.05). **CONCLUSIONS:** PAD has a potential to add significant burden to hospital costs and resources. Adopting strategies aimed at avoiding PAD may help in reducing hospital cost and resource burden and may improve patient outcomes.

PHP26

CRESCIMENTO DE ÓBITOS PÓS PARTOS CESARIANOS NO BRASIL VERSUS PARTOS NORMAIS

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OBJETIVOS: Identificar o crescimento de mortes em partos cesarianas no Brasil e compara-las com a quantidade de mortes em partos normais. **MÉTODOS:** Foram analisados um banco de dados com 16 milhões de vidas pertencentes à hospitais particulares existentes no Brasil (amostra de 35% do mercado) e analisado a quantidade de óbitos pós partos e o tipo de parto realizado todos identificados pelo CID-10. **RESULTADOS:** Dado a tendência brasileira o número de partos no Brasil é inversamente proporcional a orientação da Organização Mundial de Saúde (15% para partos cesarianos e 85% partos normais) a média nacional, de acordo com o Sistema de Informações de Nascidos Vivos (Sinasc), do Ministério da Saúde, é de 52,2% e além desta tendência nacional verificamos que o número de mortes ocorridas pós partos é proporcionalmente maior nas cesariana, além de ter crescido cerca de 135% nos últimos 3 anos, sendo que em 2012 o número de mortes foi 186% maior do que as mortes em partos normais. **CONCLUSÕES:** Este estudo é um alerta as organizações de Saúde Brasileiras quer seja do ambiente particular quanto público, tanto aos elevados números de cesarianas que vem aumentando a cada ano quanto ao riscos deste procedimentos tanto para a mãe quanto para o feto. Devendo ser levado em consideração outros fatores de custos indiretos como tempo de recuperação.

PHP28

HOUSEHOLD FEEDING PRACTICES FOR THE SICK UNDER FIVE CHILDREN; GUCHA SOUTH DISTRICT-KISII COUNTY, KENYA

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OBJECTIVES: To examine feeding practices among households with under five sick children. **METHODS:** Household baseline survey was carried out in June 2012 where 10 sub locations randomly selected were surveyed. A structured questionnaire was administered to 983 households with under fives . Mid-Upper-Arm-Circumference tapes were administered to under fives, growth monitoring and immunization cards were also examined. **RESULTS:** Fifty-six percent (550/973) fed the sick child less than usual, 14% said a child with diarrhea should not be given anything , 64% said child should not be given ORS, only 8% said sick child should be given soup and water and 13% said child should be given breast milk. After taking MUAC tape measurements 6% could be classified under severely malnourished category. 50% did not have growth monitoring cards and only 45% of the eligible children were currently being breastfed. Level of education of the mother did not seem to influence breast feeding practices, more than three quarters of the widows were not currently breastfeeding, while only 27% of salaried, 38% business and 46% farmers women were currently breast feeding. Catholic women were leading in currently breast feeding mothers with 80% followed by Seventh day Adventist -43%, Indigenous Churches - 42% and Anglican -40% respectively. **CONCLUSIONES:** Majority of the households seem to be burdened with child hood sickness. It is worrying that a significant proportion of 64% of the respondents said that a child with diarrhea should not be given ORS. Probably majority of the households do not know how to manage diarrhea among children at home. Significant proportion of the breast feeding children whose mothers were engaged in salaried and business employments are disadvantaged because they are not being breast fed. Catholic women recorded highest level of breast feeding practices compared to their counterparts in other religious affiliations.

PHP29

SOCIETAL UNMET NEEDS IN BRAZIL: EXAMINING PREVALENCE, TREATMENT RATES, AND HEALTH OUTCOMES

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OBJECTIVES: To examine how unmet needs, defined as prevalence rates, treatment rates, and quality of life, compare across the ten most common conditions in Brazil. **METHODS:** Data were obtained from the Brazil 2011 and 2012 National Health and Wellness Surveys (NHWS; N=24,000). The Brazil NHWS is a self-reported nationally representative patient survey of the adult Brazilian population (aged 18+), weighted to correct for any socioeconomic sampling bias. Among the 10 most prevalent conditions in Brazil, prevalence, treatment rates, and health utilities (using the SF-6D algorithm from the Short Form-12v2) were examined. **RESULTS:** Of the conditions respondents reported being diagnosed with, eight had prevalence rates greater than 15% (only restless leg syndrome (RLS) at 4.74% and arthritis at 4.25% were not among the top ten conditions). Despite these prevalence rates, only patients with hypertension (treatment rate=68.48%) reported a treatment rate greater than 50%. The remaining treatment rates generally varied between 19.30% (insomnia) and 40.47% (high cholesterol); patients with RLS reported the lowest treatments rates of all the top ten conditions (1.93%). Indeed, many of the debilitating conditions with respect to health utilities had particularly suboptimal treatment rates: depression (health utilities=0.606; treatment rate=39.00%), anxiety (health utilities=0.639; treatment rate=23.88%), and insomnia (health utilities=0.640; treatment rate=19.30%). **CONCLUSIONS:** Despite high prevalence rates for a variety of chronic conditions, treatment rates in Brazil are particularly poor. One of the exceptions was hypertension, which may be related to the Farmacia Popular do Brasil, which allows for the free distribution of medicines for hypertensive and diabetic patients. However, many conditions, particularly psychiatric ones, were associated with both poor treatment rates as well as significant decrements in health utilities. From a public health perspective, more emphasis should be placed on the importance of proper chronic disease management in Brazil.

PHP30

HEALTH SEEKING BEHAVIOR AMONG MEMBERS OF THE HOUSEHOLDS; CASE OF GUCHA SOUTH DISTRICT, KISII COUNTY, KENYA

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OBJECTIVES: To investigate health seeking behavior among households with sick persons. **METHODS:** Household baseline survey was carried out in June 2012 where 10 sub locations randomly selected were surveyed. A structured questionnaire was administered to heads of households. **RESULTS:** A total of 1427 households were surveyed. Questionnaire response rate was 83%. Thirty six percent (423/1181) of the respondents said they had at least one member of the household experienced sickness two weeks prior to the survey. Of those who were sick 15% did not seek treatment anywhere, 45% were still sick and 16% had been sick for more than two weeks. Sixteen percent of those who sought care took more than one hour to travel to the facility. Malaria, ARI, pregnancy related, diarrhea, Aids related and flu were mentioned to be the most common diseases the sick were suffering from. Sixty percent (681/1137) of the household heads said they were not aware of any community based referral system for the sick, 66% (467/710) of those who knew about it said a community health worker should identify a sick person in the household and initiate the referral process to a health facility. A total of 26% said the health facility should initiate and facilitate the referral process from the household while 3% mentioned of self referral to the facility for care when one is sick. **CONCLUSIONS:** Despite household members' knowledge on the diseases they were suffering from, a significant proportion did not seek treatment in health facilities even when they had been sick for more than two weeks. This finding is significant as it will inform health care providers specifically those at lower levels of care to mount behavioral change activities aimed to promote early health seeking among household members.

PHP31

MODELO PREDICTIVO PARA LA IDENTIFICACIÓN TEMPRANA DE POBLACIÓN EN RIESGO DE CRONIFICAR EN UNA ADMINISTRADORA DE RIESGOS LABORALES EN COLOMBIA

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OBJECTIVOS: Diseñar un modelo que permita identificar de manera temprana los pacientes con riesgo de cronificación basados en un análisis predictivo a partir del gasto farmacéutico, en una administradora de riesgos laborales (ARL) en Colombia. **METODOLOGÍAS:** Se revisó el gasto farmacéutico y de atenciones en salud, 2009-2011 en una ARL, identificando los pacientes con tres o más despachos en un periodo de hasta seis meses (criterio adoptado para definir paciente crónico). Los pacientes fueron analizados en 22 grupos de enfermedad basados en la clasificación de enfermedades crónicas por prescripciones (Chronic Disease Score CDS). Éstos fueron caracterizados según variables socio-demográficas y con esta información se construyeron dos modelos de costos que predicen en el gasto total y farmacéutico. Se estimó un modelo logístico binario para predecir el riesgo de llegar a condiciones crónicas. **RESULTADOS:** Se identificaron 143.626 pacientes crónicos. Se estableció que el 5,53% de los pacientes atendidos, tiende a cronificarse. Con un ajuste global, R^2: 19,1%, se evidenció que las variables: edad, salario y número de enfermedades crónicas, generan un impacto significativo, positivo y monótono sobre el gasto médico y el farmacológico. El número de prescripciones, edad del paciente, tipo de atención y origen del siniestro, tienen un impacto positivo sobre la probabilidad de que un paciente llegue a la condición crónica. El modelo fue probado sobre los últimos seis meses de datos, mostrando una sensibilidad superior al 80%. **CONCLUSIONES:** El impacto de las enfermedades crónicas sobre el gasto total es un factor importante en el resultado económico de las ARL en Colombia. El modelo construido permitiría contar mensualmente con un índice de riesgo de cronificación de todos los afiliados, útil en la toma de decisiones, y que permitiría predecir de manera más específica el gasto total y farmacéutico.

PHP32

COMPARING QUALITY OF LIFE AND CLINICAL VARIABLES FOR THE PREDICTION OF FUTURE MEDICAL EVENTS

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OBJECTIVES: Despite increased recognition that quality-of-life scores correlate with health care resource use, their relative predictive value remains understudied. This study compares a well-known quality-of-life measure against comorbidity status and current medical events in their ability to predict medical events in the subsequent 6-month period. **METHODS:** Data are drawn from panels 10 (n=12,358; rounds 2/3) and 11 (n=13,944; rounds 4/5) of the Medical Expenditures Panel Survey (MEPS), collected in 2006 and 2007. The MEPS provides information obtained from medical providers on total number of medical events and conditions associated with each panel round, as well as the physical component summary (PCS) of the SF-12 (rounds 2/4), a self-reported health status survey. Three logistic regression models were used to estimate the probability of higher resource use (6+ medical events vs. < 6) in the subsequent 6 months. Model 1 included the number of comorbidities (none; 1; 2-3; 4+) and current count of medical events as independent variables. Model 2 included just current PCS, and model 3 included all predictors from models 1 and 2. **RESULTS:** Despite being simpler, model 2 (AUC=0.80, pseudo-R2=0.11) had explanatory power close than that of model 1 (AUC=0.88, pseudo-R2=0.20). Model 3 (AUC=0.90, pseudo-R2=0.24) improved slightly on model 1. Under Model 3, a 5-point lower PCS was associated with a 33% increase in the odds of having 6+ medical events in the next 6 months, an association similar to that of having two more medical events (36% increase). **CONCLUSIONS:** Our results suggest that as compared to comorbidity counts and number of medical events, PCS has a similar ability to predict having 6+ medical events in the subsequent 6-month period.

PHP34

ANÁLISIS DE COSTO-EFECTIVIDAD DE LOS PROFESIONALES DE ENFERMERIA CON EXPERIENCIA LABORAL EN UCI VERSUS SIN EXPERIENCIA LABORAL EN EL ERROR DE LA MEDICACIÓN PARENTERAL EN PACIENTES ADULTOS HOSPITALIZADOS EN UCI

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OBJECTIVOS: Determinar la relación de costo-efectividad de los profesionales de enfermería con experiencia versus sin experiencia laboral en relación al error de tratamiento en la medicación parenteral y los eventos adversos asociados en el tratamiento de los pacientes hospitalizados en las unidades de cuidados intensivos (UCI). **METODOLOGÍAS:** Se utilizó un modelo de árbol de decisión de costo-

efectividad para establecer la comparación entre las alternativas: profesionales de enfermería con experiencia laboral en UCI (PECE) y profesionales de enfermería sin experiencia (PESE), las probabilidades del modelo se determinaron mediante una revisión sistemática de la literatura biomédica, la efectividad es cada evento adverso evitado (EAE), los costos de los procedimientos fueron calculados en pesos chilenos a valor actual desde el punto de vista de una institución de salud, mediante un método de microcosteo. Los datos fueron integrados en el modelo y analizados mediante el programa DATA 4.0 TreeAge, con los cuales se calculó la razón de costo-efectividad de cada una de las alternativas de tratamiento. Se realizó un análisis de sensibilidad y se calculó la razón de Costo-Efectividad Incremental (ICER) generada por una alternativa respecto de la otra. El horizonte de tiempo del análisis fue de un año, debido a esto no se utilizaron tasas de descuento. **RESULTADOS:** Los PECE son la alternativa dominante del análisis. La efectividad de los PECE fue de 85 EAE, en cambio en los PESE fue de 70 EAE. El ICER fue de $17.647 por cada EAE. El análisis de sensibilidad mostró que los resultados obtenidos son robustos. **CONCLUSIONES:** Es más costo-efectivo contratar para la atención y el cuidado de los pacientes en las UCI a PECE, aun cuando el sueldo de estos profesionales sea un 20% superior al de los PESE, ya que por cada EAE se produce un ahorro de $17.647 al sistema de salud.

PHP35

TREATMENT AND OUTCOME ANALYSIS OF RODENTICIDE POISONING IN TERTIARY CARE HOSPITAL IN SOUTH INDIA

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OBJECTIVES: To analyze the treatment pattern and outcome of rodenticide poisoning in tertiary care hospital. **METHODS:** A retrospective observational study was carried out in a tertiary care teaching hospital on patients admitted due to rodenticide poisoning during the period of 2004 to 2012. All the patients who diagnosed with rodenticide poisoning were enrolled in the study. Patient data like demography, social habits, co-morbid diseases, pre-hospitalization period, type of exposure, type of compound consumed, type of treatment given and outcome were collected in case record form and analyzed. **RESULTS:** Total of 137 patients were enrolled in the study. Among them 69 (50.4%) patients were male and 68(49.6%) were female. The median age of the study population was found to be 24 (11) years. Majority of the poisoning were intentional (96%). The median pre-hospitalization period was found to be 3 (5.75) hours. Among them majority of them consumed zinc phosphide poisoning (29.2%). Treatment pattern analysis showed that majority of them received gastric lavage(48.2%), charcoal(27.7%), vitamin-k (74.5%), Fresh frozen plasma (37.2%) and N-acetyl cysteine (40.1%) as a major course of treatment. Outcome analysis showed that gastric lavage and charcoal administration was found to be beneficial as an initial course of therapy. Among the other treatment modalities N-acetyl cysteine was found to be comparatively beneficial. **CONCLUSIONS:** Gastric lavage and charcoal administration were found to increase the survival rate in the initial stages of management. N-acetyl cysteine was found to be more effective as a main course of therapy.

PHP36

MONITORING HEALTH PROCESSES IN THE REAL WORLD: AN ITALIAN POPULATION DATABASE EXPERIENCE

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OBJECTIVES: To describe a functional approach of a population database for monitoring health economics, patient's outcomes and impact of new drugs. The need to use real-world data to support clinical research was the main driver for the Italian Inter-university Consortium (CINECA) to set-up a population-based patient centric database (ARNO Observatory). **METHODS:** The Italian National Health Service (NHS) is a Public Health System, providing health care assistance to all the population. Since 1987, ARNO Observatory collects and integrates administrative and clinical data for each single patient with high quality and complete information of patient demographics, NHS reimbursed drugs dispensed, hospital discharges, lab tests prescriptions. **RESULTS:** ARNO, with its patient centric approach, provides comprehensive data from a population of over 11 million of patients of a network of 32 Italian Local Health Units. Integration of administrative and clinical data is important to study patient care pathways, to evaluate appropriateness of medical prescriptions, to evaluate real world outcome and to reduce health expenditure. This patient centric approach led to the creation of disease-specific observatories such as diabetes, cardiovascular disease, osteoporosis, etc…, with access to data tailored on specific user profiles at national or local level. The aim is to examine the safety and/or effectiveness of health care products and services in the real-world by measuring performance indicators and impact of new drugs. **CONCLUSIONS:** ARNO Observatory is an important source of information able to show both economical indicators and the good practice of treatment. In particular ARNO enables Health Units and Professionals to conduct research projects on disease management, and benchmarking and it is a valid instrument for epidemiological and economic planning for decision making in Italy.

PHP37

RELATIONSHIP BETWEEN FALLS AND CNS DRUGS AT A ACUTE CARE TEACHING HOSPITAL IN JAPAN

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OBJECTIVES: Central nervous system drugs (CNSDs) are commonly used at acute care settings. However, the relationship between falls and CNSDs has not been explored. This study aims to try to address the relationship. **METHODS:** We used data of CNDs prescribed for over fifteen years old in-patients in 2012. There were CNSDs including 20 benzodiazepine agents, two non-benzodiazepine agents, one barbiturate agents, and five others. With regard to CNDs, we examined duration of prescription, duration of administration, and number of patients for falls within 24 hours after immediately being administered. Falls due to CNDs administration is defined as follows: Fall rate for CNDs = number of falls / prescription days x 100. **RESULTS:** There were 344 falls including 142 cases (41.3%) with CNDs administration, and the duration of prescription were 62,622 prescription-days. From the viewpoint of length of drug effectiveness, Fall rate for CNDs were 0.16% in short-acting CNDs, 0.25% in intermediate-acting CNDs, and 0.26% in long-acting CNDs. **CONCLUSIONS:** This result suggested that long-acting CNDs were strongly related with falls. To prevent falls within a hospital, hospital personnel including nursing staff have to be educated about CNDs.

PHP38

SINGLE USE DEVICES IN ARGENTINA: ECONOMIC EVALUATION OF A "REUSE" VERSUS A "SINGLE USE" POLICY

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OBJECTIVES: Several medical devices are labeled for single-use only. The popularity of several "off-label" processes - re sterilization, reprocessing and reuse of single use devices (SUDs)-is mainly due to the cost saving and environmental benefits, but also from scarcity of evidence of adverse safety data. This study objective was to compare differential costs of a reuse vs. a single use policy of SUDs and estimate its implications considering 4 device types (Trocars, endo-cutters, lineal-cutters and harmonic scalpels) from a perspective of an Argentinean private health care organization. **METHODS:** A literature review was performed to identify the clinical outcomes after the use of re sterilized SUDs, which was supplemented with a Delphi-like panel to inform missing parameters. An economic model was built to estimate the cost difference between a surgical procedure performed with SUDs or with a reused sterilized SUD. Costs were expressed in USD of 2012 and were grouped in three categories: device related costs, adverse events, and the incremental surgical time associated to reuse of SUD. Deterministic and probabilistic sensitivity analyses were performed. **RESULTS:** A private health care payer in Argentina would expect to spend USD 425 per surgery if new trocars are used and USD 244 if sterilized material are utilized instead. For endo-cutters the equivalent results were USD 1667 and USD 1102, for linear-cutters USD 1228 and USD 1046 and for harmonic scalpels USD 1041 and USD 292. Results were robust in the sensitivity and scenario analysis. **CONCLUSIONS:** In all the devices and scenarios analyzed, reutilization of SUD resulted less costly than using only new material even after considering the additional cost associated with potential adverse events related to reuse. If we consider total surgical costs, these differences represent savings that range from 2.5% to 14.8%. More research is needed to assess effectiveness and safety of these off-label policies.

PHP39

SERIOUS ADVERSE EVENTS FOR BIOLOGIC RESPONSE MODIFIERS INDICATED FOR THE PROPHYLAXIS AGAINST TRANSPLANT REJECTION. AN INSIGHT FROM SPONTANEOUS ADVERSE EVENT REPORTING SYSTEM

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OBJECTIVES: Immunosuppression by biologic response modifiers is essential for successful organ transplantation. These medications have safety concerns that complicate organ transplantation. This study aims to identify and characterize safety signals of serious adverse events associated with exposure to BRM among organ transplant patients. **METHODS:** Empirica Signal (version 7.3) was used to apply pharmacovigilance disproportionality analysis to the FDA Adverse Event Reporting System to identify serious adverse events. Associations between drugs and events were measured by Empirical Bayes Geometric mean (EBGM) and corresponding 95% confidence intervals (EB05-EB95). Associations with EB05 >1 are considered identified safety signals, and associations with EBGM ≥2 are considered significant safety signals that warrants regulatory follow up and possible actions. **RESULTS:** From Q4 1997 to Q2 2012, a total of 12,151 serious adverse event reports for biologic response modifiers were reported and 15.6% of them met safety signal threshold. About 12% of these signals were significant. Sirolimus and Mycophenolate accounted for the majority of all signals, and Antithymocyte Immunoglobulin and Cyclosporine contributed to the majority of significant signals. The following significant signals were identified for Antithymocyte Immunoglobulin (reduced therapeutic response, pulmonary edema, hypotention, serum sickness, infusion related reaction, and anaphylactic reaction); for Azathioprine (alternaria infection, fungal skin infection, and lymphoproliferative disorder); for Cyclosporine (neurotoxicity, graft versus host disease, and thyroid cancer); for Cyclophosphamide (disease progression); for Daclizumab (cytomegalovirus infection); and for Tacrolimus (coma and tremor). Approximately 34% of these events contributed to patient death; 7% were life-theratening; 32% lead to initial or prolonged hospitalization; and 28% contributed to other serious outcomes. **CONCLUSIONS:** Exposure to biologic response modifiers for the prophylaxis against transplant rejection is associated with serious adverse events that could be fatal or life-threatening. Pharmacoepidemiological studies are required to evaluate the identified signals to help understand the benefit-risk profile of these medications.

PHP40

ASSESSMENT OF ADVERSE EVENTS BY USING TRIGGER TOOLS IN SURGERY DEPARTMENT OF AN INDIAN TERTIARY CARE TEACHING HOSPITAL

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OBJECTIVES: An adverse event (AE) is defined as 'unintended physical injury resulting from or contributed to by medical care. A Trigger is a clue that helps a health care organization to identify adverse events. The objective of this work was to assess adverse events by using trigger tools in surgery units of the study hospital to identify AEs. **METHODS:** The study was carried in a tertiary care teaching hospital. Trigger list was developed and used to review cases (n=333). The severity of harm was categorized as per National Coordinating Council for Medication Error Reporting

and Prevention (NCC MERP) severity scale. **RESULTS:** When the list of triggers was used for the review of AE case reports, 61 triggers were identified in 167 (50.2%) cases. Transfusion / use of blood products (15%), infection of any kind (6.9%) were the commonly noted triggers in the critical care module. In the surgical module, return to surgery (6%) and occurrence of any post surgical complication (6%) were predominantly noted. In the medication module, repeated request for lab investigations (13.2%), use of laxatives (13.2%), pyrexia (10.8%), use of nebuliser/steam inhalation (7.5%), use of analgesics (6.6%) and anti-emetics (5.7%) were commonly noted. When the harm was studied category E was 24.9% followed by Category F-13.8%. **CONCLUSIONS:** The developed trigger list was able to flag 167 case profiles with potential adverse events. This tool has potential application in reviewing the cases for adverse events.

PHP41

EFFECTIVENESS OF DIFFERENT DOSAGE REGIMEN OF PRALIDOXIME IN ORGANOPHOSPHORUS POISONING IN TERTIARY CARE HOSPITAL

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OBJECTIVES: To identify the most appropriate dosage regimen of pralidoxime that can be recommended for the management of OP poisoning. **METHODS:** An open labeled cross-sectional, nonrandomized observational study was carried out in emergency wards of tertiary care hospital. A total of 256 OP poisoned patients were admitted between 2009 to 2013. The basic demographical, clinical characteristics and severity were assessed at admission. Based on the pralidoxime dosage regimen patients were categorized into 4 different groups viz. control, intermittent, 500mg/ hour, 1g/ hour groups. The clinical outcome analyzed in terms of hospitalization days, ventilatory days, total atropine required, and incidence of intermediate syndrome and outcome were assessed for comparison with pralidoxime regimen **RESULTS:** The results showed that majority of OP poisoned patients were in the age group of 21-30 years, and males predominated the females (2.3:1). Clinical Severity assessment of these patients showed that most of them had moderate to high severity. Outcome analysis showed that patients of continuous infusion of pralidoxime had significantly improved recovery rate with least sequel and fatality rate. The incidence of intermediate syndrome, number of ventilation days, total atropine requirement, number of hospitalization days and mortality rate significantly reduced in continuous infusion group. **CONCLUSIONS:** Continuous infusion of pralidoxime at 500 mg/hour resulted in significantly better clinical outcome than other dosing regimens and not associated with adverse derug reactions.

PHP42

ANALYSIS OF BRAZILIAN PUBLIC FUNDING PROCESS FOR NEW BIOLOGIC DRUGS

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OBJECTIVES: To ascertain if the Brazilian HTA body CONITEC, which replaced CITEC in December 2011, is delivering on Ministry of Health (MoH) promises of transparency and set assessment timelines whilst adopting mandatory evidence requirements for new biologic drug funding decisions via the Unified Healthcare System (SUS). **METHODS:** Secondary research based on CONITEC's final reimbursement recommendation reports, evaluating existing and sponsor submitted data. These reports include deliberations from a plenary assembly of representatives from the MoH, drug regulator ANVISA and supplementary health regulator ANS, as well as public consultation contributions. **RESULTS:** CONITEC has delivered on transparency with publications of the rationale behind each of its recommendations, thus enabling pharmaceutical firms to understand how to respond. The 180 day initial analysis phase deadline is being met but evaluation of the implementation phase timeline is premature. Out of the final recommendations published to date for biologics, about 40% correspond to a funding rejection. Biologic medicines have been denied funding from psoriasis to wet AMD due to lack of cost-effectiveness as well as efficacy and safety studies of short duration and small patient populations. The rejection of everolimus for a rare brain tumour shows that orphan drugs are not being treated differently. Positive endorsements of biologics from breast cancer to rheumatoid arthritis come with recommendations of significant price cuts and creation of clinical guidelines. **CONCLUSIONS:** Manufacturers are struggling to adjust to evidence requirements needed in supporting funding applications for new biologics, including orphan drugs. Transparency is evident in CONITEC's analysis phase but is absent after a positive recommendation, when the MoH ascertains how the medicine will be offered by SUS. Nonetheless, this is an advance compared to the CITEC process, whereby decisions were not made public and there were no clear timelines.

HEALTH CARE USE & POLICY STUDIES – Health Care Research & Education

PHP43

COSTS OF DENGUE CONTROL AND PREVENTION PROGRAM IN BRAZIL

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The burden of dengue is significant in Brazil. Between 2002 and 2010 approximately four million probable dengue cases were reported, with significant epidemics in 2002, 2008 and 2010. It is expected that a dengue vaccine, currently under phase 3 clinical trials, will reduce the number of cases, costs of the disease and costs of dengue prevention and control programs, in particular during epidemic peaks. **OBJECTIVES:** Estimate the costs of dengue control program (PMCD) in the municipality of Goiânia-GO, Brazil. **METHODS:** We conducted a retrospective analysis, considering epidemic (October/2009-April/2010), and endemic (May-September/2010) periods of dengue transmission. The public health care system perspective was considered. We considered the following cost components: human resources, training, infrastructure, equipment and office supplies, transportation, personal protective equipment (PPE), field and laboratory equipment, insecticides and social mobilization, considering capital and recurrent costs. Capital costs were estimated for both transmission periods combined. **RESULTS:** The total and monthly recurring costs of the PMCD during the epidemic period was R$8.307.590 (US$4.988.345) and R$1.400.819 (US$841.131) respectively; and in the endemic period was R$ 5.848.678 (US$ 3.511.876) and R$950.619 (US$570.805), with human resources being responsible for the majority of costs in both periods (83 and 86%, respectively). Capital costs for both periods were R$683,315 (U.S.$410,301), with a high cost share for transportation (80%) and infrastructure (13%) components. The Municipal health department was responsible for 83% of total costs, followed by state (13%), and federal (3%) levels. **CONCLUSIONS:** Although the estimated costs of the PMCD is under-estimated, we demonstrate a significant incremental costs (R$3.050,211 or U.S.$1.831.518) during the epidemic period. Our results can provide inputs for cost-effectiveness studies of dengue vaccines, which are important to support decision making regarding its introduction into public health programs.

PHP44

THE ECOLOGY OF MEDICAL CARE IN POOR SETTINGS: SELF REPORTED HEALTH CARE UTILIZATION IN SANTIAGO DEL ESTERO, ARGENTINA

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OBJECTIVES: Health services utilization in poor provinces in Argentina is poorly known, due to data poor environments. We utilized a population based health care survey to analyzed the ecology of medical care, and to estimate self reported health care services utilization (SRHCU) patterns among adults (≥18 years old). **METHODS:** A health Survey was performed, with probabilistic, stratified, polyetapic sampling, adding health utilization questions to the National Risk Factor Survey of Argentina (ENFR 2009) questionnaire. We obtained SRHCU stratified as ambulatory visits, emergency, hospitalizations, stratified into age, sex, rural, urban, health status and prior health problem. Analysis was performed with SPSS 17, 95%CI for single proportions was obtained. **RESULTS:** Among 2064 persons that responded de survey, 78,9% were urban-21,1% rural, 41,2% males, mean age was 39,9% (SD 15,8) years old, age range 18-93. The General Health Status was regular or bad (16,08%) (95%CI 14,5-17,7%). Likert scale of health status provided Mean = 86,65 (SD 104,35); Median 80 (25P =70; 75P =90). Acute illness events in prior 4 weeks occurred in 24,8% (95%CI 22,9-26,7%). 70,4% had an ambulatory visit in the prior 6 months (95%CI 68,4-72,4%), while, in prior month 17,0% (95%CI 15,4-18,7%) consulted a physician office [generalist 10,36% (95%CI 9,1-11,7%) and 6,7% specialist (95%CI 5,6-7,8%)]. Office visits rate was 261 per 100 persons per year [increased with age 65+ (305), regular or bad health (458), and rurality (289), decreased for males (197)]. Emergency visits occurred in 106 persons (5,1%) (95%CI 4,18-6,09%); Hospitalization was 10,6% during prior year (95%CI 9,3-11,9%), 78% admitted once and 20% readmitted to the hospital in the same period. **CONCLUSIONS:** Results provide an estimate of SRHCU data, and show lower ambulatory and emergency visit rates, while hospitalization admissions and readmissions is similar to other ecology of medical care studies in other areas of the world.

PHP45

REVISIÓN DE ESTUDIOS DEL COSTE DE LA ENFERMEDAD

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OBJECTIVOS: Revisar la respuesta que aportan diferentes analistas a la pregunta: ¿qué es lo que obtenemos del sistema sanitario (SS)? **METODOLOGÍAS:** Se han revisado las propuestas de la OMS, la OCDE y el enfoque del NHS británico. También las aproximaciones de investigadores como D. Cutler y J. Puig-Junoy. **RESULTADOS:** La OMS combina diferentes dimensiones: resultados en salud, equidad, equilibrio financiero y respuesta del sistema sanitario, obteniendo un indicador de medida absoluta y proponiendo dos índices relativos de eficiencia: uno relacionado con el nivel de esperanza de vida ajustada por incapacidad y otro que valora la eficiencia del SS en general. En la OCDE consideran que debe adjudicarse la prioridad a la medición de la relación costo-efectividad. Actualmente sus esfuerzos se orientan a la búsqueda de indicadores de calidad. El tercer enfoque estudia la variación de la productividad en el seno del NHS, definida como el output obtenido en relación con los inputs utilizados. Se considera que la efectividad no puede determinarse dado el grado de incertidumbre con respecto a los efectos específicos del SS y aboga por ponderar los resultados con medidas de calidad. Cutler et al obtuvieron un valor de $19.900 como coste por año de vida ganado (C/AVG) en el período 1960-2000 en EEUU, asumiendo que el SS es el responsable de la mitad del resultado. Puig-Junoy y Merino-Castelló estudiaron para el período 1960-2001 la productividad marginal del gasto sanitario en España y obtuvieron un C/AVG entre 10.045 y 12.937. **CONCLUSIONES:** No hay consenso en cuanto al estudio de la efectividad del sistema sanitario. La indeterminación que supone la influencia de elementos ajenos al mismo en el resultado final supone un inconveniente importante. La incorporación de la calidad puede ayudar a superar, en parte, este problema.

PHP46

COMPARACIÓN DEL TRABAJO EN EQUIPO EN SALAS DE CIRUGÍA ENTRE UN HOSPITAL PRIVADO Y UNO PÚBLICO DE BOGOTÁ, D.C

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OBJETIVOS: Determinar las diferencias del trabajo en equipo en salas de cirugía entre un hospital privado y uno público de Bogotá, D.C. **METODOLOGÍAS:** Estudio observacional analítico. *Muestra:* n= 90 equipos de cirugía, 49 de hospital privado (54%) y 41 de hospital público (46%). Criterios de inclusión: Equipos de cirugía general de hospitales de tercer nivel de complejidad de la ciudad de Bogotá, D.C.

Procedimiento: Los datos usados en este estudio hacen parte de la validación del instrumento OTAS (Observational Teamwork Assessment for Surgery) en Colombia. Una observadora experta en el OTAS ingresó a las salas de cirugía y registró los puntajes otorgados a cada subequipo (anestesiólogos, cirujanos, enfermeros e instrumentadores quirúrgicos) en cinco comportamientos (comunicación, coordinación, cooperación, liderazgo y conciencia situacional) para las tres fases quirúrgicas (pre, intra y post operatorio). Se aplicó la prueba U de Mann-Whitney, se hizo la corrección de Bonferroni para el alfa rechazando la hipótesis nula cuando el alfa era igual o menor a 0,004, manteniendo así un margen de error para el estudio de 5%. **RESULTADOS:** Se encontró que los puntajes obtenidos en el OTAS fueron diferentes en la institución privada comparada con la pública (Z=4,77; p=0,0000), al realizar comparaciones discriminadas se encontraron diferencias significativas en los subequipos de anestesiología (Z=12,17; p=0,0000), en los comportamientos de liderazgo (Z=3,56; p=0,0004) y conciencia situacional (Z=3,20; p=0,001) y en las fases pre quirúrgica (Z=4,41; p=0,0000) y post quirúrgica (Z=4,20; p=0,0000), en todos estos casos los puntajes fueron mayores en los equipos de la institución privada. **CONCLUSIONES:** Teniendo en cuenta el diseño los resultados no pueden ser generalizados. Los hallazgos sugieren una diferencia en algunas habilidades no técnicas e interacción en los equipos de salud según el tipo de institución, esto puede estar relacionado con cumplimiento de protocolos y mayor control de calidad implementados en la institución privada.

HEALTH CARE USE & POLICY STUDIES – Health Technology Assessment Programs

PHP47
APPLICATION OF HEALTH TECHNOLOGY ASSESSMENT AND PHARMACOECONOMICS IN THE DECISION-MAKING PROCESS IN SELECTED EU MEMBER STATES

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BACKGROUND: The application of Health Technology Assessment (HTA) and Pharmacoeconomics (PE) into real health policies in selected European countries (Austria, Bulgaria, Croatia, Czech Republic, Germany, Hungary, Latvia, Poland, Romania, Serbia, Slovakia, Slovenia, UK) was analyzed based on the outputs from the conference "Optimalization of Methods of PE and HTA: Importance for National Health Policy and Cross-Border Cooperation" (Slovakia, 10/2012). **OBJECTIVES:** The objective of the paper was to compare the systems and to find the most transparent one based on the pre-defined criteria. **METHODS:** The primary method used for the analysis was structured evaluation of the outputs from the conference. The other relevant information resulted from the systematic review of PUBMED, EMBASE and CENTRAL in years 2011-2012 extended to official websites of public health institutions and officially published data with the objective to select all papers on HTA/Pharmacoeconomics related to selected European countries. We evaluated 9 characteristics relevant for the decision-making process: legislative background, implementation, binding force, institutionalization, qualified personal resources availability, existed methodology/guidelines, clarity of the process, patient involvement in the process, and respecting the deadline of 180 days for issuing a decision. **RESULTS:** Resulting from the analysis, of selected countries, the UK was shown to have the most transparent system. Germany and Austria ranked second. Hungary and Poland ranked third, followed by Slovakia. The least transparent system was found in Bulgaria and Romania. **CONCLUSIONS:** One of the criteria was qualified personal resources availability that immediately discriminate systems in smaller central and eastern European countries. This should result in developing tailored approaches rather than copying technocratic "western" systems. The system prepared in Romania based on multiple criteria decision analysis principle could be regarded as a positive example.

PHP48
EXPERIENCIA INICIAL CON UN NUEVO TIPO DE DOCUMENTO DE EVALUACIÓN DE TECNOLOGÍA SANITARIA: "INFORMES DE MESA DE AYUDA"

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OBJECTIVOS: Si bien la utilización de Evaluación de Tecnologías (ETS) para la toma de decisiones es cada vez más utilizada en Argentina, es habitual la disociación entre el tiempo para la toma de decisiones cotidianas y el que demanda la realización de informes tradicionales. El Instituto de Efectividad Clínica y Sanitaria (IECS), una de las principales agencias de ETS de Latinoamérica, provee informes a instituciones públicas, de seguridad social y seguros privados. Se diseñó un nuevo tipo de documento orientado a responder una consulta puntual (motivada por un caso real), de respuesta en 48-72 hs, denominado Informe de Mesa de Ayuda (IMA). El objetivo es describir la experiencia del primer año y evaluar cuáles son las tecnologías más solicitadas como IMA por un grupo de decisores de Argentina y Uruguay. **METODOLOGÍAS:** Descripción y análisis de las bases de datos de IMA realizados por IECS. **RESULTADOS:** Entre enero de 2011 y febrero de 2013 se realizaron 110 IMA. El 78% de los pedidos correspondieron tecnologías terapéuticas (54% dispositivos, 26% procedimientos y 20% radioterapia), 15% a drogas y 7% a tecnologías diagnósticas. Esta distribución fue significativamente diferente a la observada en los informes de ETS donde se observa que el 52% de los pedidos correspondieron a tecnologías terapéuticas, 34% a drogas y 14% a tecnologías diagnósticas. En cuanto a las áreas de interés el 17% de los IMA fueron relacionados con cáncer, el 14% con alteraciones neurológicas, el 12% con patologías traumatológicas, 11% gastrointestinal, 11% con trastornos urinarios, siguiendo en frecuencia motivos quirúrgicos, cardiovasculares, endocrinológicos, trastornos genéticos y oftalmológicos. **CONCLUSIONES:** Es factible implementar los IMA en 48-72 hs, para responder a consultas puntuales acotadas. El perfil fue diferente al de los informes de ETS tradicionales. Los IMA más solicitados fueron aquellos relacionados con tecnologías terapéuticas, siendo el área oncológica la más frecuente.

PHP49
FOLLOWING THE WESTERN HTA MODEL IN LATIN AMERICA: A SELF-FULFILLING PROPHECY?

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OBJECTIVES: Health technology assessment in Latin America has been relatively more mature than other similarly developed health systems. This research explores the trends of development of HTA in the region to understand similarities to the European HTA model. It further looks at relevance of having such a model in Latin America, the relevance of the complexity of the methodologies and utilities used and finally, the implications of these trends. **METHODS:** The study was conducted in Brazil, Mexico, Argentina and Columbia. Opinions of 18 stakeholders were collected via telephone interviews. Respondents included senior clinical oncologists(3), academics(4), policy advisors(2), senior bureaucrats in the health ministries(3), senior members of HTA bodies(4) and senior executives from manufacturers(2). A scoring system was devised to plot the level of complexity and maturity of the HTA systems / agencies both in Latin America and then comparing it with scores of a similar study across Europe and Australia. The responses around the relevance of the model and implications were analysed qualitatively adding perspective from the author's experience in these countries. **RESULTS:** The level of maturity of HTA processes in all the countries studied was seen to be generally high. The level of association with reimbursement processes was seen to vary. There was a split on the relevance of the European model to the Latin American context. Majority of the academics (n=3/4) and members of HTA bodies (n=2/4) felt that following highly complex European models was a necessary natural progression to the HTA development curve. This was not the observation with the rest of the stakeholders. **CONCLUSIONS:** There is thought to be a trend where there is a push by academics and HTA-related professionals towards making it similar to the European model, and thus increasingly complex. Greater international attention can be a reason, although it must be further explored.

HEALTH CARE USE & POLICY STUDIES – Patient Registries & Post-Marketing Studies

PHP51
IT APPLICATION FOR POST MARKETING DRUG REGISTRIES

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OBJECTIVES: Establishing an active postmarketing safety surveillance and analysis system, used by health professionals, regulatory bodies and sponsors. **METHODS:** The solution consists in making available to the entire community a set of online tools aimed to the data collection and analysis on innovative drugs. The introduction of online integrated environments ensures the appropriate use of drugs, help to monitor drug consumption and related costs and improves the real-time reporting of suspected adverse drug events. The surveillance system collects patients data in a common IT infrastructure within the same network. For 24 antineoplastic drugs the system provides also automatic procedures to manage the 'risk sharing' & 'payment by result' approach, that foresees partial or total refund of the cost sustained by the hospital pharmacy for the drug in case of progressive disease or unacceptable toxicity. **RESULTS:** This presentation will illustrate the Cineca methodological IT approach used also by the Italian National Medicines Agency. The system has been used for 70 innovative drugs from eleven different drugs categories: antineoplastic, antidiabetics, neurological, dermatological, antiasmatics, ophtalmologic, antireumatics and others. More than 500.000 patients were registered by more than 900 health structures in a timeframe of 7 years. **CONCLUSIONS:** The introduction of an online integrated environments ensures a more appropriate drug usage, help to monitor drug consumption and related costs and improves the real-time reporting of suspected adverse drug events.

HEALTH CARE USE & POLICY STUDIES – Population Health

PHP52
EXPLORING INCOME INEQUALITY IN SELF-REPORTED HEALTH STATUS IN CHILE AFTER THE HEALTH CARE REFORM OF 2005

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OBJECTIVES: Chile carried out a health care system reform in 2005 aimed at reducing health and health care inequities. This study assessed whether household income-related inequality in adult self-reported health status (SRHS) was reduced after this reform. **METHODS:** Before and after study design using the 2000 and 2009 CASEN surveys (252 748 and 246 924 participants, respectively) we compared the Erreygers concentration index (CI) for SRHS (binary variable: poor=0, fair/good=1) between these two years. Factors associated with good health were explored using weighted logistic regression models. Decomposition analysis of the CIs by "legitimate" (age, sex, marital status, number of household members) and "illegitimate" (income, ethnicity, rural/urban, education, occupation, type of health care provision) factors was conducted. **RESULTS:** Results indicated that there was a significant concentration of fair/good SRHS favoring the rich people in Chile in both years (Erreygers corrected CI for bounded binary variables was 0.165 [Standard Error 0.007] in 2000 and 0.053 [0.002] in 2009). We standardized the 2000 and 2009 CIs to assess horizontal inequity and decomposed them into "legitimate" factors such as age and sex and "illegitimate" factors, mostly socioeconomic conditions. Despite the fact that the CIs are not directly comparable between 2000 and 2009, our findings suggest that the CI might have decreased after the reform, but good SRHS continued

to be concentrated among the rich in both years. Decomposition indicated that "illegitimate" factors remained large contributors to income-related inequality in SRHS even after the equity-centered reform of 2005. **CONCLUSIONS:** Findings suggest that income-related inequality in SRHS might have decreased in Chile after the health care reform. Beyond this observed difference over time, the remaining inequality is still largely due to illegitimate factors that should be tackled through broader policies in the country.

HEALTH CARE USE & POLICY STUDIES – Quality of Care

PHP53
PERCEPTION OF USERS OF DRUG DISTRIBUTION PROGRAM IN BRAZIL

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OBJECTIVES: To characterize the users of access to medicines program developed in Brazil, known as *Aqui Tem Farmácia Popular* Program (PAFP), by identifying those users who migrated from other supply of basic medicines programs by means of a survey explicitly developed for this purpose. This work also seeks to evaluate the meeting customers' needs by the Program and its satisfaction level. **METHODS:** The survey instrument used gathering the users of *Aqui Tem Farmácia Popular* program has been applied in 15 counties from 14 Brazilian states. 1073 interviews composed the sample, in 27 establishments of private pharmacies, during august 2012. The collection instrument was composed by three blocks: questions concerning the use of the PAFP and other programs of medicines supply; user's profile information; and identification of the medicine supplied. **RESULTS:** The evaluation of the users migration from other programs identified that, before the PAFP, 52% of interviewed users was buying the medicines in the private pharmacy and more than 30% was using the Public Service in a Health Center of SUS, a piece of 11% began the treatment after the PAFP. More than 58% of users would use the service of the SUS if there was no PAFP. However, 36% of users reported that they would not use the SUS system for withdrawal of medicines. It was observed that 61% of users gave out to be economizing while withdrawing the medicines with gratuity or at a discount. **CONCLUSIONS:** The conducted survey made possible to characterize the users of PAFP showing aspects concerning the participation and the range of the program. Generally, it was found that the persons are satisfied and they reported to have saved with the program. They also pointed out the convenience they have with the possibility of the access to the medicine in any pharmacy with the PAFP.

PHP54
A NATIONWIDE SURVEY ON PATIENT SAFETY CULTURE IN JAPAN

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OBJECTIVES: To explore safety culture dimensions among health care professionals using Hospital Survey on Patient Safety Culture (HSOPSC) by developed by AHRQ (Agency for Healthcare Research and Quality). **METHODS:** We surveyed nationwide the situation of patient safety culture in 13 hospitals (5,760 persons) allowed for additional costs on patient safety countermeasures under the social insurance medical fee schedule. The questionnaire consists of seven unit-level aspects of safety culture including 24 items, three hospital-level including 11 items, and four outcome variables including nine items. **RESULTS:** An average number of beds was 360 beds (63 - 1,354 beds). With regard to ownership, 13 hospitals included three municipality and local incorporated agency hospitals, one public hospital, two juridical person with social insurance hospitals, six medical corporation hospitals, and one other hospital. Number of all respondents was 5,118 persons (response rate: 88.9%), and included 295 physicians (90.8%), 2,909 nurses (95.5%), and 146 pharmacists (96.7%). In terms of 12 dimensions, the overall average positive response rate (RR) for the 12 patient safety dimensions of the HSOPS was 49.2%, extremely lower than the average positive RR for the AHRQ data (61%). In terms of health care professionals, the overall average positive RR for pharmacists (46.2%) was lower than that for physicians and nurses (49.6% and 49.4%).With regard to pharmacists, the average positive RRs for 8 dimensions of the 12 dimensions were the lowest among three professionals, and three average positive RRs were the highest; Frequency of event reporting (pharmacists: physicians: nurses=73.6%:53.3%:67.9%), Non-punitive response to error (48.8%:42.6%:40.4%), and Staffing (29.1%:27.0%:25.4%). **CONCLUSIONS:** The HSOPSC measurement provides the evidence for assessment of patient safety culture in Japan's hospitals. This result that patient safety culture has been in a state of development, compared with the US hospitals.

PHP55
COST AND QUALITY OF DYING IN HOSPITAL: RESULTS FROM THE ARGENTINE-HEALTH CARE COST AND UTILIZATION PROJECT (A-HCUP)

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OBJECTIVES: Little is known about dying in Argentina, we studied costs and readmissions (ReH) <30 days of hospital dying adults. **METHODS:** A cross sectional study of 1 year hospital discharges, with HCUPs methods, of patients ≥19 yrs old. We obtained deaths, first admission (1 adm) and ReH ≤365 days and ReH <30 days; total direct medical cost (TC I$), mean (I$) (SD), median I$ (Q1-Q3) discharge cost, (in I$ PPP, 2008), stratified by age/sex, admissions and ReH <30 days and <365 days. **RESULTS:** Total mortality for ≥19 yrs old patients was 4,70%. Among 2137 deaths, Total cost of those dead in hospital, TC I$: 40 540 842 ; mean cost per discharge (I$) was 19853 (SD 45 599); Median cost per discharge I$ 4182; (Q1: 1452-Q3: 17730 I$), comprising 8,31 % of TC I$. Among 43321 discharges, TC$ of those alive, TC: 447 300 754 I$; mean cost per discharge ($) was 10569 I$ (SD 21 217); Median cost per discharge 14 091 I$; (Q1: 2 496- Q3:10 054 I$). Relative dead /alive I$ was 1,88 times higher. Mean discharge cost of deceased stratified by age group (mortality 19-64 yrs. old: 1,52%, I$ 48332, age 19-64/≥19 yrs old ratio: 2,43; 65-74 yrs old: 4,72%,I$ 25968, age ratio: 1,31; 75-84 yrs old: 8,45%; I$ 15471, age ratio: 0,78; 85+ yrs old: 14,09%, I$ 7832, age ratio: 0,39), and sex, males (47,4%) had a I$: 22679 (M/F I$ ratio: 1,45). In 1 adm.(53% of deaths), mean cost was I$ 23 792; while ReH ≤365 days (47% of deaths), I$ 13 530, cost ratio ReH/1 adm= 0,57 ; and if ReH <30 days (29,5%), I$ 12354, cost ratio ReH<30/1 adm=0,52. **CONCLUSIONS:** Understanding the economic burden of dying helps promote better and cost-effective ways of promoting palliative care, old and readmitted deaths are less costly.

HEALTH CARE USE & POLICY STUDIES – Regulation of Health Care Sector

PHP56
FROM "GENERIC SCHEME" TO "BRAND-GENERIC SCHEME": THE EFFECT OF NEW POLICY (2003-2004) ON EFFICIENCY OF IRANIAN PHARMACEUTICAL INDUSTRY

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OBJECTIVES: Brand-Generic scheme was implemented in Iran to improve the competition in the market. In this study we aim to assess if this new policy has had any positive effect on efficiency of Iranian pharmaceutical companies. **METHODS:** We used Data Envelopment Analysis (DEA) to evaluate the relative efficiency of pharmaceutical companies for the years 1999-2008. The Wilcoxon matched-pairs signed-rank test and also sign test were used to assess the difference between mean relative efficiency of companies before and after policy. **RESULTS:** Although the Wilcoxon matched-pairs signed-rank test did not show any significant difference between before and after new policy in term of both technical and pure (managerial) efficiency of included companies (Pvalue: 0.079 and 0.07, respectively) but the one–sided sign test indicated that only relative pure (managerial) efficiency has improved after this policy (Pvalue: 0.031). **CONCLUSIONS:** The "Brand-Generic scheme" does not seem to be enough policy to improve efficiency of pharmaceutical companies in Iran. To achieve this aim, paying special attention to infrastructural requirements including non-discriminating and transparent laws and regulations for supporting competition, the competitive pricing policies, the presence of international companies in the market and full privatization of companies had to be also considered by policy makers.

PHP57
REGULATING THE ACCESS TO AN ADEQUATE AND AN INTEGRAL ASSISTANCE IN BRAZILIAN PRIVATE HEALTH PLANS

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OBJECTIVES: To describe the main actions promoted by the The Federal Regulatory Agency for Private Health Insurance and Plans (ANS) to regulate the access of private health plans beneficiaries to an adequate and an integral assistance. **METHODS:** A retrospective analysis of data about coverage in health plans since ANS creation (1999) was done to identify the main actions promoted by the agency in this area. It included the set of rules published and ANS periodic publications. **RESULTS:** A very important identified mechanism that ANS employs for regulating the users access to a full assistance is the elaboration of a list of medical procedures. This list constitutes the minimum obligatory coverage for all plans. It is periodically reviewed and incorporations and/or exclusions are made according to some precepts like: clinical evidence, epidemiological relevance, among others. The guidelines implementation is another important instrument identified in this study to the improvement of private health assistance. ANS established a collaboration term with the Brazilian Medical Association (AMB) to develop guidelines, to spread and to monitor their implementation. **CONCLUSIONS:** The actions presented are the main one promoted by ANS to regulate the access to an adequate and an integral assistance. They can also improve the sector efficiency along with the rational use of techniques and medical technologies. The instruments discussed will be a guide to upgrade the health plans management and their efficiency. The patients will have safer end more effective treatments and ANS keeps the balance and promotion of health in private health with a new model.

PHP58
A MEDIAÇÃO DE CONFLITOS NA AÇÃO FISCALIZATORIA DO SETOR DE SAÚDE SUPLEMENTAR BRASILEIRO

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OBJETIVOS: Demonstrar a eficácia da utilização de meios consensuais de mediação de conflitos pela Administração Pública no controle e fiscalização do cumprimento das normas que regulam a assistência suplementar à saúde no Brasil. **MÉTODOS:** Desde 2010, a ANS – Agência Nacional de Saúde Suplementar implementou o procedimento NIP (Notificação de Investiação Preliminar), cujo objetivo é realizar a mediação de conflitos entre operadoras de planos de saúde e consumidores, no que tange a situações que envolvem negativa de cobertura assistencial. A NIP é um processo totalmente eletrônico, que confere maior celeridade e eficácia na resolução das reclamações dos consumidores, induzindo uma melhora na relação operadora/consumidor. Com a NIP, as operadoras têm prazo de 5 dias para solucionar o conflito junto ao beneficiário e responder à ANS sobre as medidas tomadas. Após processamento na NIP, a reclamação pode ser finalizada por inexistência de infração, reparação de conduta ou encaminhada para abertura de processo administrativo, nos casos em que o conflito não foi resolvido. **RESULTADOS:** Desde sua implementação, a resolutividade dos conflitos na NIP manteve-se acima de 70% do total de reclamações recebidas, o que em 2012 significou a conclusão de 42.672 das 54.412 denúncias de negativa de cobertura assistencial (78,4% de resolutividade). Antes de seu advento, as reclamações eram analisadas por meio de instituição de processo administrativo sancionador, que duravam, em média, 18-24 meses para sua conclusão, podendo levar ao arquivamento da denúncia ou lavratura de auto de infração contra a operadora. **CONCLUSÕES:** A NIP conferiu maior eficácia ao processo fiscalizatório da ANS, proporcionando maior

satisfação aos beneficiários de planos de saúde. Os dados obtidos na NIP são utilizados para monitoramento da garantia de atendimento e acesso às coberturas obrigatórias, que podem gerar a suspensão de comercialização dos planos identificados com falhas assistencias, bem como instauração de regimes especiais de recuperação pela ANS.

PHP59
CONSTRUCCIÓN DE UN MODELO DE PRIORIZACIÓN APLICABLE A LATINOAMÉRICA – EL CASO DE COLOMBIA
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OBJECTIVOS: Los sistemas de salud deben enfrentar el desafío de hacer uso eficiente de recursos limitados ante necesidades crecientes de salud. Colombia no ha sido ajena a éste desafío. El Ministerio de Salud ha entendido la importancia de articular un sistema de salud que incorpore un sistema de priorización del gasto sistemático, transparente y legítimo. En el marco de lo anterior, fue creado el "Instituto de Evaluación Tecnológica en Salud (IETS)", que tiene como objetivo proporcionar recomendaciones sobre tecnologías en salud y mejores prácticas, basadas en evidencia, para el gobierno nacional y demás actores, como insumo para la toma de decisiones. En este proceso, uno de los primeros pasos es diseñar un proceso para la priorización y selección de tecnologías a evaluar. **METODOLOGÍAS:** A partir de una revisión de diferentes metodologías de priorización, se propuso un mecanismo de análisis de decisión de múltiples criterios, que fue discutido en panel de expertos del gobierno y otros actores. Se realizó un piloto de priorización que permitió detectar los principales riesgos y desafíos en cada etapa del proceso. A partir de la discusión, construcción colectiva y experiencia del piloto, se seleccionaron, definieron y ponderaron los criterios de priorización, y se diseñaron las diferentes etapas e instrumentos para llevar a cabo el proceso. **RESULTADOS:** Los criterios seleccionados fueron la gravedad de la enfermedad, la población afectada, el costo de adquisición de la tecnología, la atención a grupos vulnerables, el interés de salud pública y la solicitud de la ciudadanía. **CONCLUSIONES:** Emplear criterios explícitos facilita que la priorización sea un proceso legítimo y transparente. La propuesta permitirá al Ministerio de Salud, como líder del proceso con el concurso de otros actores, contar con herramientas para priorizar y seleccionar tecnologías para evaluación. La experiencia colombiana dará herramientas metodológicas a otros países interesados en la construcción de este tipo de procesos.

PHP60
THE NOTIFICATION OF PRELIMINARY INVESTIGATION (NIP) OF THE FEDERAL REGULATORY AGENCY OF PRIVATE HEALTH AND INSURANCE AND PLANS (ANS): A TOOL TO FACILITATE THE ACCESS TO THE MANDATORY COVERAGE
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OBJECTIVES: To describe the instrument NIP (Notification of Preliminary Investigation) and it's role on solving conflicts related to the obligatory coverage access, between health plans and patients. **METHODS:** A critical analysis of the rule that created NIP (Regulatory Resolution nº 226/2010), established by The Federal Regulatory Agency for Private Health Insurance and Plans (ANS), was done to characterize the tool. **RESULTS:** The Notification of Preliminary Investigation (NIP) consists of a communication time to mediate the relationship between consumers and providers of health plans in cases of unauthorized procedures by the provider. NIP is an electronic process to solve the conflicts before a process that can lead to the punishment of the health plan provider. A contact is previously made to notify the health plan provider about the problem and it has five business days to answer it. This way, the health plan provider has the opportunity to solve the question without punishment and the beneficiaries can have a faster access to the procedure prescribed by the doctors. If the procedure doesn't have coverage according to the supplementary health rules (it is not listed on ANS Medical List of Procedures), the demand is filed. If the provider's answer is not enough to conclude the question, it's sent to the Inspection Department to a more detailed analysis before being finished. **CONCLUSIONS:** The NIP is a mediation instrument that can help ANS to solve the problems between beneficiaries and health plan providers, giving a fast answer to both interested actors of the process. It can be positive because sometimes the questions are solved without the provider punishment and the beneficiaries' injury. The conflict mediation by NIP can contribute to the change in the entities attitude and culture and can also promotes the interaction and the active participation of the actors involved.

PHP61
THE QUALITATIVE PROFILE OF THE COVERAGE COMPLAINTS MADE BY HEALTH PLAN USERS TO THE FEDERAL REGULATORY AGENCY FOR PRIVATE HEALTH INSURANCE AND PLANS (ANS)
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OBJECTIVES: To define the qualitative profile of the coverage complaints made by health plan users, to The Federal Regulatory Agency for Private Health Insurance and Plans (ANS). **METHODS:** A retrospective analysis of the Notification of Preliminary Investigation (NIP) registers in 2011 and in the first half of 2012 was performed. The data were extracted from Inspection System (SIF). The variables considered were: the subject of the coverage complaints (Medical List of Procedures, Time for Coverage Access, Managed Care, etc.), the date of the contract (before or after ANS regulation) and the type of the plan (individual/ family or collective). **RESULTS:** The study shows a change on predominant coverage subject: In 2011 43,5 % of the complaints were about " Medical List of Procedures". In 2012, the main subject was "Time for coverage access" (36,2% of he coverage complains)." It was possible to verify that, in both years considered, there was a prevalence of ANS regulated contracts of individual/familiar type (44.8% in 2011 and 47.7% in 2012). **CONCLUSIONS:** This study helped to know the qualitative profile of the coverage complaints in brazilian supplementary health. The increased number of complaints about "Time for coverage access" in 2012 may indicate that the services offered are not being enough to attend the users. The higher percentage of NIPs of individual/family plans, compared to collective ones, may be a reflection of a greater weakness in consumer-provider relationship in this type of contract.

PHP62
PODER POPULAR Y REGULACIÓN DEL PRECIO DE LOS MEDICAMENTOS EN VENEZUELA
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OBJECTIVOS: Explorar el rol del Poder Popular en el proceso de regulación del precio de los medicamentos en Venezuela, articulado por la Superintendencia Nacional de Costos y Precios (SUNDECOP) en conformidad con lo establecido en la Ley de Costos y Precios Justos y las Providencias Administrativas relacionadas. **METODOLOGÍAS:** Estudio exploratorio documental basado en la búsqueda y revisión de los artículos de prensa disponibles y publicados en la página Web oficial de la SUNDECOP. La búsqueda y recuperación de la información fue realizada el 10 de marzo de 2012. Se tomaron en cuenta para la revisión los artículos que incluían en su contenido las palabras: participación o poder popular y regulación del precio de medicamentos. **RESULTADOS:** Se identificaron 172 artículos noticiosos publicados desde 13 julio 2011 hasta 27 de febrero de 2013. Se revisaron 12 artículos de prensa que cumplían con el criterio de inclusión. El 50% de los artículos revisados resaltan la participación del Poder Popular en la definición de las políticas de precios y los criterios a tomar en cuenta por el Sistema Nacional Integrado de Costos y Precios para la fijación del precio de medicamentos, mientras que en 10 de los artículos se desprende el papel del Poder Popular como controlador social para vigilar el cumplimiento de la regulación una vez sea decretada por la SUNDECOP. **CONCLUSIONES:** Además de las eventuales acciones de inspección y fiscalización, el Poder Popular en Venezuela está aportando insumos a la SUNDECOP que serán incorporadas en el proceso de tomas de decisiones para fijar el precio a los medicamentos durante el año 2013. Se sugiere profundizar en un posterior estudio para conocer y analizar cómo y en qué medida esos aportes del Poder Popular están siendo incluidos en el análisis metodológico para establecer la definitiva regulación del precio de los medicamentos.

HEALTH CARE USE & POLICY STUDIES – Conceptual Papers

PHP63
NOVEL PRICING STRATEGIES TO SUPPORT SUSTAINABLE ACCESS TO MEDICINE IN LATIN AMERICA
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With lower returns from price pressures in developed markets, it is imperative for pharma companies to seek growth in emerging markets such as Latin America. Simultaneously, with rising incomes, a growing middle class in emerging markets is increasing demand for access to innovative medicine, especially in diseases such as oncology, CV and diabetes. Achieving commercial expansion as well as increasing access to innovative medicine in Latin America needs new pricing strategies and funding models. We discuss and evaluate alternative pricing strategies and funding models to support commercial expansion and increase access to innovative medicines in Latin American markets such as Brazil, Argentina, Mexico and Colombia. These include current industry strategies, equitable pricing strategies and strategies focused on local market conditions. We model the impact of these strategies on both specialty and primary care medicines. The modelling is based on insights and assumptions drawn from analogue analysis in pharmaceuticals and other industries. It is supplemented by interviews with industry experts in Latin American market strategies. For the modelling we assume current market and public and private insurance coverage structures. We find that in primary care medicines there is considerable opportunity for commercial and access gain through more differentiated pricing strategies. These strategies are more commercially (revenue and profit) optimal than current industry strategy. At the same time, they are also access optimal in terms of the eligible patients they provide access to. In the case of specialty medicines, differential pricing strategies can increase commercial potential, but there is a gap between commercially optimal and access optimal strategies. This gap can be bridged through increased financing for these medicines. Based on this analysis, we suggest a path forward in which pharmaceutical companies can collaborate with governments and other stakeholders to achieve increased access to innovative medicines in a commercially sustainable manner.

PHP64
ACCESS TO MEDICINES INDEX: MEASURING HOW WELL COUNTRIES PROVIDE ACCESS TO MEDICINES
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Developing countries are now following the steps of developed countries in implementing universal health coverage. Health care systems and policies differ across countries resulting in various levels of medicine access. To evaluate which systems and policies lead to better access, we need a measure to compare how well countries provide access to medicine for their populations. Using IMS proprietary data as well as public sources, our analysis proposes a Country Access to Medicines Index that compares and ranks countries on access to medicine outcomes across four pillars: medicine reimbursement coverage, time to reimbursement, medicine affordability and support for innovation. Medicine reimbursement coverage measures private or public insurance cover for a representative basket of medicines across major communicable and non-communicable diseases. It has three components: share of population covered, share of medicines covered and share of costs covered. The time to reimbursement pillar measures average time to reimbursement for the selected basket. The affordability pillar measures relative cost of medicine basket compared to the international average both in absolute terms and as a share of per capita GNI in each country. The innovation pillar measures local patents and investment in R&D. We used this index to compare and rank more than 30 developed and developing countries. We then look at the policies in these countries to identify features that lead to better index scores. We find that five broad factors can help explain

access to medicines performance. First is the level of health financing. Second is a structured and transparent pricing and patient access system that prioritises resource allocation to high need diseases and sets economically justifiable or value based prices. Third is the development of health care infrastructure. Fourth is the provider and pharmacy incentives that promote appropriate use of medicine. And finally, a system that protects intellectual property rights.

PHP65

GUIDING PRINCIPLES FOR EFFECTIVE PRIVATE HEALTH INSURANCE IN EMERGING MARKETS

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While emerging market governments are investing more in health care, there is still a large gap between demand and supply. The gap can be primary cover in some countries; while in others, it can be health care services or costs that are not covered publicly. Private health insurance is stepping in to bridge some of this gap. We studied private health insurance across major emerging markets in Asia, Latin America and Africa to understand current situation and future trends. We found that private health insurance is growing across these markets. Its main role has been to extend primary cover to certain segments of the population. In most cases, these are the relatively affluent or employed segments. However, we also see the emergence of community based private health insurance as well as public subsidization of private insurance to cover the less well off. However, several barriers prevent private insurance from significantly increasing health coverage. These are the lack of information to properly assess actuarial risks and make proper claims settlements, moral hazard, adverse selection and the non-coverage of pre-existing conditions. We then studied specific innovative examples which have tried to address some of these barriers. For example, Roche is partnering with Swiss Re to provide actuarial expertise to local insurance companies to enable affordable premium for cancer medicine coverage in China. India's Yeshasvini community-based health insurance programme provides coverage to rural poor through well-specified procedures for enrollment, treatment and claim settlement and monitoring. GSK Brazil increased reimbursement of oncology drugs with some health insurance companies through risk-sharing agreements. Learning from such cases, we developed specific guiding principles on how private insurance can be used to provide increased and effective access to health care in emerging markets. These principles can help inform appropriate policy setting on private health insurance in emerging markets.

PHP66

THE ECONOMICS OF REPRODUCTION: HOW 'PRIMACY OF SUCCESSION' HAS INFLUENCED ACCEPTANCE AND PROVISION OF ASSISTED FERTILITY TREATMENTS THROUGHOUT HISTORY

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Viewing human history through a medical lens can offer a renewed appreciation for today's vexing reproductive challenges, as some dilemmas encountered in modern times are actually continuations of similar economic challenges experienced long ago. Succession crises have been an inherent feature of many national systems, which can lead to complex rules of inheritance to preserve dynastic patrimony. Assuming fertility is unimpaired, this system can work well to maintain market stability and intergenerational order. However, on more than one occasion infertility has disrupted this seamless transition of control; posthumous birth, while less common, has also made its own contribution to human culture. The details of an individual's reproductive life are typically impervious to formal study. Yet, archival sources including ancient literature and formal court records do occasionally provide evidence of otherwise deeply personal concerns of a different era. This survey depicts posthumous birth and infertility as crucial gears in the mechanism of economics, demonstrating how each has drawn considerable social interest, occasionally even impacting national security and dynastic succession. This assessment describes issues, worries, and desires of patients of antiquity and finds that these align closely with contemporary reproductive challenges. Because children and family are so central to the human experience, the consequences of reproduction (or the lack thereof) make substantial imprints upon the cultural, economic, and political landscape—irrespective of civilization or century. This research places selected reproductive motifs in a broad historical context to suggest that some fundamental tenets in the human condition remain essentially unchanged, despite a vast accumulation of knowledge made possible by impressive gains in science and technology.

PHP67

A LEI DE ACESSO À INFORMAÇÃO FORTALECE O PAPEL DA AVALIAÇÃO DE TECNOLOGIAS EM SAÚDE (ATS) DE FORNECER INFORMAÇÕES SÓLIDAS E TRANSPARENTES AOS USUÁRIOS DO SISTEMA ÚNICO DE SAÚDE

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OBJETIVOS: A Lei de acesso à informação (LAI), lei nº 12.527, de 2011, recentemente sancionada no Brasil, tem mudado o cenário jurídico nacional, permitindo uma maior participação popular e o controle social das ações governamentais. Essa lei regulamenta o direito constitucional de acesso dos cidadãos às informações públicas, amplia a participação da sociedade, nas diferentes esferas do governo, e permite melhoria na gestão pública. Desde a institucionalização do Sistema Único de Saúde (SUS), a participação popular vem sendo um dos pilares da sua organização. No início, essa participação limitava-se ao envolvimento da sociedade nos Conselhos e Conferências de Saúde, conforme a lei nº 8.142, de 1990. Entretanto, para garantir o caráter universal e integral imputado ao SUS, é mister que se incorpore a participação popular na formulação, fiscalização, execução e manutenção de políticas de saúde. Além dos Conselhos e Conferências, o empoderamento do usuário, um processo que reconhece o direito de participação nas decisões que afetam o cotidiano e promove espaços democráticos para o controle social das instituições, representa forma de participação popular mais contemporânea, inclusive consoante com a ideologia da LAI. Esse movimento ativo da sociedade, demandar o sistema, provoca a percepção por unidades gestoras da importância do envolvimento do usuário. Para essa interlocução é necessário adaptar a linguagem para que se disseminem informações compreensíveis e, de fato, úteis à sociedade. Com isso, a área de avaliação de tecnologias em saúde do Ministério da Saúde teve que se mobilizar para fornecer informações direcionadas aos usuários, fortalecendo seu papel de informá-los a respeito do valor relativo das tecnologias com informações confiáveis, sólidas e transparentes, inclusive seus impactos ético e social. Nesse contexto, a LAI, como instrumento oportuno de participação social, é uma ferramenta capaz de direcionar as demandas e ações de saúde, conferindo maior transparência ao processo.

PHP68

PATHOLOGICAL GAMBLING: A GROWING ADDICTION

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Gambling is a popular activity of humankind across most cultures and throughout history. Gambling disorders affect 0.2–5.3% of adults worldwide. During the last decades researchers had found that pathological gamblers (PG) are not a homogenous group and some of the patients diagnosed as PG better resemble some other categories characteristics: 1-*The impulsive subtype* is characterized by young adult male predominance, high levels of risk taking behavior and lack the ability to plan ahead. They tend to lose large sums of money in one sitting and associated with attention deficit disorder (ADD), alcohol and other substance abuse and dependence and other impulse control disorders. 2-*The obsessive- compulsive* (OC) subtype, which usually prefers slot machines, lottery and scratch tickets, is characterized by female predominance which has midlife onset (probably as a response to a perceived psychological trauma) and tend to be associated with higher rate of depression and maladaptive coping mechanisms. 3-*The addictive subtype*is characterized by betting a small amount of gambling at a time in a repetitive and compulsive fashion. In this group there is a male predominance and higher rates of alcohol abuse and dependence. Various treatment models have been suggested for gambling disorders. In general, post-treatment effects were positive for different types of therapy (eg, behavioral, and cognitive) and method of therapy However, treatment outcome studies that compared GA to CBT have indicated poor outcomes and attendance of GA. Treating PG according to its subtype: For the impulsive subtype they suggested starting with mood stabilizer. For OC subtype start with SSRI's, if not effective switch to mood stabilizers. For addictive subtype start treatment with bupropion, if not effective switch to naltrexone or nalmefen.

DISEASE-SPECIFIC STUDIES

CANCER – Clinical Outcomes Studies

PCN1

TRASTUZUMABE PARA CÂNCER DE MAMA COM SUPEREXPRESSÃO DE HER-2: EVIDÊNCIA DE EFICÁCIA, SEGURANÇA E ESTIMATIVA DE CUSTO

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OBJETIVOS: Trastuzumabe é um anticorpo monoclonal humanizado derivado de DNA recombinante, que se liga ao domínio extracelular do receptor do fator de crescimento epidérmico humano, HER-2. Esse anticorpo bloqueia o ligante natural e infra-regula o receptor. Sua utilização isolada ou em associação com quimioterápicos proporciona desaceleração na progressão do câncer de mama metastático HER-2 positivo. Este estudo avalia a eficácia, segurança e custo estimado do trastuzumabe comparado com outras opções terapêuticas para o tratamento de câncer metastásico com superexpressão HER-2. **MÉTODOS:** Revisões sistemáticas (RS) de ensaios clínicos comparando trastuzumabe com outras opções terapêuticas foram pesquisadas em The Cochrane Library, Medline, Lilacs, Centre for Reviews and Dissemination and Tripdatabase. O custo médio mensal do tratamento foi estimado com base nos preços do Banco de Preços em Saúde, do Ministério da Saúde. **RESULTADOS:** Foram incluídas nove RS. Todas elas mostraram moderada a alta qualidade de evidência. Nas nove RS os principais desfechos avaliados foram sobrevida global, sobrevida livre de doença e tempo até a recorrência tardia. Trastuzumabe apresentou melhores resultados quando comparado com placebo. Trastuzumabe, em associação com taxanos, capecitabina e anastrozol apresentou melhores resultados que os medicamentos sem a associação. O risco de desenvolvimento de disfunções cardíacas faz com que o uso combinado de antraciclinas com trastuzumabe seja desaconselhado. O custo médio mensal do tratamento é de R$34.181,24. **CONCLUSÕES:** Com base na evidência disponível, é recomendado o uso de trastuzumabe no tratamento de câncer metastásico com superexpressão HER-2, em associação com paclitaxel ou docetaxel. O uso em monoterapia não é indicado.

PCN2

O USO DE TEMOZOLOMIDA NO TRATAMENTO DE ASTROCITOMA DE BAIXO GRAU – CÂNCER NO CÉREBRO

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OBJECTIVOS: Avaliar a eficácia e segurança da temozolomida, no tratamento isolado ou adjuvante do Astrocitoma de Baixo Grau comparado com outras opções terapêuticas e com a radioterapia – tratamento padrão atual, em resposta às demandas judiciais recebidas para o fornecimento deste medicamento para o tratamento do Astrocitoma de Baixo Grau no Estado de Minas Gerais, Brasil. **MÉTODOS:** Foram pesquisadas as bases The Cochrane Library, Centre for Reviews and Dissemination, Medline via Pubmed, LILACS e Clinical Trials. Avaliações de Tecnologias de Saúde

foram pesquisadas em sites de agências nacionais e internacionais. Não houve restrição de idiomas na busca das evidências. **RESULTADOS:** Foram incluídas duas Revisões Sistemáticas (RS), as quais não compararam o uso da temozolamida com outra opção terapêutica e nem com a radioterapia. A primeira RS avaliou a eficácia de três diferentes esquemas de administração da temozolomida para tratar Gliomas de Baixo Grau entre os quais estão incluídos os Astrocitomas de baixo grau (Grau I e II). A segunda RS fez uma análise qualitativa de estudos fase II para criar um guia de conduta e prescrição do uso da temozolomida para tratamento dos tumores cerebrais. Os estudos incluídos constituíram um conjunto de evidências classificadas como de baixa qualidade. As RS foram consideradas no estudo devido a escassez de evidências sobre o tema. Existem quatro ensaios clínicos em desenvolvimento que objetivam avaliar o uso de temozolamida isolada ou como adjuvante comparada à radioterapia. **CONCLUSÕES:** Até a presente data não existem evidências disponíveis que suportem o uso da temozolomida em Gliomas de Baixo Grau entre os quais estão incluídos os Astrocitomas de baixo grau (Grau I e II). Os resultados dos ensaios clínicos em andamento serão essenciais para definição da melhor estratégia de tratamento para esta condição de saúde.

PCN3

PARECER TÉCNICO-CIENTÍFICO: EFICÁCIA E SEGURANÇA DO USO DO RITUXIMABE NO TRATAMENTO DE LEUCEMIA LINFOCÍTICA CRÔNICA

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OBJETIVOS: Analisar as evidências científicas sobre eficácia e segurança do Rituximabe associado à QT convencional com fludarabina + ciclofosfamida (RFC) comparado à QT convencional (FC) isolada para o tratamento da Leucemia Linfocítica Crônica (LLC). Realizar estimativas de custo de tratamento da LLC com FC e FCR em suas indicações terapêuticas por ciclo. **MÉTODOS:** Para a elaboração do Parecer Técnico-científico, foram utilizadas as Diretrizes Metodológicas para elaboração de PTC do Ministério da Saúde do Brasil. Foi realizada ampla busca nas bases de dados Medline (via Pubmed), Embase, Lilacs e CRD que comparassem esquemas terapêuticos contendo RFC. A estratégia de busca foi geral e sensível e incluiu termos para leucemia linfocítica crônica e rituximabe. Para a estimativa de custos, foi considerado o esquema terapêutico com medicamentos oncológicos e não oncológicos e o modo de usar para o tratamento do LLC, bem como a apresentação farmacêutica e seu preço obtido de um serviço de onco-hematologia de hospital de ensino público de alta complexidade. **RESULTADOS:** Foram selecionados 3 estudos e de maneira geral o esquema de tratamento composto pela utilização de rituximabe, fludarabina e ciclofosfamida pode melhorar efetivamente a taxa de sobrevida global e a remissão completa, além de prolongar a sobrevida livre de progressão. Para os desfechos de segurança, o tratamento com RFC apresentou maiores eventos adversos comparados à FC. Nas estimativas de custo, verificou-se o alto custo para o tratamento com o esquema RFC, chegando aproximadamente a R$ 76.155,00 por ano de tratamento em contraste com a QT convencional (FC) de R$ 30.336,00. **CONCLUSÕES:** Os estudos selecionados apresentaram baixa qualidade metodológica, e os resultados devem ser avaliados com cautela. Além disso, por ser uma doença que acomete principalmente pessoas com idade superior a 65 anos, é necessário avaliar os possíveis impactos causados pela diferença de idade e estadiamento da doença.

PCN4

ESTIMACIÓN EPIDEMIOLOGICA DEL CÁCER DE PULMÓN DE CELULAS NO PEQUEÑAS EN MÉXICO

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OBJECTIVOS: Estimar la incidencia, prevalencia y mortalidad del cáncer de pulmón de células no pequeñas (CPCNP) en México, así como la prevalencia de adenocarcinomas y mutaciones EGFR o ALK en este tipo de cáncer. **METODOLOGÍAS:** En base a GLOBOCAN 2008 se estimaron la incidencia, prevalencia y mortalidad anual por CPCNP en México en 2012. La proporción de casos de CPCNP y de adenocarcinomas en CPCNP se extrajo de estudios publicados realizados en México. El porcentaje de presentación de metástasis, valoración en la escala del estado funcional de la Eastern Cooperative Oncology Group (ECOG) y la presentación de mutaciones EGFR o ALK se extrajo de fuentes del Instituto Nacional de Cancerología. **RESULTADOS:** Se estimó que la incidencia de CPCNP en 2010 ajustada por sexo fue de 9.28 y de 3.89 casos por 100,000 habitantes para hombres y mujeres, respectivamente. La incidencia para ambos sexos fue de 6.49 y la incidencia proyectada para 2030 de 11.15. Los casos fatales fluctúan entre 7,092 en 2010 a 14,573 en 2030. Los casos prevalentes estimados para el 2012 fueron 8,225 y llegan a 15,548 en el 2030. Considerando la prevalencia de CPCNP en 2012, los casos esperados del tipo histológico adenocarcinoma fueron 4,688, de los cuales 3,985 (85%) presentan ECOG 0 ó 1 (Con síntomas que le impiden realizar trabajos arduos, aunque se desempeña normalmente en sus actividades cotidianas). El 77% (3,068) presentarían enfermedad metastásica y 31% de ellos (951) presentarían una mutación EGFR o ALK. **CONCLUSIONES:** La estimación de la prevalencia de marcadores biológicos EGFR o ALK en pacientes con CPCNP del tipo adenocarcinoimoide en México es la base para la estimación del impacto presupuestal del uso de terapias blanco en este grupo de pacientes, que es un factor a considerar en el diseño de políticas y gestión de programas para la atención de estos pacientes.

PCN5

RELATIVE CLINICAL VALUE IN ADVANCED CANCER TREATMENTS

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OBJECTIVES: To evaluate clinical and economic value of ipilimumab in the treatment of advanced melanoma compared with drugs available for the treatment of advanced cancer. **METHODS:** An analysis was performed comparing ipilimumab and other drugs for advanced cancer regarding overall survival (OS) and costs associated with improvement in survival. Parameters analyzed were: improvement in median/mean OS, improvement on survival rate at 1 year and the number needed to treat (NNT) to avoid one death. Monthly costs for improvement in mean OS were evaluated. Efficacy data were obtained from clinical trials. Medications costs were obtained from official price lists, such as Banco de Dados de Preços do Sistema de Saúde do Ministério da Saúde Brasileiro and Lista da Câmara de Regulação do Mercado de Medicamentos da Agência Nacional de Vigilância Sanitária (CMED). **RESULTS:** Improvement in median OS ranged from +2.8 (sorafenib) to +4.8 (transtuzumab), and improvements in mean OS ranged from +1.6 (sorafenib) to +6.1 (ipilimumab). Only ipilimumab showed better mean OS compared with the median OS (6.1 vs. 3.7). This demonstrates the effect of ipilimumab in prolonging OS in long term, which is observed in a considerable proportion of patients treated with this drug. Major improvement in the survival rate in 1 year occurred with ipilimumab (20%). The NNT to prevent 1 death ranged from 7 (ipilimumab) to 61 (bevacizumab for lung cancer). Costs per month of mean OS improvement ranged from BRL 34,906 (sorafenib) to BRL 64,410 (bevacizumab for lung cancer). **CONCLUSIONS:** This comparative analysis of drugs used for treatment of advanced cancer used key parameters for decision making in health sciences. The results suggest that ipilimumab delivers superior clinical and economic benefits when compared with other drugs available in Brazil for the treatment of advanced cancer.

CANCER – Cost Studies

PCN6

COMPARING THE POTENTIAL BUDGET IMPACT OF NOVEL THERAPIES FOR ADVANCED MELANOMA IN SECOND-LINE UNDER BRAZILIAN PRIVATE HEALTH CARE SYSTEM PERSPECTIVE

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OBJECTIVES: Prior to availability of novel agents such as vemurafenib and ipilimumab, poor outcomes were associated with advanced melanoma treatment. In Brazil, vemurafenib (VEM) is an oral therapy for BRAF-V600E-mutated unresectable or metastatic melanoma in all treatment lines meanwhile ipilimumab (IPI) is an intravenously administered drug for metastatic melanoma in second-line. Whereas IPI is compulsorily reimbursed in private system as labeled, this study aims to estimate the potential budget impact of second-line VEM coverage in Brazilian Private Healthcare System. **METHODS:** The study focused in second-line setting since IPI has no indication for first-line in Brazil. Based on an epidemiologic approach, the potential pool of patients for each drug was estimated. It was adopted that private market accounts for 40% oncology patients. BRAF-V600E mutation positivity rates of 50% were assumed. Treatment costs were assessed evaluating drugs acquisition expenses (considering the ex-factory prices) based on labeled posology and when applicable mutation testing costs or infusion fees. Mean treatment durations were 6 months (VEM) and 3 months or 4 cycles (IPI). Reports were made in Brazilian Reais (BRL1.00~USD0.51 Feb/2013). **RESULTS:** In 2013, a potential of 408 advanced melanoma patients in second-line would be expected in the private system. Screening all patients and treating those eligible with VEM (204 patients), would result mean treatment costs per patient of BRL110,633 (VEM) and BRL182,852 (IPI). Therefore, system would be charged by expenses of BRL59,906,137 instead of BRL74,647,411 in a scenario with no testing and all second-line patients treated with IPI. **CONCLUSIONS:** Considering VEM availability in private health care system for advanced melanoma in second-line, BRL14.7Mio savings could be achieved in 2013. Testing all patients and reimbursing VEM seems to be economically advantageous mainly due to lower cost associated to VEM and the opportunity of testing patients with BRAF-mutation, identifying those who has more chance to respond to the treatment.

PCN7

BUDGET IMPACT ANALYSIS FOR THE USE OF VANDETANIB IN MEXICAN ADULT PATIENT DIAGNOSED WITH ADVANCED UNRESECTABLE MEDULLARY THYROID CANCER

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OBJECTIVES: Determine the financial impact of including vantedanib in public health institutions in Mexico, in the treatment of adult patients with advanced or metastatic unresectable medullary thyroid cancer (MTC). **METHODS:** In order to have a greater accuracy of the total population with advanced unresectable MTC with social security, we obtained the total population based on the reports in Histopathological Registry of Malignant Neoplasms (RHNM), GLOBOCAN and Wells 2012. All the related care costs were obtained by institutional references and the resource use were determined by clinical practice guidances and clinical studies. Horizon: 5 years. Comparator: vandetanib and external radiotherapy as palliative care, as there are currently no available alternative that has an impact in terms of PFS. Discount rate: 5%. The outcome measure was incremental expenditure for the use of vandetanib versus external radiotherapy in absolute terms and relative to total national health expenditure, in Mexico. **RESULTS:** The incremental expenditure for the first year was USD$663,558.50 and for the fifth year USD$716,403.10, represent 0.0082% and 0.0088% to total national health expenditure respectively. **CONCLUSIONS:** Vandetanib is the only option to patients with advanced unresectable MTC, there are no other therapies which can slow the progression of advanced disease including radiotherapy and chemotherapy. Because of the low prevalence of the disease, the use of vandetanib only represents an average annual increase of 0.0086% for total national health expenditure and should be considered the optimal choice in this population.

PCN8

COSTO E IMPACTO PRESUPUESTAL DEL TRATAMIENTO DEL CÁNCER DE PÚLMON DE CELULAS NO PEQUEÑAS DEL TIPO ADENOCARCINOMA CON GRADO ECOG 0,1,2 EN ESTADIO IV CON MUTACIÓN + (EGFR O ALK) CON TERAPIAS BLANCO EN MÉXICO

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OBJECTIVOS: El impacto económico que tendría en México la incorporación gradual de pacientes con cáncer de pulmón de células no pequeñas en estadio IV (tipo adenocarcinoma), con mutación EGFR y ALK (CPCNP+), a esquemas basados en terapias blanco no se ha estimado. Este estudio estuvo enfocado a estimar este impacto desde la perspectiva del Sector Salud. **METODOLOGÍAS:** Con datos de GLOBOCAN 2008 se estimó la prevalencia 2012 de pacientes CPCNP+ en México. Un panel de expertos (n=20, 2 centros de alta especialidad) determinó el perfil de uso de recursos para atender a estos pacientes: hospitalización, medicamentos, consulta con especialista, administración del medicamento, pruebas de laboratorio y gabinete, tamizaje EGFR y/o ALK. Los costos se estimaron mediante metodología *bottom-up* en el Instituto Nacional de Cancerología y se expresan en US$ de 2012. Se realizó análisis de impacto presupuestal en base al Presupuesto de Egresos de la Federación (PEF) 2012. **RESULTADOS:** Se estimó que en 2012 había 3,068 pacientes candidatos a ser sometidos a tamizaje para EGFR y/o ALK, de los cuales 951 (31%) serían positivos (candidatos a tratamiento con terapias blanco). El costo esperado anual por paciente tratado con terapias blanco fue US$283,180 mientras que el costo correspondiente a pacientes que reciben quimioterapia convencional fue US$247,338. Suponiendo que el 6% (61) de los pacientes CPCNP+ fueran atendidos con terapias blanco y el resto (890) con quimioterapia convencional, el impacto presupuestal hubiera sido de 0.1% y 0.65% del PEF 2012, respectivamente. **CONCLUSIONES:** La prevalencia de pacientes CPCNP+ en México es de aproximadamente 8.5/100,000 habitantes. La diferencia en el costo esperado de tratamiento entre quimioterapia y terapias blanco es de alrededor de 15%. La introducción gradual de terapias blanco por las instituciones del Sector Salud es una estrategia que permitiría planificar el impacto presupuestal de esta adopción en base a la disponibilidad de recursos.

PCN10

ANÁLISE DAS POTENCIALIDADES DE CUSTO-MINIMIZAÇÃO ATRAVÉS DA DETERMINAÇÃO DO MARKET SHARE ENTRE OS QUIMIOTERÁPICOS DE REFERÊNCIA QUE POSSUEM GENÉRICOS CADASTRADOS EM UMA OPERADORA DE PLANO DE SAÚDE

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OBJETIVOS: Identificar as potencialidades de custo-minimização através da determinação do *market share*entre os quimioterápicos de Referência que possuem Genéricos cadastrados em uma operadora de Plano de Saúde em Fortaleza, Ceará - Brazil. **MÉTODOS:** Estudo de minimização de custos em uma amostragem de medicamentos pertencentes à classe dos quimioterápicos (n=175 códigos). A fonte de dados foi a Tabela de Medicamentos padronizados na operadora e utilizados em 2012. Incluiu-se na amostra os custos com antineoplásicos pertecentes a classe A (Alto Custo - Curva ABC). Foram excluídos os medicamentos utilizados como suporte e hormonioterapia. Em seguida, fez-se a classificação das categorias, segundo Agência Nacional de Vigilância Sanitária (ANVISA) quanto a Referência, Genérico e Similar. Considerou-se a perspectiva da Operadora de Saúde. **RESULTADOS:** O câncer mais prevalente foi o de Mama (n=203; 31,28%) seguido de Brônquios e Pulmões (n=55; 8,47%). Quanto ao sexo observou maior prevalência em mulheres (n=442; 68,10%). O custo total com quimioterápicos em 2012 foi R$ 28.918.397,51, no qual 71,14% (R$ 20.571.337,18) foram com medicamento de Referência, seguido de 0,91% (R$ 261.787,42) com Genérico e 0,77% (R$ 222.507,38) Similar. Detectou-se que 27,19% (R$ 7.862.765,53) dos com quimioterápicos de Referência tem potencialidades de uso de genérico (Docetaxel, Doxorrubicina, Gencitabina, Irinotecano, Oxaliplatina, Paclitaxel,). Quanto ao impacto financeiro haveria uma redução nos custos por volta de 24,94% (R$ 1.960.973,72), se utilizássemos somente o genérico nessas potencialidades de uso, representando o melhor cenário. **CONCLUSÕES:** O mercado de genéricos é hoje uma realidade no país, tendo criado um segmento importante no mercado de medicamentos e seu incremento na quimioterapia traria economias substanciais nas diferentes instituições de saúde, como as operadoras.

PCN11

ECONOMIC IMPACT OF INCLUDING SEQUENTIAL BEVACIZUMAB FOR THE TREATMENT OF PATIENTS WITH KIRSTEN RAS WILD TYPE UNRESECTABLE METASTATIC COLORECTAL CANCER IN FOUR LATIN AMERICAN COUNTRIES

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OBJECTIVES: To evaluate and compare the economic impact in terms of drug and administration cost of first to second line (1L>2L) sequential bevacizumab (BEV) to other sequences of biologics in the treatment of patients with Kirsten Ras wild type (KRAS WT) unresectable metastatic colorectal cancer (mCRC) in four Latin American countries. **METHODS:** A previously developed Treatment Sequencing Costing tool was adapted for Argentina, Chile, Colombia and Mexico. A private payer perspective was adopted for Argentina and Chile and a public payer perspective for Colombia and Mexico. Locally sourced drug acquisition and administration costs were included in the analysis. Cost of sequences was calculated based on proxy treatment durations of 6.1 months (1L), 4.0 months (2L) and 2.7 months (3L). Sequences analyzed for the respective countries were elicited from local experts and clinical guidelines in addition to 1L>2L BEV sequences obtained from the ML18147 trial. **RESULTS:** When 1L>2L BEV replaces sequences which include 1L anti-EGFR regimens, it results in an average potential cost reduction of ARS -42,796; $CLP -13,774,258; $COL -8,922,387 and $MXN-174,606 for Argentina, Chile, Colombia and Mexico respectively. When 1L>2L BEV replaces sequences which include 2L anti-EGFR regimens it results in an average potential incremental cost of ARS +25,331; $CLP +1,769,387 and $MXN +25,515 for Argentina, Chile and Mexico. **CONCLUSIONS:** In Argentina, Chile, Colombia and Mexico, when 1L>2L BEV replaces sequences which include 1L anti-EGFR regimens, it results in an average potential cost reduction. When 1L>2L BEV replaces sequences which include 2L anti-EGFR regimens, it results in a potential incremental cost which allows for the possibility of including a 3L anti-EGFR regimen.

PCN12

COST/BENEFIT ANALYSIS OF FIRST LINE CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) TREATMENTS IN MEXICO

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OBJECTIVES: To calculate and compare the costs and costs per PFS and OS for first line CLL treatment regimens in Mexico. **METHODS:** Relevant treatment regimens were selected based on KOL input and data availability. Treatment regimen costs were calculated using the dose, number of doses per cycle, and number of cycles per regimen from published clinical trials. Drug acquisition and administration costs were obtained from IMSS. Administration costs were applied once per treatment day, regardless of the number of drugs administered. Progression-free survival (PFS) and overall survival (OS) benefits for each regimen were calculated by applying hazard ratios for PFS and OS from a recent network meta-analysis to the median PFS and OS reported for chlorambucil. Cost/ benefit ratios were expressed as the regimen cost per month of PFS or OS. **RESULTS:** Regimens assessed were chlorambucil, fludarabine, fludarabine+ cyclophosphamide+ rituximab (FCR) and cyclophosphamide+doxorubicin+vincristine+prednisone (CHOP). Costs were estimated in 2012 Mexican pesos. The regimen cost for chlorambucil ($3,101) was less than fludarabine, FCR and CHOP ($50,430, $525,481 and $105,246, respectively). Only FCR and CHOP incurred administration costs. The hazard ratios for OS and PFS showed FCR was the most effective treatment versus chlorambucil (0.24 and 0.73, respectively). The cost/PFS benefit ratio was most favorable for chlorambucil ($352/month) versus fludarabine, FCR and CHOP ($4,757, $14,318 and $18,145, respectively). Chlorambucil also had the lowest cost/OS benefit ratio ($39/month) versus fludarabine, FCR and CHOP ($639, $4,865 and $1,441, respectively). **CONCLUSIONS:** Chlorambucil was the least costly of the Mexican CLL treatment regimens assessed in absolute terms and per benefit. However, there is a need for a CLL treatment that provides greater efficacy in terms of PFS and OS than chlorambucil, but costs less than FCR. Future studies should focus on the incremental cost-effectiveness of new regimens for this indication.

PCN13

THE AFFORDABILITY OF ONCOLOGY AND HIV/AIDS TECHNOLOGIES IN BRAZIL COMPARED TO THE UNITED STATES AND OTHER OECD COUNTRIES

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OBJECTIVES: Brazil's universal access to health care program has been deemed successful by several different measures. However, given limited health care budgets, the affordability of newer, increasingly expensive technologies can become a major access barrier. This study compares the affordability of current HIV/AIDS and oncology technologies in Brazil to those in the U.S. and other Organization for Economic Cooperation and Development (OECD) countries. **METHODS:** Per patient treatment costs for HIV/AIDS and oncology technologies in Brazil, the U.S. and other OECD countries were obtained from published studies and datasets. Non-Brazilian studies were chosen for their comparability to the Brazilian counterpart studies in terms of patient populations, disease characteristics, treatments, and economic perspective. Costs compared included drugs, procedures, administrative costs, and total cost of treatment. All costs were converted to 2011 U.S. dollars. The two affordability measures utilized included: 1) Cost per gross domestic product (GDP) per capita, and 2) cost per health care spending (HCS) per capita. These measures were compared between Brazil and other OECD countries to estimate the relative affordability of HIV/AIDS and oncology technologies. **RESULTS:** A majority of technologies assessed were less affordable in Brazil compared to comparator OECD countries by both affordability measures. Under the GDP measure, oncology technologies in Brazil consumed approximately 2 to 20 times the amount of available resources compared to OECD countries. Using the HCS measure, health care resource consumption in oncology was 4 to over 40 times that of OECD countries. Differences in relative affordability of HIV/AIDS technologies were generally smaller, with resource consumption in each country generally varying by less than 3 times that of the comparator country using each affordability measure. **CONCLUSIONS:** Although oncology and HIV/AIDS technology access in Brazil has increased in recent years, these treatments may be relatively less affordable compared to other developed countries given Brazil's current resource and budget constraints.

PCN14

DIRECT MEDICAL COSTS (DMC) OF TREATING CHRONIC LYMPHOID LEUKEMIA (CLL) PATIENTS IN THE PRIVATE HEALTH CARE SYSTEM IN BRAZIL: RESULTS FROM A 12-MONTH RETROSPECTIVE ANALYSIS OF AN ADMINISTRATIVE DATABASE

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OBJECTIVES: To determine 1-year direct medical costs of treating patients with Chronic Lymphoid Leukemia (CLL) from the Brazilian Private Healthcare System perspective. **METHODS:** The Orizon database, an administrative database containing inpatient and outpatient claims to a pool of 102 HMOs representing 34% of the total Private Health System, was reviewed from Jan/2009 to Dec/2012. Eligibility criteria were patients starting CLL (ICD-10 code C911) treatment from Apr/2009 to Dec/2011. Outcome was direct medical costs (DMC) per patient-year, calculated as the sum of the medical claims for each patient included in the analysis, for a maximum period of 12-months or death or loss of follow-up, whichever comes first. DMC was categorized in chemotherapy, hospitalizations, and other outpatient costs. Further analysis was conducted for chemotherapy and hospitalizations. **RESULTS:** From 735 patients with CLL identified in the database, 164 met eligibility criteria and were included in the analysis, representing a total of 100 patients-years. Total DMC in this population was R$ 16,555,421 (mean cost of R$ 165,827 per patient-year), from which R$ 9,451,124 (57%) are related to chemotherapy, R$ 5,341,862 (32%) to hospitalizations and R$ 1,762,434 (11%) to other outpatient costs. Outpatient laboratory exams accounted for only a small fraction (R$ 176,545, 1%) of DMC, and only one patient had a record of radiotherapy (<1% of DMC). A total of 326 hospitalizations were identified in 79 (48%) patients, with an average cost of R$ 16,386 ± 29,185 per hospitalization. Chemotherapy drugs accounted for 71% of the total costs with chemotherapy, the rest divided between other drugs (12%), disposable devices (6%), hospital facility fees (5%) and other costs (6%). **CONCLUSIONS:** Patients with CLL represent a significant economic burden to private payers. Chemotherapy and hospitalization costs accounts for almost 90% of the total costs.

PCN15

COSTS OF HORMONAL RECEPTOR POSITIVE, HER 2 NEGATIVE METASTATIC BREAST CANCER (MBC-HR+) IN BRAZILIAN PRIVATE SYSTEM (BPS): A REAL WORLD AND PUBLISHED LITERATURE ANALYSIS

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OBJECTIVES: Recently, MBC-HR+ was found to have a diverse pattern of response to the treatment compared to other MBC. Our aim is to determine the costs of treatment associated with this disease, from the perspective of BPS. **METHODS:** A large private database of medical claims for chemotherapy (Ch) (Evidencias Database) was searched in order to identify MBC-HR+, that were treated in the last two years (2011-12). We extracted data regarding treatment received, length of the treatment and antropometric data for each MBC-HR+ patient. After, medical literature was performed for studies of MBC-HR+ treatments and the same data was extracted. Based on the combination of real-world (RW) and published data we constructed a decision tree, considering three groups of MBC-HR+, according to the sites of metastasis: bone exclusive (B), Visceral exclusive (V) and bone plus visceral (BV). For each group, we calculated the costs of the treatment plus adverse events, by a micro-costing approach. We simulated a cohort of 100 patients with MBC-HR+ in a decision tree, to obtain the costs for each group and a mean cost/ patient. **RESULTS:** RW data showed the following distribution of patients: B 38%, V 42% BV 20%. Lengths of treatment (in months) were B: 25.1 to 30.5; V 16.1; BV 14 to 19.6. Most commonly used treatments were, B – two hormonal lines, fulvestrant and three lines of Ch. V – Four lines of Ch; BV- one hormonal line, fulvestrant, three lines of Ch. Most used Ch drugs were docetaxel, paclitaxel and gemcitabine. Mean costs/patient/ group, considering hormones, Ch, bisphosphonates, hospitalization, infusion, evaluations of the disease, radiation therapy and adverse events were: B- R$ 135,744 (US$ 67,872); V R$ 129,079 (US$64,539) and BV R$ 117,172 (US$58,568). **CONCLUSIONS:** MBC-HR+ is associated to a high cost of treatment under the BPS perspective.

PCN16

COST-EFFECTIVENESS OF PAZOPANIB AS FIRST LINE TREATMENT FOR METASTATIC RENAL CELL CARCINOMA IN BRAZIL: UPDATED ANALYSIS

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OBJECTIVES: Targeted therapies shows marked clinical improvements over standard treatments such as interferon alfa (IFNa) in the treatment of advanced/metastatic renal cell carcinoma (mRCC). We report an updated cost-effectiveness analysis of pazopanib, sunitinib, and bevacizumab (the later associated INFa) as first line treatments for mRCC under the Brazilian public health care perspective. In previous analysis, taxation was accounted exclusively for pazopanib's price.[Value Health 2012;15(4):A218] The present analysis applied ex-factory 0% tax prices, where now all comparisons were made under tax waiver programs. **METHODS:** A Markov model was designed to simulate mRCC progression, mortality and costs. The assessed time-horizon was 2 years. An indirect comparison estimated the relative efficacy and safety of the targeted therapies in mRCC patients. Costs and consequences of disease treatment were computed for each comparator. Only direct medical costs were considered and reported in 2013 Brazilian currency (1BRL=0.50USD). Drug prices derived from official price list (i.e., CMED). Disease management costs were those from a public reimbursement database (i.e., SIGTAP). Costs and outcomes were discounted at 5% yearly. Outcomes assessed were progression-free survival (PFS) and quality-adjusted life years (QALYs). Stochastic simulations tested model robustness. **RESULTS:** The indirect PFS hazard ratio (<1 favours pazopanib [95%CI]) indicated that pazopanib is not statistically different from sunitinib (0.93 [0.56, 1.56]) or bevacizumab+IFNa (0.79 [0.48, 1.32]). A recent head-to-head clinical study (COMPARZ) of pazopanib versus sunitinib confirmed indirect results. Estimated costs and QALYs were BRL 93,389.88 and 0.90 for pazopanib, BRL 124,923.36 and 0.93 for sunitinib, and BRL 185,942.43 and 0.88 for bevacizumab+INFa. Propabilistic analysis showed favourable economic results to pazopanib in >90% of simulations when compared to sunitinib. Bevacizumab+INFa was dominated in all scenarios. **CONCLUSIONS:** Pazopanib reported significantly lower costs and similar benefits against studied comparators as first line treatment of patients diagnosed with mRCC under the Brazilian public health care perspective.

PCN17

COST-EFFECTIVENESS ANALYSIS OF INCORPORATION OF THE HPV VACCINE TO THE NATIONAL IMMUNIZATION PROGRAM / NIP OF BRAZIL

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OBJECTIVES: To estimate cost-effectiveness of adding human papillomavirus (HPV) vaccine to Brazil National Immunization Program, compared with the current strategy for control of cervical cancer, the screening program based on conventional Papanicolaou citology. **METHODS:** We used a static decision tree analysis model, CERVIVAC, software developed by PAHO ProVac Initiative. The model compared two strategies: 1) a cohort of girls aged 10 years to represent the epidemiological situation, current screening, and care of precursor lesions and cancer (without vaccination) with 2) a cohort of girls aged 10 years who were applied 3 doses of HPV vaccine, maintaining the conditions of screening and care of precursor lesions and cancer, as they are currently. National parameters for the epidemiology of cervical cancer, screening expenditures and National Cervical Cancer Control Program were estimated in depth. The estimates were based on the health information systems of the Public Health System, SUS (SIH, SIA, APAC, SIAB, SIGTAP and SISCOLO), national survey (PNAD 2008) and relevant national literature. **RESULTS:** The vaccine introduction would reduce the burden of disease. The model estimated 261 deaths avoided and 7595 DALYs averted, in each successive cohort to be vaccinated. The ICER per DALY averted R$ 18,121 would be considered cost-effective, according to the parameters adopted by WHO. In univariate sensitivity analysis, only a lower discount rate and a high incidence and mortality would make the introduction of the vaccine very cost-effective. **CONCLUSIONS:** The vaccine introduction should bring benefits for the control of cervical cancer, but it will require large investments by the NIP. It should be guaranteed the right conditions for the immunization program sustainability and equity in a population perspective as well as to improve the screening program.

PCN18

ANÁLISIS COSTO-EFECTIVIDAD DE EVEROLIMUS MÁS EXEMESTANO PARA PACIENTES CON CÁNCER DE MAMA AVANZADO CON RECEPTORES HORMONALES POSITIVOS (RE+), HER2–, QUE FALLARON A LOS INHIBIDORES DE AROMATASA NO ESTEROIDEOS (IANES) EN MÉXICO

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OBJECTIVOS: Evaluar el perfil costo efectividad de everolimus en combinación con exemestano en pacientes con cáncer de mama avanzado, RE+, HER2–, que fallaron a los IANES. **METODOLOGÍAS:** Se desarrolló un modelo de Markov con ciclos mensuales y un horizonte temporal de diez años. El modelo compara a) exemestano+everolimus seguido por tres líneas de quimioterapia y mejor terapia de soporte (MTS) con b) tres líneas de quimioterapia más MTS. Se incluyó la probabilidad de muerte desde cualquier tratamiento. La secuencia de quimioterapia se definió a través de un panel de expertos. Las probabilidades de transición para everolimus+exemestano se obtuvieron del estudio BOLERO-2. Se realizó una revisión de la literatura para las probabilidades de transición de las quimioterapias. Se incluyeron los costos de los medicamentos y de su administración, los costos asociados con eventos adversos, monitoreo y de la MTS. Los resultados se presentan en $MXN de 2012 desde una perspectiva del Sistema Público de Salud mexicano. Se aplicó una tasa de descuento del 5% para costos y efectividades. Se realizaron análisis de sensibilidad probabilístico (ASP) con mil repeticiones y diferentes análisis de sensibilidad univariados, incluyendo un análisis con horizonte temporal de por vida. **RESULTADOS:** El modelo mostró que everolimus+exemestano resulta en 1.32 años de vida ganados con un costo incremental de $314,327 dando como resultado una razón de costo efectividad incremental (RCEI) de $237,902. El ASP mostró que la RCEI está dentro del rango recomendado por la OMS (1 a 3 PIBs per capita) en la mayoría de los casos. La RCEI con un horizonte temporal de por vida fue de $209,292. **CONCLUSIONES:** El presente análisis mostró que utilizar everolimus más exemestano en pacientes con cáncer de mama avanzado, RE+, HER2–, que fallaron a los IANES es una opción costo efectiva de acuerdo a las recomendaciones de la OMS.

PCN19

ANÁLISIS DE COSTO-EFECTIVIDAD DE ERLOTINIB EN EL TRATAMIENTO DE PACIENTES CON CÁNCER PULMONAR DE CÉLULAS NO PEQUEÑAS, CPCNP, CON MUTACIÓN DEL GEN EGFR+, EN COLOMBIA

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OBJECTIVOS: Evaluar la costo-efectividad de Erlotinib como tratamiento en primera línea (1L) de pacientes con cáncer pulmonar de células no pequeñas, CPCNP estadio IIIB/IV, con mutación del gen EGFR+, en comparación con la quimioterapia estándar (carboplatino/ Paclitaxel) y con Getinib, desde la perspectiva del Sistema de Salud Colombiano. **METODOLOGÍAS:** Se empleó un Modelo de Markov que simula el curso del CPCNP, con ciclos mensuales. Los estados de salud considerandos en el modelo son: Libre de progresión de enfermedad (LPE), Libre de progresión de enfermedad con respuesta (LPER), Progresión de enfermedad (PE); y Muerte. Se consideran costos directos y eventos adversos en pesos colombianos, años de vida ganados libres de enfermedad (AVGLE), para Erlotinib y Gefitinib comparados con quimioterapia estándar. Las probabilidades de transición se tomaron de la literatura, los costos se obtuvieron a partir de consenso de expertos según la práctica habitual, los costos de

los medicamentos se tomaron de las bases oficiales (SISMED y Circular 04 de 2012). Se empleó una tasa de descuento de 3% para costos y beneficios. **RESULTADOS:** El costo total para los 60 ciclos de la terapia con Erlotinib fue de $153 millones por 1.55 AVGLE; frente a la quimioterapia estándar con $122 millones por 1.28 AVGLE; y para la terapia con Gefitinib de $158 millones para 1.43 AVGLE. La razón de costo efectividad incremental de Erlotinib empleado en 1L es de $112 millones por 0,27 AVGLE, con respecto al esquema estándar de quimioterapia. La razón de costo efectividad incremental de Gefitinib es de $245 millones para alcanzar 0.14 AVGLE. **CONCLUSIONES:** Erlotinib mantiene el costo por beneficio ganado de la terapia estándar que ya esta siendo reembolsada por el Sistema de Salud Colombiano; en ese sentido, se puede considerar una terapia eficiente.

PCN20

ANÁLISIS DE COSTO-EFECTIVIDAD DE BEVACIZUMAB PARA EL TRATAMIENTO DE PRIMERA LÍNEA EN PACIENTES CON CÁNCER COLORRECTAL METASTÁSICO, CCRM EN COLOMBIA

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OBJECTIVOS: Realizar un análisis de costo-efectividad (ACE) sobre el uso de Bevacizumab vs anticuerpos anti-receptor de factor de crecimiento epidérmico (EGFRI), utilizados con esquemas de FOLFIRI o FOLFOX/XELOX en el tratamiento de primera línea de los pacientes con CCRm con presencia de KRAS silvestre (WT) en Colombia, según la perspectiva del Sistema de Salud Colombiano. **METODOLOGÍAS:** Se empleó un Modelo de Markov, con ciclos mensuales, para estimar costos Supervivencia Libre de Progresión (SLP) en función del estado KRAS, a partir del costo por éxito clínico (Número Necesario a Tratar, NNT, para mantener un paciente libre de progresión a 12 meses). Se incluyeron costos directos y eventos adversos en pesos colombianos, para: FOLFIRI+Bevacizumab; FOLFIRI+Anti EGFR; FOLFOX/XELOX+Bevacizumab; FOLFOX/XELOX+EGFR. Las probabilidades de transición se tomaron de la literatura, los costos se obtuvieron a partir de consenso de expertos según la práctica habitual, los costos de los medicamentos se tomaron de las bases oficiales (SISMED y Circular 04 de 2012). No se empleó tasa de descuento por ser un análisis hasta un año. **RESULTADOS:** 1.*Costos FOLFOX WT ($COP):* Folfox (10.446.152), Folfox+Anti EGFR (90.221.332), Folfox+Bevacizumab (28.238.377). 2. *Costos FOLFIRI WT ($COP):* Folfiri (16.968.778), Folfiri+Anti EGFR (104.049.002), Folfiri+Bevacizumab (45.235.174), Xelox+Anti EGFR (94.513.398), Xelox+Bevacizumab (45.488.519). 3. *SLP meses WT:* Folfox (7.2), Folfox+Anti EGFR (7.7), Folfox+Bevacizumab (11.5), Xelox+Bevacizumab (10.6); Folfiri (8.7), Folfiri+Anti EGFR (9.9), Folfiri+Bevacizumab (11.5). 5. La Razón de Costo Efectividad Incremental mostró que el uso de Bevacizumab + (FOLFOX/XELOX) y FOLFIRI es una terapia dominante. **CONCLUSIONES:** El uso de FOLFIRI/FOLFOX+Bevacizumab resulta ser la opción más costo-efectiva para una disposición a pagar de apróximadamente COP$36 millones. Los cálculos de costo efectividad estuvieron en linea con los resultados para otras terapias contra el cancer.

PCN21

COST-EFFECTIVENESS AND COST-UTILITY ANALYSIS OF MIFAMURTIDE PLUS COMBINATION CHEMOTHERAPY IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA AFTER RESECTION SURGERY

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Current treatment for high-grade osteosarcoma (HGO) consists in primary tumor complete surgical excision and adjuvant multi-agent combined chemotherapy for subclinical metastatic disease. In Mexico, osteosarcoma prevalence is ≤5 cases per 10,000 people; drugs targeting the disease are therefore designated orphan medicinal products. This is the case of mifamurtide, a potent monocytes and macrophages inducer. **OBJECTIVES:** This study aimed to determine the most cost-effective treatment for resectable, non-metastatic HGO in pediatric patients. Therapies compared were combined chemotherapy (high doses methotrexate, doxorubicin, cisplatin, with or without ifosfamide) vs combined chemotherapy plus mifamurtide. **METHODS:** Efficacy data regarding combination chemotherapy alone or with mifamurtide were obtained from the INT-0133 study. A Markov model was designed using Excel™ software. According to treatment guidelines, the model considered six stages: disease-free; disease progression; recurrence; progression-free after recurrence; progression after recurrence; death. The model adopted the Mexican public health institutions' perspective over a 60-year timeframe. Univariate sensitivity analyses were conducted to determine the robustness of the model. Average utility was calculated from published studies. Costs were from the Mexican Institute of Social Security (IMSS). Outcome measures included cost, ICER and ICUR. **RESULTS:** Cost-effectiveness analysis showed that while the chemotherapy combination regimen plus mifamurtide was more effective (19.74 vs. 18.17, LYG) it was also more costly (USD $102,635.8 vs. $13,148.89), with a discount rate of 3.5%. The ICER is USD $56,746.14. The cost-utility analysis found the same results, with the chemotherapy plus mifamurtide proving to be most effective treatment (19.55 vs. 17.95 QALY), or 1.60 additional QALY. The ICER was USD $55,837.7. Sensitivity analyses showed the model to be robust. **CONCLUSIONS:** Mifamurtide is a cost-effective treatment for pediatric patients with osteosarcoma. The additional 1.60 QALYs are relevant for the population, offering longer survival with a better quality of life.

PCN22

HOW UNIVERSITY HOSPITAL OF CRETE SUCCEEDED IN DECREASING CYTOSTATICS' BUDGET IN 2012?

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OBJECTIVES: UHC is the largest hospital in Crete and among the 5 largest hospitals in Greece. With the implementation of the memorandum, all operators were asked to reduce their costs, while special emphasis was placed on decreasing health care costs. In 2012, in this context, UHC made various attempts to diminish its budget. **METHODS:** Two events happened in 2012: 1) Pharmaceutical companies were asked to offer discounts for their products' price; 2) A central unit for the cytostatics drugs' dilution for all oncologic therapies was founded. Good management and economy of scale succeeded in quantity saving of drugs that were re-entered in pharmacy's stock. **RESULTS:** The effect of these combined actions was examined in achieving the goal of reducing the pharmaceutical expenditure. In order for the data to be comparable, only the drugs used in the CU were studied. Specifically, there are 113 medications (62 prototypes, 31 generics and 20 orphan drugs), which derived from 23 companies. In 2012, 100.000 units were consumed in hospital that worth 10 M€. The combined results were impressive as a budget reduction of 21.4% was achieved (15.4% due to discounts and 6% due to the CU). As per the discounts, 82% of cytostatics' value represents prototypes and expensive drugs, which were limited to the legal rebate of 5% discount, while 17% is mostly generics whose discounts varied from 29.5 to 92.9%. Thus, 73.4% of the value benefit was due to generic and 26.6% due to the prototype drugs. As for the CU's savings, 6000 pieces were returned to the pharmacy. A total of 91.7% of the value benefit derived from the prototypes and the remaining 8.3% from the generic and orphan drugs. **CONCLUSIONS:** Taking into consideration that cytostatic drugs' cost equals 1/3 of the total pharmaceutical expenditure, even if only these two events were taking place, a 7.1% budget decrease was achieved.

PCN23

EVALUACIÓN ECONÓMICA DEL USO DE LA PERFUSIÓN AISLADA DE EXTREMIDAD CON TASONERMIA EN PACIENTES CON SARCOMA DE TEJIDO BLANDO IRRESECABLE

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OBJECTIVOS: Identificar la relación costo-utilidad de la perfusión aislada de extremidad (PAE) con tasonermina (factor de necrosis tumoral 1a (FNTα-1a) y quimioterapia, en comparación con amputación, para el control del sarcoma de tejidos blandos irresecable en extremidad con la perspectiva de salvamento de la extremidad. **METODOLOGÍAS:** El análisis se enfocó en la calidad de vida ganada gracias al salvamento de la extremidad en comparación con amputación, en el tratamiento del sarcoma de tejidos blandos irresecables. Se desarrolló un modelo Markov de cinco años, comparando cinco posibles resultados para PAE con dos estados de amputación. Los estados de salud para PAE (pierna y brazo) incluyeron: éxito del procedimiento; éxito con pérdida de movilidad y muerte. Las utilidades para la población mexicana fueron obtenidas utilizando el método TTO y estados de salud EQ-5D. Además, utilizando información de distintas dependencias públicas, el modelo consideró costos médicos directos y el costo de las complicaciones asociadas con el tratamiento. Posteriormente, se realizó un análisis de sensibilidad univariado sobre los costos directos, el costo de las complicaciones y las tasas de descuento. **RESULTADOS:** Durante el período de análisis, el tratamiento más efectivo fue la PAE con tasonermia y quimioterapia, obteniendo una ganancia de 2.88 AVACs, en comparación con los 1.39 obtenidos para amputación. Además, la RCEI de PAE utilizando tasonermia ascendió a $123,357.78 pesos mexicanos. **CONCLUSIONES:** La PAE utilizando tasonermia en pacientes con sarcoma de tejidos blandos irresecable es considerada una alternativa costo-efectiva en el contexto mexicano, ya que la RCEI fue inferior a un PIB per cápita. Adicionalmente, el impacto positivo que tiene el procedimiento sobre la calidad de vida de los pacientes, sin comprometer su esperanza de vida, convierte a tasonermia en una opción atractiva para un grupo de pacientes que carecen de opciones de tratamiento.

PCN24

COSTO-UTILIDAD DE INTERVENCIONES PREVENTIVAS CONTRA EL CÁNCER DE CUELLO UTERINO EN MUJERES PERUANAS

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OBJECTIVOS: Estimar el costo-utilidad de la vacuna bivalente y tetravalente contra el Virus de Papiloma Humano en las mujeres peruanas de 10 años de edad comparando el tamizaje de Papanicolau y el no vacunar. **METODOLOGÍAS:** Se realizó una evaluación económica de tipo costo-utilidad estructurado sobre un modelo matemático de Markov. La población de estudio fue una cohorte hipotética de niñas de 10 años de edad para la vacunación y para el caso del tamizaje de Papanicolau, se consideró a la población de 30-49 años. Los costos de la vacunación se estimaron desde la perspectiva del financiador, con base en estos costos y los años de vida ajustados por calidad (QALY) como medidas de resultado de cada una de las intervenciones evaluadas, se calcularon las razones costo-utilidad incremental y análisis de sensibilidad utilizando una tasa de descuento del 3%. **RESULTADOS:** El costo anual de la vacunación bivalente fue de USD 9'014,006.05, para el tamizaje con Papanicolau fue de USD 3'048,448.82 y el costo del CCU fue de USD 16'270,359.3. La Razón incremental de costo efectividad (ICER) para la vacunación bivalente fue de 3377 USD/QALY, para el tamizaje de Papanicolau fue de 6,554 USD/QALY, para la vacunación tetravalente fue de 19,274 USD/QALY y para el no vacunar fue de 30,904 USD/QALY. **CONCLUSIONES:** La vacunación bivalente contra el VPH resultar ser costo-efectiva, en comparación con la vacuna tetravalente y el tamizaje de Papanicolau, sin embargo los resultados no fueron robustos al incorporar la incertidumbre existente.

CANCER – Health Care Use & Policy Studies

PCN25

TRATAMENTO DO CÂNCER COLORRETAL METASTÁTICO COM BEVACIZUMABE E CETUXIMABE: ACESSO E IMPACTO ECONÔMICO EM UM HOSPITAL UNIVERSITÁRIO

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OBJETIVOS: Avaliar o acesso e o impacto econômico da introdução das terapias-alvo bevacizumabe e cetuximabe no tratamento do câncer colorretal metástico em um hospital universitário após o início do Processo Administrativo (Resolução SS 54/2012). **MÉTODOS:** Estudo retrospectivo e descritivo realizado de janeiro de 2010 a junho de 2012, junto aos pacientes portadores de câncer colorretal metastático em seguimento no Serviço de Oncologia Clínica do Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto-USP em uso de tratamento quimioterápico. Foi avaliado o número de pacientes atendidos; o tempo médio entre solicitação, avaliação pela Secretaria de Estado da Saúde de São Paulo e recebimento dos medicamentos; o intervalo médio de tempo entre início de uso do medicamento após seu recebimento; gasto financeiro total e o gasto financeiro médio por paciente. **RESULTADOS:** No período do estudo foram tratados com bevacizumabe e cetuximabe, respectivamente, 28 e 30 pacientes. Foi identificado um tempo médio entre o pedido, avaliação pela SES-SP e recebimento dos medicamentos de 43 dias; um tempo médio de 14 dias para o início do uso após o recebimento dos medicamentos e um gasto financeiro total com cetuximabe de R$1.112.145,09 e R$1.157.444,69 com bevacizumabe, sendo o gasto médio total de R$37.071,03 por paciente tratado com cetuximabe e R$41.337.31 com bevacizumabe. **CONCLUSÕES:** O Processo Administrativo proporcionou acesso dos pacientes com maior rapidez a estes medicamentos, sendo de extrema importância se conhecer os recursos financeiros empregados aos medicamentos disponíveis. A adoção dessa medida contribuiu para a garantia do acesso da população à assistência oncológica, constituindo-se em um elemento importante para o adequado enfrentamento dos desafios que a progressão da incidência de câncer representa para a saúde pública brasileira.

PCN26

IMPACT OF PUBLIC PAYER CONCENTRATION ON PUBLIC SECTOR DISCOUNTS FOR SELECTED CANCER SUPPORTIVE CARE PRODUCTS IN BRAZIL AND MEXICO

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OBJECTIVES: When contracting with large accounts, manufacturers have long understood the importance of discounting to gain the favor of high-volume customers over the competition. The objective of this research is to compare what levels of discounting is necessary to sell pharmaceutical products in the highly-competitive cancer-supportive care market to the leading public payers in two of Latin America's largest markets, the *Sistema Único de Saúde* (SUS) of Brazil and the *Instituto Mexicano del Seguro Social* (IMSS) of Mexico. As the level of concentration in terms covered lives as a percentage of their respective countries' total populations varies this will provide insight into the importance that concentration plays in securing greater discounts. **METHODS:** Quantitative analysis of SUS and IMSS tender purchase data compared with ex-manufacturer prices for selected cancer supportive care agents in Brazil and Mexico. Products will be divided into innovative and commoditized baskets to provide insight into any differences that level of differentiation may play when contracting with these payers. **RESULTS:** Due to its higher concentration of covered lives to total population, discounts on sales for the selected products to SUS were greater than on those to IMSS. This was true for innovative as well as commoditized products, although differences in coverage policies for higher-cost, innovative drugs result in greater variability of data than for the commoditized basket of products. **CONCLUSIONS:** Discounting plays a critical role in securing contracts with large accounts, and is even more important with payers that cover a larger proportion of their populations. This is especially true for commoditized products, while innovative products show greater ability to avoid more pronounced discounting with even the largest public payers in the countries due to their greater level of differentiation.

PCN27

VARIABILIDADE NO TRATAMENTO DO CANCER DE MAMA NO BRASIL

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OBJETIVOS: Descrever as taxas de utilização do tratamento para câncer de mama feminino e determinar a variabilidade geográfica no uso desse tratamento. **MÉTODOS:** Estudo descritivo ecológico de utilização de tecnologia mediante análise de áreas geográficas, cuja fonte de dados foi a Base Onco, desenvolvida por meio de relacionamento probabilístico-determinístico dos registros de autorização para procedimentos de radioterapia e/ou quimioterapia e dos registros de internação hospitalar pelo SUS, no período de 2000 a 2006. Foram incluídas as pacientes com diagnóstico de câncer de mama entre os anos de 2000 a 2005 e com idade entre 19 a 100 anos. Para conhecer a magnitude da variação do tratamento para o câncer de mama entre os estados brasileiros foram utilizadas taxas brutas e padronizadas de tratamento oncológico por idade por 100.000 mulheres (censo 2000); razão de variação (entre os valores máximos e mínimos observados do percentil 5-95), coeficiente de variação e razão de utilização padronizada (RUE). **RESULTADOS:** Foram analisadas 104.343 mulheres com idade média de 55 anos (DP 13,51), a maioria residia na região sudeste (51%), no momento do diagnóstico estava no estadio II e III (73%) e fez quimioterapia e radioterapia exclusivamente (81%). A taxa padronizada para o tratamento oncológico de câncer de mama foi de 28,61 por 100.000 mulheres com razão de variação, entre o percentil 5-95, em torno de 3,5 vezes. A razão de utilização padronizada apresenta grande discrepância entre os estados. Os estados das regiões centro-oeste norte e nordeste - exceto Ceará e Rio Grande do Norte, apresentam RUE significativamente inferiores ao esperado (2,5 vezes a 15% menos). Os estados do sul e sudeste apresentam taxas superiores de RUE (10% a 38%). **CONCLUSÕES:** As discrepâncias observadas na probabilidade de receber um tratamento oncológico para o câncer de mama poderão indicar iniquidade no acesso aos serviços públicos de saúde no Brasil.

PCN28

VALIDACIÓN DE UN CUESTIONARIO PARA MEDIR RIESGO DE CÁNCER DE PIEL

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INTRODUCTION: Actualmente se requieren estrategias para identificar a la población en riesgo de padecer cáncer de piel para implementar medidas de prevención y diagnóstico oportuno. No existen instrumentos validados en idioma español que identifiquen el riesgo de cáncer de piel. **OBJECTIVOS:** Diseñar y validar un cuestionario auto-aplicado para cuantificar el riesgo de cáncer de piel melanoma y no melanoma en población mexicana. **METODOLOGÍAS:** Se diseñó un cuestionario auto-aplicado para medir factores de riesgo para cáncer de piel, cuya validez de apariencia y contenido fue evaluada por cinco expertos. El valor de cada ítem se ponderó de acuerdo al riesgo relativo de los factores de riesgo. Se aplicó el instrumento a grupos extremos para medir la validez de constructo y la consistencia se evaluó mediante "test-retest" a las dos semanas. **RESULTADOS:** Se aplicó el cuestionario a pacientes del Centro Dermatológico "Dr. Ladislao de la Pascua" con y sin cáncer de piel, 147 y 249 respectivamente. El puntaje total del cuestionario fue diferente en ambos grupos (U=2104.5, p=0.0001) y mediante curva ROC (área 0.964, IC95% 0.946-0.981, p=0.0001) se determinó que 5 o más puntos equivalen a riesgo alto para cáncer de piel. La consistencia del instrumento fue de 0.971 (IC95% 0.943-0.986, p=0.0001). **CONCLUSIONES:** Este es el primer instrumento en idioma español válido para medir riesgo de cáncer de piel y que aplicado a nivel poblacional sería una herramienta útil para identificar a los individuos en riesgo que requieren intervenciones preventivas.

PCN29

REQUIREMENT OF CANCER HELP LINES IN INDIA AND THE PERCEPTION OF ALL THE STAKE HOLDERS

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OBJECTIVES: To analyze the telephonic cancer help lines in India and to determine their need and potential application and also evaluate their potential to enhance flawless and uniform communication in cancer health delivery. **METHODS:** A Multi-Centre survey was conducted across 9 cities pan India with a structured questionnaire. The survey participants were oncologists, paramedical staff, hospital administrators, patients, their care takers, social workers, government officials and medical representatives. Collected data was statistically analyzed. **RESULTS:** A total of 670 people were surveyed across the country. Approximately, only 25% of the surveyed subjects were aware of cancer help lines which mainly encompassed the educated class. However, almost 97% of the total surveyed people revealed complete willingness for this service and its highest need was perceived in the villages. The convenience and comfort of telephone for health education was assessed to be 90.70% and 86.20% respectively and 88% perceived it as better than internet for personalized information. 92.3% of the oncologists acknowledged it to be useful in patient follow-up and for referring physicians for palliative care and majority of the other stakeholders recognized it to be useful in rendering better medical, emotional and supportive care thereby ultimately benefitting the patients in technologically and economically underprivileged countries like India. **CONCLUSIONS:** Owing to the health education potential of cancer helplines, and its ability to link all the health care sectors, its implementation in developing countries like India that face the burden of cancer care, poor patient follow-up and poor psychosocial support will contribute towards better and cost-effective treatment approach as well as overcome the persistent problem of poor communication in the health care delivery and create means for uniform data collection.

PCN30

TRASTUZUMABE NO CÂNCER DE MAMA METASTÁTICO: UMA REVISÃO SISTEMÁTICA DE ANÁLISES CUSTO-EFETIVIDADE

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OBJETIVOS: Realizar uma revisão sistemática de avaliações de custo-efetividade do trastuzumabe em pacientes com câncer de mama metastático. **MÉTODOS:** Foi realizada uma revisão sistemática de estudos de custo-efetividade do trastuzumabe no câncer de mama metastático, em português, espanhol e inglês, compreendendo o período de 2002 a 2013. As buscas foram realizadas em seis bases de dados eletrônicas, dois ferramentas de busca na internet e pesquisa de referências citadas. Comentários, editoriais, cartas, estudos de caso, artigos de revisão, revisões sistemáticas e metanálises foram excluídos. Os estudos foram selecionados por dois revisores independentes. **RESULTADOS:** Resultados preliminares indicaram a inclusão de 15 estudos. Embora a maioria tenha cumprido com as diretrizes de custo-efetividade, a qualidade dos resultados foi limitada. Esquemas de tratamentos adotados pelas análises de custo-efetividade foram variados. Finalmente, as análises utilizaram diferentes limiares para determinar se o tratamento com o trastuzumabe foi custo-efetivo. **CONCLUSÕES:** O uso de trastuzumabe combinado ou não a taxanos ou capecitabina, foi custo-efetivo em relação a desfechos secundários, porém no que se refere ao desfecho primário sobrevida global, houve diferentes conclusões. Esses resultados variados são, provavelmente, devido a julgamentos feitos pelos autores dos estudos incluídos nesta revisão durante a tradução dos ensaios clínicos e por problemas metodológicos para avaliar custos e desfechos. Mais estudos de custo-efetividade devem ser realizados com o objetivo de avaliar o uso do trastuzumabe no câncer de mama metastático.

DIABETES/ENDOCRINE DISORDERS – Clinical Outcomes Studies

PDB1

COMPARACIÓN INDIRECTA DE LA EFECTIVIDAD DE LA COMBINACIÓN DE HIPOGLUCEMIANTES ASOCIADOS A METFORMINA EN PACIENTES DIABÉTICOS TIPO 2

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OBJECTIVOS: Comparar el porcentaje en la reducción de hemoglobina glicosilada (HbA1c) posterior al tratamiento en pacientes con Diabetes Mellitus e inadecuado

control glucémico tratados con diferentes combinaciones de hipoglucemiantes orales con metformina. **METODOLOGÍAS:** Mediante una revisión de la literatura se identificó y evaluó la efectividad de [vildagliptina, sitagliptina, saxagliptina, linagliptina, glimepiride y glibenclamida] asociados a metformina versus monoterapia de metformina (Septiembre 2012). Los estudios encontrados se evaluaron en similitud de diseño y características de los pacientes; y a partir de los resultados de éstos se reconstruyeron las distribuciones de Hb1Ac al inicio y a 24 semanas. El análisis se hizo por diferencia de medias (reducción de HbaA1c) de acuerdo al método de Bacher mediante el software Indirect Treatment Comparison. **RESULTADOS:** Los grupos tratado con vildagliptina de 50, 100 mg y glimepiride no eran similares a los tratados con las otras combinaciones respecto al nivel de Hb1Ac de inicio (8,4% *ee* 0,08; 8,3% *ee* 0,07 y 7,7% *ee* 0,03 respectivamente) limitando su comparabilidad. Las comparaciones entre las demás combinaciones de hipoglucemiantes demostraron una mayor reducción de la HbA1c frente a la monoterapia con metformina. Ninguna de las combinaciones presentó superioridad en el desenlace analizado, aunque presentan diferencias en otros aspectos que pudieran modificar el resultado final como adherencia y presentación de hipoglucemia. **CONCLUSIONES:** Se demuestra la mayor efectividad de las combinaciones de hipoglucemiante-metformina versus monoterapia de metformina, en pacientes con Diabetes Mellitus e inadecuado control glucémico. No existen diferencias de efectividad cuando se mide el nivel de cambio de HbA1C a las 24 semanas. Se requieren análisis que tengan en cuenta variables a largo plazo como los eventos micro y macro vasculares y otras variables como la tasa de presentación de hipoglucemia que entre las tecnologías analizadas.

DIABETES/ENDOCRINE DISORDERS – Cost Studies

PDB2
ANÁLISIS DE IMPACTO PRESUPUESTARIO DE LINAGLIPTINA ADICIONADA A METFORMINA EN EL TRATAMIENTO DE PACIENTES CON DIABETES MELLITUS EN COLOMBIA

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OBJETIVOS: Determinar el impacto sobre la unidad de pago por capitación (UPC) de la utilización de linagliptina adicionada a metformina en pacientes con Diabetes Mellitus tipo 2 (DM2), con inadecuado control glucémico, en el sistema de salud de Colombia. **METODOLOGÍAS:** A partir de un modelo de costo-efectividad que muestra el beneficio de uso de linagliptina adicionada a metformina en el tratamiento de pacientes con DM2, se realizó un análisis de impacto presupuestario para un quinquenio, considerando costos directos en salud asociados a la historia natural de la enfermedad, incluyendo eventos macrovasculares y microvasculares, en una cohorte móvil de pacientes. Los costos directos de atención de salud se tomaron de Registros Individuales de las Prestaciones de Salud y de aseguradores, con un reemplazo del 50% frente a glibenclamida/metformina (incluida en el plan de beneficios del sistema de salud). Se hizo un análisis de sensibilidad univariado haciendo variar la tasa de reemplazo. **RESULTADOS:** Dada una tasa de prevalencia de 0,04 e incidencia de 0,00879 de DM2 en Colombia, y el supuesto de que el 10% de los pacientes requiere la intervención, el costo acumulado a 5 años, sería de US$ 2.143.046.352 tratados solo con glibenclamida/metformina, frente a US$ 2.067.111.599 si se usa linagliptina adicionada a metformina, con una participación del 50%. En el primer año, el impacto de la inclusión de linagliptina sería del 0,21% sobre la UPC. Del segundo al quinto año, se generarían ahorros sobre la UPC de 0,004%, 0,13%, 0,27% y 0,41%, respectivamente. Es decir, al cabo de cuatro años ya sería ahorrativo. Remplazos mayores a 60% generarían más ahorros al sistema. **CONCLUSIONES:** La introducción de linagliptina adicionadaa metformina, en el plan de beneficios del sistema de salud colombianoserá notablemente menos costosa que la actual utilización de glibenclamida/metformina, en un periodo de cinco años.

PDB3
LONG-TERM COST COMPARISON BETWEEN PARICALCITOL AND CALCITRIOL FOR THE TREATMENT OF SECONDARY HYPERPARATHYROIDISM IN CHRONIC KIDNEY DISEASE IN MEXICO

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OBJECTIVES: Assess cost burden related to drug usage in a long term treatment (5 years) in patients with Secondary hyperparathyroidism (SHPT), considering hospitalization cost, erythropoietin (EPO) consumption and other direct health care costs from an institutional perspective. **METHODS:** A statistical model was developed to simulate an average Mexican patient resources usage in 5 years' time-frame treated with two alternatives paricalcitol and calcitriol based on clinical data in published literature. Resources usage considered: SHPT treatment drugs, EPO, hospitalization costs and medical supplies. Unit costs were collected from Mexican Government Databases: Instituto Mexicano del Seguro Social (IMSS) official database, Official Journal of the Federation (DOF) and Banco de Mexico. Univariable sensibility analysis was executed. **RESULTS:** SHPT medication treatment cost were US$21.92 with calcitriol and US$10,658.00 with paricalcitol during five years, while total costs for paricalcitol patients was US$5,304.20(-8.5%) lower compared to calcitriol in this time-frame. Most savings occur in hospitalization costs where calcitriol patients require in average US$35,633.36 while paricalcitol patients required just US$24,532.88. Erythropoietin consumption costs during 5 years was also lower by US$4,910.88 in paricalcitol patients compared to calcitriol ($p<0.05$). During the first two years total costs for the patients treated with paricalcitol was slightly higher than those treated with calcitriol, US$441.79(+1.7%), due to the initial paricalcitol dosage which is reasonably higher than maintenance dosage. **CONCLUSIONS:** Based on this cost comparison model, from institutional perspective, paricalcitol treatment is less costly when the patient is treated with a middle-term (more than 2 years) or long-term (5 years) perspective at IMSS in Mexico.

PDB4
ANÁLISIS COMPARATIVO DE INSULINA GLARGINA FRENTE A INSULINA DETEMIR: MODELO DE MINIMIZACIÓN DE COSTOS PARA COLOMBIA

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Las insulinas análogas basales son opciones eficaces en el tratamiento de pacientes con DM2. No obstante, el costo del tratamiento, dado su impacto presupuestal desde la perspectiva del pagador, puede afectar la elección del medicamento. **OBJECTIVOS:** Determinar los costos asociados para alcanzar metas glucémicas con el uso de insulinas análogas basales, insulina glargina (IG) vs insulina detemir (ID), a través de un modelo de minimización de costos. **METODOLOGÍAS:** Búsqueda sistemática de literatura en PUBMED de estudios clínicos comparativos entre IG y ID para pacientes DM2 insulino-requirentes para extraer datos de uso, efectividad y frecuencia de eventos adversos. La meta de control glucémico definida fue HbA1c7%. Los costos de insulinas fueron tomados del Sistema Integrado de Precios de Medicamentos 2011 del Ministerio de Salud y precios de IMS Consulting Group promedio móvil anual para noviembre de 2011. Los análisis de sensibilidad se realizaron con simulaciones de Monte Carlo en dosis y precios de las insulinas. **RESULTADOS:** Cinco publicaciones cumplieron con criterios de inclusión. La diferencia promedio entre dosis de IG e ID fue 15,99U (SD10,04U), a favor de IG. El porcentaje promedio de pacientes que requirieron dos dosis con ID fue de 56,2% (SD35,7%). No hubo diferencias significativas en eventos hipoglicémicos. Para el canal retail, en 4 estudios se apreció un mayor costo entre IG vs ID (Rosenstock USD$435, Hollander USD$532, Swinnen USD$967 y Currie USD$357 anuales) a favor de IG y solo un estudio mostró mayor costo para IG (Raskin USD$69 anuales). Para el canal institucional, en todos los estudios, el tratamiento con IG es la modalidad más económica según costos anuales. **CONCLUSIONES:** La diferencia en dosis promedio entre IG e ID genera una diferencia significativa en costos anuales a favor de IG. El uso de IG en el manejo del paciente DM2-IR es una alternativa costo/efectiva frente a detemir.

PDB5
DIRECT MEDICAL COSTS OF TREATING DIABETES-RELATED COMPLICATIONS IN ARGENTINA

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OBJECTIVES: Diabetes is a chronic disease, which when not treated appropriately, leads to increased risk of developing preventable complications, increasing the cost of care. This represents a heavy burden for the public health budget in Argentina. The objective was to collect direct medical costs of treating diabetes-related complications in Argentina. **METHODS:** Following a literature review no data on the cost of diabetes-related complications were found in Argentina. To obtain robust data, we approached 3 local key opinion leaders from both social security (SS) and private (P) health care sectors with access to local databases; they covered 3 geographic areas of Argentina: Buenos Aires city (P) and Buenos Aires and Cordoba provinces (SS). Standardized forms were used for data collection and final values represent average cost of the SS and P sectors. Direct costs were classified into 6 groups: disease management, treatment of acute-events, renal-disease, eye-disease, neuropathy/foot ulcers and cardiovascular-complications. Values are presented in 2012 US-dollars per "event occurring in the first year" and annual follow up costs (exchange rate 1USD = 4.89ARS). **RESULTS:** The diabetes-related complications with highest first year average costs were renal-complications (renal transplant 37,833USD; peritoneal-dialysis 24,655USD and haemodialysis 23,748USD), followed by cardiovascular related events (myocardial infarction 5,939USD; congestive heart failure 4,884USD; peripheral vascular disease 4,200USD and angina 3,799USD). The cost of an amputation procedure was 2,727USD while those of prosthesis and post-amputation follow up were 3,255USD and 1,470USD, respectively. The cost of eye-laser therapy was 449USD while a cataract procedure was 1,186USD. High costs were also associated with treatment of neuropathy (1,141USD), infected foot ulcer (747USD) and gangrene (1,684USD). **CONCLUSIONS:** These findings suggest that implementation of prevention strategies to reduce the development of diabetes-related complications may decrease the diabetes burden on the health care budget. Furthermore the data presented will provide useful inputs for economic evaluations in Argentina.

PDB6
DIRECT COSTS OF TYPE 2 DIABETES IN MEXICO FROM THE PUBLIC HEALTH CARE SECTOR PERSPECTIVE

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OBJECTIVES: To quantify the annual cost of type 2 diabetes mellitus (T2DM) in Mexico and explore the relative contributions of different components of cost. **METHODS:** A cost of illness model was developed in Microsoft Excel 2007 to estimate the economic burden of T2DM in Mexico from the public health care payer perspective. Cost of routine management and complications were included in the analysis. Data inputs for prevalence of T2DM (weighted to include only patients who are diagnosed and treated) and related complications, costs and routine management were sourced from the published literature and publicly available databases, where available. Primary research approaching local key opinion leaders was performed to fill data gaps. Sensitivity analyses were conducted to identify data inputs which were most likely to impact overall results when varied. Costs are presented in Mexican pesos 2012. **RESULTS:** The annual cost of T2DM in Mexico is estimated to be $107,343,890,388MXN($8,643,348,612USD). This figure represents ~13% of the national health care expenditure. The cost of complications were estimated to account for 91% of the total cost of T2DM, with cardiovascular and eye complications accounting for 49% and 18% of total costs, respectively. Routine management, including drug costs, was estimated to comprise

9% of total cost of T2DM. The cost estimate was most sensitive to incidence and event cost of peripheral vascular disease, stroke and severe vision loss. **CONCLUSIONS:** Based on the present analysis, T2DM places a significant financial burden on the health care system in Mexico, with cost of treating related complications being the main cost driver. Given the model focuses on diagnosed and treated T2DM patients, it is likely this cost is even higher when undiagnosed and untreated patients are considered. Delaying the onset of complications could result in a reduction in costs, as well as benefits for the patient and health care system.

PDB7

DIRECT COSTS OF TYPE 2 DIABETES FROM THE BRAZILIAN PUBLIC HEALTH CARE SECTOR PERSPECTIVE

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OBJECTIVES: This study aimed to quantify the annual financial cost of type 2 diabetes (T2DM) in Brazil and explore the relative contribution of different components of cost. **METHODS:** A cost of illness model was developed in Microsoft Excel 2007 to estimate the financial cost of T2DM in Brazil from the public health care payer perspective. Cost of routine management and complications were included in the analysis. Data inputs for prevalence of T2DM (weighted to include only patients who are diagnosed and treated) and related complications, costs and routine management were sourced from the published literature and publicly available databases, where available. Key opinion leader input was sought to fill data gaps. Sensitivity analyses were conducted to identify parameters which were most likely to impact overall results when varied. Costs are presented in Brazilian Reals 2012. **RESULTS:** The annual cost of T2DM in Brazil is estimated to be 11,275,921,167 BRL ($5,471,123,022USD) which represents 5.3% of national health care expenditure. Costs of complications were estimated to account for 56% of the total cost of T2DM. Cardiovascular complications accounted for 32% of total T2DM cost. Diabetes drug costs were estimated to account for 31% of total T2DM health care spending. The overall cost estimate was most sensitive to the laser eye surgery, hemodialysis and cardiovascular complications and the frequency and cost of routine physician consultations. **CONCLUSIONS:** The findings indicate that there is a high economic burden of T2DM for the Brazilian health care system. Cost of treating related complications was the main driver. An even higher burden of the disease is expected if undiagnosed and patients currently not being treated start receiving public medical attention. The burden of the disease could considerably be reduced if T2DM related complications were avoided, which not only benefits the health care system but the patients as well.

PDB8

TRENDS IN HEALTH CARE RESOURCES UTILIZATION, COST AND MEDICATION SELECTION IN THE TREATMENT OF DIABETES

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OBJECTIVES: Diabetes is one of the most common chronic diseases in Canada. It affects about 6.8% of the Canadian population. Treating and managing the disease and its complications is associated with a significant economic burden. The objective of this study was to analyse trends in terms resource utilization, cost and treatment patterns in the management of diabetes. **METHODS:** Patients covered by the Quebec provincial drug reimbursement program (RAMQ) who had a diagnosis of diabetes, in 2005 and were covered continuously by the public drug program for the period from January 2006 to December 2010 were selected. Health care resources in terms of diabetes medications and physician visits, hospitalization, intensive care unit stay, hospital outpatient clinic visits, and emergency room visits associated with a diagnosis of diabetes were estimated over a 5-year period, from January 2006 to December 2010. Trends in the proportion of diabetes medications used each year over the 5-year study period were also estimated. **RESULTS:** A total of 46,194 diabetic patients were included in the study. The mean age of the study population was 65.4 years (SD=12.3) and proportion of male/female was 47% and 53% respectively. Over the study period, annual cost of diabetes medications varied from $320 (SD=464) in 2006 to $372 (SD=546) in 2010 (+16%) while total cost of treatment associated with diabetes varied from $627 (SD=1456) to $715 (SD=1632) (+14%) during that period. Metformine remains the most widely used medication throughout the study period with 64.3% of users in 2006 and 65.6% in 2010. Proportion of insulin users increased from 15.2% to 22.7% while gliclazide users increased from 4.4% to 11.2% during the study period. **CONCLUSIONS:** Over the five-year study period cost of diabetes treatment has increased at a rate similar to inflation, while trends of increased adoption of insulin and newer medications is observed.

PDB9

COST-EFFECTIVENESS OF PARICALCITOL VERSUS PARATHYROIDECTOMY FOR SECONDARY HYPERPARATHYROIDISM TO CHRONIC KIDNEY DISEASE IN MEXICO

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OBJECTIVES: Secondary hyperparathyroidism (SHPT) affects one of every two Mexicans with chronic kidney disease (CKD) at stage five. The objective of this research was to assess cost effectiveness (CE) of Paricalcitol intravenous administration (IV) versus parathyroidectomy (PTX) from Mexican payer perspective. **METHODS:** A decision tree model was designed to simulate patient resources usage and survival rate in 5 years time-frame treated with paricalcitol IV and parathyroidectomy based on clinical data in recent published literature. Time-frame begins when a patient is refractory to Calcitriol therapy and physician decides to treat with Paricalcitol or program PTX. Resources usage considered were just directly related to SHPT treatment: drug cost, surgery and hospitalization costs and medical supplies linked. Unit costs were collected from Mexican Government Databases: IMSS official database, Diagnosis Related Groups from IMSS, Official Journal of the Federation. (Cost considered 5% annual discount rate).Incremental Cost-Effectiveness Ratio (ICER) was calculated with treatment costs and Life-years gained (LYG) offset based on incremental survival rate of compared therapies. Probabilistic Multivariable sensibility analysis was completed with 5,000 simulated patients. **RESULTS:** Survival rate and confidence interval obtained from model was 0.63 (0.60, 0.66) for paricalcitol and 0.46 (0.44, 0.48) for PTX. Average survival of both therapies resulted in an incremental 0.61 LYG for paricalcitol patients (+18%). Average five years treatment cost for Paricalcitol patients was $10,024.25, while PTX was US$5,369.74(-46%) resulting in an ICER of US$7,619.94 per LYG, which is 28.2% below Mexican Gross Domestic Product (GDP) per capita. Probabilistic analysis shown: 90.1% of patient treated had a cost-effective outcome and 7.2% of cases had a dominant outcome. **CONCLUSIONS:** According to results obtained and using a threshold of US$29,306.29 (3 x GDP per capita), Paricalcitol is a highly cost-effective treatment option compared to PTX when treating patients with SHPT at IMSS.

PDB10

COST-EFFECTIVENESS OF FIXED-DOSE COMBINATION (FDC) OF VILDAGLIPTIN/METFORMIN FOR THE TREATMENT OF DIABETES MELLITUS TYPE 2 IN MEXICO

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OBJECTIVES: Type 2 Diabetes is a major public health care problem in Mexico. Some patients may require more than one oral antidiabetic treatment to achieve glycemic control. Vildagliptin, a DPPIV inhibitor is an option in combination with the standard treatment of metformin. The objective was to assess the cost-effectiveness of Vildagliptin/Metformin FDC versus other oral treatments available in the public market. **METHODS:** Cost-effectiveness analysis of the oral antidiabetic treatments available in the public market in Mexico was conducted. The comparisons included the following options: Vildagliptin/Metformin FDC, glibenclamide, and thiazolidinediones (Rosiglitazone and pioglitazone). Cost effectiveness analysis versus other oral antidiabetics incorporated the incidence and costs of adverse events according to Ferrannini 2009 and Gonzalez-Ortíz 2009 for glibenclamide and Motola 2012 for thiazolidinediones. Drug costs were elicited from public tenders and health care services from unitary costs of the IMSS. The perspective is the public health provider and the time horizon is one year. **RESULTS:** The use of Vildagliptin/Metformin FDC (50/500 or 850 mg) BID compared to glibenclamide, is a dominant strategy if the cost per hypoglycemia exceeds US$714.03. Vildagliptin/Metformin FDC is dominant versus pioglitazone,if the cost of fractures incurred by pioglitazone exceeds US$56.56. Drug acquisition costs of Vildagliptin/Metformin FDC are 150% cheaper per patient treated vs rosiglitazone; additionally rosiglitazone is associated with myocardial infarction events. **CONCLUSIONS:** Vildagliptin/Metformin FDC is an opportunity for resource optimization in the public sector. This cost effectiveness analysis is not considering other potential adherence benefits which are related with having two treatments in one pill.

PDB11

PROBABILISTIC SENSITIVITY ANALYSIS TO ANALYZE THE COST-EFFECTIVENESS OF ORAL HYPOGLYCEMIC AGENTS IN THE INITIAL ORAL DRUG TREATMENT OF OUTPATIENTS DIAGNOSED WITH TYPE 2 DIABETES IN PRIMARY CARE

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OBJECTIVES: To perform a probabilistic sensitivity analysis to analyze previously reported results about the cost-effectiveness of oral hypoglycemic agents (OHA's) in the initial oral drug treatment of patients diagnosed with type 2 diabetes mellitus in public primary attention in Mexico. **METHODS:** A probabilistic sensitivity analysis was made in order to analyze results previously reported in which a deterministic sensitivity analysis was performed to study the cost-effectiveness of three OHA's: metformin, glibenclamide and acarbose. We used TreeAge-Pro® software for programming and simulating a Markov model of two health states ($HbA_{1C} \leq 7\%$ or $HbA_{1C} > 7\%$) and twelve cycles of 1 month for a time horizon of 1 year. The parameters of monthly success probability as beta distributions and monthly costs as lognormal distributions of therapeutic alternatives were computed through a parametrization of data. Monte Carlo's simulations were computed for cohorts of 10,000 patients for each treatment option. **RESULTS:** The results of the Monte Carlo's simulations showed very close iterations clouds for metformin and glibenclamide showing evident dominance of both over acarbose. In the acceptability curve generated, for a willingness to pay (WTP) = 0 the probabilities to be cost-effective were 49.46 %, 43.04 % and 7.50 % for glibenclamide, metformine and acarbose, respectively, whereas for a WTP = 1 mexican GDP per capita (US $ 7876.00 in 2009) were 66.26 %, 26.98 % and 6.76%. The glibenclamide versus metformin incremental cost-effectiveness analysis showed similar results as mentioned before, showing 59.72% of iterations below the WTP = 1 mexican GDP per capita line. **CONCLUSIONS:** The probabilistic sensitivity analysis showed which the initial drug therapy with glibenclamide or metformin have advantage over acarbose. There is not sufficient evidence to say glibenclamide has advantage over metformin for WTP near to cero, as in low to middle income countries where containment of expenditures is important.

PDB12

A HEALTH ECONOMIC ANALYSIS OF THE LONG-TERM OUTCOMES AND COSTS ASSOCIATED WITH USING CANAGLIFLOZIN VERSUS SITAGLIPTIN AS AN ADD-ON TO METFORMIN (MET) IN MEXICO

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OBJECTIVES: Canagliflozin (CANA) is a novel inhibitor of the sodium glucose cotransporter 2 in development for treating patients with type 2 diabetes mellitus (T2DM). In a previously reported randomized, double-blind, 4 arm parallel group (placebo, CANA 100mg, CANA 300mg and sitagliptin 100mg [SITA]) study of 1284 subjects inadequately controlled on MET monotherapy, CANA 100mg and 300mg significantly decreased HbA_{1c} versus placebo after 26 weeks of therapy by 0.62% and 0.77%, respectively; SITA decreased HbA_{1c} versus placebo by 0.65%. In this trial, both

CANA doses and SITA significantly reduced systolic blood pressure (CANA 100mg: 5.36 mmHg; CANA 300mg: 6.58 mmHg; SITA 3.34 mmHg), however, only CANA significantly reduced body weight (CANA 100mg: 2.5%; CANA 300mg: 2.9%) versus placebo. The objective of this study was to simulate the health outcomes and associated costs attributable to using CANA versus SITA in Mexico. **METHODS:** Forty-year outcomes associated with adding CANA 100mg or CANA 300mg versus SITA to MET were simulated using ECHO (Economic and Health Outcomes)-T2DM, a validated micro-simulation model. Treatment effects and patient characteristics were sourced from the trial. Simulated treatment was intensified when HbA_{1c} exceeded 7.5% by adding basal insulin, and subsequently prandial insulin. Disutilities associated with micro- and macro-vascular events were obtained from the literature and costs were adapted to the Mexican setting. **RESULTS:** Using CANA 300mg versus SITA was projected to reduce relative risks for key events (e.g. myocardial infarction 10.2%; congestive heart failure 6.6%; macroalbuminuria 6.6%; microalbuminuria 6.2%), improve QALYs (0.046), and result in lower costs per patient ($1927MXN). Simulation results of CANA 100mg versus SITA were generally similar, albeit estimates of reductions in relative risks, QALY gains and associated costs differences were smaller. **CONCLUSIONS:** These simulations suggest that using CANA versus SITA as an add-on to MET could result in improved outcomes and reduced costs in Mexico.

PDB13

ECONOMIC EVALUATION OF INSULIN LISPRO MIX 25 WITH GLARGINE IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS PATIENTS IN THE MEXICAN PUBLIC HEALTH CARE SYSTEM IN MEXICO

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OBJECTIVES: Compare expected costs and health-outcomes in patients with Diabetes Mellitus Type 2 (DMT2) in the Public Sector in Mexico treated with glargine or 25%-insulin lispro, 75%-insulin lispro protamine suspension (LM25). **METHODS:** This analysis included a hypothetical cohort of insulin-naïve patients with T2DM, aged 30–80, years, with A1C>7.0% taking antihyperglycemic drugs for 90 days. Effectiveness measures included; (1) Percentage of patients with A1C<7.0% levels at 24 weeks, (2) frequency and type of micro and macrovascular complications (MMVC) and (3) hypoglycemic events per 1000 patients considering one-year timeframe. Costs evaluated were: 1) acquisition costs; 2) cost of hypoglycemic events; and 3) MMVC. Efficacy measures and mean-daily-dose was obtained from DURABLE, parallel, open-label and randomized study comparing directly LM25 and Glargine. Incidences of MMVC were estimated using data from UKPDS study group and data from Meta-analysis by Quayum following a similar process outlined by Grima. Acquisition costs were derived from the transparency portal of the Mexican Social Security Institute. Healthcare services utilization from hypoglycemic episodes were calculated according to international published literature and IMSS Unit Costs updated to 2013 following IMSS methodology, while other associated expenses with MMVC complications come from Mexican reports and Diagnostic Related Groups (DRG) published by IMSS this data was updated to January 2013 using the Bank of Mexico inflation calculator. Costs are expressed in 2013 USD (1USD=$12.70MXN) **RESULTS:** All results consider 1000 patients treated in a 1-yeat timeframe. Acquisition costs for LM25 were lower compared to glargine ($291,395 vs $383,521, 24% lower), although costs per hypoglycemia events were higher for LM25 ($12,242 vs. $3,673). Direct medical costs for MMVC were higher for Glargine ($668,027 vs. $754,435) Total medical costs were higher for glargine compared to LM25 ($971,663 vs. 1,141,628). **CONCLUSIONS:** Results of the present study suggest that compared with LM25, health care costs are significantly higher for glargine.

PDB14

HEALTH ECONOMIC BENEFITS OF SENSOR AUGMENTED INSULIN PUMP THERAPY IN COLOMBIA

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OBJECTIVES: To estimate the health economic impact of Sensor-Augmented Insulin Pump (SAP) Therapy among Insulin-Dependent Diabetes Mellitus (IDDM) patients in Colombia. **METHODS:** The Core Diabetes Model (CDM) is highly validated, computer simulation model to determine the long-term health outcomes and economic consequences of diabetes interventions. A recent real life clinical study in Colombia evaluating 217 IDDM patients (average baseline HbA1c of 8.97%, mean age 34 years, and average diabetes duration of 14 years) who initiated SAP therapy showed that SAP therapy led to a reduction of -1.47% HbA1c as well as a significant reduction in severe hypoglycaemic events. The impact of the reduction in the fear of hypoglycaemic events on quality of life was also included. **RESULTS:** Life expectancy of patients with SAP was increased by 3.51 years and diabetes related complications were delayed on average by 1.74 years. The Incremental-Cost-Effectiveness-Ratio (ICER) for SAP was $44,889,916COP ($24,939USD) per Quality-Adjusted-Life-Year gained based on direct costs only. SAP related therapy costs were partially offset by the savings due to the reduction in long-term complications, including proliferative diabetic retinopathy (PDR), Severe Vision Loss (SVL), End Stage Renal Disease (ESRD), and Amputations (AMP). The relative reduction in incidence of these complications (PDR 42%, SVL 20%, ESRD 46%, AMP 12%) as well as the average delay in their onset (4.9 years, 4.0 years, 3.8 years, 3.7 years, respectively) due to SAP therapy is profound. When including indirect costs, SAP demonstrated an even lower ICER. Extensive sensitivity analyses showed the robustness of the results. **CONCLUSIONS:** Using a payer's perspective, our analysis showed that SAP is cost-effective over a lifetime horizon in IDDM patients in the Colombian setting (using a WTP threshold of $60,771,600COP [3x GDP]) and can lead to an increase in life expectancy. When using a societal perspective, SAP was even more cost-effective.

PDB15

SHORT AND LONG-TERM COST-EFFECTIVENESS OF SWITCHING THERAPY FROM NPH INSULIN TO INSULIN DETEMIR IN PEOPLE WITH TYPE 2 DIABETES

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OBJECTIVES: To assess the cost-effectiveness (CE) of switching from NPH insulin ± oral glucose-lowering drugs (OGLDs) to insulin detemir ± OGLDs in people with type 2 diabetes (T2DM) in countries in different economic circumstances based on observational data gathered in routine clinical practice. **METHODS:** The A_1chieve® study assessed safety and outcomes over 24 weeks in 66,726 people with T2DM starting insulin analog therapy. Most people (96%) stated better glycemic control as reason to switching therapy, with 31% also stating hypoglycemia problems as a further reason. The CE analyses included data for people switching to detemir in South Korea (n=90) and in seven Arabian Gulf countries (n=124). Data were collected on clinical effectiveness and adverse events, and health-related quality of life using the EQ-5D questionnaire. CE analyses used the IMS CORE diabetes model with 1 and 30 year time horizons, with South Korea and Saudi Arabia country-specific costs for complications and therapies and background mortality rates. CE was measured by comparing outcomes at study-end with outcomes at pre-study. Incremental cost-effectiveness ratios (ICERs) are expressed as cost per QALY in local currencies, USD and in fractions of local GDP per capita. CE was pre-defined using the WHO definition of <3 times GDP per capita. **RESULTS:** 1-year ICERs were: South Korea (KWR 3,236,798; USD 2,980; GDP 0.13), and Saudi Arabia (SAR 27,221; USD 7,258; GDP 0.36). 30-year ICERs were: South Korea (KWR 872,589; USD 803; GDP 0.04), and Saudi Arabia (SAR 6,349; USD 1,693; GDP 0.08). Sensitivity analyses covering cost of self-monitoring, deterioration of glucose control with time, and other time horizons showed the results to be robust. **CONCLUSIONS:** Switching from NPH±OGLDs to detemir±OGLDs in people with T2DM as performed in the A_1chieve® study was found to be cost-effective in both country settings at 1 and 30 year time horizons.

PDB16

SHORT AND LONG-TERM COST-EFFECTIVENESS OF SWITCHING THERAPY FROM INSULIN GLARGINE TO INSULIN DETEMIR IN PEOPLE WITH TYPE 2 DIABETES

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OBJECTIVES: To assess the cost-effectiveness (CE) of switching from insulin glargine ± oral glucose-lowering drugs (OGLDs) to insulin detemir ± OGLDs in people with type 2 diabetes (T2DM) in Saudi Arabia, South Korea and Algeria based on observational data gathered in routine clinical practice. **METHODS:** The A_1chieve® study assessed safety and outcomes over 24 weeks in 66,726 people with T2DM starting insulin analog therapy. The CE analyses included people switching to detemir in Saudi Arabia (n=102), South Korea (n=82) and in 3 North-West African countries (n=94). Data were collected on clinical effectiveness and adverse events, and health-related quality of life using the EQ-5D questionnaire. CE analyses used the IMS CORE diabetes model with 1 and 30 year time horizons, with Saudi Arabia, South Korea and Algeria country-specific costs for complications and therapies and background mortality rates. Incremental cost-effectiveness ratios (ICERs) are expressed as cost per QALY in local currencies, USD and in fractions of local GDP per capita. CE was pre-defined using the WHO definition of <3 times GDP per capita. **RESULTS:** The switch was found to be less costly and have better outcomes in South Korea after 30 years and in Saudi Arabia at both time horizons. 1-year ICERs were: Saudi Arabia (SAR -5,849; USD -1,559; GDP -0.08), South Korea (KWR 296,842; USD 273; GDP 0.01), and Algeria (DZD 267,771; USD 3,363; GDP 0.80). 30-year ICERs were: Saudi Arabia (SAR -14,839; USD -3,957; GDP -0.19), South Korea (KWR -1,133,202; USD -1,043; GDP -0.05), and Algeria (DZD 226,818; USD 2,849; GDP 0.68). Sensitivity analyses on the 30 year time horizon showed the findings to be robust. **CONCLUSIONS:** Switching from glargine±OGLDs to detemir±OGLDs in T2DM as performed in the A_1chieve® study was found to be cost-effective across all country settings at 1 and 30 year time horizons.

PDB18

IMPACTO DE LA DIABETES SOBRE LA PRODUCTIVIDAD EN ARGENTINA

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OBJECTIVOS: Estimar y caracterizar el impacto de la enfermedad sobre la productividad laboral de personas con diabetes (DM) en Argentina. **METODOLOGÍAS:** Estudio descriptivo observacional relevando información mediante el cuestionario WPAI-GH (Work productivity and activity impairment - General Health version) en personas adultas (18 a 75 años) con DM, que concurrieron a su consulta habitual a dos centros asistenciales de La Plata. Los encuestados también respondieron sobre aspectos socioeconómicos y complicaciones de su enfermedad. La pérdida de productividad se estimó por el método del capital humano. Los resultados se presentan como media ± desvío estándar (DS) o proporciones. Para las comparaciones se utilizaron los test t de student, Kruskal-Wallis y Chi cuadrado, según correspondiera. Se consideró significativo p<0,05. **RESULTADOS:** Aceptaron participar en el estudio 73 personas con DM; 54,8% hombres con edad de 57 ± 15 años. El 42,5% poseía estudios superiores (nivel terciario o universitario completo). El 60,3% trabajaba, 6.4% estaba desempleado y el 33,3% inactivo (jubilado, pensionado). El tiempo promedio de trabajo fue de 43 ± 17 horas/semana y el 38% faltó/retiró de su trabajo por su enfermedad. El tiempo de trabajo perdido por ausentismo fue 9.1%, y por disminución de la productividad el 22%. La diabetes también disminuyó un 25% la capacidad para realizar actividades regulares diarias, afectando más a mujeres que a hombres (30 y 20,3%, respectivamente). La pérdida de productividad monetaria por ausentismo

debido a la DM se estimó en $21,516 ± 8062 año/persona. **CONCLUSIONES:** La DM afecta significativamente la productividad laboral en nuestro medio.

PDB19

COSTO DEL AUTOMONITOREO GLUCÉMICO EN PACIENTES EN TRATAMIENTO COMBINADO ORAL Y CON INSULINA EN ARGENTINA

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OBJECTIVOS: Aunque el automonitoreo glucémico (AMG) es una herramienta útil para optimizar el control de la diabetes, no existe en Argentina evidencia de su uso e impacto económico. Este estudio trata de estimar en Argentina, el número de tiras reactivas (TR) para AMG utilizadas en el Sistema de la Seguridad Social (SSS) y su impacto en el costo total de la prescripción terapéutica, en la transición de terapia combinada de antidiabéticos orales (ADO) al agregado de insulina. **METODOLOGÍAS:** Estudio observacional retrospectivo, utilizando registros de una organización del SSS (OSPERYH, consumo de TR de 681 afiliados durante 2012) y de otras dos entidades de la SSS, a través de 8.115 recetas anónimas de medicamentos y TR prescriptas en el período Febrero-Abril 2012 y registradas por el Colegio Farmacéutico de la Provincia de Buenos Aires (COLFARMA). Los resultados representan la media ± desvío estándar (DS) o proporciones. Evaluación estadística: utilizamos los test t de student, Kruskal-Wallis y Chi cuadrado, según correspondiera. Se consideraron significativas diferencias con p<0,05. **RESULTADOS:** *OSPERYH:* las TR fueron provistas bajo sistema de auditoría que incluye educación diabetológica, tipo de tratamiento y grado de control metabólico. Los tipos de tratamiento afectaron significativamente el consumo mensual de TR: combinación ADOs 25±12 *vs.* , ADO+insulina 36±15. El costo total combinación ADOs fué $456 *vs.*ADO+insulina $669 y las TR representaron el 42% y 32% del costo total, respectivamente. COLFARMA: también el tipo de terapia afectó significativamente el consumo mensual de TR pero con valores tres veces superiores: combinación ADOs 75±47 *vs.* ADO+insulina 89±63. El costo total combinación ADOs fue $711 *vs.*ADO+insulina $983, y las TR representaron el 63% y 54% del costo total, respectivamente. **CONCLUSIONES:** El consumo de TR para AMG aumenta en función de la incorporación de insulina al tratamiento y auditorías como la descripta optimizan su consumo e impacto económico.

PDB20

RELACIÓN DEL ÍNDICE DE MASA CORPORAL Y GASTO EN MEDICAMENTOS EN PERSONAS CON DIABETES EN ARGENTINA

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OBJECTIVOS: Evaluar la relación entre el Indice de Masa Corporal (IMC) y el gasto en medicamentos de personas con Diabetes (DM) en Argentina. **METODOLOGÍAS:** Estudio descriptivo observacional relevando el IMC y el consumo de medicamentos de la Base QUALIDIAB. El gasto mensual en medicamentos se determinó mediante técnicas de microcosteo, considerándose el precio promedio de las presentaciones disponibles en el mercado, sin ajustes. Los valores se expresaron en pesos argentinos (Diciembre 2012). Las personas se estratificaron según IMC de acuerdo a la clasificación de la OMS (Normal: ≥18,5 y < 25; Sobrepeso: ≥25 y < 30; Obesidad: IMC≥ 30). Los resultados se expresaron como media ± desvío estándar (DS). Para las comparaciones se utilizaron los test t de student, ANOVA y Kruskal-Wallis, según correspondiera. Coeficientes de correlación de Pearson (r) se utilizaron para evaluar el grado de asociación. Se consideraron significativos p<0,05. **RESULTADOS:** Se analizaron 1134 registros, edad 63 ± 12 años, 55,4% mujeres. El gasto promedio mensual en medicamentos fue de $ 975, el gasto en medicamentos para la DM fue $779, para la Hipertensión $ 241 y para la Dislipemia $ 128. El gasto en medicamentos aumentó en función del IMC: Normal: $782; Sobrepeso: $936 y Obesidad: $1149. El gasto fue significativamente mayor en Hombres ($1045 vs. $919). El gasto total de medicamentos se correlacionó significativamente con IMC (r: 0,164), al igual que el correspondiente a medicamentos antihipertensivos (r: 0,113) y los utilizados para controlar la hiperglucemia (r: 0,079). **CONCLUSIONES:** En pacientes con DM en Argentina, el IMC se asocia positivamente con el gasto en medicamentos. Estrategias terapéuticas que disminuyan efectivamente el IMC generarían beneficios tanto médicos como económicos.

DIABETES/ENDOCRINE DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PDB21

PSYCHOMETRIC PROPERTIES OF THE HYPOGLYCEMIA PERSPECTIVES QUESTIONNAIRE (HPQ) IN TYPE 2 DIABETES MELLITUS

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OBJECTIVES: The Hypoglycemia Perspectives Questionnaire (HPQ) was developed with clinician and patient input to assess symptoms, behaviors, and impact of hypoglycemia on diabetic patients. **METHODS:** The HPQ was administered to adult patients with type 2 diabetes mellitus (T2DM) on antidiabetic treatment as part of a cross-sectional, epidemiological study evaluating hypoglycemia and health-related quality of life (HRQoL) in Cyprus. Demographic and clinical data were collected. Patients also completed the Audit of Diabetes Dependent Quality of Life (ADDQoL-19), treatment satisfaction questionnaire, and EuroQol-5 Dimensions (EQ-5D). The original HPQ consisted of 45 items rating current status or behavior related to hypoglycemia on an 11-point numeric rating scale (NRS) and 7 additional descriptive hypoglycemia event frequency items. Analyses included examination of HPQ item performance, item reduction, and factor structure. Measurement properties (reliability, construct validity, known-groups validity) of the final HPQ were evaluated. **RESULTS:** A total of 500 T2DM patients completed the HPQ with a mean age of 61±10 years; 32.6% women. Based on item evaluation, the original HPQ item pool was reduced to 22 items. Exploratory and confirmatory factor analysis identified 21 items contributing to 3 hypoglycemia domains (Symptoms [8 items], Compensatory Behaviors [7 items], Worry [6 items]) and a single-item of global symptom awareness. HPQ domains had high internal consistency reliability (Cronbach's alpha=0.78-0.92). Construct validity was demonstrated by significant correlations between HPQ scores with HRQoL, treatment satisfaction, and health status. HPQ also demonstrated ability to discriminate between known groups. Compensatory behaviors and symptom awareness were higher for patients with a recent low blood sugar event (p<0.001) and high symptom awareness corresponded to less concern about experiencing symptoms of low blood sugar and worry (p<0.05). **CONCLUSIONS:** These results provide preliminary evidence that HPQ is reliable and valid for assessing the experience and impact of hypoglycemia on T2DM patients.

PDB22

TRANSLATION AND VALIDATION OF HINDI VERSION OF DIABETES QUALITY OF LIFE – MEASURE (DQOL-M) IN INDIAN TYPE 2 DIABETES PATIENTS

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OBJECTIVES: To test the reliability and validity and of newly translated Hindi version of DQOL-M instrument in Indian type 2 diabetic populations. **METHODS:** Backward and forward translation was carried out and intermediate version was compared with original instrument to check the linguistic equivalence. After pilot testing the final Hindi version of DQOL-M was administered to 250 patients with type 2 diabetes twice at the interval of four weeks. Psychometric parameters like treatment satisfaction, Impact of treatment, worries of social vocational issues of diabetes were assessed. Cronbach alpha for total score was calculated to study the reliability of instrument. **RESULTS:** Internal consistency was assessed using Cronbach alpha and value of 0.86 was gained for the summary score. Cronbach alpha for treatment satisfaction was found to be 0.77, for Impact of treatment it was 0.73 and for worries of social vocational issues score of 0.83 was gained. No significant difference was observed in test-retest analysis. Pearson correlations were assessed for all the four subscales and were found to be significant. **CONCLUSIONS:** This modified and final translated version of instrument confirms the linguistic validity of the questionnaire for the Hindi language and evaluates the psychometric properties of the questionnaire for psychometric validation. Indian Hindi version of DQOL-M is valid and reliable instrument for measuring HRQOL of diabetic type 2 patients.

DIABETES/ENDOCRINE DISORDERS – Health Care Use & Policy Studies

PDB23

PHARMACEUTICAL COST ANALYSIS OF DIABETES MELLITUS USING CLINICAL RISK GROUPS IN VALENCIAN COMMUNITY

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OBJECTIVES: Metabolic agents have the highest expense (130 million Euros per year in the Valencian Community) among the top five therapeutic categories of drugs for adults aged 18 and over. Treatment of Diabetes Mellitus (DM) is the main cause of this. Moreover, diabetes is a chronic illness that requires continuous medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. Clinical Risk Groups (CRGs) are a tool claimed as valid for diabetes patient management. In this context we use this methodology to conduct a pharmaceutical cost analysis of diabetes in an Eastern Spanish region where the prevalence reaches approximately 8 %. **METHODS:** A database of 5,200,000 subjects was used to analyse the prevalence of patients with DM, comorbidity and complications. The patients with DM diagnoses were classified into CRGs to know their severity levels and pharmaceutical cost was also assigned. A multivariable statistical analysis was performed to evaluate the correlation and level of explanation between CRGs' severity level and pharmaceutical expenditure. **RESULTS:** Identified 300,698 patients with DM type 2 for a prevalence of 7.85% in men and 6.77% in women being the 13.2% and 7,98% in unders 50 years old, respectively. The 69,1% treated with orals hypoglycemics being combied therapy in over 75% of these. The use cosumption ratio glucometer strip, increaes with disease progression. It Was posible to identify the presence of complicactions in patiens analysed. A high correlation between pharmaceutical costs and CRG severity level was found. Comorbidity is a predictor for adjusting the risk of pharmaceutical expenditure. **CONCLUSIONS:** The model obtained could be a useful tool for managing pharmaceutical budget policies and patient management. The use of this measurement technique is useful for monitoring the health medical expense.

PDB25

INFLUENCE OF ONE WEEK EDUCATION PROGRAM ON THE KNOWLEDGE AND APPROACH OF PHARMACY STUDENTS TOWARDS DIABETES MELLITUS

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OBJECTIVES: To assess the improvement in knowledge and attitude of Pharmacy student towards diabetes by implementing one week education program. **METHODS:** Study was conducted between January 7, 2013 to January 11, 2013 which engaged pharmacy students comprising two groups: experimental and control groups. Lectures and visual presentations on diabetic education and practice were conducted. Three surveys were performed on two group's i.e. non intervened control, non- intervened experimental and intervened experimental surveys. Questionnaire was used as survey tool. **RESULTS:** Mean score on knowledge about diabetes was increased from 68.81% to 88.90% after educational intervention while that of control group was 74.75%. General knowledge of diabetes was increased from 66.37% to 89.90% while that of control was 69.28%. Risk factors knowledge was increased from 61.05% to 90.20% while that of control was 70.20%. Symptoms knowledge increased

from 80.70% to 95.58% while that of control was 88.56%. Therapeutic complications knowledge was increased from 71.58% to 88.57% while that of control was 78.82%. Medication knowledge of diabetes was increased from 80.26% to 83.67% while that of control was 74.51%. Lifestyle knowledge of diabetes was increased from 72.81% to 89.80% while that of control was 84.64%. Knowledge about preventions in diabetes was increased from 69.47% to 86.53% while that of control was 80.78%. Knowledge about diet was increased from 48.68% to 77.55% while that of control was 42.16%. Knowledge about monitoring diabetic conditions was increased from 84.21% to 92.35% while that of control was 86.27. Scores in all diabetic knowledge aspect was increased after education intervention and was significantly ($P<0.05$) different from that of control group. **CONCLUSIONS:** Institutions may ethically help in the reinforcement of student's knowledge by implementing such educational programs which may increase the educational skills, efficiency and confidence of pharmacy students as well as professionals.

PDB26

ACUTE EXPOSURE OF BISPHENOL-A FROM ELECTRONIC GADGETS DOES NOT INDUCE OXIDATIVE STRESS IN THE RAT BRAIN

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OBJECTIVES: To investigate the effects of BPA on oxidative damage in terms of activity level of antioxidant enzymes in different regions of the rat brain. **METHODS:** In this study, BPA migration was estimated through physio-chemical parameters and leachate (equivalent to 4mg/kg body weight) was used for animal dosing. Three groups of Albino Wister rats (190+20grm) were used for control, sham, and treated. The antioxidant enzymes including superoxide dismutase (Mn-SOD), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione level (GSH) were measured in different brain regions i.e. corpus striatum, frontal cortex, thalamus and midbrain. **RESULTS:** No significant changes were observed in most of the brain regions yet the level of GPx activity in corpus striatum (29.65±0.98 nmoles/min/mg protein) and level of GSH activity in frontal cortex (2.33±0.12 µmoles/g protein) was found to decrease significantly ($p<0.05$) when compared to controls. In addition, no significant effects were observed for the oxidative damage in brain regions of sham group when compared to control group. **CONCLUSIONS:** Thus study suggests that acute exposure (4mg/kg body weight per day up to 28 days) of BPA does not induce significant oxidative damage in the rat brain. Furthermore, study might re-examine before affirm the final remark for subscribers and regulatory bodies at similar doses.

GASTROINTESTINAL DISORDERS – Clinical Outcomes Studies

PGI1

COSTS OF PRIMARY BILIARY CIRRHOSIS TREATMENT WITH URSODEOXYCHOLIC ACID IN BRAZIL

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OBJECTIVES: To estimate the cost of treatment of primary biliary cirrhosis with ursodeoxycholic acid (UDCA) in Brazil and to evaluate the efficacy and safety of this treatment. **METHODS:** We considered the doses of 8, 12 and 15mg/Kg and a patient weighing 70Kg to estimate the cost of treatment. We used the maximum price to the producer in the CMED (Drug Market Regulation Chamber) list of 03/15/2013 with 18% of ICMS (Circulating Goods and Services Tax), and applied CAP (Adequacy Coefficient of Prices)of 25% . We used Purchasing Power Parity of 1,0USD=1,8BRL. To access efficacy and safety we searched the databases The Cochrane Library, CDR, Tripdatabase, MEDLINE and LILACS to identify systematic reviews (SR) of clinical trials that reported data on mortality, biochemical improvement measurements and adverse events. **RESULTS:** The estimated annual cost of treatment was USD2,239.24 with the dose of 8mg/Kg; USD3,168.97with the dose of 12mg/Kg; and UDS4,098.71 with the dose of 15mg/Kg. We included seven SRs; four evaluating UDCA versus placebo/observation; one UDCA versus colchicine; one UDCA versus methotrexate; and one UDCA versus bezafibrate. Generally, until four years of treatment there were no difference between UDCA and placebo/other interventions with respect with mortality, hepatic transplant incidence, worsening or arising of itching and fatigue, and incidence of hepatic complications. In the other hand there were improvements in surrogate outcomes like hepatic function markers, especially bilirubin. In all studies UDCA was well tolerated by patients. **CONCLUSIONS:** Improvements in the blood levels of hepatic markers did not match mortality rates or the incidence of transplant. The main symptoms of the disease, itching or fatigue, were not altered by the use of UDCA. There is a lack of evidence of studies evaluating quality of life of the patients, which perhaps could be improved by the use of UDCA. Besides, long observational studies could connect biochemical improvement and mortality rate.

GASTROINTESTINAL DISORDERS – Cost Studies

PGI2

COST-EFFECTIVENESS OF TELAPREVIR IN GENOTYPE 1 CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IN ARGENTINA

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OBJECTIVES: Direct acting antiviral therapies (DAA) in addition to PEG 2a + RBV (PR) are a new therapeutic option with higher rates of sustained virological response (SVR) than dual therapy (PR) alone in chronic hepatitis C. Currently, two alternatives of DAA, telaprevir (TVR) and boceprevir (BOC), are available in Argentina. The aim of this study was to evaluate the cost-effectiveness of adding TVR to PR in treatment naive and previously treated patients with HCV in Argentina compared to PR alone and with the addition of BOC. **METHODS:** A lifetime Markov model was developed including HCV, cirrhosis, liver transplant and death as health states. QALYs as an outcome measure, a private health subsector perspective and a 5% discount rate for health benefits and costs have been used. Costs are expressed in local currency. A review of the literature to obtain epidemiologic and resources utilization data was performed and when data were not available or validation was needed a Delphi panel with local experts was carried out. Deterministic and probabilistic sensitivity analysis was performed. **RESULTS:** In comparison with PR, TVR avoided 166 cirrhosis cases and 13 deaths per 1,000 patients and shown an ICER of $141,922/QALY and $74,332/QALY for the naïve and for the previously treated patients respectively. TVR presented extended dominance (lower ICER) against BOC in naïve patients and complete dominance (less costly and more efficacious) in most of the previously treated ones, except in the partial responders subgroup. Against the WHO criteria TVP versus PR presented a 42% of probability of being cost effective for naïve and 75% of probability of being cost effective for previously treated patients. **CONCLUSIONS:** TVR dominated BOC and its ICER against double therapy was slightly above WHO 3x GDP criteria in Argentina from a private subsector perspective.

PGI3

ANÁLISIS DE COSTO EFECTIVIDAD DE ACIDO GADOTERICO FRENTE A OTROS MEDIOS DE CONTRASTES BASADOS EN GADOLINIO

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OBJECTIVOS: Evaluar la costo efectividad del uso de ácido gadotérico en resonancia magnética para pacientes con insuficiencia renal crónica tipo 4 y 5, versus otros medios de contraste gadolínicos (gadopentetato de dimeglumina, gadoversetamida, gadodiamida, gadobutrol) analizando como desenlace la sobrevida del paciente que presenta como evento adverso Fibrosis Sistémica Nefrogénica (FSN). **METODOLOGÍAS:** La efectividad de medios de contraste ha sido evaluada en términos de seguridad. Al revisar la literatura se encontraron diferencias en la probabilidad de desarrollo (FSN) como principal complicación del uso de estos medios de contraste en pacientes con enfermedad renal avanzada, siendo letal en más del 56% de los casos. Mediante un modelo de árbol de decisión desde la perspectiva del tercero pagador se compararon los diferentes medios de contraste tomando como desenlace de análisis la sobrevida medida en años de vida ganados, para una esperanza de vida de 64,5 años y una edad promedio de 60 años, sobre las características del caso base. Los costos fueron obtenidos de precios de mercado de bases de datos de aseguradoras en pesos colombianos, 2012. El costo usado para las tecnologías fue el de la presentación 15 ml. **RESULTADOS:** No se encontraron reportes de casos de FSN con gadotérico o gadobutrol. El ácido gadotérico mostró un promedio de año de vida de 1,706 mejor que gadodiamida, gadopentetato de dimeglumina y gadoversetamida; y fue el menos costoso frente a todos los analizados (COP$ 132.000) seguido de Gadobutrol (COP$ 161.202) siendo dominante en todos los escenarios analizados. En el análisis tipo Montecarlo con variaciones de +/-50% mantiene su dominancia en el 95% de las iteraciones. **CONCLUSIONES:** El acido gadotérico es la opción más favorable por su dominancia dada por su menor costo, y mejor o igual efectividad frente a los demás comparadores, justificando con esta información su mayor preferencia en el uso.

PGI4

RULING OUT IBD IN THE UNITED KINGDOM AND BRAZIL: IS THE USAGE OF F-CALPROTECTIN IN PRIMARY CARE COST-EFFECTIVE?

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OBJECTIVES: The inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the gastrointestinal tract; the irritable bowel syndrome (IBS) is a functional disorder (prevalence 10%-20%). They present overlapping symptoms, making diagnosis difficult in primary care. Endoscopy is the gold standard for IBD, but it often turns negative due to IBD's low prevalence, it is expensive, uncomfortable and risky for the patient. F-Calprotectin is a marker of intestine inflammation: as IBD patients exhibit levels higher than the general population and IBS patients, F-Calprotectin can be used to rule out IBD. The only CE evaluation on F-Calprotectin has been published by NHS (CEP09041, 2010); based on new evidence, we propose a refined model to evaluate the CE of F-Calprotectin compared to the standard pre-endoscopic serologic test (CRP+ESR) to distinguish IBD from IBS in the UK and Brazil. **METHODS:** F-Calprotectin sensitivity (0.96) and specificity (0.96) were evaluated from a meta-analysis performed in March 2013; CRP+ESR sensitivity (0.35) and specificity (0.73), and the costs come from CEP09041. Published HRQoL values for IBD and IBS were transformed in QALYs with transfer-to-utility techniques. The outcomes included cost savings, cost per QALY. Uncertainty was addressed with a probabilistic sensitivity analysis. **RESULTS:** Results for UK show that F-Calprotectin is CE with respect to CRP+ESR: a) it results in more corrected IBD diagnoses at a lower price (it costs 113£ less per patient); b) it reduces the number of unnecessary endoscopies, increasing the number of correctly diagnosed IBD (N=59) and IBS (N=195) patients; c) it brings about a QALY gain per patient equal to 0.0034QALYs; the ICER of the CRP+ESR diagnostic strategy is 47,783£, and it falls well outside the cost-effectiveness bounds (20,000–30,000£ per additional QALY). Similar results were found for Brazil. **CONCLUSIONS:** F-Calprotectin is CE to rule out IBD in primary care in UK and Brazil.

PGI5

COST-EFFECTIVENESS OF TELAPREVIR IN GENOTYPE 1 CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IN CHILE

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OBJECTIVES: Direct acting antiviral therapies (DAA) in addition to PEG 2a + RBV (PR) are a new therapeutic option with higher rates of sustained virological response (SVR) than dual therapy (PR) alone in chronic hepatitis C. Currently, two alternatives of DAA, telaprevir (TVR) and boceprevir (BOC), are available in Chile. The aim of this study was to evaluate the cost-effectiveness of adding TVR to PR in treatment naive and previously treated patients with HCV in Chile compared to PR alone and with the addition of BOC. **METHODS:** A lifetime Markov model was developed including HCV, cirrhosis, liver transplant and death as health states. QALYs as an outcome measure, a health care system perspective and a 6% discount rate for health benefits and costs have been used. Costs are expressed in local currency. A review of the literature to obtain epidemiologic and resources utilization data was performed and when data were not available or validation was needed a Delphi panel with local experts was carried out. Deterministic and probabilistic sensitivity analysis was performed. **RESULTS:** In comparison with PR, TVR avoided 174 cirrhosis cases and 16 deaths per 1,000 patients and shown an ICER of $14,730,736/QALY and $8,300,511/QALY for the naïve and for the previously treated patients respectively. TVR dominated BOC in naïve patients and in most of the previously treated ones (was less costly and more efficacious), except in the partial responders subgroup. Against the WHO criteria TVP versus PR presented 80% of probability of being cost effective for naïve and 96% of probability of being cost effective for previously treated patients. **CONCLUSIONS:** TVR dominated BOC and was cost-effective against WHO 3x GDP criteria in comparison to double therapy from the national health care system perspective in Chile.

PGI6

ECONOMIC EVALUATION OF DIRECT ACTING ANTIVIRAL (DAA) TREATMENTS FOR HEPATITIS C VIRUS (HCV) INFECTION IN PREVIOUSLY TREATED PATIENTS FROM THE PERUVIAN HEALTH CARE SYSTEM PERSPECTIVE

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OBJECTIVES: DAA treatments in addition to Ribavirin (RBV) and peginterferon (Peg-INF) (PR), provides the greatest opportunity to fully achieve sustained virological response (SVR) in HCV infected patients. Currently, two alternatives of DAA, telaprevir (TVR) and boceprevir (BOC), are available in Peru. The objective of this study is to assess: which is the most efficient DAA treatment to compliment the PR in previously treated patients. **METHODS:** A Markov model was used from the payer perspective to estimate costs and benefits throughout the whole life. Transition probabilities, utilities and resources usage were obtained from literature and through a mixed treatment comparison. Only direct costs were considered as medications, laboratory tests, complications costs and adverse events by using tariffs and tender prices from EsSalud. Outcomes were measured as SVR, quality adjusted life years (QALY) and events of cirrhosis per 1,000 treated patients. Two alternatives were assessed: 1) 12 weeks of TVR plus PR and 2) 24-44 weeks of BOC plus PR. Discount rate 3% and exchange rate (1 USD = 2,6 S/). **RESULTS:** 1) *Total costs (USD)*: TVR plus PR ($56,058), BOC plus PR ($64,536). 2) *Medication costs (USD)*: TVR plus PR ($47,297), BOC plus PR ($54,649). 3) *SVR*: TVR plus PR (76%), BOC plus PR (60%). 4) *QALY*: TVR plus PR (6,02), BOC plus PR (5,87). 5) *Cirrhosis per 1,000 treated patients*: TVR plus PR (311), BOC plus PR (363). Incremental Cost Effectiveness Ratio (ICER) was negative, showing that 12 weeks of TVR plus PR is a dominant therapy. **CONCLUSIONS:** When a DAA is considered, in addition to PR, for previously treated patients, TVR is the preferred choice because of its potential cost-savings versus BOC and incremental health benefits versus BOC.

PGI7

COST-EFFECTIVENESS OF TELAPREVIR IN GENOTYPE 1 CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IN COLOMBIA

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OBJECTIVES: Direct acting antiviral therapies (DAA) in addition to PEG 2a + RBV (PR) are a new therapeutic option with higher rates of sustained virological response (SVR) than dual therapy (PR) alone in chronic hepatitis C (HCV). Currently, two alternatives of DAA, telaprevir (TVR) and boceprevir (BOC), are available in Colombia. The aim of this study was to evaluate the cost-effectiveness of adding TVR to PR in treatment naive and previously treated patients with HCV in Colombia compared to PR alone and with the addition of BOC. **METHODS:** A lifetime Markov model was developed including HCV, cirrhosis, liver transplant and death as health states. QALYs as an outcome measure, a health care system perspective and a 3% discount rate for health benefits and costs have been used. Costs are expressed in local currency. A review of the literature to obtain epidemiologic and resources utilization data was performed and when data were not available or validation was needed a Delphi panel with local experts was carried out. Deterministic and probabilistic sensitivity analysis was performed. **RESULTS:** In comparison with PR, TVR avoided 172 cirrhosis cases and 24 deaths per 1,000 patients and shown an ICER of $21,260,647/QALY and $8,461,107/QALY for the naïve and for the previously treated patients respectively. TVR dominated BOC in naïve patients and in most of the previously treated ones (was less costly and more efficacious), except in the partial responders subgroup. These results were robust in the sensitivity analysis. **CONCLUSIONS:** TVR dominated BOC and and was cost-effective against WHO 3x GDP criteria in comparison to PR from the national health care system perspective in Colombia.

GASTROINTESTINAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PGI8

QUALITY OF LIFE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE IN SLOVAKIA

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OBJECTIVES: The estimated prevalence of complicated gastroesophageal reflux disease (GERD) is approximately 2% in the European population and showing 10-fold increase over the past 20 years. The objective of this paper was to find out the level of QoL in patients with GERD in Slovakia. **METHODS:** The primary method used for the analysis of QoL was the presence of transient disability period and combined questionnaire consisting of 4 parts: A. Demography and socioeconomics (13 items), B. Generic questionnaire (SF-36), C. Visual scale (4 items), D. Complementary (information and habits, 13 items). The Likert scale was used in closed questions. The sample included 100 patients treated in the gastroenterological outpatient clinic (34 men and 66 women). Of these, 72 patients were in productive age. The patients were chosen according to the order in which they visited the clinic. **RESULTS:** One month and two months of sick days were recorded in 8.3% and 7% of patients, respectively; 84,7% of patients did not report any sick days. The loss of money of up to 400 € and between 401 and 800 € was recorded in 11.1% and 4.2 % of patients, respectively; 84.3 % of did not report any loss of money. Present level of QoL was identified as 5.12 on the scale of 10, while in the time of the GERD diagnosis it was 3.86. QoL was 8.25 in the time without GERD and 8.17 in optimal state of health, respectively. Future expectations were perceived as positive in 56% of patients and negative in 44% of patients. **CONCLUSIONS:** A total of 95% of patients were well and very well informed about its characteristics. Paradoxically, only 48% of them used their medications regularly, although regular and occasional administration of medications was shown to have positive impact on health status in 56% and 44% of patients, respectively.

GASTROINTESTINAL DISORDERS – Health Care Use & Policy Studies

PGI9

A LOW ANTIVIRAL TREATMENT RATE IN CHRONIC HEPTITIS C PATIENTS IN TAIWAN- A NATIONWIDE PHYSICIAN-BASED SURVEY

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OBJECTIVES: Hepatitis C virus (HCV) infection is the most common cause of liver cirrhosis and liver cancer worldwide. In addition to low disease awareness both in public and affected patients, a low disease treatment rate remains to be an important issue regarding disease control in primary care. The nationwide prevalence of anti-HCV seropositivity in Taiwan is 4.4%. However, there are scattered hyperendemic areas in Southern Taiwan with an extremely high prevalence rate reaches 57.9% high. Therefore, several public health strategies with periodic assessment aiming to promote liver health have been performed for two decades. **METHODS:** We aimed to elucidate the reasons of lower treatment rate in our country. In this hospital-based, physician-oriented study, a proportional sampling based on previous documented HCV prevalence of geographic locations in Taiwan was conducted. An anonymous questionnaire regarding treatment status in anti-HCV-positive patients was collected from these selected physicians. Patient's information including sex, age, anti-HCV therapy, and the reason for not receiving antiviral therapy was inquired by their primary care physicians. **RESULTS:** Seventy-six physicians were recruited into this survey (Medical center n=46; regional hospital n=23; primary clinic n=7). A total of 2,722 anti-HCV-positive subjects in Taiwan were enrolled into this analysis. Among them, 54.5% (1,479/2,722) had ever received anti-HCV treatment before. The treatment rate of medical centers was 63.1%, which was higher than 52.7% of regional hospitals, and 33.8% of primary clinics, respectively ($p<0.0001$ for pair-wise chi square test; $p<0.0001$ for trend test). Males had a significantly higher motivation for receiving antiviral therapy than females (58.6% vs. 50.5%, $p<0.0001$). The main reason for not receiving anti-HCV therapy was fear of side effects (38%), followed by ineligibility for insurance reimbursement (18%), and lack of awareness (11%). **CONCLUSIONS:** In Taiwan, half of the HCV-infected patients have not received antiviral therapy. The low treatment rate may contribute to HCV hyperendemic status.

MENTAL HEALTH – Clinical Outcomes Studies

PMH1

EVALUATION OF FACTORS AFFECTING TREATMENT RESPONSE AND RISK FACTORS FOR PATIENTS DIAGNOSED WITH NON-PSYCHOTIC MAJOR DEPRESSIVE DISORDER: A LITERATURE REVIEW

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OBJECTIVES: To conduct a systematic review of literature on factors that are affecting patient treatment response and risk factors for patients diagnosed with Non-Psychotic Major Depressive Disorder (MDD). **METHODS:** A literature search was performed using relevant search terms to identify articles published from 2000 to 2010 on the factors affecting treatment response and risk factors for MDD. Studies were identified through electronic Embase, Cochrane, Medline, and PubMed databases. Additional parameters were placed on the final search strategy to limit the retrieval to articles written in English, involving human subjects. **RESULTS:** The initial search revealed 874 articles for factors affecting treatment response and 590 articles for risk factors affecting MDD from PubMed/Medline/Embase/Cochrane databases. After removing duplicates and non-rele-

vant articles, the final articles that were considered for review were 82 for treatment response and 13 for risk factors. Fifty-one studies examined non-genetic factors, serotonin-related genetic factors and variety of genes and polymorphism biomarkers to determine their association with MDD treatment response. Thirty-one studies focused on variables that were found to be associated with some aspect of MDD and their impact on treatment response and include: comorbidity (n=12), demographic and socioeconomic (n=6), and depression-related (n=13) variables. Thirteen studies examined the risk factors for MDD. Of these, 2 studies focused on the role of biomarkers in MDD risk. And, 11 studies focused on variables that were found to be associated with some aspect of MDD and their impact on MDD risk, and focused on comorbidity (n=5), demographic and socioeconomic (n=2), depression-related (n=3), and environmental variables (n=1). **CONCLUSIONS:** The majority of the biomarker studies examined associations between the serotonin transporter, genes and polymorphisms in response to various MDD treatments. With respect to correlate studies, younger age of MDD onset, as well as family history of mood disorders, were both associated with a longer duration of MDD illness.

PMH2

LENGTH OF STAY AND OUTCOMES FOR ADOLESCENTS TREATED FOR SUBSTANCE USE DISORDER: AN ANALYSIS OF DOSE RESPOSE USING PROPENSITY SCORES

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OBJECTIVES: This research uses propensity score methods to identify the relationship between amount of treatment and treatment outcome for adolescents with psychoactive substance use disorder (PSUD). The objective is to describe the dose response relationship in terms relevant in economic evaluation. Outcomes studies in this population show that longer treatment leads to more positive outcomes. The standard for residential programs is a minimum of 21 days of treatment and ideally up to 90 days. **METHODS:** The subjects are 377 adolescents who successfully completed primary treatment from 2004-2010. All were placed at ASAM level III.5 (Clinically-Managed, Medium/High Intensity Residential). The data are from treatment records and a 234-item questionnaire. The questionnaire responses were matched to variables in treatment records creating a rich source of pre-treatment characteristics. This research operationalizes dose with four one-month categories (1 dose=1 month) to capture nonlinearities between service use and outcomes. The outcome is three-month post-treatment drug/alcohol abstinence. The categories were fairly even and captured 92% of variation in dose. The first stage of statistical analysis used multinomial logistic regression to predict dosage with pre-treatment variables while adjusting for characteristics influencing both dose and treatment outcome. Propensity scores were then created for each dosage category. The dose response relationship was assessed using a binomial logistic regression including the four dose categories as dummy variables (lowest dose category as reference). **RESULTS:** The overall relationship between dose and outcome was significant (p=0.01) as were outcome improvements over the four doses. Improvements were significant ($p \leq 0.01$) decreasing as dose increased—Exp.(B) was1.204 (1.2 times more likely to abstain) for one month, 1.532 two months, 1.643 three months, and 1.794 for four months (% correctly classified=94.2; – 2LL=44.712; Cox and Snell R^2=0.475.) **CONCLUSIONS:** This research shows a significant dose response relationship between treatment length and treatment outcome with response diminishing on the margin.

PMH3

CLINICAL OUTCOMES OF PATIENTS WITH MAJOR DEPRESSIVE DISORDER TREATED WITH EITHER DULOXETINE OR SELECTIVE SEROTONIN REUPTAKE INHIBITORS IN MEXICO

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OBJECTIVES: To compare treatment outcomes in patients with major depressive disorder (MDD) treated with either duloxetine or a selective serotonin reuptake inhibitor (SSRI) for up to 6 months in a naturalistic setting in Mexico. **METHODS:** Data in this *post hoc* analysis were taken from a 6-month prospective, non-interventional, observational study that included a total of 1,549 MDD patients without sexual dysfunction in twelve countries (N=591 in Mexico). Depression severity was measured using the Clinical Global Impression (CGI) and the 16-item Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR_{16}). Pain was measured using the pain related items of the Somatic Symptom Inventory (SSI), and quality of life (QoL) was measured using the EQ-5D instrument with the UK population tariff and the EQ-VAS. Probabilities of initiating duloxetine (vs. SSRIs), expressed as propensity scores, were first constructed using logistic regression. Mixed effects modelling with repeated measures (MMRM) analysis was then used to compare treatment effectiveness and QoL between the duloxetine (N=168) and SSRI (N=413) groups, controlling for the propensity scores and other patient characteristics. **RESULTS:** The severity of depression was comparable between the two groups at baseline. Duloxetine-treated patients, however, had a higher level of pain severity and a lower level of QoL (EQ-5D) than SSRI-treated patients at baseline ($p \leq 0.001$). Both descriptive and MMRM regression analyses showed that patients treated with duloxetine had better outcomes during follow-up, compared with patients treated with SSRIs. At 6 months, duloxetine-treated patients had lower levels of CGI (2.25 vs. 2.52, p=0.005), QIDS-SR_{16} (3.95 vs. 5.35, p<0.001), and SSI-pain related (8.52 vs. 9.64, p<0.001), and higher levels of EQ-5D (0.92 vs. 0.87, p<0.001) and EQ-VAS (64.62 vs. 57.63, p=0.006) (MMRM results). **CONCLUSIONS:** Duloxetine-treated patients had better 6-months outcomes in terms of depression severity, pain and QoL, compared with SSRI-treated patients.

PMH4

A COMPREHENSIVE REVIEW OF EPIDEMIOLOGY AND ECONOMIC STUDIES FOR PATIENTS DIAGNOSED WITH NON-PSYCHOTIC MAJOR DEPRESSIVE DISORDER

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OBJECTIVES: To conduct a systematic review of literature in on epidemiology and economic studies for patients diagnosed with Non-Psychotic Major Depressive Disorder (MDD). **METHODS:** The initial search strategy was developed in the PubMed/Medline database, and was then translated for the Cochrane and Embase database searches. Search strings for epidemiology and economics studies for MDD were constructed using varied approaches that included the use of MeSH terms, as well as keywords that would afford the best retrieval. Search statements were then combined to produce a final search set. Additional parameters were placed on the final search strategy to limit the retrieval to articles written in English, involving human subjects and published between 2000 and 2010. **RESULTS:** Our search revealed 289 articles for epidemiology and 200 articles for economic studies on MDD from PubMed/Medline/Embase/Cochrane databases. After removing duplicates and non-relevant articles, 17 for epidemiology and 26 for economic studies were included in the final analysis. Fifteen studies on epidemiology were focused on MDD prevalence, one study was on cumulative incidence. Prevalence estimates were higher for lifetime than past year and ranged between 3.1% and 26.6% for lifetime prevalence and between 1.5% and 11.7% for past-year prevalence. Two studies examined burden of illness, one study budgetary impact of MDD, 14 studies examined cost effectiveness of MDD treatments, 3 studies examined cost utility analysis and 6 other studies examined retrospective claims analysis. **CONCLUSIONS:** MDD prevalence was higher in the lifetime estimates, when compared to the estimates reflecting shorter time frames, although there appeared to be greater variability in the lifetime estimates. Overall, the cost of treating MDD varied with type of study, study time frame, study perspective, the year in which the costs were calculated, and the pharmacotherapy prescribed.

PMH5

EVALUATION OF ASSOCIATIONS AMONG BIOMARKERS, CORRELATES AND TREATMENT EFFICACY IN CLINICAL STUDIES IN PATIENTS DIAGNOSED WITH NON-PSYCHOTIC MAJOR DEPRESSIVE DISORDER: A LITERATURE REVIEW

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OBJECTIVES: To perform a systematic review of literature in peer-reviewed journals on clinical biomarkers, correlates and treatment efficacy in clinical studies on patients diagnosed with Non-Psychotic Major Depressive Disorder (MDD). **METHODS:** The initial search strategy was developed in the PubMed/Medline database and was then translated for the Cochrane and Embase database searches. Search strings for biomarkers, correlates and treatment efficacy in patients with MDD were constructed using varied approaches that included the use of MeSH terms, as well as keywords that would afford the best retrieval. Also included were search terms that used an asterisk as a wildcard applied to a word stem. Search statements were then combined to produce a final search set. Additional parameters were placed on the final search strategy to limit the retrieval to articles written in English, involving human subjects and published between 2000 and 2010. **RESULTS:** The initial search revealed 871 articles from PubMed/Medline/Embase/Cochrane databases. After removing duplicates and non-relevant articles, the final articles that were included in the review were 131. Forty-eight studies examined biomarkers and primarily focused on the relationship between biomarkers and MDD treatment response. Only 29 of the 48 studies found a significant association between a biomarker and treatment response. Twenty-nine studies examined MDD correlates such as comorbidity or demographic variables. A poorer response to treatment was found for those patients who experienced comorbid anxiety, irrespective of the type of treatment. Fifty-four studies focused on treatment efficacy and are divided into 3 groups: SSRIs only, SNRIs only, and a comparison across SSRIs, SNRIs, and bupropion. Overall, the SSRIs showed comparable efficacy when compared to each other or placebo. **CONCLUSIONS:** Most of the biomarker studies examined associations between the serotonin transporter and response to various MDD treatments. The majority of efficacy studies found that the treatments that are within the class had comparable efficacy.

MENTAL HEALTH – Cost Studies

PMH6

THE IMPACT OF ANTIPSYCHOTICS POLYPHARMACY ON HEALTH CARE COSTS OF PEOPLE WITH MENTAL DISORDERS IN SÃO PAULO CITY, BRAZIL

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OBJECTIVES: Antipsychotics polypharmacy (AP) has been associated with more adverse drug effects, higher treatment costs, worse clinical outcomes and sudden death. Though, the frequency of such practice may reach 50 % in some clinical settings. The aims of this study were to estimate AP costs and its influence on the direct costs of health care package in a sample of people with mental disorders in São Paulo city, Brazil. **METHODS:** We used a bottom-up approach for the estimation of direct costs according to public health service provider perspective. Direct costs included costs with accomodation (residential service), inpatient, outpatient and emergency services and treatment received in the previous month, in 147 subjects with mental disorders living in twenty residential services during the year 2011. We evaluated quality of life, social behavior problems, psychiatric diagnosis, severity of symptoms, sociodemographics characteristics and pattern of health service use. **RESULTS:** AP was found in 38% of the sample and it was not related with gender, age, severity of psychiatric symptoms, quality of life and social behavior problems. Antipsychotics monotherapy costs were related with the type of antipsychotic: Atypical antipsychot-

ics costs were 167.4 times higher than typical antipsychotic costs. AP mean monthly costs per person varied with the type of association between antipsychotics: typical-atypical associations costs were U$257.5± U$228.5, while mean costs between two typical antipsychotics were U$4.36 ± U$4.02. Polypharmacy added U$300.00 dolars per person per month to direct costs of health care (excluding accomodation). For each additional antipsychotic associated, it was observed an additional montlhy costs per person of U$87.5 in the total costs of health care package (health services, treatment and accomodation). **CONCLUSIONS:** AP added substantial costs and risks to treatment and to health care costs and quality. This should be taken in account in resource allocation in public policies, especially in low-resources settings.

PMH7

MODELIZACIÓN ECONÓMICA DEL GENOTIPADO DEL CITOCROMO P450 CON EL TEST BRAINCHIP EN EL TRATAMIENTO DE LA DEPRESIÓN MAYOR

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OBJECTIVOS: BrainChip es un test genético que predice la respuesta al tratamiento farmacológico de la depresión mayor (DM) determinando los polimorfismos de las isoenzimas CYP450. El objetivo ha sido valorar la eficienciade la incorporación del test BrainChip previa a la prescripción farmacológica en DM tras fallo en primera línea. **METODOLOGÍAS:** Se desarrolló un modelo de Markov de ciclos bimensuales para cada fármacode una cohorte hipotética depacientes adultos con DM tras fallo en primera línea. La cohorte se adecuó a la distribución del mercado actual y a su modificación tras incorporar BrainChip. Los datos de eficacia (no respuesta, respuesta y remisión) provienen de revisiones de la literatura y el uso de recursos y costes fue adaptado para el análisis inicial a España. Se analizaron los resultados en un horizonte temporal de 1, 3, 5, 7 y 10 años desde la perspectiva del sistema sanitario aplicando un descuento del 3% sobre los efectos y los costes (euros 2011). **RESULTADOS:** BrainChip mejora la remisión entre un 9,5%-11,7% y la respuesta entre 5,5%-10,2%, alcanzando a los 10 años una respuesta del 72%. Los pacientes con DM mejoran la calidad de vida con BrainChip entre 0,04 y 0,25 años de vida ajustados por calidad. El coste de Brainchip se compensa a los 2 años resultando siempre coste-efectivo a corto plazo y dominante a partir del tercer año, mostrando ahorros de 1399€/paciente tras 10 años. **CONCLUSIONES:** BrainChip en DM es dominante, permite prescribir los tratamientos con menos riesgos y costes y más eficacia. El modelo desarrollado permitiría la adaptación del análisis a cualquier país de Latinoamérica utilizando datos de costos locales.

PMH8

COST EFFECTIVENESS OF PALIPERIDONE PALMITATE VERSUS RISPERIDONE LONG-ACTING INJECTABLE, QUETIAPINE AND OLANZAPINE FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA IN COLOMBIA

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OBJECTIVES: Schizophrenia is a chronic disorder that requires long-term treatment with antipsychotic medication to minimize relapse and provide clinical benefit to patients. For patients with schizophrenia, non-adherence to medication is a risk factor for relapse and re-hospitalization. Long-acting Injectable (LAI) formulations of atypical antipsychotics provide constant medication delivery and the potential for improved adherence. The objective of this study is to assess the cost-effectiveness of paliperidone palmitate (PP) versus risperidone long acting injectable (RLAI), olanzapine (OP) and quetiapine (QP). **METHODS:** A Markov decision analytic model was developed to simulate multi-episode patients transitioning through different states on monthly basis over a 5 year time horizon from the perspective of the Colombian Health System. Probability of relapse, level of adherence, side effects, utilities and treatment discontinuation were derived from scientific literature. Only direct costs were considered as medications, laboratory tests, relapses and adverse events by using national tariffs and prices from Ministry of Health medication database. Outcomes were measured as relapses rate and Quality Adjusted Life Years (QALY). Discount rate 3%, exchange rate (1 USD = 1,794 COP) and threshold considered 3xPIB per capita (USD 20,066 / QALY). **RESULTS:** *Total costs (USD):* PP (13,338), RLAI (12,635), OP (11,481) and QP (13,247). *Hospitalization relapses costs (USD):* PP (3,276), RLAI (3,341), OP (4,881) and QP (6,840). *QALY:* PP (3.09), RLAI (3.00), OP (2.93) and QP (2.87). *Relapses rate:* PP (1.35), RLAI (1.38), OP (2.01) and QP (2.81). *Incremental Cost Utility Ratios (ICUR: USD / QALY):* PP vs. RLAI (4,517), PP vs. OP (6,713) and PP vs. QP (230). **CONCLUSIONS:** Considering a willingness to pay of USD 20,066 per QALY, the incremental cost of PP versus other alternatives could be compensated by its incremental benefits in terms of relapses avoided and QALY gained. From Health Care Provider perspective, PP demonstrates savings in terms of less hospital setting relapsing costs.

PMH9

THE COST-EFFECTIVENESS AND COST-UTILITY OF PALIPERIDONE PALMITATE IN THE TREATMENT OF SCHIZOPHRENIA IN GUATEMALA

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OBJECTIVES: To compare from the Guatemaltecan third payer perspective the cost-effectiveness of paliperidone palmitate with oral quetiapine. **METHODS:** A Markov model was developed to assess the cost-effectiveness and the cost-utility of treatments available for schizophrenia in Guatemala. The model was adjusted to reflect the compliance of the patient and the real world effectiveness of both treatments. A 10 year time horizon was used. All direct medical costs relevant for the third payer were included. Four types of side effects were considered in the model: extrapyramidal symptoms, weight gain, diabetes and tardive dyskinesia. Deterministic and probabilistic sensitivity analyses were performed. **RESULTS:** Effectiveness outcomes were reported both in QALYs and relapses avoided. The costs were reported in the local currency Quetzales and all cost and outcomes were discounted at 5% per year. Paliperidone palmitate dominated oral quetiapine by being less expensive (14% less) and more effective (44% less relapses and 20% more QALYs). The sensitive analyses confirmed the robustness of the results. **CONCLUSIONS:** Paliperidone palmitate appeared to be a cost-saving treatment option in comparison with oral quetiapine for patients with schizophrenia in Guatemala. The model reflected a better compliance with paliperidone palmitate that is related to less relapses, a better quality of life and reduced hospitalization costs.

MENTAL HEALTH – Patient-Reported Outcomes & Patient Preference Studies

PMH10

NEEDS ASSESSMENT OF PATIENTS TREATED IN COMMUNITY PSYCHOSOCIAL CENTERS IN SÃO PAULO, BRAZIL

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OBJECTIVES: To describe the needs of patients treated at community psychosocial centers in Sao Paulo, Brazil. **METHODS:** Cross-sectional study with 373 patients who were attending psychosocial care activities at least three times per week in community psychosocial centers, during 2007-2008. Needs were assessed using the "Camberwell Assessment of Need" (CAN). Psychotic symptoms were assessed using the "Positive and Negative Symptom Schedule" (PANSS). **RESULTS:** Mean age of patients was 40.0 years (standard deviation, SD = 12.6 years); 57.6% were male, 57.9% had fundamental education, 40.5% have schizophrenia, 15.9% have worked during last 12 months and 14.7% were living alone. Median time attending in community psychosocial centers was two years (range of 15 days to 30 years) and mean number of weekly therapeutic activities was 3.6 (SD = 2.3). The mean score for the total number of needs was 7.1 (SD = 2.8), with a range of 0 to 15 (maximum = 22). Basic needs were reported by 38 (10.2%) patients; at least one social need was reported by 90.9%. At least one functioning need was reported by 94.4% patients; 85.5% have at least one health need; 86.3% have at least one service need. Women showed higher number of needs than men ($p = 0.02$) and educational until fundamental level was also associated with more needs ($p = 0.02$). We did not observe associations between weekly activities, unemployment, age, diagnosis and number of needs. Patients with higher PANSS scores showed more needs ($p < 0.001$). **CONCLUSIONS:** We observed higher number of needs than in studies conducted in Europe, in all conceptual domains assessed by CAN. Many patients showed needs related to health and services, despite the time that they were attending in community psychosocial centers. Patients' needs should take in account in order to improve the quality of care offered in mental health services.

MENTAL HEALTH – Health Care Use & Policy Studies

PMH11

CLINICAL PRACTICE GUIDELINE MAJOR DEPRESSIVE DISORDER FOR GENERAL PRACTITIONERS

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OBJECTIVES: To develop the clinical practice guideline major depressive disorder for general practitioners in primary and secondary health care setting included the diagnosis, differential diagnosis, severity classification and medical treatments. **METHODS:** A list of 13 key elements of a CPG development process were developed that consisted of 1) setting the review teams; 2) determining the problems; 3) determining health outcomes;4) evidence based literature review; 5) meeting to draft the CPG; 6) formulating draft of CPG; 7) apprising the content of CPG by experts; 8) trail phase; 9) evaluating for trail phase; 10) developing the curricular for CPG training; 11) preparing for CPG training; 12) evaluating; and 13) improving the CPG related with evaluated results. **RESULTS:** There were 3 main processes in clinical practice guideline major depressive disorder for general practitioners in primary and secondary health care setting (CPG-MDD-GP) which were 1) Assessment of major depressive disorder (clinical assessment using 9Q screening tool and DSM-TR diagnostic criteria, differential diagnosis, diagnosis for major depressive disorder and coding of diagnosis); 2) Management of major depressive disorder; and 3) Management of hospitalized patients. General practitioners were satisfied with the CPG-MDD-GP in trial phase. A total of 416 general practitioners in all provinces were trained to use the CPG-MDD-GP then they would be followed and evaluated. Psychiatrists in psychiatric hospitals/ institutes would be available for consultation from the general practitioners. **CONCLUSIONS:** The CPG-MDD-GP should be distributed to all general practitioners in primary and secondary health care setting. Next step, it would be useful for developing the CPG for MDD in the tertiary health care setting.

PMH12

CONTRIBUTION OF LATIN AMERICA TO MENTAL HEALTH IN PREGNANCY

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OBJECTIVES: To identify and describe published articles dealing with issues of mental health in pregnancy from Latin American counties **METHODS:** Medline, Embase and LILACS databases were searched for published studies originating from Latin America regarding mental health issues in pregnancy. Search terms included the names of all countries in the United States Census Bureau International Database + mental health + pregnancy. We included all research and review articles dealing with pregnancy and/or lactation, epidemiology of mental disorders, prevention or treatment of mental disorders, outcomes assessment, and counseling/drug information dissemination. Excluded were papers dealing exlusively with postpartum depression, HIV transmission, induction of abortion, in vitro fertilization, contraception or the use of alcohol or drugs of abuse. Data were analyzed descriptively. **RESULTS:** The search identified 701 studies; 110 (16%) met the criteria. The earliest was published in 1984 and the contribution has increased exponentially [Y=-1E-125*exp(0.1452X), where X is the year; R-squared=0.97). The majority (n=80; 73%) consisted of original research and the other 27% were reviews (23 overviews, 3 systematic reviews/meta-analyses, 4 other). Most frequent topics were depression (37%) as well as mixed anxiety/depression (6%), mental health during pregnancy (32%;), psychotropic drug use in pregnancy (13%), suicidality (6%), and quality of life (1%). By country, 58 (53%) were produced by Brazil, followed by Mexico (n=18, 17%), Chile (n=10, 9%), Colombia

(n=9, 8%), Peru (n=5, 5%), Argentina and Ecuador (each with 3, 3%), and one each from Costa Rica, Paraguay, and Venezuela. Contributions were positively correlated with the size of the population (Spearman's rho=0.76, P=0.03). **CONCLUSIONS:** Latin America has begun to make a small but significant contribution to the literature, However, more than 50% were from Brazil, so other countries will benefit from further research, addressing their unique social and economic needs regarding mental health in pregnancy.

PMH14

STANDARDIZED TOOL FOR MEASUREMENT OF HEALTH SERVICES COSTS AND UTILIZATION IN A SAMPLE WITH MENTAL DISORDERS: TRANSLATION, CULTURAL ADAPTATION AND INTERRATER RELIABILITY OF THE CLIENT SOCIODEMOGRAFIC AND SERVICE RECEIPT INVENTORY BRAZILIAN VERSION

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OBJECTIVES: Information on health service utilization and costs is scarce in the mental health. The *Client Socio demographic and Service Receipt Inventory (CSSRI)*, developed by Knapp and Chisholm, has been widely used for the measurement of health care costs including mental health services. The aims of this study were the translation, cultural adaptation and feasibility and the interrater reliability of the Brazilian version of the CSSRI. **METHODS:** CSSRI was translated to Portuguese (Inventário Sociodemografico de Utilização e Custos de Serviços ISDUCS) by mental health researchers. Structure and cultural adaptations were made according to the Brazilian public health system. Two independent researchers applied it in a sample of 30 subjects with mental disorders living in residential services in São Paulo city, Brazil. **RESULTS:** The ISDUCS was consisted by six sections and one additional annex covering data on: Sociodemographic information; accommodation, employment and income, medication and services use. Application lasted from twenty to sixty minutes. The sample had 50 years on average, with 60% females, with 18% illiterates, 51.6 % primary education, with length of psychiatric hospitalization of 10 years on average, 45% had severe psychiatric symptoms, 20% had moderate symptoms and 35% mild symptoms. Subjects had difficulties to answer the following questions: 24.4%, did not know about his/her education level, 76.7% did not know about the name of the medication in regular use, 58.8% did not know about visit to health professionals in the previous month, 36.4% did not know about receiving their benefits. Interrater reliability was calculated using kappa coefficient, varying from 0.8 to 1.0 for all items, showing excellent reliability. **CONCLUSIONS:** ISDUCS was feasible and reliable to be applied in Brazilian mental health settings. Additional sources like medical records and carers information were necessary to collect all data probably due to low education and severity of psychiatric symptoms of this sample.

SENSORY SYSTEMS DISORDERS – Clinical Outcomes Studies

PSS1

EFECTIVIDAD Y COSTO-EFECTIVIDAD DE LA FLUORACIÓN DEL AGUA EN LA PREVENCIÓN DE CARIES DENTAL

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OBJECTIVOS: Determinar si la fluoración del agua a concentraciones de 0,6 a 1 ppm es más efectiva y costo-efectiva que la no fluoración del agua en la prevención de la caries dental. **METODOLOGÍAS:** Se realizó una revisión sistemática de la literatura en MEDLINE, EMBASE, COCHRANE, SCIELO, LILACS, CRD database, BBO, PAHO y WHOLIS, limitada desde el 2002 al 2012. Se incluyeron meta-análisis, revisiones sistemáticas, cohortes, casos y controles, estudios económicos y corte transversal con al menos dos poblaciones comparadas. Dos investigadores de forma independiente realizaron una evaluación de la calidad de los artículos seleccionados y que cumplieron los criterios de inclusión. **RESULTADOS:** La búsqueda arrojó 468 artículos de los cuales 27 cumplieron los criterios de inclusión y 8 fueron incluidos como evidencia para evaluar la efectividad, y 4 para evaluar costo efectividad. Se concluye una reducción del riesgo de caries del 15.4 % (95% CI 10.8%, 20.1%) p<0.001 en población infantil y adolescente, y de un 34.6% (95%CI: 12.6%-51.0%) p<0.001 en población adulta de acuerdo a las revisiones sistemáticas incluidas. Todos los estudios incluidos concluyen que la fluoración del agua es altamente costo-efectiva, con Indices de Costo-efectividad bajos, aun cuando la medida de resultado es dimensionada en formas distintas (Daly, Qaly, dólares ahorrados). **CONCLUSIONES:** Existe evidencia tipo I que la fluoración del agua potable, a concentraciones de 0,6 a 1 ppm, es más efectiva y costo efectiva que la no fluoración del agua en la prevención de la caries dental.

SENSORY SYSTEMS DISORDERS – Cost Studies

PSS2

A COST–EFFECTIVENESS AND BUDGET IMPACT ANALYSIS OF DIFFERENT BIOLOGIC TREATMENTS FOR PSORIASIS IN COLOMBIA

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OBJECTIVES: There are three subcutaneous biologic therapies approved for psoriasis in Colombia: ustekinumab, etanercept and adalimumab. A network meta-analysis demonstrates a better incremental efficacy of ustekinumab versus the other two alternatives. However, considering that the medication cost is higher for ustekinumab, this analysis evaluates the cost-effectiveness and budget impact of the three alternatives assuming the Colombian Health System perspective. **METHODS:** A decision tree was designed from the payer perspective to estimate costs and benefits for one year time horizon. Clinical data were obtained from a network meta-analysis in order to model treatment response and second line treatment progression. Benefits were measured as probability of achieving a PASI 50 response at the end of 12 weeks of treatment. Only direct costs were considered using national tariffs and prices from Ministry of Health medication database. For budget impact analysys a target population of 550 patients is estimated and three scenarios of ustekinumab adoption were assessed: current scenario (13% market share), middle penetration scenario (28% market share) and a high penetration scenario (50% of market share). No discount rate was used. Exchange rate (1 USD = 1,794 COP). **RESULTS:** *Total cost per patient (USD)*: ustekinumab (23,229), etanercept (25,079) and adalimumab (23,825). *PASI 50 response (% of patients)*: ustekinumab (90%), etanercept (76%) and adalimumab (81%). *Cost per responder patient*: ustekinumab (25,810), etanercept (32,999) and adalimumab (29414). *Budget Impact* (USD): current scenario (13,387,999), middle penetration scenario (13,262,955) and high penetration scenario (13,114,969). **CONCLUSIONS:** When a subcutaneous biologic is considered as the first line choice of treatment for psoriasis, ustekinumab is the prefered first line therapy. Ustekinumab progressive adoption, in the Colombian Health System, demonstrates potential savings driven by its better efficacy and less probability of requiring a second line more expensive treatment.

PSS3

THE DIRECT COSTS OF DRUG-INDUCED SKIN REACTIONS IN POLAND

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OBJECTIVES: Drug-induced skin reactions (DISR) may be a serious medical problem, and economical in every country. **METHODS:** The aim of the study was to analyze the direct costs (costs of medication, laboratory costs, costs of physician visits) of 164 patients (57M, 107 W, mean age 53.7years) hospitalized in the Department of Dermatology, Military Institute of Medicine, Poland between 2002 - 2012 due to DISR from the public payer (NHF) and hospital perspective. **RESULTS:** In the group of the most common forms of DISR there were toxic - allergic dermatitis (n=85) and erythema multiforme (n=41). The most common cause of drug-induced skin reactions were beta lactam antibiotics, cephalosporins and NSAIDs. Symptoms of DISR appeared on an average after 7.4 days of treatment. The average hospital stay was 4.54 day per patient. Direct average cost of treatment from the NHF perspective was 717€ per patient and from the hospital perspective was 680 € per patient. **CONCLUSIONS:** Treatment of DISR is expensive, but well priced by the public payer in Poland.

PSS4

EVALUACIÓN DE COSTO-EFECTIVIDAD DE LA TRABECULOPLASTIA LÁSER SELECTIVA COMO PRIMERA OPCIÓN DE TRATAMIENTO EN GLAUCOMA PRIMARIO DE ÁNGULO ABIERTO EN COLOMBIA

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OBJECTIVOS: Evaluar la costo-efectividad de la Trabeculoplastia Láser Selectiva (TLS), como primera opción de tratamiento del Glaucoma Primario de Ángulo Abierto (GPAA) sin manejo previo versus el tratamiento médico con latanoprost, desde el punto de vista del tercero pagador en Colombia. **METODOLOGÍAS:** Se diseñó un modelo de Markov en ciclos bimestrales que simuló una cohorte hipotética de 100 pacientes adultos, con GPAA recientemente diagnosticados y que inician tratamiento ya sea con TLS o latanoprost (agonista de la prostaglandina), en un horizonte temporal de cinco años, con variaciones de +/-20% en las variables. Con este modelo se evaluó el tiempo libre de enfermedad medido en años. Se utilizaron probabilidades variables en el tiempo, del estudio cabeza-a-cabeza de Katz 2012. Los costos directos de salud fueron estimados con información de dos aseguradoras de Colombia. Se asumió una tasa de abandono del tratamiento médico referidas por Iskedjian 2011. Se aplicó una tasa de descuento del 3% a costos y desenlaces. Finalmente, se realizó un análisis de sensibilidad univariado y multivariado tipo Montecarlo. Se estimó que el fallo de primera línea en cualquiera de los dos brazos sería de COP$ 810.596 (umbral propuesto). **RESULTADOS:** El uso de TLS como primera línea de tratamiento mostró la mayor efectividad (286,9 años) frente a latonoprost (98,3 años) en los 100 pacientes. Al aplicar el descuento la razón de costo-efectividad incremental fue de $391.122,24 por año libre de enferemedad ganado. El analisis tipo montecarlo mostró que TLS se mantiene costo-efectiva en el 100% de los casos. **CONCLUSIONES:** El uso de TLS mostró ser muy costo efectivo frente al uso de latanoprost en las condiciones del caso base y el umbral propuesto. Teniendo en cuenta que el costo de la TLS se aplica al inicio del tratamiento, resulta conveniente estimar el impacto presupuestario para apoyar la toma de decisión.

PSS5

COSTO-EFECTIVIDAD DEL SCREENING Y TRATAMIENTO DE HIPOACUSIA BILATERAL EN RECIÉN NACIDOS (RN) EN CHILE

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OBJECTIVOS: El objetivo principal es determinar la costo-efectividad incremental de pasar de una estrategia selectiva (RN prematuros) de screening y tratamiento oportuno de hipoacusia bilateral congénita a una estrategia de screening universal. **METODOLOGÍAS:** El análisis se realizó desde la perspectiva del sector público y consideró como horizonte temporal la sobrevida de una cohorte de RN. La información epidemiológica se obtuvo de fuentes oficiales del Minsal, literatura y de una encuesta realizada a expertos. La precisión de los test diagnósticos se obtuvo de la literatura y la caracterización del proceso de *screening* de las Guías Clínicas nacionales. La efectividad de los tratamientos de amplificación se obtuvo por consulta a expertos. Para la medición de beneficios se determinaron *outcomes* intermedios (caso pesquisado) y *outcomes* finales (QALY). Para el análisis de la información se utilizó un modelo de árbol de decisión. Se realizaron análisis de sensibilidad determinístico (ASD) univariado y análisis de sensibilidad probabilístico (ASP) considerando los principales parámetros. **RESULTADOS:** Los costos totales por RN de la estrategia de *screening* selectivo fueron de $26.486,4 (pesos chilenos) y para la estrategia universal de $32.620,5, en tanto que la efectividad en QALY fue de 30,0523 y de 30,0708, respectivamente, obteniéndose un ICER $331.368,22. El costo por caso extra de hipoacusia bilateral congénita detectado precozmente al pasar de una estrategia a otra es de

$4.215.913 (US$8.875,61). **CONCLUSIONES:** El pasar de la estrategia selectiva focalizada en RN prematuro a una estrategia universal resulta costo-efectivo. Este resultado no se modificó con la variación de parámetros con incertidumbre asociada en los ASD y ASP. Con una disposición a pagar de $6,97 millones (PIB per cápita Chileno) la probabilidad de que la ampliación a una estrategia universal de tamizaje resulte costo-efectiva es de un 99,3%.

PSS6

ANÁLISIS DE MINIMIZACIÓN DE COSTOS DEL USO DEL AFLIBERCEPT EN DEGENERACION MACULAR RELACIONADA CON LA EDAD EN COLOMBIA

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OBJECTIVOS: Hacer una evaluación económica del uso de aflibercept versus ranibizumab para el tratamiento de la Degeneracion Macular Relaciona con la Edad de tipo exudativa, desde el punto de vista del tercero pagador en Colombia. **METODOLOGÍAS:** Se hizo un análisis de minimización de costos partiendo de una revisión de literatura que analizó la efectividad y seguridad entre las tecnologías. Se diseñó un modelo de árbol de decisiones basados en la historia natural de la enfermedad y el modelo de atención, incluyendo las dosis en cada una de las tecnologías y otros costos directos de atención, en un horizonte temporal de dos años. Los costos fueron obtenidos de del Sistema de Información de Precios en Medicamentos (SISMED) y de los Registros Individuales de la Prestación de Servicios de Salud (RIPs) expresados en dólares de 2012. Se efectuó un análisis de sensibilidad univariado en una sola vía, modificando la dosis estándar a dosis a demanda, como sugiere el estudio de Rosenfeld et al., 2006. **RESULTADOS:** Estudios cabeza a cabeza encontrados (VIEW1 y VIEW2) no mostraron diferencias significativas en términos de seguridad y efectividad, medida como ganancia en letras; aunque aflibercept demostró un 33,4% de ganancia frente al 31,6% de ranibizumab. El modelo en un paciente promedio mostró que el uso de aflibercept generaría un ahorro de US$11.468,78 a los 2 años. El análisis de sensibilidad del modelo a demanda muestra que aflibercept se mantiene ahorrativo frente a ranibizumab. **CONCLUSIONES:** No se encuentraron diferencias de efectividad entre las tecnologías evaluadas; sin embargo, aflibercept se mostró como la tecnología ahorrativa en el tratamiento de la Degeneracion Macular Relaciona con la Edad exudativa, desde el punto de vista del tercero pagador en Colombia. El menor número de dosis requeridas en el tratamiento con aflibercept podría generar adherencia que asegure mayor efectividad.

PSS7

EVALUACIÓN ECONÓMICA DEL USO DE DOS TRATAMIENTOS FARMACOLÓGICOS EN DEGENERACIÓN MACULAR RELACIONADA CON LA EDAD DE TIPO EXUDATIVA (DMRE) PARA VENEZUELA

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OBJECTIVOS: Estimar mediante un modelo de minimización de costos, el precio máximo al que sería favorable la inclusión dentro del sistema de salud venezolano el uso de aflibercept como tratamiento de la DMRE de tipo exudativa. **METODOLOGÍAS:** La revisión de la literatura no mostró diferencias en cuanto a efectividad y seguridad entre al aflibercept y el ranibizumab en los estudios cabeza a cabeza (VIEW1, VIEW2). Por lo que mediante un análisis de minimización de costos basado en el modelo de atención de la enfermedad y en un horizonte temporal de dos años se estimó a las dosis utilizadas en el estudio clínico el precio máximo a que podría ingresar el aflibercept al mercado tomando como referencia el precio de ranibizumab de $VEF 4.640,83, los costos de atención y del medicamento fueron tomados de información proveniente de aseguradores en Bolívares fuertes. Se efectuó un análisis de sensibilidad univariado en una sola vía, modificando a dosis por demanda, como lo sugiere el estudio de Rosenfeld PJ y colaboradores. **RESULTADOS:** El estudio clínico muestra mejor resultado para aflibercept pero las diferencias no son significativas. El análisis económico arrojó como costo máximo por dosis de Aflibercept, un valor de $VEF 10.598,46; un valor inferior al anterior generaría un ahorro al sistema de salud venezolano. El análisis de sensibilidad univariado en una sola vía al utilizarlos por demanda determinó que Aflibercept se mantendría como tecnología ahorrativa a un precio de $VEF 7.201,13. **CONCLUSIONES:** Aflibercept sería una opción favorable al sistema de salud, por cuanto genera menos dosis de aplicación facilitando una mayor adherencia y sería ahorrativo en el tratamiento de la DMRE exudativa para Venezuela sí su costo en el mercado se encuentra entre $VEF 7.201,13 y 10.598,46 según el esquema de tratamiento que se utilice y de acuerdo a los escenarios evaluados.

URINARY/KIDNEY DISORDERS – Clinical Outcomes Studies

PUK1

EVOLUCIÓN CLÍNICA DE UNA COHORTE DE PACIENTES CON ENFERMEDAD RENAL CRÓNICA INTERVENIDOS EN UN PROGRAMA DE SALUD RENAL

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OBJECTIVOS: El objetivo es describir la velocidad de progresión de la ERC, la permanencia, los meses ahorrados en diálisis, los desenlaces y causas de egreso de una cohorte de pacientes en estadíos 3, 4 y 5 que estaban en el programa Clínica de Salud Renal (CSR) de RTS Colombia y Mutual Ser entre el periodo comprendido entre diciembre 2010 y diciembre 2012. **METODOLOGÍAS:** En esta cohorte histórica de pacientes con ERC se analizan los desenlaces clínicos del programa, en términos de la mediana de progresión de la enfermedad renal crónica, medida como delta de tasa de filtración glomerular en ml/min/año; se reportan las proporciones de pacientes con velocidad de progresión menor que -4 ml/min/año y menor que -2 ml/min/año. Específicamente para los pacientes de ERC estadio 5, se calculan los meses trascurridos en estadio 5 libres de diálisis. Se reporta además la mortalidad de esta cohorte. **RESULTADOS:** En diciembre de 2010 habían 634 pacientes en el programa, de estos 510 permanecieron en el programa hasta diciembre de 2012 (80,44%). La velocidad de progresión fue menor a -4ml/min/año en el 82,2% de los pacientes y en un 60,8% menor de -2ml/min/año. Los meses ahorrados en diálisis en los pacientes en estadio 5 fueron 11 meses. El 19,5% (n=124) de pacientes habían egresado del programa al final de periodo de observación. Las causas de egreso fueron: mejoría a TFG >60 ml/min/año (40,3%), muerte (29,0%), ingreso a diálisis (12,1%), suspensión voluntaria (5,7%), otros (12,9%). Seguimos a los pacientes 31582 pacientes-mes, equivalente a 2631 pacientes-año y la mortalidad fue 0.0137 muertes por paciente-año en el programa. **CONCLUSIONES:** Los meses evitados de diálisis por paciente en ERC 5 son 11. Una proporción sustancial de pacientes alcanzaron las metas de progresión de ERC. La principal causa de egreso del programa fue por mejoría de la TFG.

PUK2

CLINICAL BENEFITS OF IMMUNOSUPPRESSION THERAPY IN RENAL TRASPLANT PATIENTS. SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: To study the clinical benefits of immunosuppression therapy for renal transplantation, through systematic review and meta-analysis **METHODS:** Two independently searches were performed in biomedical databases: Medline, Embase, Cochrane, Health Virtual Library and clinical trials from NIH website. Specific selection criteria were followed to collect the majority of evidence, items as temporality, methodology design, patient population, drug, therapy stage(induction/starting, maintenance, acute-rejection treatments), algorithms details and outcomes(acute rejection, graft loss, deaths, and rate of infection and malignancy). According to "Grades of Recommendation Assessment, Development and Evaluation"(GRADE-criteria) we assessed the quality of articles in order to run a meta-analysis. **RESULTS:** The study included 9 RCT of basiliximab vs ATG, and after heterogeneity test, the meta-analysis was performed with FEM (fixed effects model). In acute rejection, we obtained an OR of 1.092 CI95% [0.85–1.4] (in favor of Basiliximab). Infection risk and neoplasm development were in favor of basiliximab with (OR 1.6[CI95% 1.1–2.3] and OR 3.2[CI95% 1.1–9.4], respectively). Basiliximab vs Non-induction included 5 RCT, resulting in OR 1.8 [CI95% 1.4–2.4] and NNT of 8 (in favor of basiliximab) in acute rejection, also basiliximab had a better infection risk profile (OR 4.2 [CI95% 3–5.9]). Cyclosporine vs Tacrolimus included 26 RCT, with an OR estimate for acute rejection of 1.9 ([CI 95% 1.6-2.1] in favor of Tacrolimus). Mycophenolate-Sodium(MPS)/Mycophenolate-Mofetil(MMF) vs azathioprine included 5 RCT (2 with MPS), with an OR for acute rejection of 2.2 (CI 95%1.7–2.8) in favor of MPS/MMF, and NNT of 7 (CI95% 5–10). Additionally, we evaluated the GI AE's profile of MMF vs MPS, and we obtained an OR 0.65 (CI95% 0.5–0.8), in favor of MPS. **CONCLUSIONS:** The present study assessed the clinical outcomes of treatments for renal transplantation. Basiliximab, Tacrolimus and MMF/MPS proved to have better clinical effects for outcomes like acute rejection, infection risk and neoplasm development.

URINARY/KIDNEY DISORDERS – Cost Studies

PUK3

BUDGET IMPACT ANALYSIS OF RENAL POST-TRANSPLANT PROPHYLAXIS WITH BELATACEPT IN COLOMBIA

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OBJECTIVES: Renal transplantation is currently the most effective treatment for End Stage Renal Disease (ESRD) and its success is linked to effective immunosuppressive regimes. A new immunosuppressive agent, belatacept has recently entered the market. The mechanism of action of belatacept focuses on selective blockade of T cell activation, improving renal graft survival for a prolonged period of time with less toxicity compared to standard immunosuppressive regimes. The objective of this study was to estimate the budgetary impact to the health care system in Colombia after the introduction of Belatacept for renal post-transplant prophylaxis. **METHODS:** An Excel-based budget impact model was used to estimate over a 5 years period the average per-member-per-year (PMPY) costs of adding belatacept to the health insurance coverage in Colombia. We considered a base case scenario with prevalence of ESRD is 0.05%; annual incidence of renal transplant of 3.5% and mortality after transplant of 4%. The model considers doses and costs of belatacept, cyclosporine, everolimus, sirolimus and tacrolimus, management and costs for adverse events and clinical resources used. Data for the model inputs was extracted from published literature and local sources. A market share of belatacept increasing from 1% in year one to 10% by year five was assumed for this analysis. **RESULTS:** It was estimated that including belatacept in the health insurance coverage would increase health system spending for renal post-transplant prophylaxis on COP$7.700 (USD 4.31) PMPY, an aggregated budget impact of COP$13 million (USD 7,283) (4.44%) over the five years (additional annual investment of COP$2.6 million). Belatacept presents lower adverse events costs in comparison with other alternatives. **CONCLUSIONS:** The availability of belatacept in post-transplant prophylaxis treatment for patients in Colombia would provide a new therapeutic option for immunosuppression with lower adverse events at a limited budget impact to the Colombian health care system.

PUK4

IMPACTO PRESUPUESTAL DE LA ENFERMEDAD RENAL TERMINAL EN COLOMBIA CON UN INCREMENTO DEL NÚMERO DE TRASPLANTES

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OBJECTIVOS: La prevalencia de enfermedad renal terminal (ERT) en Colombia viene creciendo a cuatro veces el crecimiento poblacional (5% vs. 1,2%). El número de trasplantes renales, sinembargo, se viene reduciendo. El objetivo es estimar el impacto presupuestal de un incremento en el número de trasplantes. **METODOLOGÍAS:** En pesos colombianos y dólares americanos de 2012 (1 USD = 1785 COP), y desde la perspectiva del sistema de salud, estimamos los costos asociados a dos escenarios: Escenario 1: una reducción progresiva de 2% anual del número de trasplantes (tendencia histórica); o Escenario 2: un aumento gradual (5% anual) del número de trasplantes

durante el período 2013-2017. La prevalencia de ERT se proyectó a partir de datos oficiales. Los costos se obtuvieron de distintas fuentes: casos reales para determinar uso de recursos, tarifarios oficiales (ISS 2001 ajustado) para procedimientos, y SISMED para medicamentos. Todos los datos fueron validados en reuniones de expertos, se siguieron las guías ISPOR para impacto presupuestal. **RESULTADOS:** Según nuestros estimados, el número de pacientes con ERT pasará de 27.890 en 2013 a 33.900 en 2017. En el Escenario1 el costo pasará de COP$837.882 millones (USD$469,4 millones) a COP$ 1.009.782 millones (USD$565,7 millones), un crecimiento en pesos constantes de 20,5 %. En el Escenario 2 el costo llegaría COP$1.044.883 millones(USD$585,4 millones), un incremento absoluto de 3 % con respecto al Escenario 1. El número de pacientes trasplantados pasaría de 3.601 a 4.145 mientras los muertos en el quinquenio se reducirían en 14; ello equivaldría a COP$64,5 millones (USD$36.134) por paciente trasplantado adicional o COP$2.507 millones (USD$1,4 millones) por muerte evitada. **CONCLUSIONES:** Un incremento del 5% anual del trasplante renal representa un aumento del 3% del costo de la atención de la ERT en Colombia. Parte del "ahorro" actual con la diálisis se debe a mayor mortalidad.

PUK5

COST-EFFECTIVENESS OF PARICALCITOL IN END STAGE CHRONIC KIDNEY DISEASE SECONDARY HYPERPARATHYROIDISM PATIENTS ON DIALYSIS, IN BRAZIL

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OBJECTIVES: To understand from the perspective of the Brazilian National Health System (SUS) the cost-effectiveness of treating secondary hyperparathyroidism with IV paricalcitol versus IV calcitriol in dialysis patients diagnosed with end stage chronic kidney disease. **METHODS:** A decision-analytic Markov model comparing the use of IV paricalcitol versus calcitriol. Main outcomes include parathyroidectomy, hospitalizations or death, life time costs and the results are reported as incremental cost-effectiveness ratios (ICER). The treatment costs are based on the DATASUS administrative claim database which includes individuals with an end stage chronic kidney disease secondary hyperparathyroidism diagnosis, who underwent hemodialysis at SUS, from 2009 to 2012. The main clinical outcomes are based on clinical trials or cohort studies reporting those outcomes. **RESULTS:** The reference case analysis was a 5-year time horizon based on a comparison of treatment with paricalcitol versus calcitriol, of end stage chronic kidney disease secondary hyperparathyroidism dialysis patient. The use of paricalcitol leads to savings amounting R$ 113.999.601,06 to SUS and an increase in life-years gained (0.52 years). Paricalcitol was dominant over the comparator (calcitriol), indicating better health outcomes and lower costs. One-way sensitivity analyses and probabilistic sensitivity analyses confirmed the robustness of the model. **CONCLUSIONS:** In our model the substitution of IV calcitriol by IV paricalcitol can be a more cost-effective choice in the management of secondary hyperparathyroidism.

PUK6

CATHETER-ASSOCIATED URINARY TRACT INFECTIONS: COST COMPARISON STUDY FROM THE PUBLIC PAYER PERSPECTIVE

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OBJECTIVES: To compare costs of catheter-associated urinary tract infection (CAUTI) with the reminding intervention (RI) and without reminding intervention (WRI) from the public payer perspective. Urinary catheter (UC) is one of the most invasive devices used in health care, and its insertion contributes to the development of urinary tract infections (UTI), which accounts for 40% of all nosocomial infections. About 12%-16% of patients in the intensive care unit have a UC inserted at some point during hospitalization. Unnecessary use of UC may lead to CAUTI, which represents about 80% of UTI, contributing not only to excess morbidity and mortality, but also increasing costs. A prospective study published (Apisarnthanarak 2007) evaluated the effectiveness of a program to improve hospital quality, which included an intervention to remind physicians to remove unnecessary UC. **METHODS:** Efficacy data was obtained from the literature which compared RI to WRI. Data from the Brazilian Hospital Information System (SIH/DATASUS) from 2012 was used to define the annual number of high complexity admissions of adult patients in public hospitals, assuming WRI as current practice. Resource utilization was estimated through published data and unit costs were obtained from Brazilian official price lists. **RESULTS:** A total of 659.934 hospitalizations were identified in the database, with a mean length of stay of 6.7 days. According to Apisarnthanarak 2007, RI to WRI showed reductions of CAUTI of 9.4%. The estimated consumable costs associated were 1,222.45BRL/pacient/7 days of treatment. For all admissions in 2012, the total cost of CAUTI represented 247,091,949.90BRL for WRI and 223,865,239.68BRL for RI, respectively (medical supplies only). The estimated savings were 23,226,710.22BRL/year for the Brazilian public system. **CONCLUSIONS:** RI showed that staff education generates benefits for the hospital and patients, decreasing costs and unnecessary hospitalization. Further researches including other clinical outcomes, longer follow-up and complications could result in higher savings for the public payer.

PUK8

FRECUENCIA Y COSTOS DE HOSPITALIZACIÓN EN UNA POBLACIÓN DE PACIENTES EN DIALISIS EN COLOMBIA

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OBJECTIVES: Chronic renal disease patients are often hospitalised. The present study was carried out as no studies have measured such population's hospitalisation frequency and duration in Colombia nor has their economic burden been analysed. **METHODS:** This was a dynamic retrospective cohort study of 223 patients receiving dialysis therapy during 2010. Haemodialysis (HD) and peritoneal dialysis (PD hospitalisation frequency was measured, as were the number of days spent in hospital, total hospital bill and average cost per day of hospitalisation. Multivariate analysis was used for evaluating factors related to hospitalisation cost (i.e. a generalised linear model with log link). **RESULTS:** Hospitalisation rate was 0.72 hospitalisations per patient/year, 6.32 days were spent in hospital per patient/year and average hospitalisation rate was 8.68 days. No differences were observed between haemodialysis patients and peritoneal dialysis regarding such rates. Average hospitalisation bill was $2,567,680. **CONCLUSIONS:** The study population had higher hospitalisation rates and spent less days in hospital than that stated in other reports. No differences were observed between HD and PD patients regarding these rates.

PUK9

COSTO-EFECTIVIDAD DE LAS PRUEBAS PARA LA TAMIZACIÓN DE BACTERIURIA ASINTOMÁTICA DURANTE LA GESTACIÓN

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OBJECTIVOS: Estimar la razón de costo-efectividad de las pruebas para tamizar la bacteriuria asintomática (BAS) durante la gestación en Colombia. **METODOLOGÍAS:** Se diseñaron dos árboles de decisión que presentan como unidad de desenlace el número de casos de pielonefritis evitados y el número de partos pretérmino evitados, respectivamente. La perspectiva es la del sistema de salud. Las cifras monetarias fueron expresadas en pesos colombianos de 2010. Se hicieron análisis de sensibilidad univariados y probabilísticos. **RESULTADOS:** La razón de costo-efectividad incremental (RCEI) del urocultivo para pielonefritis evitadas es de $877.494; para partos pretérmino evitados es de $13.895.576. La RCEI de la tinción de Gram para pielonefritis evitadas es de $314.914 y para partos pretérmino evitados es de $.1 399.593. El urocultivo confirmatorio ante resultado positivo del parcial de orina es una estrategia dominada en todos los casos. **CONCLUSIONES:** El urocultivo es la alternativa que más casos de pielonefritis y de partos pretérmino evita. Si el umbral de disponibilidad a pagar es superior a $970.000 por caso adicional de pielonefritis evitado, o superior a $14.550.000 por caso adicional de parto pretérmino evitado, el urocultivo será costo-efectivo. Para umbrales entre $350.000 y $970.000 por caso adicional de pielonefritis evitada, o entre $2.500.000 y $14.550.000 por caso adicional de parto pretérmino evitado, la tinción de Gram será costo-efectiva. Para umbrales menores, el parcial de orina sin urocultivo confirmatorio será costo-efectivo.

PUK10

COST-EFFECTIVENESS OF CINACALCET CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS WITH SECONDARY HYPERPARATHYROIDISM IN BRAZILIAN PUBLIC HEALTH CARE SYSTEM (SUS)

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OBJECTIVES: Cinacalcet effectively reduces elevated levels of parathyroid hormone (PTH) in patients with CKD and consequently may reduce cardiovascular events, mortality and bone metabolism. This study assesses the cost-effectiveness of cinacalcet plus standard of care for the treatment of SHPT patients on dialysis compared to standard of care (SoC) alone, which includes vitamin D and phosphate binders, under the SUS perspective. **METHODS:** A Markov (state transition) cohort model with monthly cycles and 10-year time horizon was developed using published data from randomized controlled trials. The impact of cinacalcet treatment on mortality, cardiovascular events, fractures and parathyroidectomy were calculated based on a retrospective analysis. The Markov model consisted of the following health states: patient in target according to National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) targets (SHPT parameters in target range), patient not controlled (one or more parameters out target range) and death. Extensive one-way sensitivity analysis was conducted. Costs were extracted from official databases of prices of SUS. **RESULTS:** The life years gained (LYG) obtained with cinacalcet plus SoC and SoC alone was 4,42 and 3,55, respectively, resulting in an incremental cost-effectiveness ratio of USD 17,032 in a 10 year time horizon. Additional analysis showed that compared to SoC, cinacalcet was associated with more adequate levels of serum PTH, reduced the number of cardiovascular events (0,66 vs. 0,70), bone fractures (0,14 vs. 0,24) and parathyroidectomies performed (0,01 vs. 0,15). The sensitivity analysis showed that the main drivers of the result were the mortality probability in each of the SoC and cinacalcet groups, and the cost of cinacalcet acquisition. **CONCLUSIONS:** This model with data from the Brazilian Public Healthcare System shows that cinacalcet was cost-effective (cost per LYG gained) when compared to SoC.

PUK11

COST-EFFECTIVENESS ANALYSIS OF RABBIT ANTITHYMOCYTE GLOBULIN COMPARED TO BASILIXIMAB IN THE INDUCTION OF RENAL TRANSPLANT PATIENTS

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Rabbit antithymocyte immunoglobulin (r-ATG) and basiliximab are used as induction treatment for renal transplant patients. Since the cost associated with these procedures is a limiting factor in their availability, it is necessary to determine the cost-effectiveness ratio, given the differences in clinical outcomes among them. **OBJECTIVES:** To determine the incremental cost-effectiveness ratio between r-ATG and basiliximab for defined clinical outcomes in patients undergoing induction treatment for renal transplantation. **METHODS:** We completed meta-analyses for r-ATG and basiliximab in induction treatment. The data was used to define global effectiveness outcome measures (i.e. relative risk-RR) necessary to perform a cost-effectiveness analysis for Colombia. The attributable risk was calculated using the RR for each clinical outcome. **RESULTS:** The quadrant analysis for the cost-effectiveness ratio showed that the simulations are in the first quadrant (I), except for the fatal outcome of high-risk patients located in quadrant IV. For every other outcome and analysis group, there was an increase in effectiveness and cost. The costs of reducing 1% the attributable risk

for each outcome (incremental cost-effectiveness) using r-ATG vs. basiliximab were: acute allograft rejection USD$5,4 (standard-risk) - $8,7 (high-risk); delayed graft function for high-risk patients USD$57,4; graft failure USD$20 (standard-risk)-$31 (high-risk); death USD$19,9 (standard-risk) -$39,1 (high-risk). **CONCLUSIONS:** The results of the comparative analysis of r-ATG vs. basiliximab in induction of renal transplant patients showed that r-ATG is a cost-effective alternative for a significant proportion of the population for the examined outcomes in Colombia. The investment necessary to reduce the risk of the considered outcomes can be low considering its benefits, especially in a context where the availability of donors is limited.

PUK12
COST-EFFECTIVENESS OF BASILIXIMAB AS INDUCTION THERAPY FOR KIDNEY TRANSPLANTATION IN MEXICO
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OBJECTIVES: In Mexico 2,200 kidney transplantations were performed in the last 5 years. The objective of this study was to assess the cost-effectiveness of Basiliximab, which is a chimeric interleukin (IL)-2 receptor monoclonal antibody, versus antithymocyte globulins (ATG) or do not apply an induction therapy. **METHODS:** Cost-effectiveness analysis of three strategies: Basiliximab, ATG, and no induction, for the induction stage of kidney transplantation. Effectiveness was measured by the incidence of acute-rejection within 12 months. Time horizon was 1 year, and no discount rate was applied. Brenan D, et al, 2006 showed non-statistically difference in efficacy between Basiliximab and ATG. However, Nashan B, et al., 1997 found a difference on acute-rejection risk in ~17 percentage points (37.9% vs. 54.8%) between Basiliximab versus no-induction strategy. The costs included were the drugs cost and the kidney transplantation cost that was estimated in US$29,334 according to DRGs at IMSS. Drug costs were from public tenders and from public health institution's perspective. **RESULTS:** The induction cost with Basiliximab was US$31,191 and US$76,621 with ATG. Basiliximab has the less average cost-effectiveness ratio (C/E) per acute rejection avoided with US$512.46 compared to ATG. Basiliximab has the similar efficacy as ATG in patients at high risk for acute rejection, but with a lower cost which equals to 146% less per patient treated during the induction stage. Basiliximab compare to no-induction the Incremental cost-effectiveness ratio (ICER) per rejection avoided was US$14,642. **CONCLUSIONS:** The analysis is not considering the whole opportunity cost of a kidney transplant beyond the cost of the intervention itself. However, Basiliximab represents a cost effective therapy for of acute-rejection in kidney transplantation with the lower average cost-effectiveness compared to no-induction and dominant vs ATG.

PUK13
COSTO-EFECTIVIDAD DEL TRASPLANTE RENAL COMPARADO CON LA DIÁLISIS EN COLOMBIA
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OBJECTIVOS: Evaluar costos, utilidad y efectividad del trasplante renal comparado con terapia dialítica en adultos con enfermedad renal terminal en Colombia, desde la perspectiva del sistema de salud. **METODOLOGÍAS:** Se diseñó un modelo de Markov con 60 ciclos mensuales (horizonte 5 años) y 8 estados, incluyendo muerte como estado absorbente. Las transiciones entre estado se obtuvieron de los registros internacionales (Collaborative Transplant Study, University of Heidelberg, y US Renal Data System). Los costos se presentan en dólares de 2012 (1 USD = COP$ 1785) y se obtuvieron de diferentes fuentes locales: casos reales y validación de expertos para uso de recursos, tarifarios oficiales (ISS 2001 ajustado) para procedimientos, SISMED para medicamentos. Las utilidades, en años de vida ajustados por calidad (AVAC), se obtuvieron promediando las reportadas en la literatura. Los datos se validaron en reuniones de expertos. Se hicieron análisis de sensibilidad univariados, multivariados y probabilísticos. Otros indicadores de efectividad fueron meses de vida ganados, meses de diálisis evitados y muertes evitadas. La tasa de descuento fue 3% y el umbral de costo-utilidad de 3 veces el PIB = USD$ 20,168. **RESULTADOS:** El costo promedio total del paciente trasplantado a 5 años fue de $87,342, y el de diálisis $77,451, para una utilidad de 2.9832 y 2.1037 AVAC respectivamente (razón de costo-efectividad incremental RCEI = $11,246). Otros resultados fueron $1434 por mes de vida ganado, $282 por mes de diálisis evitado y $48,487 por muerte evitada. Parte de la diferencia en costos entre las terapias es debida a la mayor sobrevida del paciente trasplantado. Si igualamos la mortalidad de ambas terapias los costos se igualarían al comenzar el tercer año. **CONCLUSIONES:** El trasplante renal es más costo efectivo, tiene mayor sobrevida y mejor calidad de vida; a partir del tercer año es costo-ahorrador al ajustar por mortalidad.

URINARY/KIDNEY DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PUK14
QUALIDADE DE VIDA EM PACIENTESTRANSPLANTADOS RENAIS
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OBJETIVOS: Descrever o estado de saúde autopercebido e quantificar a qualidade de vida relacionada à saúde dos pacientes submetidos a transplante renal em hospitais públicosde Fortaleza- Ceará. **MÉTODOS:** A amostra foi composta de 50 pacientes submetidos a transplante renal entre 30 a 90 dias de pós-operatório, atendidos nos ambulatórios dos hospitais do estudo, no período de janeiro a julho de 2012 e que concordaram em participar do estudo. A amostra foi aleatória sendo aplicado o Euroqol-5D-5L (EQ-5D-5L) para mensuração indireta de preferências por estados de saúde, acrescentado questões sobre perfil sociodemográfico. **RESULTADOS:** Os 5 domínios de avaliação do instrumento EQ5D mostraram que no item mobilidade, 42(84%) pacientes não apresentam problemas, quanto aos cuidados pessoais, 44(88%) não tem problemas em realizá-los, 22(44%) deles não referiram problemas para realizar suas atividades habituais, enquanto 9(18%) sentem problemas moderados e outros 9(18%) se sentem incapazes de realizar suas atividades habituais. No domínio dor/mal-estar, 33(66%) não refere dores ou mal estar. Sobre ansiedade e depressão, 36(72%) não se sentem ansiosos ou deprimidos. O estado de saúde autopercebido, medido pela escala analógica visual, mostra uma pontuação mínima de 30 e máxima de 100, numa média de 78,5. A grande maioria dos pacientes 24(48%) considera sua saúde excelente, 17(34%) afirmam estar com saúde regular. Apenas 9(18%) da amostra considera sua saúde ruim.Quanto às condições socioeconômicas da amostra, 40(80%) pacientes estão em idade produtiva (20-59 anos), média de 41 anos, sendo a predominância do sexo masculino 34(68%). A maioria dos pacientes entrevistados, 27(54%), recebe apenas o salário mínimo como renda individual, obtida por aposentadoria ou auxílio doença. **CONCLUSÕES:** Pelo resultado obtido nessa pesquisa infere-se que os pacientes transplantados renais apresentam uma boa qualidade de vida nos primeiros meses após transplante. Sugere-se pesquisa prospectiva com o intuito de observar sobrevivência e as mudanças na qualidade de vida desses pacientes.

PUK15
HEALTH-RELATED QUALITY OF LIFE OF HEMODIALYSIS PATIENTS IN INDONESIA
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OBJECTIVES: Health-Related Quality of Life (HRQoL) is one important outcome that should be monitored especially in chronic diseases. The long periode of treatment and the progress of diseases can give significant influence to patietns' HRQoL. The study about HRQoL in developing countries will be important as one success parameter of treatment outcome. We conducted this study to understand the quality of life of the hemodialysis patients in Indonesia. **METHODS:** . We carried out observational study in the public hospital during 2 months. The subjects involved in this study were chronic renal failure patients which have been at least two times hemodialyzed in a public hospital. All of the patients were covered with national health insurance to avoid to finance impact of quality of life. The quality of life was measured by Indonesian version of WHO-QoL questionnaire which included physical health function, mental health function, environmental function, and social function. The association between quality of life domain and other functions were evaluated as well. **RESULTS:** This study showed that in average the scale of fifty hemodialysis patients' quality of life was 70.38. In the other hand, the scale of physical, emotional, environtmental and social function were 23.58, 18.10, 14.86 and 7.76, respectively. There were positive correlations between the functions and quality of life domain. The function that had highest impact on quality of life domain was physical function and the function smallest impact on quality life of domain was social function. **CONCLUSIONS:** We understand that patients' physical function during hemodialysis could deteriorate their quality of life. Thus the better service of health care given to the hemodialysis patients in Indonesia could increase their quality of life.

RESEARCH POSTER PRESENTATIONS – SESSION II
RESEARCH ON METHODS

RESEARCH ON METHODS – Clinical Outcomes Methods

PRM1
EFFICACY AND SAFETY OF PULMONARY VEINS ISOLATION WITH CRYO TECHNIQUE
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OBJECTIVES: Pulmoanry vein isolation using cryoablation represents a recently developed technology for atrial fibrillation management. Its safety and efficacy need to be evaluated. **METHODS:** From February 2011 to December 2012, 58 patients underwent pulmonary veins isolation by cryoablation with Arctic Front Cryoballoon (40 men and 15 women) with a mean age of 64.2 ± 11.3 years (range 44-71), symptomatic paroxysmal atrial fibrillation refractory to medical therapy and at least two antiarrhythmic drugs. In 12 patients (20.6%) there was a normal left atrial diameter, while in the remaining 36 (79.4%)there was a documented mild to moderate dilatation (mean diameter 50 mm). The ejection fraction (EF) measured by echocardiography was normal in 47 patients (81%, mean FE 58.3%), while in 11 patients (19%) there was a moderate left ventricular dysfunction (mean EF 43 %). 76% of patients underwent 2 cryo applications for pulmonary vein, while in the remaining 24% of patients was not possible the cannulation of the lower right pulmonary vein for technical-anatomical reasons. We performed a clinical follow-up at 3 and 6 months with 24h Holter ECG (27 pts) and subcutaneous implant of Loop Recorder (28 pts). **RESULTS:** At the end of follow-up: 51 patients (87.9%) were asymptomatic for palpitations and in sinus rhythm, 4 patients (6.9%) went to the emergency department for palpitations with electrocardiographic evidence of typical atrial flutter and underwent SVC-tricuspid isthmus ablation and 3 patients (5.21%) experienced episodes of AF lasting less than 24 hours. **CONCLUSIONS:** The isolation of pulmonary veins ostium by cryoablation with Arctic Front Cryoballoon in our series is a safe and effective technique with a low incidence of recurrence of the arrhythmia in the short term.

RESEARCH ON METHODS – Cost Methods

PRM3
ESTUDIOS DEL COSTE DE LA ENFERMEDAD
Crespo C, Gisbert R, Brosa M
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OBJECTIVOS: Analizar la producción de estudios del coste de la enfermedad (CoE) en el mundo durante 2000-2010. **METODOLOGÍAS:** Se realizó una revisión de los estudios de "Coste de la enfermedad" en inglés y español en PubMed y otras fuentes. Tras

la selección de artículos por el abstract o el título (si no existía abstract), se revisaron directamente los artículos. Los criterios de inclusión fueron estudios donde apareciera un coste total para la patología o bien un coste por año y paciente siempre que no fuera de un estudio de evaluación económica. **RESULTADOS:** Se hallaron 233 trabajos que cumplían la palabra clave. Esta cifra se redujó a 153 cuando se pasó al estudio sobre de los artículos completos. La distribución temporal de los estudios es desigual, mostrando 25 en 2009 y 4 en 2000. Las enfermedades del sistema nervioso con 33 (21,6%) trabajos figuran en primer lugar siendo la EPOC con 13 (8,5%) las patologías más frecuentes. Se obtuvieron los costes directos en 127 y los indirectos en 92, en tres casos se utilizó el enfoque del período de fricción. Se obtuvo el coste total en 81 estudios y por paciente-año en 91. Domina el enfoque de la prevalencia 129 frente al de incidencia 7 y el método "bottom up" 94 frente al "top down" 46, y USA, con casi un tercio de los estudios, el país del mundo con mayor peso en este tipo de análisis. **CONCLUSIONES:** Se mantiene –y de hecho crece- el interés por CoE con enfoque de prevalencia y "bottom up", detallando los costes indirectos y no sólo los sanitarios.

PRM4

CONSUMPTION PATTERNS, MARKET CHARACTERISTICS AND REGULATION IN THE PHARMACEUTICAL INDUSTRY: EVIDENCE FROM TWO THERAPEUTIC GROUPS IN INSURED POPULATION IN ARGENTINA

Maceira D

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OBJECTIVES: Using a theoretical framework based on estimating demand functions under uncertainty, this paper proposes to highlight the importance of including economic variables of market structure and actors' strategic organization in the design of regulations on the pharmaceutical sector, beyond the relevance of pharmacological and clinical tools. The specification of regularity standards in social health insurance schemes requires of dynamic tools to improve the decision-making process within a framework of evidence-based medicine and cost-effectiveness analysis. **METHODS:** With a sample of 9,147 and 27,647 observations on prescriptions by population covered by social insurance in Argentina, the paper two analyzes therapeutic groups: hypertensive and lipid lowering, respectively. Econometric implementation implied classical least squares estimation and logistic models for therapeutic group, product and brand. **RESULTS:** The data provides consistent messages about the presence of differentiation mechanisms that overshadow the traditional inverse relationship between price and sales. In particular, the interaction between brand and drugs, which can be extended to technological changes in a dynamic context, implies a complementary perspective in designing a regulatory framework. **CONCLUSIONS:** The power of negotiation and establishment of rules of producers must be considered in each particular therapeutic class, allowing coordinated incentives to encourage rational prescription behavior, moving in a pattern of more cost-effective and equitable use of resources.

RESEARCH ON METHODS – Databases & Management Methods

PRM5

A EVOLUÇÃO DA REDE BRASILEIRA DE AVALIAÇÃO E TECNOLOGIA EM SAÚDE

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OBJETIVOS: A Rede Brasileira de Avaliação e Tecnologia em Saúde (REBRATS), composta por 53 membros, atua no incentivo ao acesso livre à informação científica através do banco de dados criada em 2009 o SISREBRATS, visando divulgar os estudos em Avaliação de Tecnologias em Saúde (ATS) no Brasil. Além disso, a iniciativa destina-se a aumentar a visibilidade das pesquisas, dos pesquisadores, das instituições e da rede e auxiliar a sociedade no processo da educação científica e educação em saúde. O objetivo desse estudo é avaliar o crescimento da rede e a evolução da disseminação das informações científicas no Brasil através da REBRATS. **MÉTODOS:** Levantamento dos dados da base da REBRATS através da contabilização das informações computadas, do número de usuários, estudos cadastrados e o aumento dos membros da rede. **RESULTADOS:** Em uma análise realizada entre de abril de 2010 e março de 2013, houve expressivo aumento do número de usuários que podem incluir estudos no banco de dados, que passou de 29 para 226, são representados pelos pesquisadores que fazem parte da REBRATS. Neste mesmo cenário, observa-se a ampliação dos membros que formam a rede, representando 20,5% de crescimento. Neste mesmo período observou-se aumento de 85,6% de novos cadastros dos estudos que são disponíveis para acesso da sociedade e dos gestores de saúde do Brasil. **CONCLUSÕES:** Os resultados demonstraram que houve um crescimento significativo de pesquisadores e de instituições na REBRATS. Como consequência desse aumento, observou-se a ampliação dos estudos cadastrados na base. O SISREBRATS é um sistema de acesso livre e com potencial para prover informações que podem subsidiar a tomada de decisão dos gestores de saúde do pais. Apesar do crescimento, é necessário realizar contínuos esforços para ampliação da base, considerando a magnitude e a quantidade de instituições membros da REBRATS.

PRM6

DIFERENCIAS EN LA CONSECUCIÓN DE INFORMACIÓN SOBRE COSTOS DEL MANEJO DE LA DIABETES MELLITUS EN COLOMBIA

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OBJECTIVOS: La información sobre costos y uso de recursos en salud es indispensable para desarrollar evaluaciones económicas. En Colombia, los diferentes actores del sistema de salud tienen fuertes restricciones para brindar acceso a su información, la cual en su mayoría no es pública. El objetivo de este análisis fue cuantificar el acceso a la información y las diferencias reportadas en la información disponible sobre costos de la Diabetes Mellitus en Colombia. **METODOLOGÍAS:** En el desarrollo de una evaluación económica, se identificaron los recursos en salud para el manejo de la enfermedad a partir de guías nacionales y protocolos institucionales. Los costos médicos directos fueron buscados en múltiples fuentes, incluyendo: el Sistema de Información de Medicamentos del Ministerio de Salud, manuales tarifarios oficiales, bases de datos de instituciones prestadoras y aseguradoras en salud y bases de datos de precios en farmacias. **RESULTADOS:** Un total de 24 instituciones fueron contactadas para obtener información sobre costos médicos directos. Sólo 6 (25%) suministraron los datos requeridos, que correspondían a costos de hospitalización, procedimientos, manejo ambulatorio, pruebas diagnósticas y medicamentos asociados con el manejo de la enfermedad. Ninguna de las instituciones entregó más del 70% de la información solicitada. La mayor parte de instituciones con restricciones de acceso a los datos, adujo políticas internas que no permitían hacer pública su información de costos. Las diferencias reportadas en costos para el manejo de la Diabetes de las instituciones que suministraron datos fueron: 56% en costos de hospitalización, 82% en procedimientos, 88% en manejo ambulatorio, 59% en pruebas diagnósticas y 91% en medicamentos. **CONCLUSIONES:** Existen dificultades para la consecución de costos y uso de recursos para evaluaciones económicas en Colombia y amplia variación en la información obtenida, lo que genera altos niveles de incertidumbre y la transparencia y representatividad de los resultados puede verse seriamente afectada.

PRM7

USO DE BASES DE DATOS O SISTEMAS DE INFORMACIÓN PARA SOPORTAR LA TOMA DE DECISIONES EN SALUD EN COLOMBIA

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OBJECTIVOS: Actualmente existe una tendencia global en el uso de información de la vida real para soportar la toma de decisiones en salud. En Colombia, hay poca información respecto al uso de la información generada por los diferentes actores del sistema de salud. El objetivo de este estudio fue identificar las fuentes de información disponibles y su uso actual para soportar la toma de decisiones en salud. **METODOLOGÍAS:** Usando una encuesta semi-estructurada auto-diligenciable dirigida a diferentes grupos de tomadores de decisiones de instituciones aseguradoras y prestadoras de servicios de salud, autoridades de salud, industria farmacéutica e instituciones académicas y de investigación, se evaluó la información disponible y su uso actual en la toma de decisiones. **RESULTADOS:** Un total de 39 tomadores de decisiones en 30 instituciones respondieron la encuesta (40% aseguradores, 17% prestadores, 14% industria farmacéutica, 3% entidades gubernamentales y 26% de otras entidades). De ellos 95% reportaron tener bases de datos relacionadas con sus actividades en el sistema de salud; de éstos, 83% usan datos de costos para soportar la toma de decisiones; 58% reportaron que indicadores como años de vida ganados por calidad, años de vida perdidos por discapacidad y desenlaces reportados por el paciente no se tienen en cuenta para la toma de decisiones. En contraste, el 50% de las instituciones usan sistemáticamente indicadores de desempeño y perfiles epidemiológicos. **CONCLUSIONES:** Si bien existen mecanismos de almacenamiento y análisis de datos sobre prestación de servicios, eventos de interés en salud pública y costos de atención, su uso en Colombia es incipiente, limitando la realización de estudios más complejos como evaluaciones económicas o estudios de efectividad comparativa, necesarios para favorecer la toma de decisiones mejor informadas. La participación activa de los actores en el uso sistemático de esta información, puede ser de gran utilidad para mejorar la eficiencia del sistema de salud.

PRM8

ÁNALISE DE SIGNIFICÂNCIA DO BANCO DE DADOS DE HOSPITAIS PARTICULARES BRASILEIRO

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OBJETIVOS: Avaliar o grau de importância do banco de dados da Orizon (informações de hospitais particulares) para a sociedade Brasileira. **MÉTODOS:** Foram realizadas análises quantitativas e qualitativs da base de dados da Orizon comparada com os dados conhecidos da ANS (Agência Nacional de Saúde) que regulamenta os planos de saúde no Brasil. Os dados quantitativos analisados foram: número de vidas, tipo de operadora existente na base, volume de transações e histórico da base. Quanto aos dados qualitativos foram mensurados os tipos e qualidade das informações e analisados dados estatístico descritivo. **RESULTADOS:** A Base de dados Orizon possui 16.161.999 vidas que corresponde à 35% do mercado de saúde suplementar, comparado com os dados da ANS por pagador obteve-se a seguinte representatividade: autogestão a base possui 24% de todo o mercado, 16% de cooperativa médica, 14% filantropia, 8% medicina de grupo e 94% de todas as seguradoras especializas em saúde, além de 1.141.316 vidas pertencentes à grupos não regulamentado pela ANS, sua distribuição por média nos Estado Brasileiro por beneficiários que possui plano de saúde corresponde à 22%. Somente nos dois anos o volume de transações (consultas, internações, cirurgias e exames) correspondeu à 285.353.901. As informações existentes são: tipo de internação, motivo da alta, tipo do gasto, tempo de internação, descrição do item (material, exame, procedimento, taxa, medicamento e alimento), quantidade, valores, localização geográfica, gênero e idade. **CONCLUSÕES:** No Brasil existe somente a base de dados pública do sistema único de saúde (SUS) com informações do mercado público de saúde não sendo possível mensurar a saúde total brasileira, desta forma o banco de dados Orizon vem para auxiliar à mensurar todo mercado brasileiros de forma totalmente significante e necessária.

RESEARCH ON METHODS – Modeling Methods

PRM9

ANALYSIS OF MANDIBULAR TEST SPECIMENS USED TO EVALUATE BONE FIXATION SYSTEMS

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OBJECTIVES: To evaluate, through biomechanical tests, which synthetic material used for the manufacturing of test especimens (ABS plastic, polyamide, and polyurethane) shows a better biomechanical behavior for *in vitro*simulations of load resistance of a fixation method established to mandibular SSRO [Sagittal Split Ramus Osteotomy]. **METHODS:** 30 synthetic and standardized replicas of human hemimandibles with SSRO were divided into 3 groups of 10 samples each: Group A - ABS plastic, Group B - Polyamide, and Group C - Polyurethane. These were fixed by three positional bicortical screws (16 mm length, 2.0 mm system), in an inverted "L" pattern, using drilling guides and advancement of 5 mm. Each sample was subjected to a vertical linear load and the load resistance values recorded at 1, 3, 5, 7, and 10mm displacement. The standard deviations and means were compared using analysis of variance ($p<0.05$) and Tukey's test. **RESULTS:** It was observed a tendency for lower values in group B than in groups A and C. In displacements of 3 and 5 mm, there was a difference between groups A and C to group B ($p<0.05$). In displacements of 7 and 10 mm, there was a difference among the 3 groups, the highest values being found in group C and the lowest ones in group B ($p<0.05$). **CONCLUSIONES:** Taking into consideration the results achieved and the behavior of each material used as substrate, we can consider that ABS plastic was very flexible and polyurethane very rigid. On the other hand, polyamide samples behaved more likely to the human cortical bone, which can be validated to perform load tests, for SSRO, compared to other tested materials.

PRM10

CALIBRATION OF A COST-EFFECTIVENESS MODEL TO EVALUATE THE INCORPORATION OF A QUADRIVALENT HPV TYPES 6, 11, 16, 18 VACCINE IN ARGENTINA: DISEASE BURDEN COMPONENT

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OBJECTIVES: To calibrate the disease burden component (mortality and incidence rates from cervical cancer) of a cost-effectiveness model that aims to evaluate the incorporation of a quadrivalent HPV Type 6, 11, 16, 18 vaccine in Argentina. **METHODS:** We adapted a previously developed mathematical model (Elbasha 2010) to evaluate the health and economic impact of routine vaccination of 11 years old females. The model is a dynamic transmission model which estimates the direct and indirect (via herd immunity) health benefits of vaccination. Individuals enter the model as they are born; move between successive age groups at an age, gender and sexual activity specific rates, and exit the model as they die. A systematic search on effectiveness, local epidemiology, resource use and costs was undertaken to populate the model. Selected intermediate parameters (probability of transmitting genital HPV infection per sexual partnership by HPV genotype, and percent of females with cervical cancer that recognize their symptoms and seek treatment) were used for calibration. The perspective used was that of the health care system, with a horizontal span of 100 years and a rate of discount of 5% for costs and health effects. **RESULTS:** The model was properly calibrated with results in a range of +/- 1% as compared to national vital statistics and Globocan. The model showed an incidence of 5,285 new cases of HPV 16&18 related cervical cancers per year in Argentina and 1,511 deaths for 2013. Eighty-seven and 80% of incident cases and deaths were concentrated in the 35 to 85 age group, and a median age of death of 55 years. **CONCLUSIONS:** The model proved to be an evidence-based, internally valid tool for the assessment of the main HPV related disease burden and can serve as the basis for the further evaluation of the cost-effectiveness of HPV routine vaccination in Argentina.

RESEARCH ON METHODS – Patient-Reported Outcomes Studies

PRM11

MEDICIÓN DE LA CALIDAD DE VIDA POR MEDIO DEL "DERMATOLOGY LIFE QUALITY INDEX" EN PACIENTES CON PSORIASIS: UNA REVISIÓN SISTEMÁTICA

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OBJECTIVOS: Evaluar la calidad de vida relacionada con la salud en pacientes con psoriasis, medida a través del Dermatology Life Quality Index (DLQI). **METODOLOGÍAS:** Se realizó una revisión sistemática en Pubmed, Cochrane Library, Embase y CINAHL sobre la calidad de vida relacionada con la salud en pacientes con psoriasis leve, moderada y severa. Se incluyeron artículos que evaluarán la calidad de vida en su condición basal mediante la escala DLQI y se reportó el resultado utilizando el Psoriasis Assessment and Severity Index (PASI) como resultado secundario. La búsqueda sólo incluyó estudios en inglés publicados desde 1994 hasta agosto de 2012. Se excluyeron los artículos que comparaban diferentes tipos de tratamiento en términos de mejoría de la calidad de vida antes y después de la administración del medicamento, así como la evaluación de la calidad de vida en diferentes variantes de la enfermedad tales como la artritis psoriática y psoriasis de las uñas. **RESULTADOS:** Se identificaron ocho artículos que cumplieron con los criterios de inclusión y exclusión que evaluaban la calidad de vida relacionada con la salud en pacientes con psoriasis leve y moderada mediante la escala DLQI. Se evidenció una pérdida de la calidad de vida en los pacientes con psoriasis, en sus actividades diarias y de trabajo, así como en la vida sexual. El promedio de DLQI estuvo entre 6,4 a 10,8; se observó una gran variabilidad en la duración de la enfermedad entre 17,6 y 28,9 años. Un total de dos estudios reportaron el PASI, el cual estuvo entre 6,53 y 10,5, lo que indica enfermedad leve y moderada. **CONCLUSIONES:** La psoriasis afecta la calidad de vida de los pacientes que padecen la enfermedad tanto en su forma leve como moderada, y este deterioro es superior a los encontrados en enfermedades tales como acné, vitíligo, alopecia y urticaria, entre otras enfermedades.

RESEARCH ON METHODS – Statistical Methods

PRM12

THYROID DYSFUNCTION DETECTION IN PREGNANCY: UNIVERSAL SCREENING OR TARGETED HIGH-RISK CASE FINDING? A META-ANALYSIS

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OBJECTIVES: Recent consensus guidelines do not advocate universal thyroid function screening during pregnancy but recommend testing high-risk pregnant women with a personal history of thyroid or other autoimmune disorders or with a family history of thyroid disorders. Maternal subclinical hypothyroidism during pregnancy is associated with various adverse outcomes. The present study aims to assess efficiency of the targeted high-risk case-finding approach in identifying women with thyroid dysfunction during early pregnancy. **METHODS:** A comprehensive literature search was done in PubMed and EMBASE databases till July 2012 for studies related to screening of thyroid dysfunction. Data was extracted from each relevant article. The primary estimate was pooled odds ratio with 95% CI. Data analysis was done by Comprehensive Meta Analysis software. Heterogeneity was assessed by I^2 statistics. Publication bias was assessed using Begg and Egger test. Sensitivity analysis was also performed. **RESULTS:** A total of 5 studies (published between 2007 and 2011) were found to be pertinent after exclusion of irrelevant studies. Because of significant heterogeneity, a random effects model was chosen. For the effectiveness of universal screening, pooled odds ratio was found to be 2.87 (95% CI, 1.60-4.94, p=0.00). **CONCLUSIONS:** Targeted thyroid function testing of only the high-risk group would miss about one third of pregnant women with overt/ subclinical hypothyroidism.

PRM13

DESARROLLO DE UNA ESCALA DE ESTRUCTURAS Y PROCESO PARA LA EVALUACIÓN DE LOS CENTROS DE HEMODIÁLISIS

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OBJECTIVOS: Desarrollar una escala de indicadores de calidad de estructuras y procesos para los centros de hemodiálisis del Uruguay. **METODOLOGÍAS:** Un conjunto de expertos nacionales elaboró una lista de indicadores basados en estándares que fueron evaluados mediante visitas técnicas en los centros desde 2004 hasta la actualidad. Mediante el Análisis de Coordenadas Principales (ACoP) y la distancia de Gower se estudió el conjunto de indicadores buscando obtener un número reducido de factores que expliquen una proporción importante de la varianza del sistema de indicadores en el período 2007 a 2010. Se construyó la escala de estructuras y procesos empleando como ponderación la mediana de la distancia euclidea entre los indicadores para el espacio de factores obtenidos en el ACoP. Mediante estadística descriptiva se analizó el comportamiento de la escala en el tiempo y respecto de los indicadores originales. Aplicando el criterio de Kaiser se seleccionaron los dos primeros factores del ACoP (varianza explicada 37,63%), el análisis presentó un índice de estrés de 0,1646. **RESULTADOS:** La escala desarrollada mostró una tendencia temporal de mejora en la calidad de las estructuras y procesos brindados por los centros de hemodiálisis. También se observó una asociación significativa con varias de las dimensiones de estructuras y procesos evaluados. **CONCLUSIONES:** Se considera que el instrumento desarrollado es adecuado para la valoración global de las prestaciones en hemodiálisis en las áreas de estructura y procesos.

PRM14

APPLIED COMPARISON OF META-ANALYSIS TECHNIQUES

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Meta-analysis is an approach that combines findings from similar studies. The aggregation of study-level data can provide precise estimates for outcomes of interest, allow for unique treatment comparisons, and explain differences arising from conflicting study results. Proper meta-analysis includes five basic steps: identify relevant studies; extract summary data; compute study effect sizes, perform statistical analysis; and interpret and report the results. **OBJECTIVES:** This study aims to review meta-analysis methods and their assumptions, apply various meta-techniques to empirical data, and compare the results from each method. **METHODS:** Three different meta-analysis techniques were applied to a dataset examining the effects of the bacille Calmette-Guerin (BCG) vaccine on tuberculosis (TB). Fixed-effect, random-effect modeling and meta-regression were applied for analysis, with added study-level covariates. Overall and stratified results, by geographic latitude were reported. **RESULTS:** Estimates of treatment effect differed depending on the technique applied. When a fixed effect model was applied to estimate the effect of a vaccination against tuberculosis, the log odds ratio was -0.436 (confidence interval [CI: -0.528, -0.344]). After testing for heterogeneity and fitting a random effects model, the estimate was reduced to -0.741 (CI [-1.12, -0.352]), and the CI became wider. When covariates were added to the model to explain the heterogeneity, the treatment effect was reduced even further. All three techniques showed statistically significant effects from the vaccination. However, once covariates were added, efficacy diminished. Independent variables, such as the latitude of the location in which the study was performed, appeared to be partially driving the results. **CONCLUSIONS:** Meta-analysis is useful to draw general conclusions from a variety of studies. However, proper study and model selection are important to ensure the correct interpretation of results. Basic meta-analysis models are fixed-effects, random-effects, and meta-regression.

RESEARCH ON METHODS – Study Design

PRM15

DISPONIBILIDAD Y FUENTES DE LA INFORMACIÓN PARA LA TOMA DE DECISIONES EN REUMATOLOGÍA: USO DE LOS ESTUDIOS ECONÓMICOS

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OBJECTIVOS: Identificar el impacto de la obligatoriedad de presentar una Evaluación Económica (EE) para la inclusión de medicamentos en el Cuadro Básico Nacional en las publicaciones de EE relacionada con el área de reumatología en México. **METODOLOGÍAS:** Se realizó una búsqueda sistemática de las publicaciones de EE y reumatología publicados entre 1995 y 2011. Los estudios de EE fueron clasificados por tres expertos en economía de la salud con base a los criterios de Drummond, Sí los estudios contemplan comparación de dos o más alternativas y sí valoran los costos y consecuencias de las alternativas examinadas se dice que es un estudio de evaluación económica completa (EEC). Se valoró sí la modificación en el año 2003 tuvo impacto significativo en términos de número de publicaciones. **RESULTADOS:** Se identificaron un total de 263 artículos de EE entre 1995 y 2011, 93(35%) de fueron EEC. En el periodo 1995-2002 se identificaron 56 estudios, 19(34%) EEC. En el periodo de 2003-2011 (después de la modificación del reglamento) se identificaron un total de 207 publicaciones de EE, 74(36%) EEC. El 79% de las publicaciones se concentra en el periodo 2003-2011, con un total de 207 publicaciones. Del total de publicaciones las relacionadas con reumatología fueron 3% (n=9) de las cuales 33% fueron completas, 67% fueron parciales. Se destaca que antes de la modificación del reglamento en 2003 se detectó un estudio de EE/reumatología mientras que después del año 2003 el número de publicaciones ascendió a 8 artículos. **CONCLUSIONES:** La EE en México a través del número de publicaciones se ha ido desarrollando notablemente, asimismo el hacer obligatorio el presentar un estudio de EE para la inclusión de un insumo al Cuadro Básico y Catálogo de Insumos del Sector Salud fue un punto de partida para el desarrollo de la EE en México.

RESEARCH ON METHODS – Conceptual Papers

PRM16
A UNIFIED METHODOLOGICAL FRAMEWORK FOR THE ECONOMIC EVALUATION OF THERAPEUTIC MEDICAL DEVICES

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To inform policy decisions economic evaluation (EE) studies require the systematic identification and (quantitative) synthesis of the relevant evidence base on the clinical effectiveness, quality of life (QoL) and costs associated with the use of competing health technologies. Existing methods for EE are linked to principles of evidence-based medicine and, as such, are geared primarily towards the evaluation of pharmaceuticals. Some authors have claimed that medical devices (MDs) cannot be evaluated using the same principles. We take the opposite viewpoint and argue that used within the right evaluative framework existing EE methods are indeed appropriate to assess the cost effectiveness of therapeutic MDs. What makes the (economic) evaluation of MDs challenging is the fact that the quantity, quality, and characteristics of the evidence base around them, is often fragmented, heterogeneous and associated with high levels of uncertainty. In these circumstances it is important to acknowledge the value of eliciting and quantitatively summarising physicians and other experts' beliefs regarding the effectiveness and resource use demands associated with MDs already in use. Using real life examples this paper shows how a Bayesian stepwise iterative approach has helped address some of the challenges associated with the EE of MDs, while guiding policy decisions regarding technology adoption, research funding and design. Relevant steps include: a) identification of existing evidence base and elicitation of experts' beliefs on clinical effectiveness , QoL and costs - i.e. "a priori evidence base"; b) quantitative synthesis of this a priori evidence base to inform the parameters of an EE model; (c) initial estimation of the model; d) assessment of the economic value of conducting further research (VoI); e) collection of new patient level data (PLD) in a pilot study; (f) new evaluation of the EE model updating the prior estimates using primary PLD; g) further VoI analysis.

DISEASE-SPECIFIC STUDIES

CARDIOVASCULAR DISORDERS – Clinical Outcomes Studies

PCV1
COSTS AND CONSEQUENCES OF ORAL ANTICOAGULATION IN ATRIAL FIBRILLATION IN COLOMBIA

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OBJECTIVES: To determine the clinical consequences and it's associated costs of the usage of oral anticoagulation therapy for the treatment of atrial fibrillation (AF) in Colombia by establishing the cost per disease related event. **METHODS:** We used a 6-week cycle length, 17 functional state Markov model of the main clinical outcomes in the lifetime of a hypothetical cohort of 1,000 patient with AF per treatment arm. The pivotal clinical studies for apixaban, dabigatran, rivaroxaban compared to warfarin were the source of safety and efficacy data. Data for the analysis was extracted from this literature using indirect comparison methods. Costs in Colombian pesos 2012 are expressed in American dollars (1 US$ = COP$ 1785). To estimate costs, we analyzed resource use of a sample of 53 stroke, 148 myocardial infarction, 6 systemic embolism patients in San Ignacio University Hospital. Results were validated by an expert panel. **RESULTS:** The number of events associated with each anticoagulant therapy (apixaban, dabigatran 110mg, dabigatran 150mg, rivaroxaban and warfarin, respectively) were: stroke and systemic embolism 349, 363, 351, 360, 369. ISTH major bleedings 235, 212, 233, 280, 277; clinically relevant non major bleedings 342, 337, 357, 395, 383; myocardial infarctions 102, 114, 116, 101, 104; and event related deaths 459, 485, 475, 469, 481. Apixaban could be associated with savings in non pharmacological cost of $ 360, $170, $145 and $311 per treated patient compared to dabigatran 110mg, dabigatran 150mg , rivaroxaban and warfarin, respectively. **CONCLUSIONS:** In this non-pharmacological cost avoidance assessment we determined that apixaban can be a cost saving alternative in the long term. Versus SoC (warfarin), apixaban may be the only NOAC with consistent benefit on all relevant events. Consistent with trial data, lifetime modeling suggested reduction in the mortality.

PCV2
COMORBIDITIES ASSOCIATED TO ATRIAL FIBRILLATION (AF) IN SELECTED LATIN AMERICA COUNTRIES

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OBJECTIVES: AF is the most common chronic cardiac arrhythmia worldwide and is an important risk factor for morbidity related mainly to an increased risk of cerebrovascular events and heart failure. This study examined the prevalence of comorbidities among patients receiving treatment for AF in 4 Latin America countries to convey a more comprehensive picture of the total disease burden. **METHODS:** For study purposes, co-morbidity was defined as the presence of one or more disorders in addition to a primary disease, or the effect of such additional disorders. A 3-step process was conducted in order to understand treatment patterns for patients suffering from AF: 1) health care assessment per country; 2) evaluate patient's information; and 3) data analysis to understand and determine treatment algorithms. Data were collected through 59 face-to-face interviews with cardiologists in Argentina, Brazil, Chile, and Venezuela. **RESULTS:** Analysis per country suggested that, in Chile and Venezuela, 98% and 94% of patients, respectively, reported at least one co-morbidity. In Argentina this pattern was observed in 81% of the patients, whereas in Brazil this was 78%. Findings revealed that the main 5 comorbidities associated with AF were: 1) Hypertension: LatAm 43%, Argentina 28%, Brazil 45%, Chile 43%, Venezuela 33%; 2) Dyslipidemia: LatAm 22%, Argentina 11%, Brazil 25%, Chile 21%, Venezuela 18%; 3) Diabetes: LatAm 13%, Argentina 8%, Brazil 11%, Chile 10%, Venezuela 18%; 4) Cardiopathies: LatAm 8%, Argentina 4%, Brazil 8%, Chile 8%, Venezuela 9%; and 5) Thyroid disease: LatAm 7%, Argentina 4%, Brazil 3%, Chile 12%, Venezuela 9%. **CONCLUSIONS:** Overall, the analysis suggests that hypertension is the main co-morbidity associated with AF, followed by dyslipidemia and diabetes. The health burden carried by patients often extends far beyond AF. Physicians should carefully consider comorbidities and concomitant medications when managing patients.

PCV3
ICEBERG PHENOMENON OF HEART FAILURE IN HOSPITALIZED PATIENTS: A MULTICENTRIC CROSS SECTIONAL STUDY

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OBJECTIVES: Heart failure (HF) ranks high in hospital utilization, cost and quality/safety consequences. We studied occult HF as secondary diagnosis (2Dx) in a multicentric study of the A-HCUPs. **METHODS:** A multi-centric cross sectional study of 1 year hospital discharges adapted HCUPs for Argentina. We estimated HF by HCUPs' CCS#108 SL (heart failure) in 2Dx to measure submerged HF; obtained HF in first diagnosis (1Dx), and 365 day readmissions (ReH), <30 day ReH, mortality and case fatality. 2Dx1=in first secondary Dx; 2Dx5=fifth 2Dx, etc. International dollars PPP, (UN Data: 1Arg$ = 1.608 PPP, 2008) were used. **RESULTS:** Among 45466 discharges ≥19 years old, we found 1178 discharges with CCS#108 among 1Dx (incidence: 2,59%*; 95%CI 2,44-2,74%); mortality 0,24% ** (95%CI 0,20-0,29%); 365 days ReH was 60,9% (95%CI 58,1-63,7%) and <30 day ReH of 18,1% (95%CI 15,9- 20,3%). 864 discharges had CCS #108 (HF) among any 2Dx (from 1 to 10 2Dx), (incidence: 1,90%; 95%CI 1,77-2,03%) (p<0,001 vs*), descending from 2Dx1: 316, 2Dx5: 89; and 2Dx8: 36 discharges. HF was one among several multi-morbid conditions. Outcomes of discharges with 2Dx1 are 365 day ReH: 57,3 % (95%CI 51,8-62,7%) and <30 day ReH: 17,1% (95%CI 12,9- 21,2%), mortality 0,09 (95%CI 0,06-0,12%,(p<0,001 vs**), case fatality: 12,66% (95%CI 8,99- 16,32%). Mean cost per discharge was 7 907 I$ PPP and median cost 1 917 I$PPP for HF in 1Dx; while mean was 23316 I$PPP and median cost 12796 I$PPP for CCS #108 in 2Dx5. **CONCLUSIONS:** HF is the leading CCS among several criteria of ranking of discharges. Is one of the leading causes of admissions as detected by 1Dx. However, HF is frequently submerged as a 2Dx, causes significant mortality, costs and readmissions (ReH). Quality, safety and economic studies should consider HF as secondary diagnosis.

PCV4
PERMANENT TRANSVENOUS LEAD EXTRACTION: FACTORS INFLUENCING THE DIFFICULTY OF THE PROCEDURE

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OBJECTIVES: Transvenous lead extraction is increasingly required. The aim of this study was to determine which factors influence the difficulty of a lead extraction procedure through the analysis of a high-volume centre database. **METHODS:** A total of 889 permanent leads were extracted from 469 patients. Factors influencing the difficulty of a procedure were assessed using a multivariate logistic regression model. The fluoroscopy time of the procedure was taken as index of difficulty. **RESULTS:** From January 2003 to December 2012 , 932 of 946 (98.5%) leads were completely removed. Major complications occurred in 1.3% patients. No deaths occurred. Median fluoro time was 8.4 min (3.2 - 17.1). A procedure was classified as difficult when fluoro time was greater then 31.2 min (90th percentile). At a multivariate analysis the predictors of a difficult procedure were the number of extracted leads (OR 1.71, 95%CI 1.06 – 2.8), the presence of screw leads (OR 5.68; 95%CI 1.9 – 16.9), the presence of dual coil shock leads (OR 5.01, 95%CI 1.27 – 19.8), the years since the oldest lead was implanted (OR 1.23, 95%CI 1.15 – 1.31), the absence of leads with vegetation (OR 6.76, 95%CI 1.35 – 33.3). The female gender, the patient age at extraction, the presence of tachy leads, the presence of lead failure weren't predic-

tors of a difficult procedure. **CONCLUSIONS:** Factors influencing the difficulty of an extraction procedure are the number of leads, the presence of screw leads, the presence of dual-coil tachy leads, the years since the oldest lead was implanted and the absence of leads with vegetation.

PCV5

LA UTILIDAD PREDICTIVA DEL EUROSCORE PUEDE SER MEJORADA AL ADICIONAR VALORES DE PEPTIDO NATRIURÉTICO TIPO B O DE HEMOGLOBINA

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OBJECTIVOS: El Euroscore(EU) es el modelo predictivo más usado en cirugía cardiaca; sin embargo, sobreestima el riesgo y la información necesaria para calcularlo no siempre está disponible. Este estudio fue diseñado para: 1). Definir si adicionar el valor preoperatorio de hemoglobina (HB), péptido natriurético tipo B(BNP) o ambos, al EU, mejoran su capacidad predictiva sobre morbimortalidad a 6 meses de seguimiento postoperatorio en toda la muestra y en los pacientes diabéticos; y 2). Evaluar la utilidad de EU en nuestro medio. **METODOLOGÍAS:** Se incluyeron 492 pacientes quirúrgicos cardiacos. Se comparò directamente la capacidad predictiva de BNP y/o HB vs EU. Luego se evaluó en que tanto la incorporación de BNP y/o HB al EU, adicionaron en términos de lograr mejor discriminación. Para cada uno de los desenlaces se construyeron y compararon curvas ROC. **RESULTADOS:** Sobre mortalidad, BNP o HB no adicionan capacidad predictiva al EU ni en la muestra global ni en diabéticos. La mortalidad intrahospitalaria fue mejor discriminada por EU aislado: área bajo la curva ROC (ABC-ROC): 0.83(IC95%0.75-0.92) y a 6 meses, ABC-ROC 0.73 (IC95% 0.64-0.83); en pacientes diabéticos, ABC-ROC 0.95 (IC95%0.91-1.00) para mortalidad intrahospitalaria y a 6 meses, ABC-ROC 0.84 (IC95% 0.74-0.98). La discriminación obtenida con BNP fue buena para bajo gasto cardiaco: ABC-ROC, 0.72 (IC95% 0.67-0.77); e insuficiencia renal aguda ABC-ROC 0.75 (IC95% 0.76-0.84). Los mejores predictores de transfusión fueron EU+HB ó BNP+HB. EU mostró buena capacidad predictiva (ABC-ROC≥0.70) sobre morbilidad combinada, estancia prolongada en cuidado intensivo, bajo gasto cardiaco e insuficiencia renal y a 6 meses en la discriminación de evento cerebrovascular, tanto en el grupo total como en diabéticos. **CONCLUSIONES:** La capacidad discriminatoria de EU para mortalidad en nuestro medio es muy buena, especialmente en diabéticos. BNP o HB no adicionan capacidad predictiva. En la mayor parte de los desenlaces de morbilidad la discriminación obtenida con BNP aislado es comparable a EU.

PCV6

INDIRECT TREATMENT COMPARISON BETWEEN FIXED-DOSE-COMBINATIONS OF LOSARTAN/AMLODIPINE AND VALSARTAN/AMLODIPINE IN BLOOD PRESSURE CONTROL

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OBJECTIVES: To compare changes in blood pressure after 8 weeks of therapy between a fixed-dose combination (FDC) of amlodipine/losartan and amlodipine/valsartan using a network meta-analysis because there are no trials directly comparing amlodipine/losartan to amlodipine/valsartan. **METHODS:** A systematic search identified six randomized controlled trials of study FDCs and their component monotherapies; 3 included amlodipine/losartan and 3 included amlodipine/valsartan. Conventional fixed-effects methods were used to conduct the comparisons. The change in sitting diastolic and systolic blood pressure (sitDBP, sitSBP) at 8 weeks post-randomization was the primary and secondary effect measures. **RESULTS:** Amlodipine/losartan 5/50 mg produced greater reductions in sitDBP (-1.27 mmHg, 95% confidence interval (CI) -5.7 - 2.2) and sitSBP (-3.7 mmHg, 95% CI -9.0 - 2.9) than amlodipine/valsartan 5/80 mg. Amlodipine/losartan 5/100 mg produced a greater reduction in sitDBP (-0.45 mmHg, 95% CI -3.7 - 2.7) than amlodipine/valsartan 5/160 mg while amlodipine/valsartan 5/160 mg had a greater reduction in sitSBP (0.2 mmHg, 95% CI -6.2 - 6.0) than amlodipine/losartan 5/100 mg. The confidence of superior antihypertensive efficacy for COZAAR XQ 5/50 mg than amlodipine/valsartan 5/80 mg is 77% for sitDBP and 89% for sitSBP, while the confidence of greater efficacy for amlodipine/losartan 5/100 mg than amlodipine/valsartan 5/160 mg is 61% for sitDBP and 48% for sitSBP. With 95% CI, the reduction difference in sitDBP and sitSBP between amlodipine/valsartan 5/80 mg and amlodipine/losartan 5/100 mg is not expected to exceed 1.6 mmHg and 1.26 mmHg, respectively, and not expected to exceed 2.31 mmHg and 5.38 mmHg, respectively with amlodipine/valsartan 5/160 mg versus amlodipine/losartan 5/100 mg. **CONCLUSIONS:** The blood pressure lowering effect with amlodipine/losartan and amlodipine/valsartan was comparable. The findings from this network metaanalysis do not indicate a potential superiority of the reductions realized with amlodipine/valsarta relative to amlodipine/losartan.

PCV7

COMPARATIVE EFFICACY OF BLOOD PRESSURE LOWERING DRUGS IN PRIMARY PREVENTION FOR ELDERLY PATIENTS

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OBJECTIVES: Differences in efficacy of different classes of blood pressure lowering drugs (BPLDs) have been observed in elderly primary prevention populations, with beta-blockers (BBs) reported to be less efficacious for primary prevention. In this study, we assessed if these differences remained significant in patients that use statins concurrently. **METHODS:** We conducted a series of population-based nested case-control studies using administrative data from 104,023 diagnosed hypertensive patients without recent antecedents of diabetes or cardiovascular disease (CVD) in the province of Quebec (Canada) between 2000 and 2004. Follow-up ended either with an outcome event, or at the end of 2009. Individuals with an outcome event (all-cause death, CVD event) were considered cases. Controls were matched according to age, sex, date of cohort entry, and comorbidity index. Conditional logistic regression was used to estimate the odds ratio of the outcome events for patients whose treatment in the week before event date included statins and BBs as compared to patients whose treatment included statins and other BPLD(s). **RESULTS:** Patients on statins and BBs showed substantially higher risks for cardiovascular death (OR=2.12, 95%CI: 1.81–2.49), all-cause death (OR=1.64, 95%CI: 1.49–1.81), CVD events (OR=1.96, 95%CI: 1.80–2.12) and hospitalization for CVD (OR=1.99, 95%CI: 1.82–2.17) as compared to patients on statins and other BPLDs. Sensitivity analyses suggest that this higher risk is not due to differences in prescription patterns based on perceived disease severity (indication bias). **CONCLUSIONS:** In elderly hypertensive patients, the concurrent use of statins and BBs is associated with less effective primary prevention in comparison to the use of statins in combination with other BPLDs. Consequently, the difference observed in the efficacy of different classes of BPLDs in elderly populations in primary prevention remains significant in the subpopulation receiving statins. Further studies should be conducted to confirm this finding.

PCV8

DIFFERENCES IN THE WEIGHTED AVERAGE DAILY DOSES OF STATINS IN LATIN AMERICA AND THEIR POTENTIAL IMPACT ON CARDIOVASCULAR OUTCOMES

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OBJECTIVES: We examined the potential clinical implications of prescribing patterns of generic statins within 11 Latin American markets (LA11). In LA11, generic versions of pravastatin, simvastatin and atorvastatin are available, however, each statin has a different LDL-cholesterol (LDL-C) lowering efficacy that may ultimately result in differences in the incidence of CV events. 2011 LA11 prescription data indicate that statins are prescribed at doses that do not yield equivalent LDL-C lowering. Thus we calculated the weighted average daily doses (WADDs) of pravastatin, simvastatin and atorvastatin within LA11 and estimated the average LDL lowering with each statin, and the incidence of CV events. **METHODS:** The WADDs of prescribed simvastatin, pravastatin and atorvastatin in LA11 were derived from IMS data. The LDL-C modifying potencies of the WADDs were interpolated from dose response curves from Nicholls et al (Am J Cardiol, 2010), and Law et al (BMJ, 2003). The relationship between LDL-C reduction and the resultant impact on cardiovascular events was derived from the Cholesterol Treatment Trialists' Collaboration (CTTC, Lancet 2010), where a 1mmol/L reduction in LDL-C, translated to a 22% reduction in major cardiovascular events. **RESULTS:** Across LA11, the WADDs for pravastatin, simvastatin and atorvastatin were 24.9mg, 22.4mg and 20.6mg, respectively. The corresponding reductions in LDL-C at these doses were estimated to be 25.0%, 33.4% and 40.6%. Assuming a pre-treatment LDL-C of 4.0mmol/L, these lipid changes would lead to reductions in the risk of a major coronary/stroke event of 22.0%, 29.4% and 35.8%, respectively. **CONCLUSIONS:** At currently prescribed WADDs in LA11, the real world use of atorvastatin provides a superior reduction in LDL-C to either simvastatin or pravastatin, and hence would be expected to result in a greater reduction in cardiovascular events.

PCV9

ANALYSIS OF CONSUMPTION OF DIURETICS IN SERBIA FROM 2006 TO 2010

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OBJECTIVES: Diuretics are drugs of first choice in the treatment of hypertension. The aim of this study was to analyze the consumption of diuretics in Serbia in the period from 2006 to 2010 year. **METHODS:** The data about the use of drugs were taken from the Agency for Drugs and Medical Devices of the Serbia. **RESULTS:** The use of diuretics during the observed period in Serbia is quite small and it ranged from 5 to 6% of the total consumption of all drugs from the C group. Furosemide was the most frequently used diuretic. In the five year period furosemide consumption ranged from 33-55% of the total consumption of all diuretics. The second largest consupmtion during first four years of the study was that of indapamide. Indapamide consumption in the fifth year was at the fourth position. At the third position in drug consumption in the first four years was hydrochlorothiazide. Use of hydrochlorothiazide in 2010 took second place. Spironolactone has occupied the fourth position in the first four years. During the last years of the period spironolactone occupied the third position. Consumption of all other diuretics was small and it was only a few percent of the total consumption of all diuretics. **CONCLUSIONS:** In Serbia, in the observed period, consumption of diuterics is two to three times lower in comparison with the consumption of diuretics in Norway and Finland. This research was supported by Provincial Secretariat for Science and Technological Development, Autonomous Province of Vojvodina project No 114-451-2458/2011 and by Ministry of Science, Republic of Serbia, project no 41012.

PCV10

ANALYSIS OF CONSUMPTION OF ANTIHYPERTENSIVE DRUGS IN SERBIA FROM 2007 TO 2011

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OBJECTIVES: Drugs of first choice in the treatment of hypertension are: β-blockers, tiazide diuretics, ACE inhibitors, angiotensin receptor inhibitors and Ca channel blockers. The aim of this study was to analyze the consumption of antihypertensive drugs in Serbia in the period from 2007 to 2011 year. **METHODS:** The data about the use of drugs were taken from the Agency for Drugs and Medical Devices of the Serbia. **RESULTS:** The use of diuretics during the observed period in Serbia is quite small and it ranged from 5 to 6% of the total consumption of all drugs from the C group. Consumption of β-blockers was around 12% during all 5 years. Consumption of calcium channel blockers was less than 12% of the total consumption of all drugs from group C in the first 2 years of the observed period. However, consumption of such drugs in the last 3 years growing over 18% of the

total consumption of all drugs from the C group. Total consumption of drugs acting on the renin-angiotensin system (C09) in Serbia in opserved period was over 41 % of the total consumption of all drugs from the C group. The highest percentage in this group belonged to the ACE inhibitors. Consumption of angiotensin receptor inhibitors is small and it is only a few percent of the total consumption of all drugs from C09 group. However, consumption of drugs in this subgroup recorded steady growth in recent years. **CONCLUSIONS:** In Serbia in the observed period, ACE inhibitors are the most frequently used drugs within the group of drugs which is used for treatment of hypertension. This research was supported by Provincial Secretariat for Science and Technological Development, Autonomous Province of Vojvodina project No 114-451-2458/2011 and by Ministry of Science, Republic of Serbia, project no 41012.

PCV11

IMPACTO ECONÓMICO Y EN DISCAPACIDAD DEL INCREMENTRO DE UTILIZACIÓN DE TROMBOLISIS EN EL CUIDADO AGUDO DE L ICTUS ISQUÉMICO EN CHILE

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OBJECTIVOS: Estimar el impacto en discapacidad y económico del incremento de utilización de trombolisis para el manejo agudo de ictus isquémico (IS) en Chile, aplicando un modelo de simulación de eventos discretos. **METODOLOGÍAS:** Se modeló la historia natural y el manejo agudo de los IS para población adulta chilena, incorporando tiempos desde el inicio de síntomas al tratamiento y cuatro escenarios de utilización de trombolisis: a) utilización actual (1,7%), b) utilización de 11,6% tratando todos los pacientes que son atendidos dentro de la ventana terapéutica, c) 25% de utilización, y d) 100% de utilización. Se usaron distribuciones empíricas y teóricas para incluir la probabilidad y tiempos de los eventos. Se realizó una simulación entre 2002-2017, usando el software ARENA. Los resultados fueron la prevalencia de discapacidad por escenario. Se realizó un análisis de impacto presupuestario desde la perspectiva del asegurador público de salud, considerando los costos directos del tratamiento y de rehabilitación. **RESULTADOS:** En 2017 manteniendo la actual utilización de trombolisis (1,7%), la tasa de prevalencia por IS es 360,8 por 100.000 habitantes, presentando una disminución entre los escenarios, siendo 299,8 cuando todos los pacientes son tratados. Con respecto a la utilización actual, aumentar el tratamiento al 11,6% evita 779 discapacitados, al 25% evita 1.783 y tratar a todos los pacientes evita 8.534. A lo largo de la simulación, los costos ahorrados por casos de rehabilitación evitados son más bajos que los costos de la trombolisis. **CONCLUSIONES:** La tasa de prevalencia de discapacidad disminuye moderadamente al incrementar la utilización de trombolisis. El impacto poblacional en discapacidad manteniendo la utilización actual es marginal, siendo recomendable incrementar su utilización. Los costos directos aumentarían por sobre el costo de rehabilitación evitados, sin embargo, es necesario considerar la limitada cobertura de atención de la discapacidad en Chile y los costos sociales.

PCV12

PREVALENCE OF RISK FACTORS OF ST ELEVATED MYOCARDIAL INFARCTION

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OBJECTIVES: There is no enough data available in our country about the prevalence of risk factors for ST elevation myocardial infarction (STEMI) and which has the highest mortality rate in hospitals of Pakistan. The purpose of study was to access the age distribution, location of infarct, risk factors, sign & symptoms and in-hospital management of STEMI patients in Bahawalpur region, southern Punjab, on of the regions with high risk of coronary heart disease. **METHODS:** A retrospective study of 400 patients diagnosed as STEMI admitted to Bahawal Victoria Hospital (BVH), Bahawalpur, Southern Punjab, Pakistan was done by following their hospital record. **RESULTS:** The mean age of STEMI patients were 40 ±10. Smoking, Diabetes and Hypertension were the risk factors (51.5%), (28%), (20.5%) respectively. Anterior wall Myocardial infarctions were seen (51.5%). Sweating, vomiting, shortness of breath (SOB) & nausea accounted for more than 60% of the symptoms with chest pain mostly in left arm. Among the patients who reached early to hospital & received Streptokinase (SK) were 150 (75%), those late for SK were 44(22%), thrombolytic therapy was contraindicated only in 6 (3%) patients. Most prescribed medication are aspirin (100%), clopidogrel (98%), statin (96%), ACE-I (77.5%), nitrates (69.5%), beta blocker (60%), anticoagulant (50%), LMW-heparin (33 %). **CONCLUSIONS:** The result of our study, in which the risk factors especially smoking were found to have a prevalence in patients with STEM1 living in southern Punjab, suggested that STEM 1 can be prevented by the modification of these risk factors.

CARDIOVASCULAR DISORDERS – Cost Studies

PCV13

A BUDGET IMPACT ANALYSIS (BIA) OF TRANSCATHETER AORTIC VALVE IMPLANTATION (TAVI) IN HIGH-RISK PATIENTS WITH SYNTOMATIC SEVERE VALVE STENOSIS (SSVS) UNDER THE BRAZILIAN PUBLIC HEALTH CARE SYSTEM (SUS) PERSPECTIVE

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OBJECTIVES: Aortic valve stenosis is a progressive valvular heart disease with a standard care that involves a major open surgery. However, part of the patients is ineligible for surgery, therefore drug therapy is the only option available. Once TAVI is a less invasive surgical option, clinical trials demonstrated significant benefits, although procedure and device are costly. The aim of this study was to estimate the incremental budget impact with this new procedure incorporation under the SUS perspective. **METHODS:** The BIA was based on a Markov model with quarterly cycles and 5-year time horizon in order to predict clinical and economic outcomes in a scenario with TAVI incorporation compared to the actual scenario – drug therapy (amiodarone, furosemide and digoxin) with or without aortic balloon valvoplasty. Epidemiological data were obtained from DATASUS and survival was extrapolated from PARTNER cohort B trial by using a Weibull distribution. Resource use, also gathered from this trial, included early perioperative complications (30 days) and late events (rehospitalization, dialysis, stroke, pacemaker implantation and major vascular complications). Costs were taken from the official Brazilian public official lists (DATASUS and BPS). Market-share data was obtained from Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista. **RESULTS:** The estimated number of Brazilian patients eligible for SSVS treatment was 795, 922, 1,180, 1,335 and 1,402 respectively for years 1-5 of analysis. Compared to the current scenario, the inclusion of TAVI procedure with a 13% market share during the analysis period shows an additional budget through year 1-5 of 3.5M, 5.0M, 6.7M, 8.1M and 9.4M, consecutively. **CONCLUSIONS:** The incremental budget impact to include TAVI as a treatment option in the Brazilian Public Healthcare System for SSVS high-risk patients was estimated to be USD 65 million in 5 years.

PCV14

ANÁLISE DE IMPACTO ORÇAMENTÁRIO DO OCLUSOR SEPTAL PERCUTÂNEO PARA O FECHAMENTO DE COMUNICAÇÃO INTERATRIAL (CIA) DO TIPO OSTIUM SECUNDUM

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OBJETIVOS: Analisar o impacto orçamentário do implante de oclusor septal percutâneo para o fechamento de comunicação interatrial do tipo *ostium secundum*em comparação a cirurgia cardíaca convencional. **MÉTODOS:** Análise sob a perspectiva do Sistema Único de Saúde (SUS) em um horizonte temporal de cinco anos, para uma população de pacientes portadores de CIA do tipo *Ostium Secundum*.O modelo considerou os custos com as intervenções durante o período de internação e a análise da incorporação do oclusor seguiu o pressuposto de uma taxa de utilização de 75% dos pacientes portadores de CIA OS. **RESULTADOS:** Apresentou uma redução de mais de sete milhões de reais a favor da incorporação do oclusor percutâneo em relação a cirurgia como procedimento exclusivo. As análises de sensibilidade confirmaram uma economia favorecendo o oclusor percutâneo para o fechamento de CIA *ostium secundum*. E ao cruzar as variações de custos da cirurgia, do oclusor e das taxas de utilização para uma melhor aproximação da realidade, o resultado permaneceu favorável e demonstrou uma concentração do número de casos na faixa entre zero e R$40.000.000,00 em economia. **CONCLUSÕES:** A análise demonstrou a possibilidade de redução dos custos para o fechamento de CIA do tipo *ostium secundum*com a incorporação de uma tecnologia que já vem sendo bem indicada e utilizada ao longo dos últimos 36 anos, como uma alternativa segura e eficaz ao fechamento cirúrgico tradicional. O implante de oclusor septal percutâneo é uma opção repleta de méritos ao evitar que o paciente sofra os traumas físicos e riscos associados ao procedimento cirúrgico, bem como os riscos psicológicos causados pela estética gerada pela cicatriz cirúrgica e trauma da internação para as crianças.

PCV15

ECONOMIC EVALUATION OF COLLAGENASE VERSUS HYDROGEL DRESSINGS FOR CHRONIC-WOUND TREATMENT FROM THE PUBLIC PAYER PERSPECTIVE

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OBJECTIVES: To develop cost-effectiveness analysis of collagenase (CO) versus hydrogel (HG) dressings for chronic-wound treatment in adults, under the perspective of Brazilian public payers. **METHODS:** Data from the Brazilian Hospital Information System from January 1st to December 31st 2012 was used to define the annual number of hospital admissions due to chronic wounds (only non-surgical records with L89 ICD-10 code included). The model assumed that CO is the current practice in Brazilian public hospitals and patients are discharged at the time their wound heals. The difference in MHT was applied to the average length of stay (LOS) reported in the database. Resource use was estimated through expert panel and unit costs were obtained from Brazilian official price lists. **RESULTS:** A total of 280,440 hospitalizations were identified with mean LOS of 4.47 days. The model estimated costs for the inpatient period assuming one dressing change for CO and HG. The cost per dressing change was estimated as 13.83BRL for CO and 11.95BRL for HG and the overall treatment costs were 61.82BRL and 53.42BRL according to the LOS. HG-related incremental costs were -8,40BRL indicating a cost-saving profile. Addopting HG as wound management protocol would save 527,227.20BRL for the 2012 cohort. Benefits in terms of reduction in LOS were not accounted in the base case scenario. **CONCLUSIONS:** HG dressing has shown higher efficacy when compared to CO dressings, with fewer costs. The clinical and economic incremental results between different dressings reinforce the need of evidence-based decision making and rational resource allocation.

PCV16

COST ANALYSIS OF PULMONARY ARTERIAL HYPERTENSION IN A TERTIARY CARE SETTING IN MEXICO CITY

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OBJECTIVES: The present study determined the total direct health-care costs for the management of PAH patients with differing degrees of disease severity. The study also aimed to find the key cost drivers in the management of PAH. **METHODS:** PAH patients were recruited from a tertiary care hospital between January 1, 2009 and

2011. One-year costs were identified by applying cost data to medical information obtained by review of medical records. Costs included those for medications, laboratory and diagnostic tests, clinic visits, emergency room visits and hospital stays. Contemporary data were obtained from epidemiological studies, government datasets, and other sources to estimate prevalence. National costs (US dollar 2012) of treatment for PAH were estimated by extrapolation of mean cost estimate per person to national incidence data for PAH. Because of uncertainties surrounding some of our estimates such as prevalence, one way sensitivity analyses were undertaken. **RESULTS:** A total of 113 PAH patients were identified and their demographic and clinical characteristics, patterns of care were examined. The mean age was 38 years, and 83% were female. The average per patient annual cost was $ 10,869 without specific treatment (min $ 137; max $155,928). The annual cost for the treatment of a single PAH patient per year with specific therapy (Bosentan) was calculated in $31.433. Aggregate national health care expenditures for treatment of PAH were USD 46.6 million In multivariate analysis, length of hospital stay, stay in ICU, were all significant independent predictors of treatment. **CONCLUSIONS:** There is a correlation between the cost of HAP and disease severity with hospitalization owing to disease severity being a major contributor to cost. With the expected increase in the incidence of PAH in Mexico over the coming decades, these results emphasize the need for effective preventive and acute medical care.

PCV17

COST-OF-ILLNESS STUDY OF PATIENTS SUBJECTED TO CARDIAC RHYTHM MANAGEMENT DEVICES IMPLANTATION: RESULTS FROM A SINGLE TERTIARY CENTRE

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OBJECTIVES: To estimate the procedure (implantation) cost, the total hospitalization cost and annual follow-up cost, in patients subjected to pacemaker (PM) and implantable cardioverter-defibrillator (ICD) implantation. **METHODS:** A single-center, prospective, cost-of-illness study was conducted between August 2008 and July 2009. In total, 464 consecutive patients were recruited (370 were subjected to PM implantation and 94 to ICD implantation). Resource data were assessed at patients' enrolment in the study and at 6th and 12th months of patients' follow-up. Then, the procedure cost, the total hospitalization cost as well as the annual patients' follow up costs were calculated using a bottom-up approach. **RESULTS:** The mean (95% confidence interval) procedure cost of PM and ICD implantation (including the costs of devices, electrodes, other supplies, and personnel's time) was calculated to be €1803 (€1758–€1858) and €13 521 (€13 153–€13 892), respectively. The mean total hospitalization cost (including procedure cost, hospitalization cost, cost of laboratory and imaging diagnostic examinations and the indirect cost attributed to productivity lost due to patient's hospitalization) was €3926 (€3711–€4167) for PM and €17 764 (€16 852–€18 692) for ICD. The mean annual cost (direct and indirect) was €1816 (€1433–€2421) for PM and €2819 (€2115–€3703) for ICD. No difference was detected in the annual cost between patients with initial implantation and replacement. **CONCLUSIONS:** These data revealed that although these devices are associated with a relatively high upfront cost, the annual societal cost following the implantation is low. Therefore, implantation of such devices should be encouraged since these devices reduce the morbidity and mortality without a high economic burden to society.

PCV18

ECONOMIC BURDEN OF CORONARY HEART DISEASE IN THE PATIENTS ATTENDING NATIONAL HEART CENTER, KATHMANDU, NEPAL

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OBJECTIVES: To calculate cost of illness due to coronary heart disease in the patients attending National Heart Center, Kathmandu, Nepal. **METHODS:** Descriptive cross sectional survey was conducted. The total number of sample was 120. The sample was selected by non-probability purposive sampling method. Data entry and analysis was done using SPSS 16.0. Categorical variables were compared using Independent Sample t-test and cross tabulation was done and chi- square test was applied to show significant difference between variables. **RESULTS:** Agriculture was the main source of income of the coronary heart disease household and the average annual household income was NRs. 1, 54,000 (US $ 1792). The study estimated the average cost of illness to be NRs. 30,888.14 (US $ 360) for an outpatient episode of coronary heart disease which was 20.05% of the average annual income of CHD household. The average total time loss of the CHD household was 8.75 person days. The average total direct cost was NRs. 29,600 (US $ 344) of which medical cost was the largest component. The average monetary value of time loss by the household was found to be 2,981.18 (US $ 35). **CONCLUSIONS:** The study found high cost of illness due to centralised system of health care. The findings of the study showed that households struggled to cope and adopted unsustainable strategies that damaged asset and caused or sustained impoverishment. Thus, estimated cost appears to be sustained economic burden on the individual household.

PCV19

AFFORDABILITY OF ANTIHYPERTENSIVE TREATMENT IN MEXICO

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OBJECTIVES: Hypertension (HT) is one of the most prevalent chronic diseases in Mexico. In the last two decades, a substantial increase in the prevalence of HT was observed in Mexico from 25% in 1993 to 43.2% in 2006 in adult population (≥20 years old). Almost 50% of population is not under a social security scheme and many patients pay for medicines out-of-pocket. This study's aim was to calculate the affordability of different kinds of antihypertensive drugs in Mexico. **METHODS:** Price data for 5 classes of antihypertensive drugs (diuretics, beta blockers, calcium channel blockers, ACE inhibitors and angiotensin II receptor antagonists or ARBs) were obtained from public internet sources, and the lowest price identified for each generic was used to estimate one month's cost of hypertension treatment; considering the maximum and minimum dosage for each generic. The affordability of treatments was calculated by comparing the total cost of medicines to the daily official minimum wage ($63.12MXN, 2013 prices) **RESULTS:** The number of days' wages required to pay one month of antihypertensive therapy ranged from: 0.08-4.18 for diuretics, 0.67-1.90 for beta blockers, 1.7-3.99 for calcium channel blockers, 0.71-3.31 for ACE inhibitors and 2.38-8.11 for ARBs. **CONCLUSIONS:** Cost could be a substantial barrier for permanence in antihypertensive treatment, so that should be discussed measures to prevent this from happening.

PCV20

TREATMENT COSTS OF ISCHEMIC STROKE PREVENTION AND MANAGEMENT IN PATIENTS WITH ATRIAL FIBRILLATION (AF) IN LATIN AMERICA: ARGENTINA, BRAZIL, CHILE, AND VENEZUELA

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OBJECTIVES: AF is the most common chronic cardiac arrhythmia worldwide. Most patients with AF need life-long treatment to be protected from ischemic stroke. The aim was to conduct a high level cost assessment for stroke prevention and management in patients with AF [SPAF & SMAF] in 4 Latin American countries. **METHODS:** Overall the costs of SPAF & SMAF were determined through 59 face-to-face interviews with cardiologists in Argentina, Brazil, Chile and Venezuela. Treatment costs were estimated using benchmarks from major private and public hospitals in each country. **RESULTS:** On average, the largest component of real-life medical expenditures for SPAF, under appropriate treatment given CHADS2 scores, was prescription drugs, which ranged from 68% in private to 75% in public. Annual SPAF treatment ranged in price from US$425 in Argentina to US$1,935 in Chile in private institutions and US$85 in Brazil to US$1,199 in Venezuela in public institutions. Moreover, overall treatment costs in Chile were 5X higher than the least expensive country in each sector. For SMAF, using rivaroxaban vs the common Vitamin K antagonists resulted in a 24%-46% cost reduction for disease treatment at a national level due to better patient adherence. This would decrease the stroke incidence/year, which would translate to US$143 M /yr in savings. **CONCLUSIONS:** AF is an important source of health care resource utilization because of repeated medical examinations, extensive use of laboratory tests and pharmacological treatments. Private and public institution cost differences are common in all 4 countries. Improving access to novel drugs, such as rivaroxaban, could help improve cost allocation, inducing a savings opportunity in each country.

PCV21

HEALTH-ECONOMIC ASSESSMENT OF THE USE OF CATHETER-BASED RENAL DENERVATION IN PATIENTS WITH RESISTANT HYPERTENSION IN MEXICO

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OBJECTIVES: Catheter-based renal denervation (RDN) is a new therapy for resistant hypertension, a condition that affects approx. 10-15% of hypertensive patients, in which blood pressure is uncontrolled despite the simultaneous use of three or more antihypertensive drugs. Our objective was to assess clinical and cost-effectiveness of RDN compared to standard of care (SoC) from the Mexican public payer perspective. **METHODS:** A previously published lifetime Markov model was adapted to the Mexican setting to predict clinical endpoints (death, myocardial infarction, stroke, heart failure, coronary heart disease, end-stage renal disease) and costs - based on Mexican epidemiological and cost data. We evaluated the impact of a 32 mmHg reduction in systolic blood pressure, from a baseline of 178 mmHg, in a 58-year old 43% female, 34% diabetic, and 16% smoking cohort, as observed in the Symplicity HTN-2 randomized controlled trial. Direct public health care costs were estimated from the published literature and from governmental databases. The incremental cost-effectiveness ratio (ICER) was computed as incremental costs per life-year gained, discounted at 3%. Deterministic sensitivity analyses were performed. **RESULTS:** RDN was projected to reduce cardiovascular endpoints by 22-32% over 10 yrs., and 7-17% over lifetime. The lifetime ICER was estimated at MXN$ 194,128 (US$ 14,750) per LY gained, and had an incremental cost of MXN$ 117,916 (US$ 8,959) compared to SoC. Application of higher discount rates led to a measured increase in the ICER. **CONCLUSIONS:** Our model projections suggest that RDN reduces and delays cardiovascular events and is a cost-effective therapy in Mexico when considering most international willingness-to-pay thresholds, but remains above the current national government threshold of one GDP/capita of MXN$ 139,900 (US$ 10,630) per additional life year.

PCV22

COST-EFFECTIVENESS OF TRANSCATHETER AORTIC-VALVE IMPLANTATION FOR SEVERE SYMPTOMATIC AORTIC STENOSIS IN INOPERABLE PATIENTS IN THE BRAZILIAN PUBLIC HEALTH CARE SYSTEM

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OBJECTIVES: Aortic stenosis is the most common valvular heart disease in the elderly – its prevalence is estimated to be up to 5% in individuals over 75 years. Surgical replacement of the aortic valve is considered the standard care and in the absence of serious coexisting conditions, the procedure is associated with low operative mortality. However, a significant proportion of patients can not undergo surgery due to a high surgical risk associated with advanced age or with the presence of multiple coexisting conditions. Treatment with transcatheter aortic-valve implantation (TAVI) is a therapy with potentially lower peri-procedure risk and has been used as a therapeutic option in this group of patients considered inoperable. Therefore, this study aims to develop a cost-effectiveness analysis of TAVI in patients with severe aortic stenosis who are not suitable for surgical treatment. **METHODS:** A Markov model was developed to compare the TAVI *versus* standard therapy (drug treatment

with or without aortic balloon valvuloplasty). Outcomes in the model were based on safety and effectiveness (as measured by clinical outcomes of chance of successful implantation procedure and survival from PARTNER cohort B trial). Resource use included early perioperative complications (30 days) and late events. Cost data were obtained from Brazilian public lists (DATASUS and BPS). Results were expressed as the reason of incremental cost-effectiveness ratio (ICER) per years gained. Probabilistic sensitivity analysis was performed to confirm robustness of the results. **RESULTS:** Compared with standard therapy with or without aortic balloon valvuloplasty, the use of TAVI improves survival in 0.97 life years with an incremental cost of US$35,071, resulting an ICER of US$36.260/ life year gained. **CONCLUSIONS:** Use of TAVI results in improved survival with a low risk of serious adverse events, and demonstrates a cost-effectiveness profile when compared to other technologies already incorporated by the Brazilian public health system.

PCV24

ANÁLISE DE CUSTO-EFETIVIDADE PARA UTILIZAÇÃO DE OCLUSORES SEPTAIS NO FECHAMENTO DE COMUNICAÇÃO INTERATRIAL (CIA) DO TIPO OSTIUM SECUNDUM COMPARADO COM A CIRURGIA CONVENCIONAL

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OBJETIVOS: Análise de custo-efetividade comparando as técnicas de fechamento de comunicação interatrial do tipo ostium secundum: cirurgia convencional e implante percutâneo com oclusor septal; na perspectiva do sistema único de saúde (SUS) brasileiro. **MÉTODOS:** Realizada revisão sistemática da literatura através de busca em bases de dados primárias. Avaliação da qualidade da evidência apresentada feita através do GRADE (*Grading of Recommendations Assessment, Development and Evaluation*). A partir da metanálise de 15 artigos foram selecionados os desfechos de fechamento do CIA, complicações e reprocedimento. Proposto um modelo matemático de árvore de decisão que foi utilizado para estimar a razão custo efetividade entre o procedimento de cirurgia convencional e o implante percutâneo com oclusor septal, através do software TreeAge 2012 Pro. O desfecho utilizado como dado de eficácia foi o número de cirurgias realizadas. Determinação dos custos: calculou-se o consumo de recursos variáveis de acordo com o volume de atendimentos entre 2007 e 2010, em um hospital especializado em cardiologia de alta complexidade do Ministério da Saúde. Custos fixos específicos: procedimentos e serviços hospitalares e profissionais foram determinados a partir de valores tabelados retirados do Sigtap (Sistema de Gerenciamento da Tabela de Procedimentos, Medicamentos e OPM do SUS, versão 1.2.0909141204; competência novembro de 2012). **RESULTADOS:** Reprocedimento: cirurgia = 0,37%; implante = 1,44% ; complicações: cirurgia = 12,87%; implante = 3,89%; fechamento: cirurgia = 99,11%; implante imediato = 93,23% e implante Follow-up = 95,21%; custos cirurgia: procedimento = R$ 22.045,70; complicações = R$ 1.038,28; custos implante percutâneo: procedimento = R$ 17.671,87; complicações= R$ 421,02. Ao rodarmos o modelo de árvore de decisão; o resultado foi favorável ao implante percutâneo, com um custo de R$18.408,86, com a probabilidade de ocorrência de cirurgia em 7% dos casos. **CONCLUSÕES:** O fechamento da comunicação interatrial por implante percutâneo de oclusor septal demonstrou ser o procedimento mais custo efetivo, quando comparado a cirurgia convencional.

PCV25

ANÁLISIS DE COSTO-EFECTIVIDAD DE IOXAGLATO VERSUS IODIXANOL EN ANGIOGRAFÍA CORONARIA

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OBJECTIVOS: Realizar un analisis de costo-efectividad del uso de ioxaglato en angiografía coronaria comparado con iodixanol, en pacientes con evento coronario agudo (ECA), desde la perspectiva del tercero pagador en Colombia. **METODOLOGÍAS:** Se diseñó un árbol de decisiones que simula los eventos clínicos relacionados con la angiografía en pacientes con ECA, en un horizonte temporal de un mes. Para un paciente con síndrome coronario agudo con edad promedio de 40 años, esperanza de vida de 74 años y peso promedio de 65 kg, sometido a angiografía coronaria con el uso de ioxaglato o idioxanol en dosis de 320 mgI/ml, se estimó como desenlace la sobrevida medida en años de vida salvados (AVS). El modelo incluye la posibilidad de presentar re-infarto y/o muerte durante y después de la realización del procedimiento (hasta un mes). Los costos de las tecnologías y los eventos fueron estimados de la base de datos estatal de costos y del sistema de precios de medicamentos (SISMED) en pesos colombianos del 2012. **RESULTADOS:** El ioxaglato mostró mayor efectividad (1,1 AVS) frente a iodixanol (29,3 frente a 28,2 respectivamente) y un ahorro de COP$ 833.079, mostrando así dominancia en las condiciones evaluadas. El análisis de sensibilidad probabilístico tipo Montecarlo, mostró que se mantenía la dominancia en el 65% de los casos en 1.000 iteraciones y con variaciones de +/- 50% de los datos. **CONCLUSIONES:** El uso de ioxaglato frente a iodixanol, en las condiciones del caso base y tomando como referencia el desenlace analizado basado en la probabilidad de re-infarto durante el procedimiento de angiografía secundario a un ECA, se muestra como la opción de elección por su mayor efectividad y menores costos, desde el punto de vista del tercero pagador en Colombia.

PCV27

COSTO-EFECTIVIDAD DE CLOPIDOGREL VERSUS TICAGRELOR, AMBOS EN COMBINACIÓN CON ASA, PARA EL MANEJO DEL SÍNDROME CORONARIO AGUDO, DESDE LA PERSPECTIVA DEL SISTEMA DE SALUD PRIVADO EN MÉXICO

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OBJECTIVOS: Realizar una evaluación económica de clopidogrel versus ticagrelor, ambos en combinación con ASA, para el manejo del síndrome coronario agudo en México. **METODOLOGÍAS:** Se utilizó un modelo de markov para evaluar distintos desenlaces clínicos a partir del grado de función renal de los pacientes con síndrome coronario agudo, desde la perspectiva del sistema de salud privado en México. Los parámetros clínicos incluyeron riesgos de hemorragia, EVC, infarto y muerte, los cuales fueron extraídos de ensayos clínicos y estudios epidemiológicos. Los datos de costos fueron tomados de los tabuladores de reembolso disponibles en los sitios de internet de las compañías aseguradoras, y las estimaciones de costos estuvieron apoyadas por opiniones de expertos. Se realizaron análisis de sensibilidad univariados. Los resultados están expresados en dólares americanos a un tipo de cambio de 12 pesos mexicanos por dólar. **RESULTADOS:** En la cohorte de pacientes con función renal alterada el costo por año de vida ganado con ticagrelor fue de 4168 dls; sin embargo, en los pacientes con función renal normal clopidogrel resultó dominante sobre ticagrelor. En cuanto a hemorragias evitadas y EVC evitados, clopidogrel también resultó dominante sobre ticagrelor en ambas cohortes de pacientes. El costo por infarto evitado con ticagrelor fue de 20,493 dls en los pacientes con función renal alterada y de 2486 dls en los pacientes con función renal normal. **CONCLUSIONES:** Clopidogrel resultó una estrategia dominante sobre ticagrelor en la mayoría de los desenlaces evaluados, tanto en pacientes con función renal como alterada, por lo que puede generar ahorros para los pacientes, mientras ofrece un mejor perfil de seguridad.

PCV28

COST-UTILITY OF DAGIBATRAN FOR CHRONIC ATRIAL FIBRILLATION IN ARGENTINA

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OBJECTIVES: Dabigatran has shown to be effective in preventing embolic events in chronic atrial fibrillation patients, but it's cost-utility has not been assessed in Argentina. Therefore, our objetive was to estimate the cost-utility of dabigatran used in recomended doses (220mg and 300mg) for the prevention of thromboembolic events in chronic atrial fibrillation. **METHODS:** A Markov model was constructed to simulate a national cohort of patients aged 65 or more, with chronic atrial fibrillation. The strategies compared were dabigatran (220 or 300 mg according to age and kidney function) or coumarins. Markov states were no events, ischemic stroke (with different severities), hemorragic strokes (with different severities) and death. Baseline characteristics were introduced in the model from a recent National Registry. Stroke risk was estimated from baseline characteristics using CHADSVASC2 score. Mortality was estimated from events and age specific mortality. Relative risks both preventing embolic events and bleeding were obtained from RELY study. Resource use was obtained from the National Admissions Database for stroke admissions and major bleedings. Costs were obtained from national health providers, both for anticoagulation costs and admission costs. Discount rate was 3%, costs and effects. The results were expressed in incremental cost-utility ratios (Argentinean pesos-ARS-per QUALY, 1 USD=5 ARS). Sensitivity analysis variables: stroke risk, 95% CI of relative risks of RELY study, stroke costs. **RESULTS:** In the base case analysis, dabigatran in 220 or 300mg doses shown to be more effective than coumarins (incremental QUALYs 0.49), with and incremental cost of ARS 5,923, resulting in an ICER of 12,040 ARS per QUALY gained. Dabigatran was associated with higher drug costs, but lower events costs. In all one way sensitivity analysis, dabigatran remained as a cost-effective strategy. **CONCLUSIONS:** Dabigatran is a cost-effective strategy for anticoagulation in chronic atrial fibrillation patients in Argentina, even considering different population characteristics, resource use and costs of ower local setting.

PCV29

COST-UTILITY OF APIXABAN COMPARED TO WARFARIN FOR STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION IN COLOMBIA

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OBJECTIVES: To evaluate the cost-utility of apixaban vs warfarin for stroke prevention in patients with atrial fibrillation (AF) from the Colombian health care system perspective. **METHODS:** A validated Markov decision model was adapted from the Colombian Healthcare system perspective. For efficacy and safety inputs, the model is based on data from the ARISTOTLE trial and clinical trials of warfarin therapy for AF. Resource utilization and costing of events were estimated using a reference hospital's billing records and validated with local experts. Costs of procedures were obtained from official tariffs (adjusted ISS 2001). The cost of medications were obtained from SISMED. The study set the price of apixaban at parity price per day to dabigatran 150mg. A discount rate of 3.5% was used for both costs and outcomes. A cohort of 1,000 patients was modeled using a lifetime horizon. Probabilistic sensitivity analysis (PSA) to account for variability in outcomes due to statistic uncertainty in inputs as well as univariate sensitivity analyses to examine the effects of changes in key model parameters were performed. **RESULTS:** Warfarin therapy resulted in a quality-adjusted life expectancy of 8.20 years at a cost of $14,906,026 COP. Treatment with apixaban led to a quality-adjusted life expectancy of 8.64 years at a cost of $23,064,028 COP. The cost-utility ratio was calculated at $ 18,392,415 per QALY. Our findings were robust in univariate sensitivity analyses varying model inputs across plausible ranges. In Monte Carlo analysis, apixaban was cost-effective in 80% of simulations using the recommended threshold for Colombia by the Ministry of Health of $36,000,000 COP per QALY. **CONCLUSIONS:** Apixaban is a cost-effective alternative relative to warfarin for stroke prevention in patients with AF in Colombia, assuming that it is introduced at a price similar to that of dabigatran.

PCV30

CORRELACIÓN ENTRE LOS NIVELES DE LDL-C FRENTE AL RIESGO DE PRESENTACIÓN DE EVENTO CARDIOVASCULAR

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OBJECTIVOS: Encontrar la correlación entre la presentación de eventos cardiovasculares, infarto agudo de miocardio (IM) y evento cerebro vascular (ECV), con los niveles de colesterol de baja densidad (LDL-c) en prevención primaria, que sirva como una herramienta para la toma de decisiones sobre acciones específicas para el manejo del tema en Colombia. **METODOLOGÍAS:** Se realizó una revisión de literatura científica en diferentes bases de datos, seleccionando estudios clínicos que mostraran el uso de las estatinas en prevención primaria, en pacientes con alto riesgo cardiovascular, y que reportaran desenlaces discriminados por eventos cardiovasculares. Los desenlaces de los estudios de presentación de eventos cardiovasculares se ajustaron a tasas por cada mil pacientes. Se realizó un análisis econométrico por medio de una regresión lineal, con el fin de encontrar el término de correlación de una variable frente a otra, como lo han sugerido previamente varios autores. **RESULTADOS:** Se seleccionaron ocho estudios que utilizaban diferentes estatinas y placebo con resultados en los desenlaces analizados (IM y ECV) ajustados en periodos por año de exposición. Los pacientes de los estudios no eran diferentes en sus características generales, excepto el nivel de LDL-c. Se encontró que la tasa de presentación de IM presenta un coeficiente de correlación de 0,015 frente al cambio de 1 mg/dL de LDL-c para niveles de LDL-c>130 mg/dL ($p<0,05$). Para el riesgo de presentación de ECV, se presentó un coeficiente de 0,003 ante el cambio de 1 mg/dL, ($p<0,05$). **CONCLUSIONES:** Se evidenció una relación positiva estadísticamente significativa entre los niveles de LDL-c y la tasa de presentación de los eventos. Sin embargo la probabilidad de presentación de un IM es mucho más sensible comparado con el de ECV ante cambios en los niveles de LDL-c en prevención primaria. Aunque esta aproximación sugiere una corelación, es necesario estudios clínicos que lo comprueben.

CARDIOVASCULAR DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PCV31
PROXY UTILITY ASSESSMENT IN ACUTE HEART FAILURE

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OBJECTIVES: Acute heart failure (AHF) is amongst the most common causes of hospitalisation in the U.S. with direct costs estimated to be $20.9 billion in 2010. Reducing the duration of hospitalisation for such conditions can have a significant impact on resource use and may also have substantial benefit for individual patients.The aim of this study was to estimate quality of life (utilities) for patients hospitalised with AHF, expressed as a utility score between 0 [dead] and 1.0 [full health] . These data could be used to support an analysis of the cost effectiveness of an intervention in AHF. **METHODS:** Proxy assessments of HRQL were collected from 50 experienced cardiac nurses (formal caregivers) and 50 family caregivers of individuals who had experienced AHF events leading to hospitalisation (informal caregivers). Data were collected retrospectively for four time points (day 1, 3, 5 and 7 post cardiac event) using the EQ-5D health status instrument. **RESULTS:** The results suggest that HRQoL is poor for hospitalised patients but quickly improves over time in response to treatment. Formal caregivers reported HRQoL to be substantially poorer for individuals immediately after admission to hospital when compared to informal caregivers. By day 7 however, formal caregivers rated patients' HRQoL as being better when compared to informal caregivers' assessments. **CONCLUSIONS:** Collection of utility data in severe acute conditions is challenging. This study represents an attempt to capture such values through the use of proxy assessment. The data suggest that hospitalization due to AHF is associated with very poor HRQoL, at least in the short term. Utility values for early assessments approximate those for conditions such as advanced cancers or major stroke. By day 7 however these values demonstrate significant improvement and a return to near normal general population levels.

PCV32
DISPOSICIÓN A PAGAR Y ANÁLISIS DE CONJOINT PARA DETERMINAR LAS PREFERENCIAS POR LOS PRODUCTOS MEDLEY EN MÉXICO

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OBJECTIVOS: Identificar los atributos que definen a un producto como Accesible. Considerando las preferencias de los médicos para prescribir y los pacientes. **METODOLOGÍAS:** Estudio analítico semi cuantitativo, cualitativo y prospectivo en pacientes con enfermedades crónicas que usan productos farmacéuticos y médicos prescriptores de productos de estas enfermedades, desde el punto de vista del sector privado en México. Se aplicaron dos técnicas complementarias, disposición a pagar y análisis de Conjoint. Se elaboraron instrumentos de recolección de datos tanto para la prescripción como adquisición por parte del paciente. Se utilizaron métodos estadísticos tanto descriptivos como inferenciales (regresiones simples, modelos ANOVA y modelos LOGIT). **RESULTADOS:** Se entrevistaron entre 15 y 20 médicos por cada especialidad. Los aspectos más importantes para los médicos al momento de prescribir un medicamento son tanto la eficacia como la seguridad, en tercer y cuarto lugar queda la tolerabilidad y el apego al fármaco. Cuando se les cuestionó sobre prescribir un fármaco genérico se encontró que para el 50% de los medicamentos el precio representa el principal atributo. Se entrevistaron 120 pacientes que padecieran alguna enfermedad crónico-degenerativa, los cuales dieron mayor pesos para elegir un medicamento de patente fueron la eficacia y la seguridad. Para los medicamentos genéricos, la eficacia fue el atributo mayor pero el precio desplazó a la seguridad. Se identificó que la cantidad a pagar por un medicamento Genérico es del 63.93% del precio del medicamento de patente. Por otra parte importa la escolaridad de la gente para elegir el medicamento. **CONCLUSIONES:** Al considerar los atributos de accesibilidad los productos Medley son productos que se consideran accesibles, ya que ofrecen eficacia y seguridad y a su vez, tienen un precio accesible para la población.

CARDIOVASCULAR DISORDERS – Health Care Use & Policy Studies

PCV33
EVOLUÇÃO DO USO DE MEDICAMENTOS GENÉRICOS NO TRATAMENTO DE DOENÇAS CRÔNICAS – PBM BRASILEIRA

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OBJETIVOS: Analisar a evolução na aquisição de medicamentos genéricos ao tratamento de doenças nos últimos quatro anos em amostra brasileira. **MÉTODOS:** Utilizou-se uma amostra de 14.425 participantes do programa de benefício de medicamentos da PBM (Programa de Benefício de Medicamentos) Orizon, que consumiram medicamentos de uso crônico para tratamento de Hipertensão Arterial Sistêmica Sistêmica (HAS), Dislipidemia (DL) e Diabetes Mellitus (DM), nos últimos 4 anos (2009 à 2012) e verificou a evolução do uso destes medicamentos. **RESULTADOS:** Houve aproximadamente 56% em unidades vendidas de medicamentos genéricos ao longo dos últimos 4 anos, contra 44% dos medicamentos de marca (referência ou similar). A diferença no percentual da quantidade de unidades de medicamentos genéricos vendidos, comparados com os de marca foi de 9,44% em 2009, 11,42% em 2010, 13,84% em 2011 e 16,28% em 2012. Os medicamentos genéricos atingiram cerca de 1% de aumento ao ano representou cerca de R$ 430mil nos anos de 2009 a 2011, sendo que em 2012 houve um decréscimo na quantidade de medicamentos utilizados no ano. **CONCLUSÕES:** A adesão ao tratamento das doenças crônicas HAS, DL e DM foi em sua maioria com o uso de medicamentos genéricos que representaram aproximadamente 56% das unidades vendidas nos últimos 4 anos, crescimento no qual foi progressivo e constante no período. Dado a vasta cadeia de descontos fornecida por fabricantes de medicamento genérico auxilia na adesão e persistência ao tratamento de crônicos, demonstrado que o valor do medicamento na compra influencia o tratamento.

PCV34
PROJEÇÃO DE GASTOS COM MEDICAMENTOS DE USO CRÔNICO (AMBULATORIAL)

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OBJETIVOS: Projetar gastos com medicamentos de uso contínuo para patologias crônicas, para usuários com plano de beneficio farmácia estimando o grau de sua utilização. **MÉTODOS:** Utilizou-se um estudo descritivo de uma população no total de 574.640 vidas, com alto subsidio na aquisição de medicamentos, utilizando o banco de dados da Orizon com mais de 16 milhões de vidas que captura informações de consumo de medicamentos pelo plano de beneficio farmácia (PBM) no ano de 2012. Foram estimadas as incidências e os gastos mensais com a compra de medicamentos para uso crônico de Hipertensão (HAS), Insuficiência Cardíaca Congestiva (ICC), Insuficiência Cardíaca Obstrutiva (ICO), Doença Pulmonar Obstrutiva Crônica (DPOC), Asma e Diabetes *Mellitus* (DM), transformando este consumo em dose diária definida (DDD), seguindo *a Anatomical Therapeutic Chemical Code*(ATC) e dividimos por faixa etária para chegar ao valor médio mensal de DDD por faixa etária. O valor da DDD para projeção do custo foi calculado baseado nos preços de janeiro de 2013, informados pela Câmara de Regulação do Mercado de Medicamentos (CMED) considerando medicamentos de A à Z. **RESULTADOS:** As patologias cardiovasculares HAS, ICC e ICO a incidência mensal foi de 6,03%, consumo médio de 89,63 DDDs e custo R$ 1,01 / DDD, as patologias repiratórias DPOC e Asma a incidência mensal foi de 0,39%, consumo médio de 35,45 DDDs e custo de R$ 3,50 / DDD e para a patologia de DM dividida em hipoglicemiantes orais e injetaveis (insulinas), o resultado para os orais foi: incidência mensal de 1,89%, consumo médio 47,14 DDDs e custo de R$ 2,26 / DDD e para os injetaveis (insulinas) a incidência foi de 0,32%, consumo médio de 35,21 DDDs e custo de R$ 7,47 / DDD. **CONCLUSÕES:** Modelo utilizado para projetar o grau de utilização e gastos com medicamentos de patologias crôncias, para beneficio de farmacia.

PCV35
ESTIMATING THE IMPACT OF STATIN THERAPY ON DIRECT AND SOCIETAL COSTS IN MEXICO: A COMPARISON TO SWEDEN

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OBJECTIVES: Recent studies have shown a high burden of cardiovascular disease (CVD) risk factors in Mexico, potentially signaling rising levels of CVD-related morbidity and mortality. This study models the cost-effectiveness of statins as a class of drugs for the secondary prevention of key coronary heart disease (CHD) and CVD events, to measure the impact of pharmaceutical innovation on a country-level basis. **METHODS:** The investigation uses a value of innovation model created for Sweden, the site of many early statin trials, and adapted to Mexico to allow a comparison between emerging and developed settings. An 8-state semi-Markov model was used to simulate the effect of statin use on key health events and disease-related societal impacts. Drug impact was modeled at the class level using relative risk reductions based on meta-analyses of international statin trials. The subject of the base-case analysis was a 55 year-old male with lifetime statin use. Individual level findings were scaled to the total population to enable an investigation of cost and health outcome trends at the country level for all incident cases in 2011. **RESULTS:** Over an individual's lifetime, the risk of subsequent myocardial infarctions (MIs) and revascularizations decreased in Mexico (MI, RVC: -3.3%,-0.5%) and Sweden (MI, RVC: -5.3%, -1.6%) due to the use of statins. At the population level, statin use produced lifetime direct cost savings (lowered outpatient, inpatient, and institutionalized costs) of USD$21M in Mexico, and USD$4M in Sweden, as well as indirect costs savings (increased productivity and reduced premature disease-related retirement) of approximately USD$50M (Mexico) and USD$88M (Sweden). **CONCLUSIONS:** In both countries, direct cost savings were smaller in scale than indirect savings, indicating the high value of societal benefits

in both developed and emerging settings. As Mexico's economy continues to grow, the value of investments in health innovation from both a public health and economic perspective will rise.

PCV36

EVALUATION OF HOME MEDICATION REVIEW IN COMMUNITY OUT REACH PROGRAM

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OBJECTIVES: To Establish the value of WHO-FIP Pharmacuetical Care in chronic conditions like diabetes, Hypertnsion and Obesity in a community out reach program. The Pharmaceutical Care program is new concept proposed in 2005, to aid the patient in improving his knowledge in the area of Drug, Disease and Life style by pharmacist. **METHODS:** The patients are approched at thier homes by a panel of health care professionals led by pharmacists. the pharmacist after interacting with the patients make the documentation regarding patient current status of knowlegde, regarding disease, drugs and life style along with his/her condition of health and the life style. The care plan is made by taking into above facts and patients are explained the correct way of using the medicine, the correct life style habits and idea about diet and physical activity. The patients were again approched after a fortnight at thier homes and measurements of Blood pressure, Body Mass Index along with Random blood sugar were carried out . All these values are recorded in a Pharmacuetical care card, which was issued to individual patients. The patients were usually followed upto 3 months in which minimum 6 visits have beed carried out. **RESULTS:** The patients are able to asses the progress of thier condition by following the advice of a health care professional. **CONCLUSIONS:** It is expected that patient will under go a cycle of knowlegde attitude and practice model. For assesing the value of the program, the pre and post evaluation by EQ 5D questionnaire and clinical parameters will be applied.

PCV37

EVOLUCIÓN EN EL URUGUAY DE TAZAS DE UTILIZACIÓN DE CATETERISMO CARDÍACO DIAGNOSTICO PAR A CARDIOPATÍA CONGÉNITA EN MENORES DE 18 AÑOS (1995-2012)

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OBJECTIVOS: Como resultado del advenimiento del ecocardiograma doppler color (EDC) a fines de los 90, muchas cardiopatías congénitas (CC) son tratadas sin Cateterismo cardíaco Diagnóstico (CCD). En el Uruguay el Fondo Nacional de Recursos financia CCD desde 1981, estando normatizada su autorización desde el 2008. Se cuenta con un registro único nacional de CCD. Objetivos: Conocer la evolución de la tasa de utilización de CCD en población pediátrica, períodos: 1°:1995 – 1999, 2°:2003 - 2007, 3°: 2008 - 2012. **METODOLOGÍAS:** Estudio descriptivo de solicitudes de CCD para CC en menores de 18 años.Las variables analizadas son : año de solicitud, edad, sexo, procedencia, cobertura asistencial, estado de autorización, y población nacional discriminada por edad en forma anual. Para analizar la evolución temporal de las tasas de solicitudes ajustada por edad y sexo se utilizó una regresión Binomial Negativa. **RESULTADOS:** Se observó un descenso significativo de la tasa de solicitudes en el devenir de los períodos analizados (RR= 0,93 IC95%= 0,91 - 0,95). Analizada la tendencia temporal y tomando como referencia el primer período se observa un descenso significativo en las tasas de solicitudes del segundo y tercer período (RR= 0,55 IC95%= 0,43 - 0,70 y RR = 0,37 IC95%= 0,29 - 0,47). Al tomar como referencia el segundo período, se observa un descenso significativo en el tercer período (RR =0,67 IC95%= 0.52- 0,85). **CONCLUSIONES:** El mayor descenso del número de CCD observado en el tercer período podría atribuirse a la introducción de normativas para autorizar la cobertura financiera de CCD por parte del FNR sumado al protagonismo del EDC. La utilización de la normativa resultó una herramienta útil para disminuir el uso de procedimientos innecesarios, optimizando la utilización de recursos.

PCV38

DESIGUALDAD EN SALUD RELATIVA AL INGRESO EN CHILE: ANÁLISIS DE DESCOMPOSICIÓN DEL ÍNDICE DE CONCENTRACIÓN EN HIPERTENSIÓN, DIABETES Y DEPRESIÓN

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OBJECTIVOS: Existe una clara asociación positiva entre ingreso per cápita y salud. Sin embargo, esta asociación no es tan clara cuando el Producto Interno Bruto percápita (PIBpc) supera de los US$18,000. Esta pérdida de asociación es en buena parte explicada por las grandes diferencias de resultados en salud entre subgrupos de la población, donde uno de sus determinantes más claramente establecidos es el ingreso económico. Chile es un país en vías de desarrollo que pretende llegar el año 2018 a un PIBpc >US$18,000. Toda evaluación de políticas en salud no debe estar circunscrita a promedios poblacionales sino a la distribución de dichos resultados en la población. El objetivo de este estudio fue estudiar la desigualdad en salud relativa al ingreso en Chile para tres enfermedades de alta prevalencia: hipertensión, diabetes y depresión. **METODOLOGÍAS:** A partir de la encuesta CASEN del 2009 (n=246 924), se estimó el índice de concentración de Erreygers ($IC_{Erreygers}$) para cada una de estas enfermedades y se realizó su descomposición basado en una regresión probit para estudiar factores asociados legítimos (edad, sexo, estado marital, número de miembros del hogar, etnia, rural/urbano) e ilegítimos (ingreso, ocupación, educación, calidad de vivienda, previsión de salud). **RESULTADOS:** El $IC_{Erreygers}$ estimado para hipertensión, diabetes y depresión fue de 0,0030; 0,0037 y -0,0012, respectivamente. La descomposición de $IC_{Erreygers}$ indica que la mayor parte de la desigualdad está explicada por la edad en todos los casos (legítimo). Ingreso y ocupación le siguieron de manera consistente en los tres problemas de salud estudiados (ilegítimos). **CONCLUSIONES:** La desigualdad en salud relativa al ingreso en hipertensión, diabetes y depresión en Chile muestra estar fundamentalmente explicada por factores legítimos como la edad. Sin embargo, factores ilegítimos como ingreso, tipo de ocupación y nivel educacional siguen explicando en algún grado la desigualdad observada en salud en esta población.

PCV39

EXPLORING GENDER DIFFERENCES IN POPULATION-BASED PREVALENCES OF CARDIOVASCULAR DISEASES IN CHILE AFTER THE HEALTH CARE REFORM OF 2005

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OBJECTIVES: Cardiovascular diseases (CVDs) are the biggest killer worldwide. Since 2002 the Cardiovascular Health Program exists in Chile and more people with CVDs are treated over time. Few focused evaluations of the equity-centered health care reform of 2005 in Chile have been conducted and none of them with a gender focus. We aimed at analysing the existence of gender differences in the prevalence of CVDs in Chile after this reform. **METHODS:** Secondary analysis of the cross-sectional Chilean Health Survey 2009-2010 (downloaded after approval from the Ministry of Health in Chile; n=5293 adult participants). We explored the relationship between CVDs (hypertension and myocardial infarction) and gender (male/female), crude and adjusted by potential confounders (individual health-risk factors, demographics, socioeconomic status, health care provision). Odds Ratios (OR) were estimated by weighted logistic regressions in Stata 12.0. **RESULTS:** The crude prevalence of hypertensions were 28.13% (95%CI [26.11-30.24]) and myocardial infarcts 3.19% (95%CI [2.47-4.12]). More than half of the population were overweight/obese (39.20%/22.92%) and any alcohol consumption in the past month was high (58.42%). Around 40.19% currently smoke. Regression models indicated that gender was a significant risk factors for hypertensions (OR 1.58, 95% CI: 1.23-2.03) as well as having public health care insurance (OR1.45, 95% CI: 1.01-2.10). However, gender was not a significant predictor of myocardial infarcts, whereas age (OR 1.05, 95% CI: 1.03-1.06) and body mass index (OR 1.05, 95% CI: 1.02-1.09) were significant to this condition. **CONCLUSIONS:** This is the first study on gender patterns of CVDs after health care reform of 2005 in Chile. It uses a national representative survey and it controls for relevant confounders. Results suggest that men were less likely to report hypertension than women. This raises the hypothesis of whether men are being underdiagnosed and whether current CVD programmes in Chile need to attract men that are not defining themselves as sick.

PCV40

TREATMENT PATTERNS OF ATRIAL FIBRILLATION (AF) IN LATIN AMERICA

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OBJECTIVES: Atrial Fibrillation (AF) is the most common chronic arrhythmia occurring worldwide in the presence of other cardiovascular disease. The objective of the current study is to determine real-life treatment patterns for patients with AF in Latin America. **METHODS:** We conducted 59 face-to-face interviews with cardiologists in four Latin American countries--Argentina, Brazil, Chile and Venezuela-- to assess medical treatment. Information from 240 patients from private and public institutions was evaluated using CHADS2 scores to identify patients' risk and to determine treatment. **RESULTS:** Patients with AF undergo a 3-step process to define their treatment course: 1) AF evaluation and diagnosis; 2) AF classification: paroxysmal, persistent, and permanent; 3) Clinical treatment focused on stroke prevention based on symptom relief, optimal treatment of concomitant cardiovascular disease, rate control and correction of rhythm disturbance. Overall in all four countries, analysis shows that the majority of patients with AF were diagnosed right before or at the time of first stroke. The most common type of AF was permanent, except in Chile which was paroxysmal. The preferred antiarrythmic was amiodarone; the primary vitamin K antagonist used was warfarin in Brazil and Venezuela and acenocumarol in Argentina and Chile. **CONCLUSIONS:** Results from the study suggest that there are no significant differences among countries and that the majority treat patients following international clinical guidelines. Although the individual health care systems need to be considered in terms of relationship of treatment patterns with resource use, it is reassuring to note that international standards of care are being embraced in major emerging markets.

INDIVIDUAL'S HEALTH – Clinical Outcomes Studies

PIH1

ANÁLISE COMPARATIVA DOS ANTICONCEPCIONAIS ORAIS COM DIFERENTES CONCENTRAÇOES DE ETINILESTRADIOL EM RELAÇÃO AOS PERFIS DE EFICÁCIA E DE ADESÃO

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OBJETIVOS: Analisar as evidências científicas disponíveis sobre anticoncepcional oral com apresentação farmacêutica Etinilestradiol (EE) 20mcg + Levonorgestrel (LVG) 100mcg, em comparação com a preparação EE 30mcg + LVG 150mcg. **MÉTODOS:** Foi realizada ampla busca nas bases de dados Medline (via Pubmed), Cochrane Library, Rebrats e CRD. **RESULTADOS:** Dos 53 estudos encontrados na estratégia de busca, apenas uma RS disponível na base de dados The Cochrane Library foi selecionada por apresentar resultados comparados dos mesmos princípios ativos nas dosagens relacionadas à pergunta do estudo. Na RS foram incluídos 21 ECRs, comparando contraceptivos orais combinados com doses de estrógenos maiores ou menores/iguais a 20 µg. Não houve diferenças significativas em termos de eficácia contraceptiva entre os 13 diferentes anticoncepcionais. Encontrou-se risco elevado de distúrbios de sangramento para os ACO de baixa dose de estrógeno (amenorréia ou sangramento irregular, infrequente ou prolongado; sangramento frequente e spotting). Mulheres em uso de EE 20 µg e desogestrel 150 µg foram mais suscetíveis a sofrer sangramento irregular (OR 1.56; 95% IC 1.10 a 2.20) e a ter maior duração do sangramento irregular durante o terceiro ciclo (diferença média de 0.7 dias; 95% IC 0.30 a 1.10) que mulheres em

uso de EE 30 µg e desogestrel 150 µg (Akerlund, 1993). Muitos ACO contendo baixa dose de estrógeno resultaram em altas taxas de descontinuação (global e através de eventos adversos como sangramento irregular). Mulheres em uso de EE 20 µg e desogestrel 150 µg tiveram um OR de descontinuação através de sangramento irregular igual a 2.59 (95% IC 1.35 a 5.00) em relação ao grupo de mulheres em uso de EE 30 µg e desogrestrel 150 µg (Akerlund 1993). **CONCLUSÕES:** Reduzir a concentração de estrógenos para melhorar a segurança pode resultar em baixa adesão em função de mudanças inaceitáveis nos padrões de sangramento.

PIH2

COST EFFECTIVENESS EVALUATION OF A ROTAVIRUS VACCINATION PROGRAM IN ARGENTINA

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OBJECTIVES: Rotavirus diarrhea is one of the most important vaccine-preventable causes of severe diarrhea in children worldwide. There are two vaccines licensed Rotarix® (monovalent attenuated human rotavirus strain) by GlaxoSmithKline and RotaTeq® (pentavalent live human-bovine reassortant vaccine) by MSD with similar results. This study aim was to evaluate the cost-effectiveness of incorporating monovalent rotavirus vaccine 2-dose scheme (Rotarix®) compared with the pentavalent vaccine 3-dose scheme (Rota-Teq®) in the national immunization schedule of Argentina. **METHODS:** A deterministic Markov model based on the lifetime follow up of a birth cohort was used. QALYs as an effect measure, health care system perspective and a 5% discount rate for health benefits and costs have been used. A review of the literature to obtain epidemiologic and resources utilization data was performed. The sources used to estimate the epidemiologic parameters were the National Health Surveillance System, the national mortality statistics and national database of hospital discharges records. Costs are expressed in local currency. PAHO 2012 Revolving Fund vaccine prices were used. **RESULTS:** Rotarix® prevented 177,254 rotavirus cases, 19,376 hospitalizations and 31 deaths while Rotateq® prevented 165,022, 17,882 and 28 events respectively. Both vaccination strategies were less costly and more effective than the strategy without vaccination (total costs $69,700,645 and 2,575 total QALYs lost). When comparing vaccination schemes Rotarix® was less expensive ($ 60,174,508 vs. $ 67,545,991 total costs) and more effective (1,105 vs. 1,213 total QALYs lost) than Rotateq®, being the dominating strategy. Probabilistic sensitivity analysis showed results to be robust of being cost-effective at a WTP threshold of 1 GDP per capita when comparing the 2-dose scheme vs. no vaccination or the 3-dose scheme one. **CONCLUSIONS:** In Argentina both rotavirus vaccination schemes dominate the no vaccination strategy and Rotateq® (3-dose scheme) was dominated by Rotarix® (2-dose scheme), being this results robust in the sensitivity analysis.

PIH3

ROLE OF ANTIOXIDANTS IN RECURRENT PREGNANCY LOSSES, LOW BIRTH WEIGHT, AND GESTATIONAL DURATION

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OBJECTIVES: To study the impact of antioxidants on the maternal and child health of women with Recurrent Pregnancy Loss (RPL) and healthy pregnancies. The three main variables studied for the purpose included (i) low birth weight (LBW), (ii) gestational duration (GD) and (iii) RPL with a history of RPL. **METHODS:** The study was conducted in two parts. Study 1 focused on the impact of antioxidants on mothers with RPL with a sample size of 123 mothers out of 200 cases. Study 2 focused on the impact of antioxidants on LBW and GD included a sample of 900 women with healthy pregnancy of 6 months. Each of the study groups were divided in to experimental (active arm) and control group (placebo arm). It was hypothesized that 1) Oral antioxidant supplementation will reduce the rate of recurrent pregnancy loss; 2) Oral supplementation of antioxidants during pregnancy will increase the birth weight of the child; and 3) Oral supplementation of antioxidants will decrease premature births. **RESULTS:** it was found in study 1 that antioxidant supplementation reduced the chances of RPL as the chances of conception in women in the active arm increased by 36%. Study 2 revealed that the chance of LBW was reduced by 15% in women that received antioxidant supplements and the average weight of their infants in the active arm increased by 0.30kg. It was found that the gestational period for women in the active arm increased by 12 days and they were 30 times more likely to give birth within their expected date of delivery (EDD). Lastly, it was also found that maternal and neonatal mortality was also reduced by 4.4% and 2.9% respectively. **CONCLUSIONS:** It is conclusion that antioxidants be made mandatory for normal pregnant women and especially women of RPL.

PIH4

CALIDAD DE PRESCRIPCIÓN DE ANTIBIÓTICOS EN EL SERVICIO DE PEDIATRIA DE UN HOSPITAL GENERAL DE CARDENAS, TABASCO, MÉXICO

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OBJECTIVOS: Evaluar la calidad de la prescripción de antibióticos en el servicio de pediatría del Hospital General de Cárdenas, Tabasco, México, en el año 2010. **METODOLOGÍAS:** Estudio de utilización de medicamentos, de tipo transversal. Se estudió un universo de N=678 expedientes de pacientes atendidos durante 2010, se tomó una muestra probabilística simple (p=0.15, d=0.05, Z=1.6) de n=152 expedientes seleccionados sistemáticamente a intervalos de k=5. Se recopiló información sobre antibióticos prescritos, diagnóstico, uso del antibiótico y esquema terapéutico; se evaluó la calidad de la prescripción comparando el esquema prescrito contra las guías de práctica clínica y la farmacopea Pediadosis. La información se sistematizó y analizó utilizando Epi Info versión 3.5.1 para Windows, se obtuvo estadística descriptiva. **RESULTADOS:** El 80.3% de los pacientes recibió antibióticos (n=122). La media de antibióticos prescritos fue 1.8, en un intervalo de 1-4, la moda fue 2. Diagnósticos más frecuentes: gastroenteritis 16.4% y bronconeumonía 9.8%. Uso de los antibióticos: profiláctico 2% y terapéutico 98%. Antibióticos más frecuentes: amikacina 37.4%, ampicilina 25.6% y dicloxacilina 13.7%. Vía de administración más frecuente: intravenosa 87%. La calidad de la prescripción fue inadecuada en 93%. Errores de prescripción más frecuentes (individuales): duración inadecuada 79.9%, dosis inadecuada 63% y medicamento inadecuado 57.5%. **CONCLUSIONES:** La calidad de prescripción de antibióticos en la unidad médica es preponderantemente inadecuada, se requieren estretegias de intervención educativas y gerenciales para dar solución al problema. Se sugiere evaluar la calidad de prescripción de otros grupos de medicamentos en todos los servicios médicos del hospital.

INDIVIDUAL'S HEALTH – Cost Studies

PIH5

ANÁLISIS DE IMPACTO PRESUPUESTAL DEL USO DE LNG SIU COMO MÉTODO DE CONTRACEPCIÓN EN COLOMBIA

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OBJECTIVOS: Analizar el impacto presupuestal de incorporar el Sistema Intrauterino Liberador de Levonorgestrel (SIU-LNG) en el sistema de salud colombiano como método de contracepción reversible de larga duración. **METODOLOGÍAS:** Tomando como referencia un modelo de costo-efectividad que muestra el beneficio del uso de SIU-LNG, se realizó un modelo de impacto presupuestal de la adición del SIU-LNG al sistema de salud. Tomando como referencia la población estimada en Colombia para 2012 y los datos de uso de estos métodos de planificación de la Encuesta Nacional de Demografía y Salud 2010, se estimó el impacto para una cohorte fija y con incremento poblacional del uso del SIU-LNG con una tasa de reemplazo anual del 30%, hasta 5 años, incluyendo costos directos de salud. Se realizó un análisis de sensibilidad univariado, realizando variaciones en la tasa de remplazo. **RESULTADOS:** El impacto que tendría SIU-LNG para el sistema de salud como método de contracepción usando cohorte fija sería de USD$ 30.422.297,03 (USD$ 0,65 per cápita) en el primer año, disminuyendo anualmente hasta llegar a un impacto acumulado de USD$ 0,31 per cápita a 5 años. Con incrementos anuales de población similar a la tasa de crecimiento poblacional, el impacto acumulado al quinto año sería de USD$ 0,42 per cápita, correspondiente a USD$ 19.969.830,10. Tomando como referencia el valor per cápita asignado para 2012, éste implicaría un impacto de 0,21% para el primer año, de -0,02% y -0,03% para el segundo año en cohorte móvil o fija, respectivamente. **CONCLUSIONES:** Los resultados muestran que la incorporación de SIU-LNG como método de planificación en el sistema de salud colombiano genera ahorro en el gasto a partir del segundo año en las condiciones del caso analizado y su impacto es bajo frente a los beneficios en calidad de vida que podría generar.

PIH6

A TIME-MOTION COMPARISON OF ITEMIZED TREATMENT COSTS IN FIRST VERSUS SUBSEQUENT CYCLES OF IN VITRO FERTILIZATION (IVF): TREATMENTS CAN OPTIMIZED FOR IMPROVING OUTCOMES WHILE INCREASING PATIENT VOLUMES IN COST-CONSTRAINED REGIONS

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OBJECTIVES: To anlayze the differences in initial versus subsequent fresh in vitro fertilization (IVF) cycles with regard to personnel time, consumables and other resources. **METHODS:** A cross-sectional observational study of 120 patients. Observations were made during regular clinic hours in the clinical rooms of a UK fertility centre and its affiliated embryology department from January 1, 2002 to December 31, 2002. The average time per task was determined for each component of treatment by averaging the observed duration for five distinct observations. For each member of staff and each component of treatment, the total time (in hours) was estimated by multiplying the duration of attendance by a) the percentage of patients undergoing each treatment component and b) the frequency of attendance by each staff member, which allowed for the weighted average of personnel time and costs along with standard deviations to be calculated. **RESULTS:** When consumables were included, each initial cycle cost the clinic approximately £2246.57 +/- £151.01. The total amount of time patients spent with staff during subsequent fresh IVF cycles was much less than initial cycles, at 6.94 +/- 2.44 hours. The time spent with staff equated to £257.53 +/- £90.77, while each subsequent fresh cycle cost the clinic approximately £1813.12 +/- £90.77. A total of 9.77 +/- 4.94 more staffing hours were spent with patients during initial IVF cycles compared to subsequent fresh IVF cycles. This decrease in staffing time created a £319.52 +/- £176.19 difference between initial and subsequent fresh cycles, while the diminished use of consumables on subsequent treatment cycles accounted for a cost-reduction of £113.93. Thus, subsequent fresh IVF cycles were, on average, £433.45 +/- £176.19 less than initial cycles. **CONCLUSIONS:** The details of our study give insight, particularly in cost-constrained regions, how clinic management may be conducted in a cost-efficient manner.

PIH7

COSTO-EFECTIVIDAD DE CARBETOCINA EN COMPARACIÓN CON OXITOCINA PARA PREVENIR HEMORRAGIA POSPARTO POR ATONÍA UTERINA EN PACIENTES CON FACTORES DE RIESGO EN COLOMBIA

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OBJECTIVOS: La hemorragia postparto (HPP) es la principal causa de mortalidad materna, el 75% de los casos de HPP son causados por atonía uterina, por lo

tanto seleccionar una terapia costo efectiva para prevenir la HPP, es vital para los países en vías de desarrollo. Los objectivos de este estudio son de evaluar lo costo-efectividad e impacto presupuestal de carbetocina en comparación con oxitocina para prevenir hemorragia posparto por atonía uterina en partos con factores de riesgo. **METODOLOGÍAS:** El modelo incluye un árbol de decisión en Excel y las medidas de efectividad fueron: el uso de dosis de uterotónicos adicionales, pérdida de sangre durante el parto y perfil de seguridad incluyendo los eventos adversos que se presentan durante la preparación y administración del medicamento, todos los parámetros clinicos fueron extraídos de evidencia científica y meta-análisis. El horizonte temporal corresponde a la duración de la estancia hospitalaria. Se incluyeron los gastos hospitalarios para atención de parto por cesárea, los costos de uterotonicos adicionales y los relacionados a la preparación y administración de medicamentos. Los valores se tomaron de manuales tarifarios y listados de precios (Farmaprecios, SISMED, ISS). A los costos de eventos adversos se les aplico un coeficiente de ajuste obtenido del Health at a Glance 2011: OECD (Organisation for Economic Co-operation and Development). **RESULTADOS:** Los pacientes que recibieron carbetocina requieren significativamente menos uterotónicos adicionales que los que recibieron oxitocina (RR 0,65, IC del 95%: 0,53 a 0,80). El costo promedio de tratamiento por paciente con oxitocina es 115USD, y con carbetocina 76USD. En una cohorte de 1000 pacientes el ahorro es de 38.530USD. El análisis de sensibilidad con +/- 10% no modifico los resultados. **CONCLUSIONES:** Carbetocina es una terapia costo ahorrativa en Colombia para prevenir HPP en pacientes con factores de riesgo.

PIH8

ECONOMIC EVALUATION OF NASOGASTRIC HYDRATION VERSUS INTRAVENOUS HYDRATION FOR INFANTS WITH BRONCHIOLITIS: A RANDOMISED TRIAL

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OBJECTIVES: Bronchiolitis is a disease of the lower respiratory tract with peak incidence in the winter. It is the leading cause of hospitalization during the first year of life and a major cause of morbidity and mortality. The estimated cost of the Victorian bronchiolitis hospital admissions for 2006 was $8.1 million dollars. Nasogastric hydration (NGH) and intravenous hydration (IVH) are two techniques for fluid replacement therapy, required in approximately 20% of children admitted with bronchiolitis, however there is a lack of agreement on which method is most beneficial. **METHODS:** The study was a multi-centre, three-year, open, randomized trial comparing NGH and IVH in children between two months and 12 months of age who were admitted to hospital with bronchiolitis and required non-oral fluid rehydration. The setting was seven hospitals in Australia and New Zealand between 2009 and 2011. The primary outcome was 'length of hospital stay', with secondary outcomes covering 'intensive care admission' (ICU), 'adverse events' (AEs) and 'number of attempts at insertion'. An economic evaluation was conducted alongside the trial to assess which approach is more cost-effective, as judged by their net 'cost per child ready for discharge' ratio. Each study site collected cost data covering treatment activities and outcome data including medical interventions, mediation received, complications, need for ICU admission and level of respiratory support. The reference year was 2009. **RESULTS:** A total of 759 infants were randomised: 378 to IVH and 381 to NGH. There was no statistically or clinically significant difference in the mean length of stay, ICU admission or AEs between treatment groups. Success at insertion on first attempt was higher in NGH (85.1%) compared to IVH (56.1%), p<0.001. **CONCLUSIONS:** The full results of the economic evaluation will be presented. With no significant difference in outcomes the economic analysis was reduced to a cost-minimisation study.

PIH9

COSTO-EFECTIVIDAD DE LAS CINTAS DE URETRA MEDIA COMPARADAS CON EL TRATAMIENTO CONVENCIONAL DE LA INCONTINENCIA URINARIA FEMENINA DE ESFUERZO EN COLOMBIA

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OBJECTIVOS: Estimar la costo-efectividad de las cintas de uretra media comparadas con la colposuspensión retropúbica y el cabestrillo pubovaginal en pacientes con incontinencia urinaria femenina de esfuerzo en Colombia. **METODOLOGÍAS:** Se construyó un árbol de decisión para comparar las cintas de uretra media con la colposuspensión retropúbica y el cabestrillo pubovaginal en el tratamiento quirúrgico de la incontinencia urinaria femenina de esfuerzo. La perspectiva fue la del tercero pagador, incluyendo todos los costos directos para el sistema de salud. Todas las cifras monetarias se expresaron en pesos Colombianos de 2011. La unidad de resultado fue la mejoría clínica definida como paciente continente o seca. Los datos de efectividad y seguridad se extrajeron de la literatura. Se calculó la razón de costo-efectividad incremental. Se realizaron análisis de sensibilidad univariados y probabilísticos para los costos, efectos y supuestos del modelo. **RESULTADOS:** Los resultados del modelo indican que el costo por un caso adicional de mejoría clínica del cabestrillo comparado con la colposuspensión fue de $10.967.742. El costo por un caso adicional de mejoría clínica de las cintas comparadas con el cabestrillo fue de $6.551.724. **CONCLUSIONES:** Desde el punto de vista económico, bajo los supuestos del modelo y desde el punto de vista del tercero pagador, las cintas de uretra media para el tratamiento de mujeres con incontinencia urinaria de esfuerzo son costo-efectivas para Colombia. Los resultados fueron sensibles a los costos de los procedimientos quirúrgicos y a la efectividad de los mismos.

PIH10

EVALUACIÓN COSTO-EFECTIVIDAD Y DE VALOR SOCIAL DE UN PROGRAMA DE INTERVENCIÓN EN POBLACIÓN INFANTIL EN SITUACIÓN DE VULNERABILIDAD, REZAGO O DÉFICIT EN EL DESARROLLO INTEGRAL - CHILE 2012

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OBJECTIVOS: En 2009 se crea el Sistema Intersectorial de Protección Social, para facilitar el pleno desarrollo de las potencialidades de los niños y niñas en Chile. Así, los niños tienen una evaluación periódica del desarrollo psicomotor, y ante la presencia de déficit o retraso, acceden a alguna de cuatro modalidades de intervención: Sala de Estimulación, Visita Domiciliaria, Ludoteca, y Servicio Itinerante de Estimulación. Estas modalidades se ejecutan en todo el país, y su implementación ha significado un importante costo. El objetivo del estudio es realizar un análisis costo-efectividad y de valor social de las intervenciones en Chile. **METODOLOGÍAS:** Se estudiaron los costos con técnica de microcosteo. Se determinaron costos sociales. La efectividad se estudió aplicando el Test Batelle antes y después de la intervención. Con estos datos se construye un modelo de simulación de la historia natural (no intervención) y de los efectos de la intervención en estudio. Para evaluar el valor social de las intervenciones, se aplica un instrumento de medición de deseabilidad y disponibilidad a pagar. **RESULTADOS:** Los costos de las intervenciones presentan importante variabilidad interregional. Las intervenciones son efectivas,y hay diferencias de efectividad entre ellas. La evaluación costo-efectividad muestra que la inversión por un niño recuperado es alta, y resulta costo-efectiva en la medición del efecto estimado a largo plazo (edad escolar y productividad). La disponibilidad a pagar y la deseabilidad social de este Programa es, en general alta, pero notoriamente mayor en las regiones más extremas del país. **CONCLUSIONES:** La evaluación costo-efectividad de un programa de intervenciones destinado a igualar oportunidades de desarrollo en las edades más precoces (0 a 4 años) es materia de desafío metodológico, pero necesario para el decisor político. Es importante destacar que además de las medidas de efectividad, se agrega la dimensión del valor social, lo cual pondera significativamente la costo-efectividad.

PIH11

ANÁLISIS COSTO-UTILIDAD DE DOS ALTERNATIVAS PARA EL TRATAMIENTO DE BEBÉS PREMATUROS EN BOGOTÁ

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OBJECTIVOS: El manejo habitual que se les da a los bebés prematuros consiste en mantenerlos hospitalizados en una unidad neonatal. Como alternativa al tratamiento habitual se considera el Método Madre Canguro (MMC), el cual busca obtener una reducción importante en los costos de hospitalización y disminuir los riesgos de infecciones nosocomiales, entre otros. Se realizó un análisis de costo-utilidad de las alternativas, el cual considera aspectos cualitativos y cuantitativos. **METODOLOGÍAS:** Se diseñó una metodología para realizar un análisis de costo-utilidad de alternativas de tratamiento médico, la cual se aplicó a los manejos de bebés prematuros en Bogotá, Colombia. Para la medición de utilidad se utilizó el enfoque de Teoría de Utilidad Multiatributo que permite, a través de una función de utilidad aditiva, evaluar el desempeño de seis variables relevantes en la valoración del estado de salud de cada uno de los bebés incluidos en el análisis. El costo se estimó con base en un procedimiento de micro-costeo de los recursos consumidos por cada bebé, bajo cada tratamiento. Finalmente, se calcularon las razones incrementales de costo-utilidad (RICU) de los tratamientos. Los modelos se realizaron con base en los resultados del estudio Charpack, Ruiz, Calume, & Charpack, 1997, el cual registra datos de 593 prematuros con mediciones desde su nacimiento hasta cumplir el primer año. **RESULTADOS:** Los valores promedio estimados para MMC y el manejo habitual, en utilidad fueron 0.876 y 0.809, y en costos Col$2'810.531 y Col$2'997.643, respectivamente. La utilidad presentó diferencia estadística significativa, a diferencia de los costos. La RICU estimada fue Col$-2'783.236, lo cual indica que el MMC no solo es más efectivo sino menos costoso. **CONCLUSIONES:** Del análisis de Costo-Utilidad realizado, se puede afirmar que el MMC como alternativa al cuidado en incubadoras de prematuros estables, con peso de nacimiento menor de 2000g, domina al manejo habitual.

INDIVIDUAL'S HEALTH – Patient-Reported Outcomes & Patient Preference Studies

PIH12

MEASUREMENTS OF ADHERENCE TO ORAL THERAPIES AMONG BRAZILIAN PATIENTS: A SYSTEMATIC REVIEW

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OBJECTIVES: To systematically review the measures of adherence to oral therapies employed in Brazilian observational studies. **METHODS:** Observational studies that evaluated adherence to oral therapies among Brazilian patients of any disease or condition were identified by searching Medline and LILACS, without time limits, using a combination of controlled vocabulary and text words for 'adherence'. To be included studies had to fully report methods to assess adherece to oral drugs and be conducted with Brazilian patients. Studies examing only persistence measures or using lost to follow-up as a proxy to adherence were not deemed eligible. Articles were independently reviewed by two researchers to identify relevant studies and abstract methodological data. **RESULTS:** Of the 472 records identified, 61 full-text articles were included in the final version of this review. The most frequent therapeutic areas were Infectious Diseases (37.7%), Cardiology (24.6%), and Endocrinology (8.2%) – HIV/AIDS represented 36.1% of all studies, while High Blood Pressure contributed with 13.1% of the included papers. Sixteen studies adopted more than one adherence measures (81 differente evaluations in 61 studies). The most frequently used adherence measures were: self-reported (n=30, 37.0%), the Morisky test (n=19,

23.5%), and pharmacy records (n=7, 8.6%). Different versions of the Morisky test were identified (modified, 4-item, and 8-item). Other validated adherence questionnaires identified within the studies (with more than one occurence) were: MAT (n=3) and MedTake (n=2). Pill counting, medical chart review, and serum drug determination were used in 4 studies each. None study used electronic monitoring of adherence. **CONCLUSIONS:** Data from the available Brazilian studies indicate a variety of methods adopted by local researchers for measuring adherence to treatment. Indirect measures are more common, particularly those based on patients' or caregivers' perception of adherence behaviors. Most studies enrolled HIV/AIDS or hypertension patients. Other chronic conditions with long term continuous oral therapies were underrepresented.

PIH13

PROMETEX - PROMEVOZ, TOOL SUPPORT OF PHARMACEUTICAL CARE FOR THE SCOPE OF PROPER ADHESION IN COLOMBIA, 2009-2012

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OBJECTIVES: To determine if the tool *Prometex – Promevoz*, helps in reducing the drug therapy use problems identified in the Pharmacotherapy Monitoring for pharmaceutics. **METHODS:** Prometex – Promevozis a tool for telephony (voice and text messages) you want, combined with other strategies, to maintain and increase drug compliance, remembering the exact times of taking medication. With prior consent, information is sent to all medications they are prescribed, coded for strictly personal interpretation and handling of confidential and bidirectional. A descriptive longitudinal, which includes users with at least two visits to Pharmacotherapy Monitoring, a pre and post-deployment of telephony tool. Demographic variables are analyzed and compared in an exploratory way in the same population type and amount of drug therapy use problems at the beginning and end of use of the tool. **RESULTS:** A total of 25.6% of patients had at least 1 drug therapy use problems during the first consultation of Pharmacotherapy Monitoring, a situation that changed after the use of *Prometex – Promevoz*, which decreased the proportion of patients with drug therapy use problems to 16.7%. A decrease between the two observations of 53.3% with a chi squeare (ji^2) of 9,56 and a p value of 0,002. **CONCLUSIONS:** The tool Prometex – Promevoz appears to contribute to the decline in drug therapy use problemsidentified in the Pharmacotherapy Monitoring.

PIH14

PATIENT-REPORTED OUTCOMES: ARE THEY WORTH IT? AN EXAMINATION IN PRO VALUE THROUGH CASE STUDIES

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OBJECTIVES: Increasing competition, pressure from payers and greater regulatory constraints require pharmaceutical manufacturers to seek methods for product differentiation. One way of differentiating pharmaceuticals is the generation of patient-centric value messages utilizing patient-reported outcomes (PROs). PROs may be primary or nonprimary endpoints in clinical trials, and commercial use is typically dependent on PROs that support key endpoints and appear in labeling (US) or in the summary of product characteristics (EU) to support reimbursement. However, despite this obvious utility, the cost and logistical complexity of including PROs may deter clinical teams. The purpose of this research is to better understand the value of PROs and the ability of PROs to provide data critical to decision making for patients, clinicians, and payers. **METHODS:** A detailed case study was conducted of three marketed products: ivacaftor, mirabegron, and botulinum type A. Selection of these products represent a range of therapeutic areas and may provide insight into the differing roles of PROs. For each product available US and European submission and review documents were analyzed. **RESULTS:** PROs were included in all three submissions. A PRO labeling claim was granted for a primary endpoint for mirabegron, and while claims for nonprimary PROs were denied, the review documents indicate that the decision for drug approval was supported by results of the nonprimary endpoints. Ivacaftor was granted a claim based on a nonprimary PRO endpoint, though the tool did not meet the specifications of the FDA's PRO guidance. Finally, health authorities recognized the impact on health-related quality of life for botulinum type A for migraine in support of a positive appraisal. **CONCLUSIONS:** The results of this review indicate that PROs included in clinical trials may have a strong influence on the drug approval process, regardless of whether a PRO labeling claim is ultimately granted. Further research is warranted.

PIH15

THE PATIENT-REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM IN SPANISH

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OBJECTIVES: The Patient-Reported Outcomes Measurement Information System (PROMIS®) provides accurate and efficient measurement of patient-reported outcomes. Developed in English using qualitative methods, PROMIS tools measure symptoms, such as pain and fatigue, and aspects of health-related quality of life across a wide variety of chronic diseases and conditions. **METHODS:** To enable participation of Spanish-speaking populations the PROMIS banks were translated into Spanish using methods that would ensure linguistic equivalence and cultural appropriateness. The Spanish translation of 825 adult and 156 pediatric items was obtained through the FACIT Multilingual Translation Methodology which consists of the following ten steps: 1) creation of item definitions; 2) two simultaneous forward translations; 3) reconciliation of forward translations; 4) back-translation of reconciliation; 5) expert review of back-translation and previous steps; 6) preliminary finalization for pilot-testing; 7) cross-cultural harmonization; 8) quality assurance; 9) cognitive testing with native speakers of Spanish; and 10) finalization of translations based on analysis of qualitative data collected during pilot-testing. In an effort to create a universal Spanish version, linguists from various Spanish-speaking countries were recruited to achieve a translation that could be used in all regions in which Spanish is spoken. **RESULTS:** After the translation phase was completed, psychometric testing was carried out. 485 adult items and 139 pediatric items from 11 subdomains were tested with native Spanish speakers (2,500 adults and 1,200 children) from an online general population panel. Different item banks exhibited various levels of differential item functioning (DIF) across Spanish and English speaking populations. In order to retain all items in each bank, a hybrid approach was used in which English calibration metrics were used for non-DIF items and Spanish calibrations were used for items exhibiting DIF. **CONCLUSIONS:** Spanish Computer Adaptive Tests (CATs) for Anxiety, Depression, Fatigue, Physical Function and Sleep Disturbance are currently available in Assessment Center (www.assessmentcenter.net).

PIH17

PRELIMINARY RESULTS QUALITY OF LIFE, PHYSICAL ACTIVITY, AND SEDENTARY BEHAVIOR IN COLLEGE STUDENTS

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OBJECTIVES: Being physically active is associated with reduced risk of chronic diseases. In this study we examined the associations of physical activity and sedentary behavior with perceived quality of life (QoL) in college students in Venezuela. **METHODS:** A convenience sample of 64 students at Central University of Venezuela, ranging in age from 17 to 43 years was surveyed using a written questionnaire. Quality of life was measured using a single-item from the Health Survey Short-Form 36 (SF-36), EuroQol health states descriptive system (EQ-5D), and a visual analogue scale (EQ-VAS). The relationships between health status, physical activity, and sedentary behavior were estimated computing Kendall's τ correlation coefficients. Statistic analysis was performed by SPSS 13.0. **RESULTS:** The sample consisted of 41 females and 22 males. The sample had a mean age of 20.54 years (s.d. 3.99 years). Two subjects (3.2%) reported some problems with mobility. Three subjects (4.8%) reported some problems with usual activity. Ten subjects (15.9%) reported some problems with pain. One subject (1.6%) reported extreme problems and 10 reported some problems with anxiety. Three subjects (4.8%) rated health status of fair or poor. Subjects reported doing vigorous physical activities on a mean of 2.05 days during the past week. Subjects reported walking for a mean of 93.49 minutes during the past week. Subjects reported spending a mean of 301.31 minutes sitting during the past week. Neither physical activity nor sedentary behavior was associated with quality of life in our population. **CONCLUSIONS:** Study limitations include the sample size and the use of a convenient sample. Overall, this exploratory study demonstrates that the quality of life of college students in Venezuela was good.

INDIVIDUAL'S HEALTH – Health Care Use & Policy Studies

PIH18

COMPARED ANALYSIS OF INEQUALITIES IN HEALTH AND INFLUENCE OF SOCIAL DETERMINANTS OF HEALTH IN CUBA AND USA

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OBJECTIVES: Equity is a desirable goal for health systems performance and the comparison of them is important to learn lessons from the best. In the present study our goal was to analyze comparatively inequalities in health and the influence of social determinants of health in two countries with different social, economical and political contexts: Cuba and USA. **METHODS:** A compared inequalities analysis was made in three health indicators related with the performance of health systems: maternal mortality rate (MMR), infant mortality rate (IMR) and life expectancy at birth (LEB) using published geopolitical unities information from USA and Cuba in 2008 and through the computation of inequality indexes suggested in literature and statistical analysis. Also there were comparatively analyzed the effects on these health indicators of three proxy indicators of social determinants of health (PISDH's): percent of rural population (PRP), percent of non white population (PNW) and physicians rate (PHR), through the computation of effect indexes for significantly Pearson correlations. **RESULTS:** Cuba showed significantly higher inequality than USA in MMR; USA showed higher inequality in LEB; the inequality in IMR was statistically not different. The PRP was a risk factor for the LEB in USA but a protector factor in Cuba; PNW was a risk factor for MMR and IMR in USA only, although with low effect index; PHR was a risk factor for MMR in USA only, perhaps by his correlation with another PISDH's. **CONCLUSIONS:** Important inequalities were identified in both countries. The PISDH's analyzed affected health indicators principally in USA. Another economic PISDH's are required for more detailed comparative analysis in the effects of PISDH's in health inequalities. There are few comparative analysis of health systems in the literature that employ quantitative methodology as used in this study.

PIH19

ATENCIÓN INTERCULTURAL DEL PARTO VAGINAL EN MÉXICO: COSTOS ECONÓMICOS, DETERMINANTES Y RETOS DE LA IMPLEMENTACIÓN DE POLÍTICAS EFECTIVAS EN BENEFICIO DE LAS MUJERES INDÍGENAS

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OBJECTIVOS: Estimar los costos de atención del parto vaginal en unidades del sector público de salud de Oaxaca y Chiapas, para dos modelos asistenciales alternativos (convencional e intercultural), durante 2008-2012 e identificar los principales determinantes de la implementación efectiva y puesta a escala de modelos interculturales de atención materna en beneficio de la población indí-

gena. **METODOLOGÍAS:** Análisis transversal con información de expedientes clínicos de 488 usuarias de los servicios estatales de salud. Se realizó un microcosteo y se estimaron los costos de la utilización de recursos, desde la perspectiva del sector salud. Se realizaron pruebas estadísticas tipo X^2 de Pearson y prueba t para identificar diferencias en las variables de estudio. Los costos se expresan en pesos mexicanos del 2012. Se realizaron entrevistas semi-estructuradas a usuarias y actores de niveles estratégicos, tácticos y operativos involucrados en el diseño e implementación de modelos interculturales en salud materna en ambos estados. **RESULTADOS:** El 66% de las mujeres eran indígenas. 80% de los costos se concentraron en consultas y hospitalización. El costo promedio por este concepto fue de $4188 (modelo convencional) y $4002 (modelo intercultural). Se identificaron dos principales modelos interculturales: el parto vertical y la vinculación entre parteras tradicionales y prestadores de servicios. Existen divergencias entre las expectativas de las usuarias y sus familiares y los actores involucrados en el diseño e implementación de las intervenciones interculturales y escasa conciencia entre prestadores de servicios y tomadores de decisiones sobre la complejidad del significado de la atención intercultural en salud materna. **CONCLUSIONES:** Incorporar elementos interculturales en la atención al parto vaginal, no añade costos adicionales al sector salud, mientras sí puede asociarse con mayor aceptación de las usuarias. Se requiere una mayor coordinación entre los actores, para la implementación efectiva de intervenciones interculturales, en apoyo a las estrategias de reducción de la mortalidad materna.

INFECTION – Clinical Outcomes Studies

PIN1
DYNAMIC MODELING OF VECTOR-BORNE DISEASES (VBD): THE EXAMPLE OF MALARIA

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BACKGROUND: VBD, such as Chagas disease, dengue, or malaria, are transmitted from to humans by insects or other organisms and can be difficult to control. VBD transmission involves a combination of interactions among multiple factors including animal hosts, vectors, and humans. Dynamic modeling methodologies used to describe infectious disease transmission processes are amenable to a situation when infection and interaction of ≥1 species, as is the case of VBD. This work demonstrates the use of such methodology for the example of malaria. **METHODS:** A dynamic, compartmental model was developed to simulate malarial disease transmission among the human and mosquito populations. The model consists of a mosquito population divided into susceptible, exposed but not infectious, and infectious and a human population including susceptible, exposed but not infectious, infectious but immune and infectious susceptible individuals. Parameters include human and mosquito birth rates and life expectancies, probabilities of disease transmission between humans and mosquitoes, and number of mosquito blood meals per day. The effect of anti-malarial treatment was modeled to assess epidemiologic outcomes under various scenarios. The model was solved analytically to determine the expected number of cases per person per year under each scenario. **RESULTS:** When transmission intensity is low, treatment of infected individuals with a therapy providing a subsequent 15-day period of immunity reduces the incidence of disease from 0.481 with no treatment to 0.475 cases per person per year (pppy). In moderate and very high transmission settings the incidence of disease is reduced from 2.385 to 2.171 cases pppy and 9.899 to 7.007 cases pppy, respectively. **CONCLUSIONS:** This model demonstrates the utility of dynamic modeling methodology to examine the spread of VBD. Several model parameters may be varied to assess the epidemiologic impact of a number of treatments and vector control mechanisms. These models may be expanded for cost-effectiveness analysis.

PIN2
ALTERNATIVE HIGH LEVEL DISINFECTANTS TO PROCESSING FLEXIBLE ENDOSCOPES

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OBJECTIVES: Endoscopy is fundamental in different medical specialties, with increasing use. Endoscopes are expensive equipment, complex, thermo sensitive, delicate materials and submitted to high-level disinfection (HLD). The most commonly used disinfectant is glutaraldehyde (GLU) due to its high compatibility with the materials and low cost. However, evidence of toxicity to professionals and the identification of mycobacteria tolerant to GLU caused changes in Brazilian legislation on the issue, pressing health services to search for alternative desinfectants. Search for evidence on the effectiveness, toxicity and potential damage to endoscopes by alternative disinfectants to GLU available in the Brazilian market. **METHODS:** The study sample was semi-critical endoscopes flexible (digestive, respiratory and cystoscope), the intervention was HLD with peracetic acid (PA), Ortho-Phthalaldehyde (OP) and Electrolyzed Acid Water (EAW), compared to GLU, with outcomes HLD effectiveness, toxicity and damage to equipment. **RESULTS:** Were identified 822 publications (2008-2013) on 13 databases, 23 studies were selected considering the best quality of available evidence. As for effectiveness, the findings draw attention to the intrinsic resistance of subclass *Coccidia spp* to all evaluated disinfectants and acquired tolerance by GLU strain of *Mycobacterium massilienses* which caused an outbreak of infection with more than 2000 cases in Brazil. About toxicity, the most frequently reported adverse events are colitis (no definitive causal relationship with the germicide used) and anaphylactic reactions by OP in cystoscopy. There is lack of published data on damage caused in endoscopes by the disinfectants; the few studies on the theme indicate the importance of adequate handling of equipment for conservation of its functionality. **CONCLUSIONS:** The publications show superiority of the PA and OP for efficacy in HLD. Only the OP clearly had adverse event related to their use. There is insufficient evidence in literature to assert the inferiority of some disinfectant for damage to equipment.

PIN3
BURDEN OF VARICELLA IN LATIN AMERICA: A SYSTEMATIC REVIEW AND CRITICAL ANALYSIS

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OBJECTIVES: Varicella is a common, vaccine-preventable illness with significant public health impact in Latin America (LA). This study aimed to review the epidemiology and economic burden of varicella, and to perform a critical analysis of available data in LA. **METHODS:** A comprehensive literature review was conducted in major databases and government websites to identify published data on epidemiology and economic burden of varicella in LA. Study data were extracted systematically including incidence rates, lifetime prevalence, mortality, type and rates of complications, as well as use of health care resources (hospitalizations, physician office visits, others) and both direct and indirect costs associated with varicella. Critical analyses of study quality and data availability are performed for each country. **RESULTS:** Published studies were identified from ten countries including Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Mexico, Paraguay, Uruguay, and Venezuela. Annual incidence rates ranged from 20 per 100,000 in Uruguay up to 381 per 100,000 in Mexico. Incidence was highest among children <10 years of age, bearing increased utilization of healt health care resources. Bimodal seasonal patterns of varicella were reported in Argentina, Mexico and Uruguay. Most frequent complications among hospitalized patients were skin and soft tissue infections, respiratory infections and neurological complications. Patients hospitalized for varicella stayed generally between 1-5 days. Critical analysis suggested that most published studies had limitations including data representativeness and study design issues. Data gaps in the epidemiology and economic burden of varicella were also found on the country level. **CONCLUSIONS:** Currently there is limited information available on burden of varicella in Latin America, potentially due to the lack of mandatory reporting and active surveillance systems for varicella in the region. Country-specific epidemiological information and varicella-related health care resource utilization data are needed to elucidate the disease burden for developing appropriate immunization recommendations and informing decision makers about the value of varicella vaccination.

INFECTION – Cost Studies

PIN4
COSTS AND OUTCOMES ASSOCIATED WITH MULTIDRUG RESISTANT STAPHYLOCOCCUS AUREUS BACTEREMIA

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OBJECTIVES: There is a dearth of studies in India that quantifies the impact of multidrug resistance on key economic and clinical outcomes. The aim of this retrospective cohort study was to determine the costs of treatment and evaluate the clinical outcomes in patients suffering from multidrug resistant (MDR) *Staphylococcus aureus* bacteremia and compare these with the costs and clinical outcomes of patients suffering from non-MDR *S. aureus*bacteremia. **METHODS:** Data was collected from 2007 through October 2010 from a private tertiary care hospital in India. Multidrug resistance was defined as resistance to ≥3 classes of antimicrobial drugs. Resistance within a class was defined as resistance to ≥1 antimicrobial agent. **RESULTS:** A total of 42 cases were included in the study of which 19 belonged to the MDR cohort and 23 to the non-MDR cohort The total mean cost for treating patients in the MDR cohort was 1.35 times higher compared to the non-MDR cohort (INR 230,000 [170,000-623,000] versus INR 171,000 [91,000-310,000]; P = 0.049). Death was reported in similar number of patients in both the groups (5 patients and 4 patients in the MDR cohort and non-MDR cohort, respectively). The number of deaths attributable to sepsis was also similar between the groups (16% vs. 13%). The total mean length of stay in hospital was significantly longer for the MDR cohort compared with non-MDR cohort (19 days [16-28] vs. 14 days [9.2-18.5]; P = .024). However, after the onset of bacteremia, the difference in the length of stay between the groups was not statistically significant (16 days [14-21] vs. 11 days [8-15.5]; P = 0.12). **CONCLUSIONS:** Multidrug resistance in *S. aureus* bacteremia was associated with a significant increase in hospital costs.

PIN5
COSTOS ECONÓMICOS ASOCIADOS A SECUELAS DE MENINGITIS EN COLOMBIA

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OBJECTIVOS: Estimar los costos económicos asociados al tratamiento de secuelas de meningitis en una serie de casos en Colombia. **METODOLOGÍAS:** De la base de datos de 253 pacientes atendidos entre 2009 y 2012 en una institución de rehabilitación ubicada en Cartagena de indias Colombia, se identificaron 37 diagnóstico de meningitis bacteriana y entre estos se confirmaron 19 casos de secuelas. De estos, se microcostearon 13 pacientes con secuelas asociadas a un episodio de meningitis meningocócica verificada por pruebas de laboratorio. Las perspectivas del costeo fueron del sistema de salud y la sociedad. En la primerara se consideraron todos los costos médicos directos originados durante el primer año de tratamiento de la secuela y en los años subsiguientes. En la perspectiva social, adicionalmente se consideraron la compra de órtesis y prótesis, adecuaciones del hogar, gastos de transporte y perdida de de productividad, cuando el cuidador tuvo que abandonar el trabajo para asistir al paciente. Los costos se expresaron en US dólares de 2012 (Tasa de cambio 31 dic 2012 1 USD por COP$ 1768.23). **RESULTADOS:** De los 13 pacientes considerados, 5 tenían secuelas de retardo psicomotor, cuatro de hipoacusia neurosensorial, tres de epilepsia y un trastorno del comportamiento. Desde la perspectiva del sistema de salud, los costos directos de tratamiento para el primer año y cada año subsiguiente fueron US$ 3,106.27 (IC95%: 454.5 – 5,758.0) y US$ 496.1 (IC95%: 449.2 - 509.3); desde la perspectiva social fueron US$ 4,647.1 (IC95%: 4,183.8 – 5,082.3)

y US$ 1,085.7 (IC95%: 1,059.9 – 1,109.14). **CONCLUSIONES:** Los costos incrementales, desde la perspectiva social, revelan una carga económica importante para las familias en el tratamiento de las secuelas de meningitis en Colombia.

PIN6

COST OF ADULTS> 50 YEARS COMMUNITY-ACQUIRED PNEUMONIA IN ARGENTINA

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OBJECTIVES: Community-acquired pneumonia (CAP) is an important cause of mortality and morbidity worldwide especially in adults > 50 years. The total cost of CAP in this population is unknown in Argentina **METHODS:** We constructed a Markov model to estimate argentinean health care services use and costs of CAP in 2010 adults > 50 years cohort. Data about incidence and health care utilization were obtained from published reports and a local database. Costs were obtained for the public, social security and private health care subsectors and are expressed in 2012 US dollars **RESULTS:** We estimated that CAP caused 321.321 illness episodes, 24.710 deaths, 189.579 hospitalizations, and 642.643 outpatient visits. Direct medical costs totaled $ USD 340.961.862,9. According to epidemiological data, the public subsector accounted for 32%, the social security for 36.20% and the private for 31.8%. **CONCLUSIONS:** Based on our model the economic burden of CAP is huge in Argentina and it remains an important cause of morbidity, mortality as well.

PIN7

APPROACHES FOR ESTIMATING BURDEN OF PNEUMOCOCCAL AND ROTAVIRUS DISEASES: CONCEPTUAL FRAMEWORK AND SYSTEMATIC REVIEW

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OBJECTIVES: Country level estimation of disease burden promotes the understanding of the problem and can help prioritize the planning and implementation of programs, and thus foster the better use of scarce resources. Our aim was to review burden of disease (BoD) estimation methods and develop a guidance for conducting local disease burden exercises for pneumococcal and rotavirus diseases in Latin America and the Caribbe (LAC). **METHODS:** We developed an algorithm to guide in a BoD study based on the availability of the different data sources and a systematic review of the different approaches used in the estimation of BoD pneumococcal and rotavirus disease studies worldwide. We followed the MOOSE guidelines for systematic reviews of observational studies, and the PRISMA statement for systematic reviews and meta-analyses. We searched studies published between January 1995 to September 2010 without language restriction on MEDLINE, EMBASE, LILACS, generic and academic Internet search and meta-search engines. **RESULTS:** The algorithm developed include five approaches: based on end results; based on the end and intermediate results (using health services); based on incidence and end results; partial approach; and based on incidence. The systematic review retrieves 1728 articles. After pair assessment, we include 92 in title/abstract phase and finally 35 in full text phase for extraction. Single or multiple approaches based on incidence were the most used (57%), based on intermediate results are in the second place (53%) and based on final results are the least used (43%). 48% of the based on final results studies/substudies, 46% of those based on intermediate results, and 36% of those based on incidence were considered to be representative for the jurisdiction of interest. **CONCLUSIONS:** The present work describes a taxonomy of BoD estimation and provides guidance for LAC and other LMIC countries according to local data availability.

PIN8

A COST-CONSEQUENCE ANALYSIS OF DIFFERENT PROTEASE INHIBITORS SCHEMES FOR HIV TREATMENT FROM THE COLOMBIAN HEALTH CARE SYSTEM PERSPECTIVE

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OBJECTIVES: First-line antiretroviral therapy selection provides the greatest opportunity to fully suppress HIV replication and prevent the emergence of drug-resistant strains that lead to treatment failure and compromise future drug treatment strategies. Currently, two alternative protease inhibitors PIs, lopinavir (LPV) and atazanavir (ATV), are included in the Colombian national formulary for the treatment of HIV patients. Darunavir (DRV) boosted with low-dose ritonavir has demonstrated to be an efficacious PI alternative for treatment of experienced and naïve patients. The objective of this study is to compare costs and benefits among different PI sequential algorithms of DRV, ATV and LPV from the Colombian Health Care System. **METHODS:** A decision tree was designed using the insurer perspective to estimate costs and benefits throughout a three years time horizon. Clinical data were obtained from the pivotal trials in order to model second line and rescue progression and benefits were measured as probability of virological response (VR). Only direct costs were considered, such as medications (first line, second line and rescue medications), laboratory tests and rescue related inpatient care costs using national tariffs and prices from Ministry of Health medication database. Four PI schemes were assessed: 1) DRV followed by ATV, 2) ATV followed by DRV, 3) LPV followed by ATZ and 4) LPV followed by DRV. Discount rate 3% and exchange rate (1 USD = 1,794 COP). **RESULTS:** *Direct costs (USD):* DRV-ATV (29,747), ATV-DRV (30,191), LPV-ATV (24,507) and LPV-DRV (24,157). *VR:* DRV-ATV (51%), ATV-DRV (49%), LPV-ATV (43%) and LPV-DRV (43%). *Cost per VR (USD / VR):* DRV-ATV (58,327), ATV-DRV (61,614), LPV-ATV (56,993) and LPV-DRV (56,179). **CONCLUSIONS:** Using DRV after LPV as a first line agent is the sequencing strategy which demonstrates the better cost per virological response. DRV in first line position save costs and improves VR versus ATV in first line position.

PIN9

COSTO EFECTIVIDAD DEL ANTIBIÓTICO ORAL VS. LOCAL EN MUJERES NO GESTANTES CON FLUJO VAGINAL SUGESTIVO DE VAGINOSIS BACTERIANA EN COLOMBIA

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OBJECTIVOS: Estimar la costo-efectividad del antibiótico oral vs local en mujeres no gestantes con flujo vaginal sugestivo de vaginosis bacteriana. **METODOLOGÍAS:** Se compararon cuatro combinaciones de antibióticos para primera opción y ante falla clínica: clindamicina vaginal y tinidazol oral dosis única; clindamicina vaginal y secnidazol oral dosis única; tinidazol oral dosis única y clindamicina vaginal; secnidazol oral dosis única y clindamicina vaginal. Se construyó un modelo de Markov para representar de manera general la historia natural de la vaginosis bacteriana. El cambio en el tratamiento ante recurrencia sin eventos adversos se modeló como un caso particular mediante un árbol de decisión. La perspectiva fue la del sistema de salud incluyendo todos los costos directos. Todas las cifras monetarias se expresaron en pesos colombianos de 2010. La unidad de resultado fue la mejoría clínica. Los datos de efectividad, seguridad, persistencia y recurrencia se extrajeron de la literatura. Se calculó la razón de costo-efectividad incremental y se realizaron análisis de sensibilidad univariados y probabilísticos. **RESULTADOS:** Tanto para el caso general como el particular, el esquema clindamicina vaginal como primera opción y tinidazol oral dosis única, para tratar persistencia con eventos adversos y recurrencia es una estrategia dominante ya que es menos costosa y más efectiva comparado con los demás esquemas de tratamiento. Para 1.000 pacientes, el costo de la alternativa dominante es de $16.795.411 con mejoría en 985 casos en el modelo general y de $23.979.230 con mejoría en 903 casos en el caso particular. **CONCLUSIONES:** Clindamicina vaginal como primera opción para el tratamiento de la vaginosis bacteriana y tinidazol vía oral dosis única para tratar persistencia con eventos adversos a la clindamicina y recurrencia es costo-efectiva para Colombia. Los resultados fueron robustos a variaciones en los parámetros del modelo.

PIN10

ANÁLISIS DE COSTO-EFECTIVIDAD DE LAS VACUNAS NEUMOCÓCICAS CONJUGADAS 10 Y 13 VALENTE PARA NIÑOS EN ANTIOQUÍA, COLOMBIA

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OBJECTIVOS: El *Streptococcus pneumoniae* es responsable de la enfermedad neumocócica invasiva [ENI] (meningitis, bacteremia) y no invasiva (neumonía, otitis media aguda [OMA]). El objetivo de este análisis es estimar la costo-efectividad de las vacunas neumocócicas conjugadas 13-valente (PCV13) y 10-valente (PCV10), en una cohorte de recién nacidos en Antioquia, Colombia. **METODOLOGÍAS:** Se desarrolló un árbol de decisiones. Los comparadores fueron: PCV13 y PCV10 (esquema de vacunación 2 + 1) contra no vacunación (NV); cobertura de vacunación del 90%. Se simuló una cohorte de recién nacidos en Antioquia (85.955 niños), con horizonte de 5 años y 3% de descuento anual. El análisis se realizó desde la perspectiva del sistema de salud. Los valores de eficacia de las vacunas fueron tomados de la literatura. Los costos médicos (US$ 2013) fueron proveídos por una aseguradora nacional, para las vacunas fueron tomados de la OPS. Los desenlaces medidos fueron: casos de enfermedad evitados y muertes prevenidas por ENI, neumonía, OMA y Años de Vida Ganados (AVG) **RESULTADOS:** En 5 años, PCV13 prevendría 52 muertes por infección neumocócica vs NV (PCV10 prevendría 41 muertes vs NV), evitaría 71 casos de ENI vs NV (PCV10 evitaría 55 casos vs NV) y generaría 3.096AVG (691AVG más que PCV10). Los costos médicos evitados serían de US$2.5M con PCV13 y US$1.8M con PCV10. PCV13 y PCV10 son alternativas costo-efectivas vs la no vacunación, con una razón de costo efectividad incremental de US$511.84 y US$737.64 por AVG respectivamente, teniendo en cuenta un umbral de disposición a pagar de 1PIB per cápita por AVG (US$7,235). PCV13 fue dominante frente a PCV10 debido al menor costo total y mejores desenlaces. **CONCLUSIONES:** PCV13 es una alternativa dominante (costo-ahorradora) vs PCV10, como parte de un programa de vacunación masiva para niños de Antioquía, menores de 1 año PCV13 generaría una mayor reducción en la mortalidad infantil a causa de enfermedades neumocócicas.

PIN11

THE HEALTH AND ECONOMIC IMPACT OF A QUADRIVALENT HUMAN PAPILLOMAVIRUS VACCINE (6/11/16/18) IN COLUMBIA: A TRANSMISSION DYNAMIC MODEL-BASED EVALUATION

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OBJECTIVES: To estimate the potential impact of a quadrivalent human papillomavirus (HPV) (6/11/16/18) vaccine for the prevention of cervical cancer, cervical intraepithelial neoplasia grades 2 and 3 (CIN2/3), CIN1 and genital warts in Colombia. **METHODS:** We adapted a previously developed transmission dynamic model (Elbasha & Dasbach; 2010) to evaluate the health and economic consequences of routine vaccination of nine year old girls in a dynamic Columbian population over the course of 100 years. We calibrated the model to the observed data of the crude incidence and mortality of cervical cancer, and genital warts attributable to HPV 16/18 and 6/11 respectively. The model assumed 85% vaccine coverage rate. **RESULTS:** At 50 years the model shows cumulative reduction in HPV 16/18 related cervical cancer cases and deaths by 18.1% and 13.9% respectively, and cumulative reduction in the CIN2/3 and HPV 6/11 related CIN1 cases by 46.9% and 59.9% correspondingly. At year 100, the vaccination reduces the annual incidence of HPV 6/11/16/18 related cervical cancer, deaths, CIN2/3 and CIN1 cases by about 99%. At

50 years the model shows 99.5% and 98% reduction in the annual incidence of HPV 6/11 related genital warts cases in females and males respectively. **CONCLUSIONS:** In Colombia, a quadrivalent HPV vaccination program for 9 year old girls can significantly reduce the incidence of cervical cancer, CIN and genital warts.

PIN12

PUBLIC HEALTH IMPACT AND COST EFFECTIVENESS OF PNEUMOCOCCAL VACCINATION FOR ADULTS IN PUERTO RICO

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OBJECTIVES: In 2012, the U.S. Advisory Committee on Immunization Practices (ACIP) revised their 1997 adult pneumococcal vaccination recommendation for certain high-risk adults with immunocompromising conditions to include a sequential regimen of 13-valent pneumococcal conjugate vaccine (PCV13) followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23), while continuing routine PPSV23 use for healthy and immunocompetent adults with comorbidities. This study aims to examine the public health impact of pneumococcal vaccination for adults in Puerto Rico (PR), and cost-effectiveness of 2012 ACIP recommendation relative to 1997 recommendation. **METHODS:** A static cohort model that incorporated lifetime costs, health outcomes, and quality-adjusted life-year (QALY) losses associated with invasive pneumococcal disease (IPD) and non-bacteremic pneumococcal pneumonia (NBPP) was developed for a cohort of 50,000 adults 50 years of age in PR. Cost-effectiveness of three vaccination strategies: 2012 and 1997 ACIP recommendations, and no vaccination, were evaluated using incremental cost-effectiveness ratios (ICERs). Public health impact of the pneumococcal vaccination strategies were examined by estimating net costs and burden of disease prevented by pneumococcal vaccination in PR. **RESULTS:** Compared to no vaccination, pneumococcal vaccination with 2012 ACIP recommendation would reduce IPD cases by 4.4%, NBPP hospitalizations by 0.6%, NBPP outpatient visits by 0.9%, and deaths by 1.0% with a net cost of $1,721,533. Compared to 1997 ACIP recommendation, vaccination with 2012 ACIP recommendation would reduce IPD cases by 0.7%, NBPP hospitalizations by 0.1%, NBPP outpatient visits by 0.1%, and deaths by 0.2% with a net cost of $228,346. Cost-effectiveness analysis showed that compared to 1997 ACIP recommendation, 2012 ACIP recommendation is a more economically efficient strategy (ICER of $14,780 per QALY gained vs. no vaccination). **CONCLUSIONS:** Pneumococcal vaccination in adults would prevent a substantial portion of pneumococcal-related morbidity, mortality, and health care resource utilization use in PR. The 2012 ACIP recommendation appears to be a cost-effective vaccination policy for PR.

PIN13

EFECTO DE LA DETERMINACIÓN DE LA CONCENTRACIÓN CAPILAR DE PROTEÍNA C REACTIVA EN LA TASA DE PRESCRIPCIÓN DE ANTIBIÓTICOS PARA EL TRATAMIENTO DE INFECCIÓN DE VÍAS RESPIRATORIAS ALTAS (ANÁLISIS DE COSTO-EFECTIVIDAD)

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OBJECTIVOS: En Infección de Vías Respiratorias Altas (IVRA) frecuentemente se prescriben innecesariamente antibióticos, lo que favorece la resistencia e incrementa los costos. Se ha demostrado que la proteína C reactiva (PCR) -marcador de respuesta inflamatoria aguda-, orienta en la prescripción de antimicrobianos. El estudio estimó desde la perspectiva del proveedor de servicios de salud el costo-efectividad de contar con la determinación de PCR en una unidad de atención primaria del Instituto Mexicano del Seguro Social(IMSS). **METODOLOGÍAS:** Entre febrero y junio de 2012, se realizó un estudio comparativo en pacientes con diagnóstico de IVRA, quienes fueron asignado aleatoriamente a un grupo con la determinación de PCR, cuyo punto de corte para apoyar el uso de antibiótico fue > 100 mg/L; o, sin la prueba. En ambos grupos la atención siguió el proceso habitual y los médicos tuvieron libertad de decisión. El seguimiento fue por 7 días. Se midió la tasa de prescripción de antibióticos y la satisfacción del paciente. Los costos se estimaron con los recursos utilizados durante el seguimiento y se expresaron en dólares norteamericanos (tasa de cambio 12.65 pesos/dólar). Se realizó análisis de sensibilidad probabilístico. **RESULTADOS:** Se incluyeron 103 pacientes con PCR y 118 sin PCR. La tasa de prescripción de antibióticos en el grupo de PCR fue 0.33(IC95% 0.23–0.42) y sin PCR 0.81(IC95% 0.73–0.88) p <0.05. El grado de satisfacción con PCR fue 79%(IC95% 71% - 86%) y sin PCR 63% (IC95% 54% - 71%), p = 0.04. El costo promedio de atención con PCR fue US$52(IC95% US$48 – US$57) y sin PCR US$49(IC95% US$45 – US$54), p< 0.05. La utilización de PCR fue dominante en ambos casos y costo-efectivo independientemente de la disposición a pagar. **CONCLUSIONES:** Incluir al proceso de atención de IVRA la determinación capilar de PCR es una alternativa costo-efectiva en el IMSS.

PIN14

ESTIMACIÓN DE LA COSTO-EFECTIVADAD DEL USO DE DAPTOMICINA VS VANCOMICINA EN PACIENTES CON BACTERIEMIA Y/O ENDOCARDITIS POR S. AUREUS RESISTENTE A METICILINA

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OBJECTIVOS: Evaluar la CE del uso de D vs V para el tratamiento de B/EI por SAMR en Argentina. **METODOLOGÍAS:** Se consideraron los datos de eficacia y seguridad de D y V en B/EI del estudio de Fowler, VG y col. (NEJM 2006; 355:653). La estrategia de análisis de costos (C) se tomó del estudio de CE publicado por Bhavnani SM y col. (CID 2009; 49:691) en 3 estratos (E): E1 C de drogas; E2 C de fallas de tratamientos y complicaciones; y E3 C de internación. La utilización de recursos médicos y los patrones de tratamiento se estimaron para los tres subsectores de salud (público, seguridad social, y privado) a través de la metodología de casos promedio con panel Delphi de expertos en infectología. Los datos de C se tomaron de una base de datos con prestadores de todo el país y de la base K@iros. Se adoptó la perspectiva del financiador. **RESULTADOS:** La eficacia (curación) reportada fue de 44% para D y 32% para V. Ante falla de tratamiento con D se rotó a V o linezolid y en el caso de V se rotó a D o linezolid. La media estimada de días de tratamiento fue de 24.4, y la de días de internación de 13, con 11.8% promedio de ingreso a UTI. Se estimó el tratamiento con dos ampollas/día de D y 4 de V. Los C por estrato (V vs D) fueron: E1= 31.112$ vs 10.655$; E2=817$ vs 81,4$; y E3=23.292$ vs 23.292$. La CE global por caso de B/EI tratado fue: V=13.5187 $/caso y D=70.901$/caso. **CONCLUSIONES:** Nuestra estimación de CE, indica que una estrategia basada en el uso inicial de daptomicina para el tratamiento de las infecciones mencionadas es más costo-efectiva que utilizar vancomicina, principalmente por los costos relacionados a la falla de tratamiento de vancomicina.

PIN15

COSTO-EFECTIVIDAD DEL DIAGNOSTICO ETIOLÓGICO CON PRUEBAS RAPIDAS VS. SINDROMICO EN MUJERES NO GESTANTES CON SINTOMAS DE INFECCIÓN CERVICAL EN COLOMBIA

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OBJECTIVOS: Estimar la costo-efectividad de la aproximación etiológica con pruebas rápidas en el sitio de atención vs el diagnóstico sindrómico en mujeres no gestantes con síntomas de infección cervical. **METODOLOGÍAS:** Se construyó un árbol de decisión para determinar la razón de costo-efectividad incremental de la aproximación etiológica con pruebas rápidas: Acon®Plate (Neisseria-Chlamydia), Acon®Duo (Neisseria-Chlamydia) y Acon®Plate (Neisseria)+ QuickVue® (Chlamydia) comparadas con el diagnóstico sindrómico, incluyendo tratamiento con antibióticos a la paciente índice y su contacto sexual, según el resultado. La perspectiva fue la del sistema de salud incluyendo todos los costos directos. Todas las cifras monetarias se expresaron en pesos Colombianos de 2010. La unidad de efectividad fue la mejoría clínica. Los datos de las características operativas de las pruebas se extrajeron de una cohorte de mujeres sexualmente activas (n=1.444). Los resultados de las alternativas diagnósticas se compararon con el patrón de oro (PCR). Los datos de efectividad de los tratamientos fueron tomados de la literatura. Se realizaron análisis de sensibilidad univariados y probabilísticos. **RESULTADOS:** La alternativa más eficaz y más costosa fue Acon®Plate + QuickVue®, seguida de Acon®Duo y del manejo sindrómico. Acon®Plate fue una estrategia dominada. La razón de costo-efectividad incremental de Acon®Plate + QuickVue® fue de $2.782.690 y la de Acon®Duo fue de $597.886. La sensibilidad probabilística confirmó el ordenamiento de las alternativas. **CONCLUSIONES:** Si la disponibilidad a pagar (DAP) por un caso adicional de mejoría clínica es mayor que $2.782.690, Acon®Plate + QuickVue® sería la mejor alternativa en términos de costo-efectividad; de otro lado, si la DAP por un caso de mejoría clínica adicional está entre $ 597.886 y $ 2.782.690, Acon®Duo sería la alternativa costo-efectiva; finalmente, si la DAP por un caso de mejoría clínica adicional es menor que $ 597.886 el manejo sindrómico sería costo-efectivo.

PIN16

COST-EFFECTIVENESS OF TELAPREVIR IN GENOTYPE 1 CHRONIC HEPATITIS-C VIRUS INFECTION IN VENEZUELA

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OBJECTIVES: Direct acting antiviral therapies (DAA) in addition to PEG 2a + RBV (PR) are a new therapeutic option with higher rates of sustained virological response (SVR) than dual therapy (PR) alone in chronic hepatitis C. Currently, two alternatives of DAA, telaprevir (TVR) and boceprevir (BOC), are available in Venezuela. The aim of this study was to evaluate the cost-effectiveness of adding TVR to PR in treatment naive and previously treated patients with HCV in Venezuela compared to PR alone and with the addition of BOC. **METHODS:** A lifetime Markov model was developed including HCV, cirrhosis, liver transplant and death as health states. QALYs as an outcome measure, a health care system perspective and a 5% discount rate for health benefits and costs have been used. Costs are expressed in local currency. A review of the literature to obtain epidemiologic and resources utilization data was performed and when data were not available or validation was needed a Delphi panel with local experts was carried out. Deterministic and probabilistic sensitivity analysis was performed. **RESULTS:** In comparison with PR, TVR avoided 174 cirrhosis cases and 20 deaths per 1,000 patients and shown an ICER of $70,149/QALY and $29,689/QALY for the naïve and for the previously treated patients respectively. TVR dominated BOC in naïve patients and in most of the previously treated ones (was less costly and more efficacious), except in the partial responders subgroup. These results were robust in the sensitivity analysis. **CONCLUSIONS:** TVR dominated BOC and was cost-effective against WHO 3GDP criteria in comparison to double therapy from the national health care system perspective in Venezuela.

PIN17

PHARMACOECONOMICS OF CERVARIX VACCINES AGAINST HUMAN PAPILLOMA VIRUS IN THE REPUBLIC OF KAZAKHSTAN

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OBJECTIVES: Based on the pharmacoeconomic analysis determine the feasibility of vaccine against HPV-associated diseases in Kazakhstan. **METHODS:** The number of prevented cases of HPV-related diseases, disability, death, and the size of damage avoided due to vaccination was determined using static pharmacoeconomic MS Excel model which focuses on 4 types of HPV-associated diseases that are targeted by the vaccine "Cervarix" (ASCUS, cervical intraepithelial neoplasia of grades 1, 2, 3 and cervical cancer), 2 outcomes of CC - disability and death. Number of CC cases expected in the cohort for the period of survival was determined based on the relative incidence rates (16.0 per 100 000 female population in Kazakhstan), the cohort of 12 year old girls (122799), and the life expectancy in Kazakhstan (73 years). To determine the value of the case of

HPV-associated diseases, medical technologies used in CC, CIN 1, CIN2, CIN3, ASCUS, the frequency of their use and the price for the services were determined. **RESULTS:** Vaccination cost for cohort of girls (122,799) resulted in 23.2 million USD. The cost of prevented damage is estimated 16.5 million. Additional cost - 6.7 million. Years of life saved - 11172. The coefficient of "cost-effectiveness" of using Cervarix vaccine was calculated for 598 USD for one year of life saved. The cost of prevented damage was identified to be 38.5 million based on the number of prevented cases of CC, CIN 1, CIN2, CIN3, ASCUS and the cost of each case of illness, disability, and death. **CONCLUSIONS:** The cost of potential annual preventative damage/gain as a result of Cervarix vaccine application may reach 38.5 million USD. When comparing the annual preventative damage to the annual cost of vaccination for 12 year old girls in Kazakhstan, the cost of prevention was estimated to be 1.7 times more than the cost of one vaccine cohort.

PIN18

ANÁLISE CUSTO-MINIMIZAÇÃO (ACM) DO CLORIDRATO DE VALGANCICLOVIR COMPARADO COM GANCICLOVIR NA PROFILAXIA DA INFECÇÃO POR CMV EM TRANSPLANTADOS RENAIS

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OBJETIVOS: Realizar Análise Custo-Minimização (ACM) do Cloridrato de Valganciclovir comparado com Ganciclovir na profilaxia da infecção por CMV em transplantados renais. **MÉTODOS:** Os dados acerca da eficácia semelhante dos antivirais foi obtido por meio de Revisão Sistemática. Foram elencadas as seguintes categorias de custo direto: medicamento e materiais descartáveis. Foram simulados três esquemas de profilaxia: Ganciclovir 1g intravenoso (IV) 3x/dia durante período de internação e Ganciclovir 1g VO por 3x/dia até cem dias (Esquema A); Ganciclovir 1g IV 3x/dia durante internação seguido pelo Valganciclovir 900mg VO uma vez/dia até cem dias (Esquema B) e Valganciclovir 900mg VO na internação e após a alta até completar cem dias de uso (Esquema C). Foram feitos os cálculos relativos aos anos de 2010 e 2011 com base no número estimado de pacientes submetidos a transplante de um hospital do Sistema Único de Saúde – Brasil. Os valores dos medicamentos foram obtidos no Banco de Preços em Saúde (BPS) do DATASUS e a lista de conformidade da Câmara de Regulação do Mercado de Medicamentos (CMED) da ANVISA. **RESULTADOS:** Em 2010, o custo médio por paciente do esquema A foi de R$ 18.097,79, do segundo foi de R$ 22.754,63 e do terceiro foi de R$ 21.096,00. Em 2011, o custo médio por paciente do primeiro esquema foi de R$ 16.393,27, do segundo foi de R$ 22.603,35 e o terceiro foi de R$ 22.346,00. **CONCLUSÕES:** Os resultados demonstraram menor custo de profilaxia para CMV com Ganciclovir 1g IV, e o segundo menor com Valganciclovir 900 mg VO. A administração IV do Ganciclovir versus a VO do valganciclovir devem ser analisadas com outros estudos, considerando-se também os riscos inerentes à administração e reações adversas.

PIN19

ECONOMIC EVALUATION OF TREATMENTS FOR CHRONIC HEPATITIS B

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OBJECTIVES: To conduct a cost-utility study in the context of Brazil's Public Health Care System of the drugs adefovir, entecavir, interferon alpha, pegylated interferon alpha, lamivudine and tenofovir for chronic hepatitis B. **METHODS:** For efficacy and safety data, a systematic review was carried out. Utility data and transition probabilities between health states were searched in the literature. The Markov model was developed in a time horizon of 40 years with annual cycles for three groups of patients with chronic hepatitis B: HBeAg positive, HBeAg negative, and all patients. These strategies were compared to a fourth group that received no treatment. Discount rates of 5% were applied and sensitivity analyses were performed. **RESULTS:** Tenofovir offered the best cost-utility ratio for the three evaluated models: U$397, U$385 and U$384 (per QALY, respectively for HBeAg positive, negative, and all patients). All other strategies were completely dominated. The sequence of cost-utility in the three models was: tenofovir, entecavir, lamivudine, adefovir, telbivudine, pegylated interferon alpha, and interferon alpha. In the sensitivity analysis, adenofovir became less cost-utility than telbivudine in some situations. **CONCLUSIONS:** In this study, tenofovir presented the best cost-utility ratio. The results obtained in this study will be valuable in decision-making and in the review of the clinical protocol, mainly involving the allocation of available resources for health care.

INFECTION – Health Care Use & Policy Studies

PIN20

EVOLUCIÓN DEL CONSUMO Y VENTAS DE ANTIBIÓTICOS EN CHILE 1998-2012

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INTRODUCTION: Desde el año 1999 en Chile se exige la receta médica para la venta de antibióticos (ATB) en farmacias. Hasta el momento se desconoce el efecto a largo plazo de esta medida sobre el consumo y las ventas de ATB. **OBJECTIVOS:** Determinar los niveles y tendencias de consumo y ventas de ATB en Chile antes y después de implementar la venta con prescripción médica. **METODOLOGÍAS:** Mediante un estudio retrospectivo de la base de datos del International Marketing System (IMS), se analizaron las ventas de ATB en farmacias entre 1998-2012. Las unidades vendidas se transformaron en Dosis Diaria Definidas (DDD), DDD/1000 habitantes/día (DHD) y costo/DDD. Las tendencias se analizaron mediante regresiones lineales. **RESULTADOS:** Se observó una disminución del 17% en el consumo de ATB con la aplicación de las medidas regulatorias (11.8 a 9.8 DHD, en 1998 y 2012, respectivamente). No obstante, las quinolonas, cefalosporinas y macrólidos aumentaron un 298%, 31%, 27%, respectivamente, durante el periodo estudiado. La mayor disminución respecto al año 1998 ocurrió en el año 2002 (-38%), mientras que entre 2002 y 2012 hubo un incremento del 34% en el consumo. El costo/DDD disminuyó un 15% entre 1998 y 2003 (0.71 a 0.60 USD/DDD), mientras que entre 2003 y 2012 aumentó en un 47% llegando a 0.88 USD/DDD en 2012. Durante el periodo 2000-2012 el consumo de ATB aumentó un 32% (de 7.4 a 9.8 DHD). El patrón de consumo total estuvo dado principalmente por las penicilinas de amplio espectro (53%, 61.1 DHD), siendo la amoxicilina el ATB más usado (44%, 50,5 DHD). **CONCLUSIONES:** Las medidas regulatorias permitieron disminuir el consumo y los costos/DDD de ATB en Chile. Sin embargo, el aumento progresivo observado indica la necesidad de revisar la calidad en la utilización de los ATB y el cumplimiento de la regulación vigente.

MUSCULAR-SKELETAL DISORDERS – Clinical Outcomes Studies

PMS1

TREATING PSORIATIC ARTHRITIS WITH BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS: SYSTEMATIC REVIEW AND META-ANALYSIS TO EVALUATE EFFICACY AND SAFETY

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OBJECTIVES: To evaluate the efficacy and safety of biological disease modifying antirheumatic drugs (DMARDs) adalimumab, etanercept, golimumab and infliximab in the treatment of psoriatic arthritis (PA) in adults. **METHODS:** We conducted a systematic review of controlled clinical trials to access the efficacy and safety of these agents in patients with active PsA which have or have not been treated with biological DMARDs before. The databases MEDLINE, EMBASE, LILACS and Central Cochrane where searched until February 2013 to identify articles that reported data on clinical improvement measurements and adverse events. Metanalysis were performed using Review Manager® 5.1 and the Random Effect Model. **RESULTS:** Seven RCTs comparing biological DMARDs with placebo where included; two comparing either adalimumabe, etanercept and infliximab to placebo, and one comparing golimumab to placebo. After 12 weeks of treatment, adalimumabe and etanercepte were more effective than placebo with respect to 20% improvement from baseline in the American College of Rheumatology response criteria (ACR 20); Risk Ratio 3.42 ([2.08, 5.63]; I^2 38%) and 4.15 ([2.71, 6.36]; I^2 0%), respectively. After 16 weeks, infliximab patients also achieved ACR20 in a greater rate than placebo; RR 5.71 ([3.53, 9.25]; I^2 0%). However, results after 54 weeks of treatment showed no significant differences between infliximab and placebo; RR 0.98 ([0.82, 1.18]; I^2 0%). Golimumab was more effective than placebo at 24 weeks; ACR20 RR 4.53 ([2.75, 7.48]). After 16 weeks infliximab shown a 50% reduction in the psoriasis area and severity index (PASI50) in a greater rate than placebo, RR 10.67 ([5.52, 20.64]; I^2 1%), however, once again 54 weeks results have shown no significant differences between infliximab and placebo, RR 0.94 ([0.80, 1.12] I^2 66%). Adverse events where similar between the biological and placebo groups, nevertheless the placebo group showed a slightly higher rate of adverse events than adalimumabe; RR 0.68 ([0.50, 0.92]; I^2 0%). **CONCLUSIONS:** Results show clinical improvement with the use of biological DMARs in the treatment of PA. Still, there is a lack of evidence to support the spread the use of these medicines especially in synthetic DMARD naïve patients.

MUSCULAR-SKELETAL DISORDERS – Cost Studies

PMS2

ESTIMATING THE BUDGET IMPACT IN BRAZILIAN PUBLIC HEALTH CARE SYSTEM OF TOCILIZUMAB REIMBURSEMENT AS A RHEUMATOID ARTHRITIS FIRST-LINE BIOLOGICAL THERAPY

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OBJECTIVES: Rheumatoid arthritis (RA) is a systemic autoimmune disease which affects 0.5% of the population in developing countries. In Brazilian public health care system (SUS) infliximab, etanercept, adalimumab, golimumab, certolizumab (anti-TNF), abatacept (T-lymphocyte activation inhibitor) and tocilizumab (IL-6 inhibitor) are available as biological treatment. However, only anti-TNF therapies are indicated as standard of care for first-line biologic therapy. As tocilizumab is a known effective and cost-saving drug for this indication, the present study aims to evaluate the budget impact of its inclusion in public RA biologics first-line setting. **METHODS:** A model was developed in order to assess the budget impact of tocilizumab reimbursement as a first-line biological therapy under SUS perspective from 2014-2018. Only expenditures with biologics were accounted according to posology presented in Brazilian Ministry of Health RA Guideline considering a mean 67kg-weighted patient. Prices were obtained from public disclosures. Forecasts were made pursuant to government sources (IBGE, DataSUS) and market research-based data. Different mix scenarios based on varying growth rate of tocilizumab usage were assessed to evaluate total savings. A two-way sensitivity analysis was conducted changing diagnosis and biologics use rates. Costs were reported in Brazilian currency (BRL1.00~USD0.51 Feb2013). **RESULTS:** Annual costs per patient were BRL20,002, BRL25,625, BRL26,899, BRL18,330, BRL22,386, BRL15,232 and BRL27,391, for tocilizumab, etanercept, adalimumab, infliximab, abatacept, certolizumab and golimumab, respectively. Concerning different tocilizumab public usage scenarios, if it reaches 20% in 2018, savings could sum BRL143,058,554 (-2.8%) in the analyzed period. Nonetheless by achieving a 40% usage savings would be even higher resulting in a potential BRL318,643,978 (-6.3%) economy in the same period. Sensitivity analysis showed savings ranges of: BRL101,782,493-BRL262,029,470 (20% usage scenario) and BRL228,085,067-BRL579,597,311 (40% usage scenario). **CONCLUSIONS:** The public inclusion of tocilizumab in 2014 as a RA first-line biologic therapy and its usage enhance would result in increasingly savings arousing significant impacts in public health care budget.

PMS3

AVALIAÇÃO DO IMPACTO ORÇAMENTÁRIO COM A INCORPORAÇÃO DE IMUNOBIOLÓGICOS EM UMA OPERADORA DE PLANOS DE SAÚDE – 2012

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OBJETIVOS: Avaliar o impacto orçamentário com a incorporação de imunobiológicos endovenosos (IMB-EV) em uma Operadora de Planos de Saúde de Fortaleza

- Brasil, no ano de 2012. **MÉTODOS:** Foi delineado em janeiro/2012 um cenário sob a perspectiva da operadora e com os pacientes potenciais de utilização de IMB-EV em primeira linha de tratamento para (Artrite Reumatóide, Espondilite Anquilosante, Artrite Psoriática e Doença de Crohn) em sua maior posologia/doses. Somente custos diretos foram considerados em Reais ($) e utilizou-se um paciente padrão com peso médio de 70 kg para o IMB-EV peso-dependente na dose. A análise da incidência das doenças na cartela epidemiológica de clientes da operadora permitiu uma extrapolação para determinação do custo/tratamento em relação ao número de infusões em relação a cada tipo de IMB-EV (Infliximab, Tocilizumab, Abatacepte). Utilizou-se Brasindice 741 para precificação dos medicamentos. **RESULTADOS:** A partir dos dados coletados foram projetados atendimentos de 50 pacientes em uso de infliximabe com um custo anual de R$ 5.051.886,00 e per capta de R$ 101.037,72. Em uso de Tocilizumab o custo anual seria de R$ 2.338.944,00 (per capta de R$ 46.778,88) e com Abatacepte o custo anual seria de R$ 2.997.498,00 (per capta R$59.949,96). Assim o total geral da incorporação com IMB-EV teve um custo projetado de R$ 10.388.328,00. **CONCLUSÕES:** A avaliação de custos com medicamentos de alto impacto nos orçamentos das instituições de saúde, como os imunobiológicos, nas operadoras tem se tornado uma importante ferramenta para um planejamento estratégico e sustentável financeiramente. A partir das análises e monitorizações, teve-se a tomada de decisão para inclusão de outros IMB subcutâneos como Etanercept, Golimumab e Certolizumabe, os quais podem apresentar uma relação custo-minimização mais favorável.

PMS4

COMPARING COSTS PER CLINICAL REMISSION OF TOCILIZUMAB MONOTHERAPY VERSUS ADALIMUMAB MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A BRAZILIAN PRIVATE PERSPECTIVE

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OBJECTIVES: Rheumatoid Arthritis (RA) is an autoimmune disease that causes chronic inflammation of the joints. Disease progression leads to a significant socioeconomic impact for the individual and for society. In Brazil, there are eight approved biologic drugs indicate to treat patients with moderate/severe RA that presented previous inadequate response to therapy with DMARDs, including tocilizumab (TCZ) and adalimumab (ADA). ADACTA trial (Gabay et al, 2012) showed positive results related to TCZ monotherapy for the treatment of moderate/severe RA in patients who presented inadequate response to methotrexate therapy or were MTX intolerant. This study aims to evaluate costs of TCZ monotherapy vs. ADA monotherapy to achieve remission after one year of treatment for adult RA, according to ACR70 and DAS28 outcomes. **METHODS:** An economic evaluation based on ADACTA study was performed. Drugs ex-factory prices were used to estimate treatment costs. Regimen was 8 mg/kg every 4 weeks TCZ and 40 mg every 2 weeks ADA. Costs to achieve remission in one year according to ACR70 and DAS28 outcomes were compared. The study was conducted from a Brazilian private health care perspective, considering only drug costs. Costs were reported in Brazilian Reais (BRL1.00=USD0.51 Feb/2013). **RESULTS:** Annual costs were BRL39,100.06 TCZ vs. BRL63,134.76 ADA. After one year of treatment, ACR70 response rates were achieved in 32.50% in TCZ group and 17.90% in ADA group. DAS28 remission was achieved in 39.90% and 10.50% in TCZ and ADA group, respectively. TCZ presented better results in costs per clinical remission than ADA (ACR70 BRL120,307.88 vs. BRL352,708.16 and DAS28 BRL97,995.14 vs. BRL601,283.43). **CONCLUSIONS:** TCZ presented better response rates in both ACR70 and DAS28 outcomes and lower annual costs per clinical remission compared to ADA, suggesting that TCZ is a better single-agent alternative to treat moderate/severe rheumatoid arthritis in Brazilian private health care system.

PMS5

ANALYZING COSTS PER CLINICAL REMISSION OF TOCILIZUMAB MONOTHERAPY VERSUS ADALIMUMAB MONOTHERAPY IN RHEUMATOID ARTHRITIS FROM A PUBLIC PERSPECTIVE IN BRAZIL

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OBJECTIVES: Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease which affects around 0.5% of adult population worldwide. ADACTA (Gabay et al, 2012) is the first study designed to compare two approved biologic drugs in monotherapy for the treatment of RA. The trial compared tocilizumab monotherapy (TCZ) vs. adalimumab monotherapy (ADA) and presented results that support TCZ alone as a single-agent therapy for RA patients who are either intolerant to methotrexate (MTX) or in whom previous MTX therapy was inadequate. Based on ADACTA, this study aims to compare annual costs per clinical remission of TCZ vs. ADA in moderate/severe adult RA treatment considering ACR70 and DAS28 outcomes. **METHODS:** Remission data of ACR70 and DAS28 outcomes were taken from ADACTA study. Annual costs of TCZ and ADA therapies considered labeled dosage and public drugs acquisition's prices. Based on these data, costs per clinical remission after one year of treatment were compared. Regimen was 8 mg/kg every 4 weeks TCZ and 40 mg every 2 weeks ADA. The average weight of 67 kg was assumed. A public health care system perspective was considered and only drug costs were evaluated. Drug acquisition prices were assessed from public disclosures. Costs were reported in Brazilian Reais (BRL1.00=USD0.51 Feb/2013). **RESULTS:** After one year of treatment, annual costs were BRL26,898.56 ADA and BRL19,945.90 TCZ. Therapy with TCZ as a single-agent showed better response rates in both outcomes (ACR70 32.50% TCZ vs. 17.90% ADA and DAS28 39.90% TCZ vs. 10.50% ADA). Costs per clinical remission considering ACR70 results were BRL61,372.00 TCZ vs. BRL150,271.28 ADA. Costs per clinical remission of DAS28 were BRL49,989.72 TCZ vs. BRL256,176.76 ADA. **CONCLUSIONS:** The analysis suggests that TCZ represents an effective strategy to treat moderate/severe adult RA patients in Brazil's public health care system and presents lower costs per clinical remission compared to ADA.

PMS6

COSTOS ASOCIADOS A EVENTOS CARDIOVASCULARES EN PACIENTES CON ARTRITIS REUMATOIDE AFILIADOS AL RÉGIMEN SUBSIDIADO EN COLOMBIA

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OBJECTIVOS: Los pacientes con Artritis Reumatoide (AR) tienen un número importante de manifestaciones extrarticulares incluyendo la enfermedad cardiovascular, la cual conduce del 30-50% de todas las muertes. El objetivo de este trabajo es estimar los costos asociados a eventos agudos (infarto al miocardio y pericarditis) y crónico (falla cardíaca) de la enfermedad cardiovascular en pacientes con AR en Colombia. **METODOLOGÍAS:** Este estudio se realizó desde la perspectiva del tercer pagador. Se identificaron los eventos generadores de costo de guías de atención aprobadas por el ministerio de salud, con ayuda de un experto clínico se construyeron los casos tipo de infarto al miocardio, pericarditis y falla cardíaca, se utilizó un costeo por actividades siguiendo la metodología del botton-up, para la valoración de procedimientos se emplearon los manuales tarifarios ISS y SOAT, los costos de los medicamentos se tomaron del SISMED y el costo de los dispositivos médicos se obtuvo de licitaciones públicas. Todas las cifras monetarias se expresan en pesos colombianos de 2013. La prevalencia de la AR y el riesgo de ocurrencia de los eventos cardiovasculares se tomaron de la literatura. Los datos de aseguramiento provienen de estadísticas nacionales. **RESULTADOS:** El costo promedio de atención de los eventos cardiovasculares objeto de estudio en pacientes con AR fueron: infarto al miocardio $ 8.518.192 (procedimientos: $ 4.364.209; medicamentos: $ 4.004.331; insumos: $ 149.652); pericarditis $ 2.638.233 (procedimientos: $ 2.430.875; medicamentos: $ 207.357); falla cardíaca $ 26.435.947 (procedimientos: $ 9.348.420; medicamentos: $ 17.087.526). Los costos globales de atención en pacientes con AR afiliados al régimen subsidiado de los eventos cardiovasculares de interés serían: infarto al miocardio $ 38.106.493.677; pericarditis $ 5.447.190.660; y falla cardíaca $ 54.582.612.447. **CONCLUSIONES:** La enfermedad cardiovascular en pacientes con AR representa una carga económica de gran impacto para el régimen subsidiado en el sistema de salud Colombiano.

PMS7

COSTOS ASOCIADOS A NEUMONÍA SEVERA Y TUBERCULOSIS EN PACIENTES CON ARTRITIS REUMATOIDE QUE HAN RECIDO TRATAMIENTO CON TERAPIA BIOLOGICA ANTI-TNF

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OBJECTIVOS: Los pacientes con artritis reumatoide (AR) tienen un mayor riesgo de padecer infecciones severas, debido a factores de mal pronóstico de la enfermedad que han sido identificados como predictores de infección y al tratamiento farmacológico con inmunosupresores. En la literatura se encuentran reportados como eventos adversos frecuentes respecto a infecciones, la neumonía severa y la tuberculosis (TBC) en pacientes que han recibido tratamiento con terapia biológica anti-TNF, el objetivo de este trabajo es presentar una estimación de costos médicos directos de dichos eventos. **METODOLOGÍAS:** Este estudio se realizó desde la perspectiva del tercer pagador. Los eventos generadores de costo para neumonía severa se identificaron a partir de una guía de práctica clínica Colombiana y para TBC se empleó un protocolo de manejo avalado por el ministerio de salud. Se construyeron los casos tipo para cada patología con ayuda de un clínico experto y se utilizó un costeo por actividades siguiendo la metodología botton-up. La valoración de los procedimientos se realizó teniendo en cuenta los manuales tarifarios ISS y SOAT, los costos de los medicamentos se tomaron del SISMED y el costo de los dispositivos médicos se obtuvo de licitaciones públicas. Todas las unidades monetarias se expresan en dólares americanos (1 US$ = 1.785 COP). **RESULTADOS:** El costo promedio de atención de la neumonía en pacientes que van a la unidad de cuidado intensivo (50%) fue US$ 2410 (procedimientos US$ 2194; medicamentos US$ 191; insumos US$ 25). El costo promedio de atención de la neumonía en pacientes que van a hospitalización (50%) fue US$ 1854 (procedimientos US$1425; medicamentos US$392; insumos $ US 37). El costo de atención de TBC fue US$16,438 (procedimientos US$ 299; medicamentos US$ 16,139). **CONCLUSIONES:** Los costos asociados a la atención de la neumonía severa y TBC representan un gran impacto económico para el sistema de salud.

PMS9

CUSTOS DAS FRATURAS OSTEOPORÓTICAS NO SISTEMA PÚBLICO DE SAÚDE BRASILEIRO

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OBJETIVOS: Descrever o custo do tratamento hospitalar das fraturas de baixa energia, típicas da osteoporose, no Sistema Único de Saúde do Brasil. **MÉTODOS:** Foi realizado um estudo de custos por procedimentos nas unidades do complexo de urgência e emergência da Fundação Hospitalar do Estado de Minas Gerais (Fhemig). O período de coleta dos dados foi de janeiro a maio de 2012. O estudo foi composto de cinco etapas seqüenciais, que englobam: i. Identificação e definição dos macroprocessos, processos e atividades relacionados às fraturas de quadril, ombros, punhos e vertebrais, decorrentes da osteoporose; ii. Elaboração de Mapeamento de Processos típicos de pacientes acometidos pela doença submetidos a tratamento cirúrgico; iii. Identificação dos recursos consumidos em cada atividade, como tempo gasto para cada atividade, materiais médico-hospitalares, órteses e próteses; iv. Construção da base de informações interligada com o Sistema de Gestão Hospitalar (SIGH – Custos ABC); e v. Realização de Painel de Especialistas para validação do estudo. Os valores foram descritos em dólar americano (31 de março de 2012 – taxa de cambio: 1 dólar =1,82 real). **RESULTADOS:** Os maiores custos encontrados foram para as fraturas vertebrais, seguido das fraturas dos quadris, ombros e punhos. Custos de fraturas vertebrais variaram de $10,054.57 a 20,313.73; das fraturas de

quadris de $2,126.41 a 11,012.42. Os custos para as fraturas de ombros variaram de $1,355.64 a 4,436.57. E, custos das fraturas de punhos variaram de $454.75 a 3,869.94. O maior percentual do custo, na maioria das vezes, estava relacionado às próteses e ao tempo de permanência pós-cirúrgico no ambiente hospitalar. **CONCLUSÕES:** Apesar de os maiores custos estarem relacionados às fraturas vertebrais, os desfechos clínicos mais relevantes da osteoporose são as fraturas de quadris, devido à sua elevada incidência. Fraturas osteoporóticas são, em grande parte, evitáveis, a partir do controle dos fatores de risco e medicação preventiva adequada.

PMS10

CUSTO-EFETIVIDADE DO TRATAMENTO PARA OSTEOPOROSE NA POS-MENOPAUSA NO BRASIL

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OBJETIVOS: Realizar uma avaliação de custo-efetividade dos medicamentos disponíveis para o tratamento da osteoporose na pós-menopausa, sob a perspectiva do Sistema Único de Saúde, do Brasil. **MÉTODOS:** Utilizou-se um modelo de Markov para simular a progressão da osteoporose na pós-menopausa presumindo-se uma coorte hipotética de mulheres de diferentes faixas etárias (40-49 anos, 50-59 anos, 60-69 anos, 70-79 anos e 80 ou mais) com fraturas prévias. O modelo levou em consideração a eficácia do tratamento nos diferentes sítios de fraturas (quadris, punhos, ombros e vértebras). Foram comparados o alendronato, risedronato, ibandronato, calcitonina, raloxifeno, calcitriol, teriparatida e denosumabe com não oferecer tratamento medicamentoso. O modelo foi utilizado para estimar os benefícios clínicos em termos de anos de vida ganhos e os custos associados ao tratamento medicamentoso. Os dados de eficácia foram baseados em revisões sistemáticas com metanálise; os custos do tratamento e com internações decorrentes das fraturas referiram-se aos custos do Sistema Único de Saúde. O tempo de seguimento foi de 50 anos ou até a morte. Utilizou-se taxa de desconto de 5% nos custos e benefícios. Foram feitas análises de sensibilidade probabilística e considerando-se diferentes taxas de desconto. **RESULTADOS:** As estratégias terapêuticas não foram custo-efetivas na faixa etária de 40-49 anos. Aos 50-59 anos, foram custo-efetivos o alendronato e denosumabe; nas faixas etárias mais avançadas (60 anos ou mais), somente o alendronato foi custo-efetivo. **CONCLUSÕES:** As estratégias terapêuticas foram custo-efetivas para algumas situações. E, apesar de existirem diferentes opções terapêuticas para o tratamento da osteoporose na pós-menopausa, poucas tem efeito em todos os sítios de ação. Nenhuma das estratégias apresentou-se *cost-saving*.

PMS11

ASSESSMENT OF COST-EFFECTIVENESS MODELS FOR BIOLOGICS IN THE MANAGEMENT OF PSORIATIC ARTHRITIS

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OBJECTIVES: Given biological therapies in psoriatic arthritis (PsA) treatment paradigm are expensive, cost-effectiveness evaluations can be a valuable tool in payer health care decision making. We sought to review the economic evidence and cost-effectiveness of all available biologics developed for treatment of PsA. **METHODS:** We conducted a structured literature search of published and unpublished literature from year 1996 to 2012. We included modeling and other economic studies that assessed cost-effectiveness of biologics and excluded studies that evaluated therapies other than biologics. **RESULTS:** A total of 9 studies involving moderate to severe active PsA patients were analyzed. Most of the cost-effectiveness studies were conducted in the UK (N=6) using direct payer perspective. As no head-to-head trials between biological therapies were present, either indirect comparison with Bayesian technique or network meta-analyses were used to synthesize evidence. Treatment clinical effectiveness was measured by psoriatic arthritis response criteria (PsARC) and/or psoriasis area and severity index (PASI). Functional status was measured by health assessment questionnaire (HAQ). Decision analytical model with underlying Markov modeling was considered by majority of the studies to build the cost-effectiveness model using cohort of patients, while few studies used patient level simulations. Disease-modifying anti-rheumatic drugs (DMARDs) were primarily considered as comparators. Time horizon varied from 10 years to lifetime. All studies employed quality adjusted life years (QALYs) as their measure of effectiveness. Costs and QALYs discounting rate varied from 3.5 to 6% and 1.5 to 3.5% respectively. Incremental cost-effectiveness ratio per QALY varied from £17,000 to £40,000. **CONCLUSIONS:** Although biologics are considered expensive, they improve patient's quality of life in the long-run. Existing cost-effectiveness studies have differences in their assumptions and methodologies, and provide valuable inputs towards building the set of disease related parameters. Next generation of biologic therapies in the near future can benefit from these analyses.

PMS12

ASSESSMENT OF COST-EFFECTIVENESS MODELS FOR BIOLOGICS IN THE MANAGEMENT OF SEVERE ANKYLOSING SPONDYLITIS

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OBJECTIVES: Current biologics provide effective clinical benefits to patients with ankylosing spondylitis (AS). We sought to review economic evidence supportive of cost-effective evaluation for currently available biologics developed for treatment of severe AS that aid in disease management decision-making. **METHODS:** A structured literature search of published and unpublished literature from year 1996-2012 was conducted. We included modeling and other economic studies that assessed cost-effectiveness of biologics and excluded studies evaluating other therapies. **RESULTS:** Ten studies (infliximab=5, etanercept=2, infliximab and etanercept=1, adalimumab=1, golimumab=1) were analyzed. Majority of studies (N=7) were conducted from societal perspective. Health payer perspective was employed by 2 studies and one study incorporated both. Cohort simulation of patients with severe AS was employed to build cost-effectiveness model by most of the studies and few used patient-level simulation. Non-steroidal anti-inflammatory drugs were considered as comparators in all economic models. Studies employed quality adjusted life years (QALY) as their unit of outcome. Euro-quality-of-life-5 dimensions was used as the instrument for quality weightings by most studies and health utilities index-3 and general health rating scale were used by others. Bath ankylosing spondylitis disease activity index and Bath ankylosing spondylitis functional index were used as response and efficacy parameters. Costs and QALYs discounting rate varied from 3%-6% and 1.5%-5% respectively. Over a longer time horizon (25-40 years), the incremental cost-effectiveness ratio per QALY varied from €7,500-€56,000 for infliximab, €22,000-€32,000 for etanercept, €23,000 for adalimumab, and €30,000 for golimumab. **CONCLUSIONS:** Although biologics are considered expensive, they are the only approved therapy options for patients with severe AS. Even though existing cost-effectiveness studies have differences in their assumptions and methodologies, they do provide valuable inputs towards building set of disease related parameters useful for economic evaluation of next generation biologic agents.

PMS13

COST-EFFECTIVENESS ANALYSIS OF ETANERCEPT IN THE TREATMENT OF RHEUMATOID ARTHRITIS IN INSTITUTIONAL MARKET IN ECUADOR

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OBJECTIVES: Rheumatoid arthritis is an autoimmune, inflammatory and chronic disease associated with significant morbidity. Due its chronic and progressive nature, functional limitations and physical disability cause an important social and economic impact. In Ecuador, the prevalence of AR is 0.9%; The incidence is higher in women (6.4:1) and the average age is 53.6 years, representing a Public Health problem. Biologic treatments represent a therapeutic alternative for patients who failed disease-modifying antirheumatic drugs. However, their high cost and the high risk of tuberculosis are the challenges for clinicians and decision makers. The aim of this study was to assess the cost-effectiveness of biologic alternatives in Ecuador from an institutional perspective. **METHODS:** A Markov model was developed to simulate the clinical course of patients treated with etanercept (25mg twice a week), adalimumab (40 mg every 15 days) and infliximab (3mg/kg initial and at 2nd and 6thweek, every 8 weeks) as first-line therapies combined with Metotrexate 20 mg/kg per week after DMARDs failure, as well as associated costs over one-year period. Effectiveness measures were: proportion of patients achieving 70% improvement in both, tender or swollen joint counts following the ACR70 criteria and quality adjusted life years gained. Costs considered included: biologics, concomitant drugs, medical follow-up and side effects management. Clinical response of alternatives was extracted from published literature, while costs were collected from Official Ecuadorian databases. **RESULTS:** The cost-effectiveness analysis showed the utility in QALYs gained of etanercept, adalimumab and infliximab is 0.79; 0,77; and 0,73 respectively, the net costs are: USD$ 17092.39 for Etanercept; USD$ 17,940.39 for Adalimumab and USD$32979.60 for Infliximab. Resulting etanercept the dominant option. **CONCLUSIONS:** The cost effectiveness analysis results determinate that etanercept is the most cost effectiveness option. Due the less production of adverse events including tuberculosis, easy and ambulatory application and differential price for institutional market.

PMS14

EVALUACIÓN DE COSTO-EFECTIVIDAD DE CERTOLIZUMAB PEGOL COMPARADO CON ETANERCEPT EN EL TRATAMIENTO DE ARTRITIS REUMATOIDEA EN COLOMBIA

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OBJECTIVOS: Los Anti TNF alfa son terapia de primera línea para el tratamiento de pacientes con Artritis Reumatoidea Activa (AR) con inadecuada respuesta a metotrexate u otros DMARs no biológicos, el objetivo del presente estudio es evaluar la costo efectividad de certolizumab pegol (CZP) en comparación con el anti TNF incluido en el listado de medicamentos del plan de salud en Colombia etanercept (ETA), bajo la perspectiva del sistema de salud con un horizonte temporal de un año. **METODOLOGÍAS:** Se construyó modelo basado en árbol de decisiones no probabilístico en Excel, la medida de efectividad fue la tasa de respuesta ACR20 a la semana 52 la cual fue extraída de los estudios pivotales de cada una de los medicamentos (TEMPO y RAPID 1), se siguió la metodología para comparaciones indirectas de Glenny et al. en donde se ajusta por metotrexato como comparador común. Se incluyen costos directos, el costo anual de la terapia se estimó usando los valores de la Circular 04 de Noviembre de 2012 de la Comisión Nacional de Precios y Dispositivos Médicos y las tarifas SOAT 2012 para gastos médicos complementarios. Se calculó la razón de costo efectividad promedio e incremental y se realizó análisis de sensibilidad con +/- 10% de los valores del caso base. **RESULTADOS:** El costo anual fue estimado en 19.270USD para ETA y 25.692USD para CZP, la tasa de respuesta ACR 20 ajustada fue de 45% para ETA Vs 77% para CZP, la razón de costo efectividad fue de 42.755USD para ETA y 33.434USD para CZP y el costo por respondedor adicional de CZP comparado con ETA es 201 USD, las conclusiones se mantienen en el análisis de sensibilidad. **CONCLUSIONES:** En Colombia certolizumab pegol resulta costo efectivo frente a etanercept en pacientes con Artritis Reumatoidea activa que han tenido respuesta inadecuada a DMARs no biológicos.

PMS15

ESTIMATED COST EFFECTIVENESS OF LOWER-DOSE SUBMICRON DICLOFENAC COMPARED WITH TRADITIONAL DICLOFENAC IN BRAZIL

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OBJECTIVES: Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed to treat pain and inflammation.Despite their effectiveness, concerns exist regarding their safety. Worldwide health authorities, including the Brazilian Society of Rheumatology, (Henrique da Mota et al., 2012) advise that NSAIDs should be prescribed at lower doses and for shorter durations. Effectively lowering NSAID dose without compromising pain relief has been demonstrated in randomized controlled trials of an investigational NSAID, lower-dose submicron diclofenac (LDSD). The objective of this study was to estimate the potential reduction in risk of NSAID dose-related adverse events (AEs), corresponding savings in health care costs, and the incremental cost-effectiveness of LDSD compared with conventional diclofenac (CD) in Brazil. **METHODS:** A decision-analytic cost-effectiveness model was developed that considered a subset of potential AEs that may be avoided by lowering NSAID dosage. Prediction equations estimating the relative risk of upper GI bleeding/perforation and major CV events, by diclofenac dosage versus non-NSAID use, were estimated by meta-regressions using data from systematic literature reviews. Utilities, lifetime costs, and health outcomes associated with AEs in Brazil were literature based. The model was validated with clinical experts in Brazil. Results were evaluated in one-way and probabilistic sensitivity analyses. **RESULTS:** The model predicted that LDSD vs CD could reduce the occurrence of modeled gastrointestinal events (by 18%), cardiovascular events (by 7%), and acute renal failure (by 19%), leading to a 10% reduction in costs of treating AEs. LDSD was predicted to be cost-effective, with a robust incremental cost-effectiveness ratio relatively insensitive to parameter uncertainty. **CONCLUSIONS:** LDSD has the potential to provide clinical and economic value to patients using NSAIDs in Brazil. Further investigation regarding the potential effect of LDSD on the risk of additional NSAID dose-related toxicities should be explored.

PMS16

COSTO-UTILIDAD DE COLÁGENA-POLIVINILPIRROLIDONA EN EL TRATAMIENTO DE OSTEARTROSIS DE RODILLA I-II FRENTE AL CUIDADO ESTANDAR ESTABLECIDO EN LOS PROTOCOLOS VIGENTES DE LAS INSTITUCIONES PUBLICAS EN MÉXICO

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OBJECTIVOS: Osteoartrosis es la enfermedad reumática más prevalente en México. El surgimiento de alternativas terapéuticas buscando un mejor pronóstico frente a los protocolos convencionales, requiere generar información científica para establecer el costo-efectividad/utilidad de las mismas. Este estudio evalúa el costo-utilidad de colágena-polivinilpirrolidona (colágena-PVP), producto desarrollado en México, frente a las alternativas del protocolo institucional del Instituto Mexicano de Seguridad Social (IMSS) en el tratamiento de la osteoartrosis de rodilla (OAR). **METODOLOGÍAS:** Se diseñó un modelo probabilístico de Markov para evaluar los costos y resultados/utilidades (QALYs) del tratamiento con colágena-PVP comparado con AINES en pacientes con OAR I-II. La selección del comparador se basó en las recomendaciones de las Guías de Práctica Clínica vigentes en México. Las utilidades y probabilidades se fundamentan en la evidencia disponible en la literatura nacional e internacional. El horizonte temporal fue el tiempo de sobrevida de la cohorte (53 años) y los costos fueron obtenidos de los listados de adquisiciones y GRDs del IMSS y de las tarifas del diario oficial. Se aplicó una tasa de descuento del 5% para costos y utilidades. Se realizaron análisis de sensibilidad que con el modelo probabilístico estableció el efecto de la incertidumbre **RESULTADOS:** Para colágena-PVP, el costo por tratamiento de OAR es de MEX$ 734,572.86. En el grupo AINES, el costo del tratamiento fue de MEX$ 806,584.02. El grupo con colágena-PVP presentó 9.88 QALYs comparado con 7.99 en el grupo AINES, con un radio costo-utilidad mayor en este último ($100,949.19/QALY versus MEX$74,349.48/QALY en colágena-PVP). El costo ahorrado para obtener un QALY adicional con colágena-PVP (RCUI) es de MEX$ 38,101. **CONCLUSIONES:** Al considerar el referente de un PIB/cápita como guía para determinar el costo-utilidad cuando no hay medidas de disponibilidad a pagar establecidas en un sistema de salud, colágena-PVP es una alternativa costo-ahorradora en el tratamiento de OAR en México.

PMS17

ESTUDIO DE COSTO/UTILIDAD DEL TRATAMIENTO HABITUAL DE LA ARTRITIS REUMATOIDEA MAS ETANERCEPT VERSUS TRATAMIENTO HABITUAL MÁS OTROS BIOLÓGICOS DEL MERCADO CHILENO Y VERSUS TRATAMIENTO HABITUAL SIN BIOLÓGICOS

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OBJECTIVOS: Determinar el costo/utilidad incremental (ICER) del esquema habitual de tratamiento en la Artritis Reumatoide (AR) más etanercept y compararlo con otros esquemas de tratamiento que incluyan agentes biológicos, usando como base el esquema habitual sin agentes biológicos. **METODOLOGÍAS:** Se realizó un estudio de costo/utilidad usando un modelo de Markov con tres estados de salud: AR activa, AR inactiva y Retiro. El punto de vista del estudio fue el del sistema público más gasto de bolsillo de los pacientes. Las utilidades fueron medidas en una muestra de pacientes chilenas con AR utilizando el instrumento EQ-5D y los costos fueron determinados de acuerdo a los costos del Sistema Público de Chile. El horizonte temporal del análisis fueron 75 años y se usó una tasa de descuento de 3%. **RESULTADOS:** Las utilidades obtenidas fueron de 0,52±0,27 para la AR inactiva (n=46) y de 0,15±0,33 para la AR activa (n=35). Usando el criterio del American College of Rheumatology de mejoría del 20% en relación a la condición basal (ACR 20), se obtuvo, usando el tratamiento habitual como base, un ICER de $24.572.914 (US$ 49.146) para etanercept; de $272.758.563 (US$ 551.614) para Adalimumab; y de $441.333.820 (US$ 932.067) para certolizumab. Rituximab, infliximab y golimumab resultaron más costosos pero menos efectivos que el tratamiento habitual. Estos resultados no fueron sensibles ni a la variación de las utilidades, ni a la variación en el número de ciclos, ni a la variación de la tasa de descuento, ni a la variación en el criterio de mejoría (ACR20 vs. ACR50). **CONCLUSIONES:** Etanercept es el producto con el menor ICER en relación al tratamiento habitual de la AR en Chile.

PMS18

IMPACTO EN LA PRODUCTIVIDAD LABORAL DE UNA COHORTE DE PACIENTES CON ARTRITIS REUMATOIDE TRATADOS CON ETANERCEPT (ENBREL®) EN COLOMBIA

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OBJECTIVOS: La Artritis Reumatoide (AR) es una enfermedad inflamatoria crónica, progresiva, incapacitante, asociada con altos costos. El objetivo de este estudio es analizar los cambios de la productividad laboral (en tiempo) y su impacto económico, en una cohorte de pacientes con AR tratados con Etanercept (Enbrel®) durante un año en el programa de gerenciamiento de la enfermedad "Evaluación día" en la Institución Prestadora de Salud Riesgo de Fractura S.A-CAYRE en Bogotá, Colombia. **METODOLOGÍAS:** En el análisis se incluyeron pacientes con AR que iniciaron tratamiento con Enbrel® entre Agosto-2009 y Enero-2011. Como criterio de inclusión se requirió la aplicación de una herramienta para medir productividad laboral: Work Productivity and Activity Impairment Questionnarie (WPAI), al menos en dos oportunidades: al inicio y a los 9-12 meses del tratamiento; los supuestos utilizados fueron: pérdida de productividad en la misma proporción que pérdida laboral, cambio del estatus laboral debido sólo a la enfermedad, productividad individual equivalente al PIB per cápita. Se calculó la pérdida económica utilizando como referencia el valor de las horas pérdidas estimadas a partir del PIB per cápita de Colombia. **RESULTADOS:** Al inicio del tratamiento, 32% de los pacientes eran trabajadores, el ausentismo fue del 12,38% y el porcentaje de discapacidad total en el trabajo (presentismo y ausentismo) fue 11,89%. A los 9-12 meses, 28% de los pacientes eran trabajadores, el ausentismo fue de 3,26% y la discapacidad total en el trabajo de 3,17%. Asumiendo que los resultados obtenidos mediante WPAI no cambian de manera importante en el tiempo, se estima que al utilizar Enbrel® los pacientes recuperan anualmente $1.086.308 (9%) del PIB per cápita/año. **CONCLUSIONES:** El uso de Enbrel® afecta de manera positiva la productividad laboral de los pacientes analizados. Los supuestos permiten apreciar el efecto de Enbrel® en la productividad, sin hacer referencia a las diferencias salariales entre pacientes.

MUSCULAR-SKELETAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PMS19

IMPROVEMENTS IN PHYSICAL FUNCTION, HEALTH RELATED QUALITY OF LIFE AND WORK PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH GOLIMUMAB: SUB-ANALYSIS OF LATIN AMERICAN PATIENTS ENROLLED IN MULITCENTRE PHASE III CLINICAL TRIALS

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OBJECTIVES: To examine physical function, health-related quality of life(HRQOL) and work productivity in patients enrolled from Latin American countries (Argentina,Chile and Mexico) in Phase III clinical trials for golimumab(GLM) in rheumatoid arthritis(RA). **METHODS:** Active RA patients not previously treated with methotrexate(MTX)(GO-BEFORE,N=637) or with inadequate response to MTX(GO-FORWARD,N=444) were randomized to SC GLM(50 or 100mg)+MTX or PBO+MTX, q4wks.At wk24(GO-FORWARD) or wk52(GO-BEFORE), PBO+MTX group switched to GLM 50mg+MTX. Physical function was assessed using HAQ(0-3). HRQOL was assessed using SF-36 PCS(0-100) and SF-36 MCS(0-100). Impact of disease on work productivity was assessed using a productivity VAS (0-10). Clinically meaningful improvement was defined as improvement of $\geq$0.25 point in HAQ, or $\geq$5 points in SF-36 PCS and MCS. **RESULTS:** At baseline, both MTX naive (N=96) and MTX experienced (N=56) RA patients enrolled in Latin American region experienced moderate to severe physical disability (mean HAQ score of 1.60 to 1.75) and impaired HRQOL (mean PCS of 30.0 to 30.3 and mean MCS of 9.4 to 42.6). The impact of RA on productivity was severe (mean VAS score of 6.3-6.7). Patients treated with GLM (50 or 100 mg)+MTX had significantly greater mean improvement than PBO+MTX group in HAQ (0.87 vs. 0.56, p=0.01), PCS (12.44 vs. 6.93, p<0.01) and work productivity (-3.69 vs. -2.25, p<0.01) at wk 24, and greater proportions of patients in GLM+MTX group than PBO+MTX achieved clinically meaningful improvement in HAQ (84.04% vs. 65.45%, p=0.01), PCS (74.47% vs. 49.09%, p<0.01) and MCS (45.74% vs. 41.82%, p=0.73). Similar results were observed in patients who were MTX naïve and experienced although the magnitudes of improvements were greater in MTX naïve patients than MTX-experienced patients. The improvements were sustained over wk52 and 104. **CONCLUSIONS:** MTX naïve and MTX experienced RA patients from Latin America treated with GLM demonstrated improved physical function, HRQOL, and work productivity.

PMS20

QUALIDADE DE VIDA DOS PACIENTES QUE UTILIZAM MEDICAMENTOS ANTI-TNF PARA O TRATAMENTO DE DOENÇAS REUMÁTICAS NO SISTEMA ÚNICO DE SAÚDE EM MINAS GERAIS, BRASIL

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OBJETIVOS: Descrever o perfil epidemiológico e qualidade de vida dos pacientes em tratamento com bloqueadores do fator de necrose tumoral (TNF) no Sistema Único de Saúde, em Minas Gerais, Brasil. **MÉTODOS:** Os entrevistados foram pacientes que receberam a primeira dispensação de anti-TNF para o tratamento de artrite reumatoide (AR), artrite psoriática(AP) e espondilite anquilosante(EA) nas Gerências Regionais de Saúde (GRS) de Belo Horizonte e Juiz de Fora, no período de agosto de 2011 a março de 2013. Foi utilizado formulário padronizado para investigação

sobre os medicamentos e reações adversas, comorbidades, atividade das condições reumatológicas e avaliação da qualidade de vida. Para avaliação da qualidade de vida foi utilizado o HAQ (*Health Assessment Questionary*), e o EuroQol 5-D (EQ-5D) um instrumento genérico de medida de qualidade de vida. **RESULTADOS:** Foram entrevistados 204 pacientes ao todo. Desses, 70,2% tinham diagnóstico de AR, 11,7% AP e 18% EA. Aproximadamente 74,8% eram do sexo feminino. A média de idade foi de 50,71 anos (DP 13,52). O tempo médio com diagnóstico da doença foi de 119,56 meses (DP=102,54). A maioria, 67,8%, utilizou adalimumabe, 25% etanercept e 7,2% Infliximabe. O valor médio do EQ-5D foi de 0,6247 (DP=0,178) no total dos pacientes. Para os pacientes com AR a média do EQ-5D foi 0,6238 (DP=0,179), para EA 0,6579 (DP=0,178) e para AP 0,5790 (DP=0,169). **CONCLUSÕES:** população predominantemente do sexo feminino e com uma média de idade de cerca de 51 anos. No geral, o score do EQ-5D foi considerado moderado e, dentre as doenças, a que apresentou score menor foi a AP.

MUSCULAR-SKELETAL DISORDERS – Health Care Use & Policy Studies

PMS21

DESCRIPCIÓN DE UNA COHORTE DE PACIENTES CON ARTRITIS REUMATOIDE TRATADOS CON ETANERCEPT (ENBREL®) DENTRO DE UN PROGRAMA DE ATENCIÓN EN UN CENTRO ESPECIALIZADO EN COLOMBIA

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OBJECTIVOS: La Artritis Reumatoide (AR) es una enfermedad articular inflamatoria que afecta al 0,5-1,0% de la población adulta mundial. El objetivo de este estudio es realizar un análisis descriptivo de la actividad de la enfermedad (DAS28), calidad de vida (HAQ – Health Assessment Questionnaire) y depresión (escala de Zung), tras un año de seguimiento del programa de gerenciamiento de la enfermedad "Evaluación día" para pacientes con AR que iniciaron tratamiento con Etanercept (EnbrelÒ) en la Institución Prestadora de Salud Riesgo de fractura S.A-CAYRE en Bogotá, Colombia. **METODOLOGÍAS:** En el programa se incluyeron 91 pacientes colombianos con AR que iniciaron tratamiento con Enbrel®, tuvieron 4 visitas de seguimiento durante un año; como parte del manejo integral de la enfermedad se incluyeron paraclínicos, evaluación por reumatólogo, psicólogo, terapeutas y clinimetría (DAS28, HAQ y Zung entre otras). Un total de 52 pacientes (57,14%) cumplieron criterios de inclusión para el análisis, con una edad promedio de 53,5 años y evolución promedio de la enfermedad de 12,2 años. **RESULTADOS:** Al año, 25% de los pacientes alcanzó el porcentaje de remisión DAS28 con una reducción de 52,9% en alta actividad entre la visita de ingreso y la última visita; 19 pacientes (37,5%) presentaron una reducción >1,2 del DAS28 respecto al inicio del tratamiento. El HAQ inicial promedio fue 1,07 y mejoró al disminuir a 0,96 en el último control. Al inicio 33,3% de los pacientes tenían algún grado de depresión mayor (Zung) y al año de la observación disminuyó a 21,9%. **CONCLUSIONES:** Los resultados obtenidos nos permiten inferir que Enbrel® afecta de manera positiva la evolución de AR en un programa de gerenciamiento de la enfermedad. Es importante contar con la descripción de programas de gerenciamiento de la enfermedad, con el fin de tener data propia de AR en Colombia y brindar el manejo integral que requieren las enfermedades crónicas.

PMS22

BARRIERS OF ACCESS TO ELECTIVE ORTHOPEDIC PROCEDURES IN RIO DE JANEIRO, BRAZIL

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OBJECTIVES: Currently, in Rio de Janeiro state, barriers to patient care who require elective surgical procedures in orthopedics are found, thus many patients remain long periods on hold until the attendance. This study aims to analyze the frequency of hospitalization procedures (HP), total inhospital cost (IC), and total number of inhospital days (ID) related to orthopedic elective procedures in Rio de Janeiro state, Brazil, from the public perspective in order to identify potential barriers of access. **METHODS:** Orthopedic procedures that require hospitalization were selected from the public official hospital information system, for the year 2011. These procedures were separated into elective or urgent according to treatment indication, and validated by an expert panel. Costs are expressed in 2012 Brazilian Real (BRL). A public secondary database was accessed to evaluate HP, IC, and ID separated by cities. **RESULTS:** Rio de Janeiro state is composed by 92 municipalities. Total population consists of 15,989,929 inhabitants, and 6,320,446 (39.53%) live in the capital (Rio de Janeiro city). In 2011, 18,564 elective HP were performed, with a total IC of 21,977,085 BRL, and 145,295 ID. Data from the capital show 10,724 elective HP, total IC of 14,399,281 BRL, and 98,458 ID, which represent 57.77%, 65.52%, and 67.76% of the state, respectively. When only urgency procedures were analyzed, these rates fell to 43.73%, 46.46%, and 49.35%, respectively. **CONCLUSIONS:** Hospitalizations for elective orthopedic procedures in Rio de Janeiro state do not present homogeneous distribution among municipalities. The capital houses less than 40% of total population and accounts for more than 65% of costs and inhospital days. Data suggest that municipalities are able to absorb urgency occurrences, but not elective ones, creating difficulties for the treatment of patients in need of elective procedures. Decentralization of care may be able to reduce such barriers.

PMS23

DRIVING AFTER DRINKING: HOSPITALIZATION, MORTALITY RATE, AND COSTS PRE AND POST PROHIBITION IN RIO DE JANEIRO, BRAZIL

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OBJECTIVES: In Rio de Janeiro, the prohibition on driving after drinking alcoholic beverage began on March 19th 2009. Media has reported since then a decrease in the number of vehicle accidents. A study on hospitalization profile and costs was developed from the public perspective to compare pre and post beginning of prohibition periods. **METHODS:** A public secondary database was accessed to evaluate three periods: pre prohibition (PRE; April 2008 to March 2009); first (FAP; April 2009 to March 2010) and second (SAP; April 2011 to March 2012) years after prohibition. For each period, number of hospitalizations, related costs and mortality rate were evaluated. Costs are presented in 2012 Brazilian Real (BRL). Filters for city (Rio de Janeiro), and group (external causes – transport accidents) were applied. No limits for procedure type, ICD-10 or patient's age were used. **RESULTS:** In FAP and SAP, total number of hospitalizations related to transport accidents showed a discrete decrease (4,485 and 4,729, respectively) when compared to PRE number (4,783). However, hospitalization costs showed a small increase in FAP (5,812,999BRL; mean cost per patient: 1,296BRL) and SAP (6,596,924BRL; mean cost per patient: 1,398BRL), when compared to PRE (5,677,670BRL; mean cost per patient: 1,187BRL). Mortality rate, as well as absolute number of deaths has decreased in FAP (165; rate: 3.7) and SAP (211; rate: 4.5) if compared to PRE (224; rate: 4.7). Surgical treatment of tibia fracture was the most impacting procedure in number of hospitalizations (294; 246; and 255 for PRE, FAP and SAP, respectively), and two most impacting cost disease were surgical treatment of politrauma (956,435BRL; 1,190,927BRL; 1,491,951BRL), and surgical treatment of tibia fracture (475,117BRL; 396,793BRL; 391,756BRL), for all three studied periods. **CONCLUSIONS:** No significant impact in costs were observed after prohibition on driving after drinking alcohol. Absolute number of hospitalizations and mortality rate showed a discrete fall.

PMS24

ESTIMACIÓN DE LA PREVALENCIA DE ARTRITIS REUMATOIDE EN MÉXICO

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OBJECTIVOS: Estimar la prevalencia de artritis reumatoide (AR) en adultos en México durante el año 2009. **METODOLOGÍAS:** Se estimó la prevalencia de pacientes con AR en México, basada en los registros de casos nuevos (consulta de especialidad en segundo nivel de atención de primera vez y subsecuente) de la base de datos de la Secretaría de Salud (datos de 2009, clasificación CIE-10). Se excluyeron los casos reportados en consulta familiar ya que de acuerdo a guías de práctica clínica, el diagnóstico de artritis reumatoide requiere de validación por parte de un reumatólogo. La estructura poblacional se extrajo de fuentes gubernamentales oficiales. Los datos fueron analizados con el software DISMOD II para generar estimados consistentes de los parámetros epidemiológicos de la AR. **RESULTADOS:** La prevalencia estimada de AR para el año 2009 fue de 0.8% de la población adulta, equivalente a 879,776 personas. La prevalencia estimada por género fue de 0.7% en hombres y de 0.9% en mujeres. De acuerdo a la edad, la prevalencia se acentúa después de los 45 años. Según el grado de discapacidad 10% de los casos se consideraron como enfermedad severa, 60% AR moderada y 30% AR leve. El 97% de los pacientes recibió atención médica institucional: 49% derechohabientes de empresas privadas, 36% del Seguro Popular, 9% trabajadores del gobierno federal, 2% trabajadores petroleros y fuerzas armadas y 1% trabajadores de gobiernos estatales. **CONCLUSIONES:** La prevalencia estimada para México es consistente con lo reportado a nivel internacional. El número estimado de casos por sexo, edad y severidad pueden emplearse como base para diseñar políticas específicas, así como gestionar estrategias de atención y realizar la planificación de los recursos necesarios para atender a esta población.

PMS25

UNMET NEEDS AND BIOLOGIC USE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN BRAZIL

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OBJECTIVES: Despite their availability, it is unclear the extent to which biologic treatments are being used in Brazil. The current study assessed the unmet needs of patients with rheumatoid arthritis (RA) in Brazil and the degree to which biologic treatments are currently used. **METHODS:** Data were obtained from the Brazil 2011 and 2012 National Health and Wellness Surveys (NHWS; N=24,000). The Brazil NHWS is a self-reported nationally representative patient survey of the adult population (aged 18+), weighted to correct for any socioeconomic sampling bias. Respondents in NHWS who reported a diagnosis of RA (n=137) were examined with respect to their sociodemographics, current treatments, health outcomes (e.g., Short Form 12v2), and biologic-related attitudes. Differences in health outcomes as a function of severity were examined using general linear models. **RESULTS:** Patients with RA were mostly female (59.12%) and had a mean age of (43.76 years). 36.50%, 43.07%, and 20.44% of patients were mild, moderate, and severe, respectively. Mean levels of physical health status decreased as severity increased (Mild=45.12; Moderate=41.50; Severe=38.49, $p<.05$). All severity levels were significantly lower than the population norm of 50 (ps<.05). Similar effects were observed for other health outcomes. Despite these unmet needs, only 60.92% of moderate-to-severe patients were currently being treated with a prescription medication and only 6.90% were using biologic therapy. Post-hoc analyses examined potential reasons for low biologic uptake among moderate-to-severe patients including significantly poorer access (20.27% of RA patients vs. 27.74% of non-RA patients had monthly household incomes above R$10,000) and attitudinal factors (29.33% reported a fear/strong fear of needles). **CONCLUSIONS:** Our analyses suggest significant decrements in health outcomes among patients with RA in Brazil and poor uptake in biologic therapies. Although future research would need to more directly test our hypotheses, preliminary analyses suggest that poor access and attitudinal factors may play a role.

NEUROLOGICAL DISORDERS – Clinical Outcomes Studies

PND1

MIXED TREATMENT COMPARISON OF ADVERSE EVENTS FOR BG-12, GLATIRAMER, AND TERIFLUNOMIDE FOR THE TREATMENT OF RELAPSING FORMS OF MULTIPLE SCLEROSIS

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OBJECTIVES: Clinical trials of two new oral treatments (Teriflunomide and BG-12) for relapsing-remitting multiple sclerosis (RRMS) have been recently published. As efficacy is similar between these products and glatiramer, a comparison of their relative safety is relevant to physicians, patients, and providers. Our objective was to conduct a mixed treatment comparison of adverse event (AEs) in placebo-controlled randomized clinical trials of BG-12 240mg BID and TID, Glatiramer 20mg SID, and Teriflunomide 7mg and 14 mg SID in RRMS. **METHODS:** Articles were selected and reviewed following Cochrane guidelines. Placebo-controlled phase III RRMS clinical trials were eligible for inclusion. Data collected were the total number of patients experiencing at least one AE. The odds ratio (OR) of AEs, Credible Interval (CrI), and confidence in OR >1 for all drug pairs were estimated using a Bayesian random effects network meta-analysis with placebo as baseline comparator, and multi-arm adjustment. The mean rank (1-5) and probability of ranking lowest (PrL) of all treatments were calculated. The Surface Under Cumulative Ranking (SUCRA) summarized overall strength of evidence of the ranking of each treatment (best 100%, worst 0%). **RESULTS:** A total of 384 studies were identified and reviewed, and 3 studies (3737 patients) were included for analysis. Preliminary results are reported. Glatiramer exhibited the lowest AEs of all treatments (OR >1 for all comparisons with ≥ 90% confidence), except for borderline non-significantly lower AEs vs. placebo (OR=.73;95%CrI=.18-1.98;PL=89.6%). Patients receiving glatiramer had the lowest AEs (rank=1.4,PrL=80.3%,SUCRA=91.7%), followed by placebo (rank=2.9,PrL=4.2%,SUCRA=62.6%), BG-12 240mg TID (rank=3.2,PrL=4.8%,SUCRA=56.8%), Teriflunomide 7mg (rank=4.2,PrL=5.5%,SUCRA=35.3%), BG-12 240mg BID (rank=4.7,PrL=1.2%,SUCRA=26.9%), and Teriflunomide 14mg (rank=4.7,PrL=4.0%,SUCRA=26.7%). **CONCLUSIONS:** Preliminary results suggest that RRMS patients treated with Glatiramer have the lowest risk of experiencing AEs, while patients taking Teriflunomide 14mg have the highest AEs risk. This evidence may be useful to perform net clinical benefit analyses on alternative RRMS treatments.

PND2

EPIDEMIOLOGY AND ECONOMIC STUDIES ON PATIENTS DIAGNOSED WITH INSOMNIA: A REVIEW OF THE LITERATURE

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OBJECTIVES: To conduct a systematic review of literature in peer-reviewed journals on epidemiology and economic studies on patients diagnosed with Insomnia. **METHODS:** The initial search strategy was developed in the PubMed/MEDLINE database, and was then translated for the Cochrane and Embase database searches. Search strings for epidemiology and economics studies for Insomnia were constructed using varied approaches that included the use of MeSH terms, as well as keywords that would afford the best retrieval. Additional parameters were placed on the final search strategy to limit the retrieval to articles written in English, involving human subjects and published between 2000 and 2010. **RESULTS:** The initial search identified 225 articles for epidemiology and 144 articles for economic studies on Insomnia from PubMed/Medline/Embase/Cochrane databases. After removing duplicates and non-relevant articles, 40 articles for epidemiology and 13 for economic studies were included in the study. Twenty-three studies were focused on the prevalence of insomnia and the estimates among all of the studies ranged from 6.6% to 56%. Two studies focused on one year incidence rates of insomnia; one in Canada and the other in the UK. There were 4 studies each on burden of illness and cost effectiveness and 5 studies on retrospective claims analysis. The average annual direct and indirect per-person costs were $5,010 for individuals with insomnia syndrome, $1,431 for individuals presenting with symptoms, and $421 for good sleepers. **CONCLUSIONS:** There was a significant variation in the prevalence rates of Insomnia across different studies and in different countries. Insomnia results in significant direct and indirect costs and indirect costs in comparison to patients who were not diagnosed with Insomnia.

NEUROLOGICAL DISORDERS – Cost Studies

PND3

NATALIZUMAB FOR 2ND LINE TREATMENT IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS: 5-YEAR BUDGET IMPACT ANALYSIS (BIA) FROM THE BRAZILIAN PUBLIC PAYER PERSPECTIVE

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OBJECTIVES: Multiple sclerosis (MS) is a neurodegenerative disease associated with long-term disability and economic impact. With the addition of new agents for the MS treatment (e.g. natalizumab), there is a need to evaluate the relative value of newer therapies in terms of cost, given health care resource constraints in Brazil. Natalizumab is an effective therapeutic option for RRMS patients. Compared to other drug options, it shows better efficacy in terms of disease progression and relapse rates. Although natalizumab is indicated for 2nd line, the Ministry of Health public guidelines recommend natalizumab only in 3rd line treatment for MS. Therefore, a BIA has been created to analyze the impact of introducing natalizumab in 2nd line treatment in the public system. **METHODS:** BIA was based in a Markov model with monthly cycles and 5-year time horizon and MS epidemiological data were obtained from DATASUS. The model compared current MS treatment options reimbursed by the Brazilian government - interferon, glatiramer acetate and natalizumab (3rd line) with an alternative scenario with natalizumab in 2nd line. **RESULTS:** Number of Brazilian patients eligible for Relapsing-Remitting Multiple Sclerosis (RRMS) treatment was estimated to be around 7,098, 2,397 and 498 patients (1st, 2nd and 3rd line treatment, respectively) in the first year. Compared to the current scenario, the inclusion of natalizumab in the reimbursement protocol for 2nd line shows an additional budget through the 5 years consecutively as: 124.9K, 365.7K, 652.3K, 912.8K and 1.0M (USD). It is expected that during the 5-year analysis, the inclusion of natalizumab as 2nd line will increase the budget for MS by 4% with average cost per MS patient of USD50.60 (USD13.061 vs USD13.112 per patient/year). **CONCLUSIONS:** The estimated budget impact to include natalizumab as a 2nd line treatment option was USD3.1M in five years (increment of 4.0% of the current budget) for MS treatment.

PND4

ANÁLISIS DE COSTO-EFECTIVIDAD DE DOS FORMULACIONES DE TOXINA BOTULÍNICA TIPO A (TBA) EN COLOMBIA PARA EL TRATAMIENTO DE LA PARÁLISIS CEREBRAL INFANTIL (PCI)

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OBJECTIVOS: La incidencia de PCI es de 1.5 a 5/1000 nacidos vivos, esta representa la mayor causa de discapacidad infantil con un alto impacto en salud pública y la TBA hace parte del tratamiento integral. Los objectivos de este estudio son de comparar la costo-efectividad e impacto presupuestal del tratamiento con TBA Dysport 500U y Botox 100U en pacientes pediátricos con PCI, bajo la perspectiva del sistema de salud colombiano en un horizonte temporal de un año. **METODOLOGÍAS:** Para valorar la efectividad y seguridad se realizó revisión sistemática de la literatura; para la estimación de costos se utilizó la metodología de caso tipo, validado por tres fisiatras. Se estimó el costo de tratamiento anual basados en la "Circular 04 de Noviembre de 2012 de la Comisión Nacional de Precios". El análisis de sensibilidad incluye una variación entre el 25% y 30% de las dosis y escenarios sin optimización de unidades. Se calculó y comparó el costo promedio de tratar un paciente con PCI durante 1 año y el impacto presupuestal en una cohorte 1000 pacientes con cada medicamento. **RESULTADOS:** Las dos alternativas son equivalentes en términos de respuesta clínica y seguridad de acuerdo a lo encontrado en la evidencia científica. El costo promedio de tratamiento por paciente con TBA 500U es USD 2592 vs USD 3888 con TBA 100U, lo que representa un ahorro anual del 33% con el uso de TBA 500U. Si se considera una cohorte de 1000 pacientes, la elección de tratar PCI con TBA 500 proyecta un ahorro de USD 1,296,000 para el sistema de salud colombiano. En el 83% los escenarios del análisis de sensibilidad el uso de TBA 500U se mantuvo costo-ahorrativa. **CONCLUSIONES:** Desde la perspectiva del sistema de salud Colombiano el tratamiento de la PCI con TBA 500U resulta costo-ahorrativo vs el tratamiento con TBA 100U.

PND5

ANÁLISIS DE COSTOS MEDIANTE UN MODELO LINEAL GENERALIZADO DE PACIENTES MEXICANOS CON SINDROME DE WEST

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OBJECTIVOS: Realizar un análisis de costos del Síndrome de West (SW) mediante un modelo lineal generalizado desde la perspectiva institucional del Sector Salud de México. **METODOLOGÍAS:** Se identificaron los costos médicos directos de la atención de pacientes con SW (CIE-10 G40X) en el período comprendido entre 2000 y 2010, en el Hospital Infantil de México Federico Gómez (HIMFG). Los costos de recursos se obtuvieron del tabulador de cuotas de recuperación del HIMFG ajustados por el índice de precio del Sector Salud al 2011, los costos se reportan en MxP.Se realizó un modelo lineal generalizado para conocer la distribución de los valores de cada concepto evaluado y con estos resultados se realizó un análisis de sensibilidad Bootstrap para observar el comportamiento en los costos y la variabilidad de los mismos, además de una simulación de Monte Carlo con los intervalos de confianza generados. **RESULTADOS:** Se revisaron 86 expedientes de pacientes con SW, 60,7% de sexo masculino, la edad de inicio de los espasmos fue en promedio 4.9 meses, el tiempo promedio de seguimiento de los pacientes fue de 2.67 años. El costo total promedio del seguimiento fue de $45.425,73 correspondiendo el 73,79% del gasto a uso de fármacos antiepilépticos, 24,39% a estudios de extensión y el 2,2% restante a atención ambulatoria, hospitalizaciones y consulta de urgencias. En relación al tiempo de seguimiento, el medicamento con mayor costo durante el seguimiento fue la vigabatrina (media $21.924,24, rango $1.051,27 - $101.347,70), seguida del valproato de magnesio (media $6.914,75, rango $50,41 - $108.176,50). El análisis de sensibilidad realizado mostró que el modelo de costos es robusto y eficaz. **CONCLUSIONES:** La mayor proporción del coste de tratamiento en pacientes con SW correspondió al tratamiento antiepiléptico, lo que coincide con otros reportes de la literatura en relación al costo generado por el tratamiento farmacológico en pacientes epilépticos.

PND6

BURDEN OF MULTIPLE SCLEROSIS AND UNMET NEEDS IN BRAZIL: COST OF ILLNESS STUDY

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OBJECTIVES: To assess both direct medical and non-medical costs of Brazilian multiple sclerosis (MS) patients. **METHODS:** This was a cross-sectional, multicenter study conducted in 8 Brazilian major MS treatment sites. Costs due to MS treatment were calculated based on the resource utilization related to inpatient days, outpatient visits, laboratory and imaging tests, disease modifying therapies (DMTs), co-medication, OTC medications, aids and/or home modifications, and professional caregiver. Unit costs derived from Brazilian official price lists were applied to the

yearly frequency and average consumption. **RESULTS:** The study enrolled 210 MS patients, mean age was 40.7 [standard deviation=11.5] years and 70.7% female. Patients with mild disability (according to self-reported Expanded Disability Status Scale [EDSS]) represented 40.4% of patients, 43.7% had moderate disability and 15.9% had severe disability. The overall yearly direct costs (mean [CI95%]) associated to patients with mild, moderate and severe disabilities were: USD18,475 [2,293-34,657], USD19,371 [4,651-34,090], and USD19,545 [0-57,659] (1BRL = 0.4937USD), respectively. Disease modifying therapies (DMTs) were the major component of the total yearly cost, ranging from 93.5% among mild patients to 53.9% in the severe group (85.5% in the total sample), followed by aids and home modifications (mild: 2.3%; moderate: 2.3%; severe: 15.1%; total sample: 4.3%). Patients with moderate disability had higher absolute costs related to inpatient care, emergency visits, laboratory and imaging tests, and DMTs than the other disability groups, while those with severe disabilities presented higher costs in the remaining categories (consultations, co-medications and OTC medications, aids and home modifications, and professional caregiver). **CONCLUSIONS:** To our knowledge, this is the first Brazilian study investigating the cost of MS patients. Our findings indicate that MS represent a significant economic burden for both the health care system and patients and their families, with different expenditures profiles depending on the EDSS level.

PND7

ARGENTINIAN SURVEY IN COST OF ILLNESS AND UNMET NEEDS IN MULTIPLE SCLEROSIS: TREATMENT EXPERIENCE & THE COSTS OF MS PATIENTS IN ARGENTINA

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OBJECTIVES: The objective of the study was to assess the cost of MS patients in Argentina categorized by disease severity using a societal perspective. **METHODS:** This was a cross-sectional study including MS patients from 21 MS centers in 12 cities of Argentina conducted to collect information on demographics, disease characteristics, disease severity, comorbidities, relapses, resource utilization and patient reported outcomes, associated with MS. Patients were stratified by disease severity using the EDSS (group 1 with EDSS score between 0 and 3; group 2 with EDSS >3 and <7; group 3 with EDSS ≥7). Direct and indirect costs included in the analysis were: inpatient and outpatient care for relapses, inpatient care for other reasons than relapses, consultations, investigations, specific MS treatments, wheelchair, professional care, informal care, sick leave and retirement due to MS. Second quarter 2012 costs were obtained from public sources and converted to US Dollars. **RESULTS:** A total of266 patients were included. 87.6% had relapsing remitting MS. Mean annual cost per MS patient was USD 36,025 (95% CI 31,985-38,068) for patients with an EDSS between 0-3; USD 40,705 (95% CI 37,199-46,300) for patients with EDSS >3 and <7, and USD 50,712 (95% CI 47,825-62,104) for patients with EDSS ≥7. **CONCLUSIONS:** This is the first Argentine study evaluating the costs of MS considering disease severity.

PND8

CHARACTERISTICS OF HOSPITALIZATIONS DUE TO AN EPISODE OF RELAPSE IN MULTIPLE SCLEROSIS BRAZILIAN PATIENTS: A RETROSPECTIVE ADMINISTRATIVE CLAIMS ANALYSIS UNDER THE PUBLIC PAYER PERSPECTIVE

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OBJECTIVES: To describe hospital admissions for managing multiple sclerosis (MS) relapses in the Brazilian Public Healthcare System (BPHS). **METHODS:** Data from the 2009-2012 period were collected from the BPHS Hospital Information System (SIH/SUS), which aggregates administrative data from inpatient admissions in public hospitals in the entire country. Individual claims coded as "MS Relapse Inpatient Treatment" in the SIH/SUS (regardless ICD-10 codes) were identified in the database and compiled by state and year. **RESULTS:** We obtained data on 5,922 individual MS relapse-related claims, homegenously distributed among the 4 years. They represented an overall cost of BRL3,729,921 for the 2009-2012 period (ranging from BRL806,722 in 2010 to BRL1,033,649 in 2012). The 4-year national average cost per inpatient admission BRL629, with mean LOS of 7.51 days and ICU days of 0.22. The in-hospital mortality rate ranged from 0.65%-1.60%. The 2012 national rate of MS relapse-related hospitalization in the general population (per 100,000, absolute number of admissions / total population) was 0.79, varying from 0.03/100,000 in Alagoas (Northeast region) to 1.78/100,000 in Santa Catarina (South region). All parameters were consistently different among Brazilian states. In-hospital deaths were very rare in this sample not allowing robust conclusions. It was possible to identify significant outliers in the mean cost per admission when states were separately considered (2012 data: from BRL323 [n=3] in Sergipe to BRL 4,596 in Espírito Santo [n=4]). São Paulo was the state with higher absolute number of hospitalizations in all years. In 2012, the state had 526 admissions, mean cost per event of BRL810, 4 in-hospital deaths (0.76%), mean LOS=6.16, and mean ICU days of 0.36. **CONCLUSIONS:** BPHS administrative hospital database can provide insightful information about MS relapse-related admissions. Both geographical and time trends can be examined using SIH/SUS secondary data, particularly for diseases with highly specific procedure codes.

PND9

ANÁLISIS DE COSTO-EFECTIVIDAD DEL TRATAMIENTO PROFILÁCTICO VERSUS A DEMANDA EN ADOLESCENTES CON HEMOFILIA A SEVERA EN COLOMBIA

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OBJECTIVOS: Algunos adolescentes con hemofilia A moderada reciben profilaxis con Factor VIII (FVIII), pero los resultados económicos de esta estrategia de tratamiento son desconocidos. El objetivo de este estudio fue estimar la razón de costo-efectividad incremental (ICER) de profilaxis con FVIII versus tratamiento a demanda para prevenir episodios de sangrado y hemorragias articulares en adolescentes con hemofilia A moderada en Colombia. **METODOLOGÍAS:** Se utilizó un árbol de decisión desde la perspectiva de un tercer pagador y con tasas de eventos anuales. La eficacia de la profilaxis se tomó de la literatura. Los costos incluyeron FVIII, hospitalización, consultas por urgencias, colocación y complicaciones del catéter venoso central y consultas médicas. La tasa de descuento fue 3% y la utilización de recursos se identificó del grupo económico de hemofilia Europeo y se valoró a partir de tarifarios locales. La prevalencia de hemofilia se determinó con datos locales. Dosis de profilaxis con FVIII: 25U/kg tres veces semanales. Dosis del tratamiento a demanda: 40U/kg dos veces diarias por 3,5 días. **RESULTADOS:** En adolescentes de 10 años y 33kg, la profilaxis con FVIII evitará 118 episodios de sangrado y 47 hemorragias articulares durante el resto de sus vidas, versus a demanda; ICER para el sangrado fue $6.749 y $17.178 para hemorragias articulares. En adolescentes de 19 años y 54kg, la profilaxis con FVIII versus a demanda, evitará 87 episodios de sangrado y 34 hemorragias articulares durante el resto de sus vidas; ICER para el sangrado fue $11.750 y para hemorragias articulares $29.938. **CONCLUSIONES:** La profilaxis con FVIII es una estrategia costo-efectiva en niños con hemofilia A moderada y que presenten 6,4 episodios de sangrado y 2,3 hemorragias articulares, en promedio cada año. Si la profilaxis se inicia a una edad más temprana, se prevendrán más episodios de sangrado y de hemorragia articular.

PND10

ANÁLISIS DE COSTO-EFECTIVIDAD DL TRATAMIENTO PROFILÁCTICO VERSUS A DEMANDA EN ADULTOS JÓVENES CON HEMOFILIA A SEVERA EN COLOMBIA

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OBJECTIVOS: La profilaxis con Factor VIII (FVIII) en hemofilia A severa se utiliza en países desarrollados, en países en desarrollo hay controversia por sus costos. El objetivo de este estudio fue estimar la razón de costo-efectividad incremental (ICER) de profilaxis con FVIII versus tratamiento a demanda para prevenir episodios de sangrado y hemorragias articulares en adultos con hemofilia A severa en Colombia. **METODOLOGÍAS:** Se utilizó un árbol de decisión desde la perspectiva del tercer pagador y con tasas de eventos anuales. La eficacia de la profilaxis se tomó de la literatura. Los costos incluyeron FVIII, hospitalización, consultas por urgencias, colocación y complicaciones del catéter venoso central, consultas médicas y días de trabajo perdidos. La tasa de descuento fue 3% y la utilización de recursos se identificó del grupo económico de hemofilia Europeo y se valoró a partir de tarifarios locales. La prevalencia de hemofilia se determinó con datos locales. Dosis de profilaxis con FVIII: 25U/kg tres veces semanales. Dosis del tratamiento a demanda: 50U/kg tres veces diarias por una semana durante la hospitalización y 25U/kg tres veces semanales por tres semanas ambulatoriamente. **RESULTADOS:** En adultos de 20 años y 70kg, la profilaxis con FVIII evitará 168 episodios de sangrado y 66 hemorragias articulares durante el resto de su vida, versus a demanda; ICER para el sangrado fue $5.676 y $14.463 para hemorragias articulares. En adultos de 40 años y 70kg, la profilaxis con FVIII evitará 79 episodios de sangrado y 31 hemorragias articulares durante el resto de su vida, versus a demanda; ICER para el sangrado fue $5.244 y para hemorragias articulares $13.417. **CONCLUSIONES:** La profilaxis con FVIII en pacientes adultos mejora los resultados clínicos versus a demanda. Si la profilaxis se inicia a una edad más temprana, se prevendrán más episodios de sangrado y de hemorragia articular.

PND11

COST-EFFECTIVENESS ANALYSES OF NATALIZUMAB FOR 2ND LINE VERSUS GLATIRAMER ACETATE IN THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS IN BRAZIL

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OBJECTIVES: Multiple sclerosis (MS) is a neurologic disease that can dramatically affect patients. The aim of this study is to conduct a cost-effectiveness analysis of natalizumab (Tysabri®) versus glatiramer acetate (Copaxone®) for treatment of Relapsing Remitting Multiple Sclerosis (RRMS) patients from the Brazilian Public Healthcare System (SUS) perspective. **METHODS:** A Markov model with a 20-year time horizon comparing natalizumab to glatiramer acetate was developed. Health states were based on EDSS and relapses (moderate or severe). We obtained relapse and disability progression transition probabilities from natural history studies on RRMS patients. In each monthly cycle, patients can discontinue treatment, remain stable, progress to higher MS EDSS state, experience Progressive Multifocal Leukoencephalopathy (PML) or die. Patients with EDSS score ≥ 7.5 receive best supportive care. Resource use and costs were validated by an expert's panel and valued using Brazilian public official lists (DATASUS and BPS). Costs and outcomes (5%) were discounted. Probabilistic sensitivity analyses (PSA) covered variability in efficacy and costs. **RESULTS:** Use of natalizumab was associated with slower EDSS progression and reduced relapse burden. The life years gained (LYG) with natalizumab and glatiramer acetate was 10.65 and 10.09, respectively. Costs associated with natalizumab were USD 119.330 and USD 102.275 for glatiramer acetate. Incremental cost-effectiveness rate for natalizumab versus glatiramer acetate was USD 30.251/LYG. PSA has confirmed the consistency of base case results. **CONCLUSIONS:** For a patient with RRMS, this model shows that natalizumab was cost-effective when compared to treatment with glatiramer acetate, assuming the threshold of USD 50.000/LYG commonly mentioned by the Ministry of Health in Brazil.

PND12

COST-EFFECTIVENESS ANALYSES OF NATALIZUMAB FOR 1ST LINE VERSUS INTERFERON BETA-1A 44 MCG IN THE TREATMENT OF HIGHLY ACTIVE RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS IN BRAZIL

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OBJECTIVES: Multiple sclerosis (MS) is a neurologic disease that can dramatically affect the patient. The aim of this study is to conduct a cost-effectiveness analysis of natalizumab (Tysabri®) versus interferon beta-1a (IFNB1a) 44mcg (Rebif®) for treating Highly Active Relapsing Remitting Multiple Sclerosis (HARRMS) patients. IFNB1a

44mcg was chosen as comparator since it is the most widely prescribed disease modifying therapy for 1st-line treatment in HARRMS patients in Brazil. **METHODS:** We developed a Markov model with 20-year time horizon comparing natalizumab to IFNB1a 44mcg. Health states were based on EDSS and relapses (moderate or severe). Since there are no published data evaluating long-term course specifically in HARRMS, we assumed transition probabilities on EDSS states based on natural history studies on unselected RRMS patients, and relapse probabilities based on a post-hoc analysis of the pivotal natalizumab AFFIRM trial. This is a rather conservative approach, since disability progression may be slower in this proposed model then expected for patients with HARRMS and so the benefit from natalizumab could be underappreciated. In each monthly cycle, patients can discontinue treatment, remain stable, progress to higher EDSS state, experience Progressive Multifocal Leukoencephalopathy or die. Patients with EDSS score≥7.5 receive best supportive care. Resource use and costs were validated by an expert's panel and valued using Brazilian public official lists (DATASUS and BPS). Costs and outcomes were discounted (5%). Probabilistic sensitivity analyses (PSA) covered variability in efficacy and costs. **RESULTS:** Use of natalizumab was associated with slower EDSS progression and reduced relapse burden. Life years gained with natalizumab and IFNB1a 44mcg were 10.90 and 10.54, and costs were USD119,977 and USD132,446, respectively. In the base-case, natalizumab was dominant versus IFNB1a 44mcg. PSA has confirmed the consistency of results. **CONCLUSIONS:** For a patient with HARRMS, the model shows that natalizumab was dominant when compared to IFNB1a 44mcg in the Brazilian Public Healthcare System.

PND13

BURDEN OF MULTIPLE SCLEROSIS AND UNMET NEEDS IN BRAZIL: HEALTH CARE RESOURCE UTILIZATION

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OBJECTIVES: To assess the health care resource utilization (HRU) of Brazilian multiple sclerosis (MS) patients. **METHODS:** This was a cross-sectional, multicenter study conducted in 8 Brazilian major MS treatment sites. HRU was evaluated as the percentage of patients self-reporting the consumption of resources. The main categories were: hospitalization, consultations, laboratory and imaging tests, disease modifying therapies (DMTs), co-medication, aidsand/or home modifications. Frequency and average consumption were annualized. **RESULTS:** The study enrolled 210 MS patients, mean age was 40.7 [standard deviation=11.5] years and 70.7% female. Patients with mild disability (according to self-reported Expanded Disability Status Scale [EDSS]) represented 40.4% of patients, 43.7% had moderate disability and 15.9% had severe disability.Hospitalization was reported by 23%, 33% and 15% of mild, moderate and severe MS patients, with average length of stay of: 7.53, 10.41, and 7.40 days, respectively. Most patients (>96%) had at least one neurologist consultation per year (average 4.94 visits/year in the total sample). Physical therapy was the most consumed non-medical consultation (mild: 11%; moderate: 38%; severe: 64%). Magnetic resonance imagingwas reported by 60%, 68%, and 55% of mild, moderate and severe patients. Patients using at least one DMT during the previous year were: 89%, 93%, and 61% of mild, moderate and severe MS patients, respectively. The most prescribed DMT was glatiramer acetate (38%, total sample). The most frequent co-medications were: anti-depressants, anti-spasticity, and analgesics. Home modification was reported by 19% and 45% of patients with moderate and severe disability, respectively. For ambulation, walking stick was used by 35% of moderate patients, while wheelchair was needed by 58% of severe patients. **CONCLUSIONS:** To our knowledge, this is the first Brazilian study investigating the HRU of MS patients. The findings can be useful to better understand MS patients' needs in terms of comprehensive care.

NEUROLOGICAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PND14

WHICH CYSTIC FIBROSIS INHALED ANTIBIOTIC MEDICINE FEATURES MATTER MOST TO ADULT PATIENTS AND PARENTS OF PEDIATRIC PATIENTS?

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OBJECTIVES: To quantify patient and parent preferences and adherence for different administration features of inhaled antibiotic medicines for cystic fibrosis (CF). **METHODS:** Adult patients with a self-reported physician diagnosis of CF and parents of pediatric CF patients (6 to 17 years) who had *Pseudomonas aeruginosa* in their lung culture at least twice in one year completed a web-enabled, discrete-choice experiment survey in the United States. Respondents answered 5 treatment-choice questions with known statistical properties. Each question required evaluating a pair of hypothetical CF treatment profiles defined by device type (nebulizer, dry powder inhaler (DPI)), total daily administration and cleaning time, dosing frequency, dry cough side effect, and personal cost per cycle. Lung function measured as forced expiratory volume in one second (FEV_1) was held constant between the hypothetical CF treatment profiles. Stated adherence questions followed two randomly selected treatment-choice questions. Random-parameters logit models were used to estimate preference weights for all feature levels and the mean relative importance of each feature for both samples. **RESULTS:** A total of 209 adult patients and 271 parents completed the survey. Mean age of adult patients was 32 (SD = 10) years and mean age of pediatric patients was 12 (SD = 3) years. Among all respondents, the average time spent taking inhaled antibiotic medicines was approximately 40 minutes. Relative importance estimates indicated that switching from a 30-minute nebulizer twice daily to a 10-minute DPI twice daily was 6.3 times more important for adult patients and 2.0 times more important for parents than an improvement in dry cough from moderate to mild. Stated adherence for adult and pediatric patients was 20-30% higher for DPIs versus nebulizers. **CONCLUSIONS:** Treatments administered with more convenient devices such as DPIs and shorter administration times are associated with higher utility and higher stated adherence in adult and pediatric patients.

PND15

BURDEN OF MULTIPLE SCLEROSIS AND UNMET NEEDS IN BRAZIL: MEASUREMENT OF FATIGUE USING MODIFIED FATIGUE IMPACT SCALE

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OBJECTIVES: Fatigue is one of the most frequent symptoms in patients with multiple sclerosis (MS). This study aimed to examine the severity and impact of fatigue in MS Brazilian patients. **METHODS:** This was a cross-sectional, multicenter study conducted in 8 Brazilian major MS treatment sites. Fatigue was assessed using the Brazilian version of the Modified Fatigue Impact Scale (MFIS), which evaluates the impact of fatigue on 3 dimensions of patients' daily life: physical, cognitive and psychosocial. The patient scores 0 (lower impact) to 84 points (higher impact). The final score was classified according to the level of impact: absent (0-38), low (39-58), and high (>58). **RESULTS:** The study enrolled 210 MS patients, of which the mean age was 40.7 [standard deviation = 11.5] years and 70.7% were female. Patients with mild disability (according to self-reported Expanded Disability Status Scale [EDSS]) represented 40.4% of patients, 43.7% had moderate disability and 15.9% had severe disability. In the overall sample, the impact of fatigue was considered absent, low and high in 49%, 32% and 19% of patients, respectively. Any impact (both low and high summed) was reported by 33%, 63%, and 66% of patients with mild, moderate and severe disability, respectively. The mean MFIS total score for mild, moderate and severe patients was 29.3, 45.0, and 45.4 (38.6 in the total sample). The mean impact scores for each domain in the total sample were 20.0 (physical, range 0-36), 14.7 (cognitive, range 0-40), and 3.9 (psychosocial, range 0-8), meaning that fatigue has a proportionally higher impact in the physical than the cognitive or psychosocial domains. **CONCLUSIONS:** Our findings indicate that over 50% of MS Brazilian patients notice some adverse impact of fatigue in their daily lives, particularly related to the physical domain.

PND16

BURDEN OF MULTIPLE SCLEROSIS AND UNMET NEEDS IN BRAZIL: MEASUREMENT OF HEALTH-RELATED QUALITY OF LIFE USING EQ-5D

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OBJECTIVES: To measure the health-related quality of life (HRQL) of multiple sclerosis (MS) patients and examine potential associations between HRQL and patients' characteristics. **METHODS:** This was a cross-sectional, multicenter study conducted in 8 Brazilian major MS treatment sites. HRQL was assessed using the Brazilian version of the EQ-5D and patients self-evaluated their HRQL and health status using five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analog scale (VAS). The EQ-5D index was calculated based on the value set derived from the UK population, since the Brazilian value set is not available. **RESULTS:** The study enrolled 210 MS patients, of which the mean age (standard deviation [SD]) was 40.7 [11.5] years and 70.7% were female. Patients with mild disability (according to self-reported Expanded Disability Status Scale [EDSS]) represented 40.4% of patients, 43.7% had moderate disability and 15.9% had severe disability. Among the 5 assessed HRQL dimensions, the ones with higher frequency of self-reported severe limitations were usual activities and anxiety/depression (11.0% each). The least impaired dimension was self-care, with 63.0% of patients reporting absence of limitation. The mean [SD] VAS score was 71.6 [18.9]. The mean EQ-5D index for each level of EDSS (mild, moderate or severe disability) was 0.73 [0.21], 0.49 [0.30], and 0.30 [0.34], respectively. In the multivariate analysis, variables related to patients' characteristics were explored and the following were associated with the presence of any limitation in at least one dimension: older age, unemployment/retirement, relapses in the previous year, emergency department visits in the previous 6 months and lower educational level. **CONCLUSIONS:** MS adversely impact patients' HRQL, especially with disability progression and clinical features that can be linked to more severe disease.

NEUROLOGICAL DISORDERS – Health Care Use & Policy Studies

PND17

EVALUATION OF TREATMENT PATTERNS AND CLINICAL TRIALS PUBLISHED ON PATIENTS DIAGNOSED WITH INSOMNIA: A LITERATURE UPDATE

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OBJECTIVES: To conduct a systematic review of literature in peer-reviewed journals on real world treatment patterns and clinical trials on patients diagnosed with Insomnia. **METHODS:** A comprehensive literature search was performed using relevant search terms to identify articles published from 2000 to 2010 on the real world treatment patterns and clinical trials conducted on patients with Insomnia. Studies were identified through electronic Embase, Cochrane, Medline, and PubMed databases. Additional parameters were placed on the final search strategy to limit the retrieval to articles written in English, involving human subjects. **RESULTS:** Our search yielded 1,153 articles for treatment patterns and clinical trials on patients diagnosed with Insomnia from PubMed/Medline/Embase/Cochrane databases. After removing duplicates and non-relevant articles, 65 articles were included for final review. A total of 16 studies had some focus on

real world treatment patterns in Insomnia patients and majority of these studies focused on benzodiazepine users. The rate of medication use in Insomnia patients is fairly low and rates were ranging from 17% to 75%. There were a total of 11 trials published testing Eszopiclone use, 10 trials each on Ramelteon and Zolpidem, 4 trials on Indiplon, 3 trials on Gaboxadol, 3 trials on Doxepin use in patients diagnosed with Insomnia. Several patient reported outcomes measures were used in the assessment of various clinical trials. **CONCLUSIONS:** There were a variety of agents being used to treat insomnia; while benzodiazepines and non-benzodiazepines were largely popular. Products in development need to be studied further to determine whether their new mechanisms of action were truly beneficial for treatment.

RESPIRATORY-RELATED DISORDERS – Clinical Outcomes Studies

PRS2
ACUTE ASTHMA CHARACTERISTICS AND ASTHMA CONTROL IN LATIN AMERICA

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OBJECTIVES: To investigate the patient's acute asthma characteristics, and identify predictors of asthma control in a population of asthma patients from five Latin American countries. **METHODS:** Adults and parents of adolescents (12-17 years) with a physician diagnosed asthma and asthma medication use or asthma attacks in the past year were surveyed as part of the 2011 Latin America Asthma Insights and Management (AIM) survey. Using Global Initiative for Asthma (GINA) guidelines as a reference, respondents were categorized into three levels of asthma control: well-controlled, partly- controlled, and uncontrolled. Chi-square tests and adjusted logistic regression were used to determine odds ratios (ORs) to assess the relation of degree of asthma control with frequency of sudden asthma episodes, frequency of asthma symptoms, duration of episodes, day-and night time symptoms, utilization of rescue medications, and asthma episodes seasonality. **RESULTS:** Data from 2168 adults and parents from asthma patients ≥12 years survey was analyzed. Seven percent (7%) of the patients are controlled, 57% partially controlled, and 36% uncontrolled. Adjusted logistic regression models showed that patients whose asthma was uncontrolled were significantly more likely to have acute sudden asthma episodes compared to patients whose asthma was controlled either partially or fully. Similarly, patients with uncontrolled asthma were significantly more likely to have higher frequency of asthma episodes in most days of the week, increased day and night symptoms than those asthmatics who were controlled **CONCLUSIONS:** Patients who did not have well-controlled asthma had more acute episodes as compared to patients whose asthma was well-controlled. Our results strongly suggest that the acute asthma requires a significant effort to decrease its severity.

PRS3
GRAPHIC HEALTH WARNINGS ON CIGARETTE PACKS IN QATAR: PRE-IMPLEMENTATION AWARENESS AND PERCEPTION AMONG THE GENERAL PUBLIC

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OBJECTIVES: Graphic health warnings (GHWs) on cigarette packages have been found to be significantly associated with increased awareness of smoking-related health hazards as well as behavior change. Legislations on GHWs have recently been endorsed and GHWs have now been introduced in Qatar. This study aims to evaluate the general public's awareness, beliefs and perceptions on anti-tobacco GHW labels on cigarette packs prior to the introduction of the new law. **METHODS:** A cross-sectional survey using a pretested 23-item questionnaire was conducted among randomly approached adults in Qatar. Data were analyzed using the IBM SPSS® version 19. Responses were analyzed by smoking status (ever-smokers vs. never-smokers) to ascertain how these two distinct groups differed in their awareness and perceptions related to health warning messages. The demographic characteristics and other outcomes of interest were compared using χ^2 or Fishers Exact tests. **RESULTS:** A total of 500 participants (59% male) responded to the survey. Most notably, ever-smokers did not significantly differ from never-smokers on awareness of GHW. About one-third of the respondents had no idea about any specific text warning messages on tobacco products sold and nearly 45% of them did not know what a GHW was. Furthermore, a substantial proportion (more than 20%) of the respondents in both groups did not believe that introducing GHWs will enhance smoking behavior change. Non-smokers generally tended to have more positive attitudes than smokers toward the perceived impact of GHWs ($p < 0.05$). **CONCLUSIONS:** A substantial proportion of the general public in Qatar had poor awareness about GHWs. This study has important implications on the needs to increase awareness about the value of GHWs as well as calls for further research to determine the effectiveness of GHW labels on cigarette packages in Qatar and the greater Middle Eastern region, where legislations on GHWs are still at infancy.

RESPIRATORY-RELATED DISORDERS – Cost Studies

PRS4
IMPACTO DO USO DO MICRODEBRIDADOR NOS DESFECHOS E CUSTOS NAS CIRURGIAS ENDOSCÓPICAS NASAIS

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OBJETIVOS: O objetivo deste estudo foi comparar as técnicas cirúrgicas com uso do microdebridador em relação à técnica convencional nos procedimentos de septoplastia com turbinectomia e sinusectomia, quanto ao tempo de cirurgia, tempo de hospitalização, uso de colas e hemostáticos, escore de dor, taxa de readmissão hospitalar e custo do procedimento. **MÉTODOS:** A partir do sistema de faturamento do HIAE foram selecionados 538 procedimentos de septoplastia com turbinectomia e sinusectomia realizados no ano de 2011 que utilizaram as técnicas comparadas neste estudo. Foram incluídos na análise 517 pacientes, 56 procedimentos utilizando o microdebridador e 461 utilizando a técnica convencional. Em média, os pacientes que utilizaram o microdebridador possuíam uma faixa etária mais elevada e um percentual maior dos pacientes apresentaram diagnóstico de sinusite crônica. **RESULTADOS:** Em relação à média de tempo de permanência hospitalar esta foi maior no grupo do microdebridador (28 horas versus 22 horas no grupo da técnica convencional, p= 0,002). A quantidade média de unidades de cola e de hemostático foi maior no grupo que utilizou o microdebridador. Não houve diferença estatística entre os grupos nos desfechos de tempo de cirurgia e nas taxas de readmissão hospitalar. No desfecho de dor no pós operatório imediato a diferença entre os grupos foi estatisticamente significativa (p = 0,006), indicando um percentual maior de pacientes com escore de dor acima de 5 sendo tratados com o microdebridador, quando comparado com o grupo convencional. Considerando-se o custo do procedimento com a técnica convencional como referência, o uso do microdebridador resultou em um aumento médio de 17,4% em relação à técnica convencional. **CONCLUSÕES:** O uso do microdebridador não se mostrou favorável nos desfechos avaliados, tendo em vista um aumento do tempo de permanência do paciente, uso de colas e hemostáticos em maior quantidade que a técnica convencional e o custo do procedimento foi significativamente mais alto.

PRS5
COMPARING COPD COSTS BY EXACERBATION FREQUENCY AND DYSPNOEA LEVEL IN A PRIMARY CARE SETTING IN THE UNITED KINGDOM

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OBJECTIVES: Economic burden in Chronic Obstructive Pulmonary Disease (COPD) patients with varying levels of dyspnoea is largely unknown. The objective of this retrospective analysis was to estimate the resource use and the associated costs incurred by COPD patients with increasing levels of dyspnoea with or without frequent exacerbations. **METHODS:** A retrospective cohort of prevalent COPD patients was identified in the Clinical Practice Research Datalink (CPRD). All patients who had at least 12 month pre- and post- cohort entry date (1st prevalent COPD diagnosis confirmed by spirometry ≥April 1, 2009) recorded were included in the analysis. Patients were categorised as having none, 1 or 2+ exacerbations in the 12 months post cohort entry and further classified using Medical Research Council (MRC) dyspnoea scale. Study outcomes included general practitioner (GP) visits, community treated exacerbations (medical dg for exacerbation or ATB+OCS Rx), hospital treated exacerbations and all-cause hospitalisations excluding COPD exacerbations. The costs associated with the estimated resource use were calculated using National Health Service (NHS) reference costs for 2010-11. **RESULTS:** The cohort consisted of 51,641 COPD patients with 27,764 (53.8%), 12,585 (24.4%) and 11,292 (21.9%) having experienced none, 1 and 2+ annual exacerbations post cohort entry. Among all patients, the estimated annual COPD management costs, excluding the costs of medications, were £1,597, £1,849, £2,298, £2,745 and £3,579 with increasing levels of dyspnoea (MRC grade 1-5). The equivalent cost ranges by exacerbation frequency were £1,267-£2,235, £2,021-£3,447 and £2,627-£4,709 for patients with none, 1 or 2+ annual exacerbations, respectively. **CONCLUSIONS:** Increase in COPD management costs with increase in level of dyspnoea occurred in all exacerbation frequency groups. Better symptom control and disease management strategies in primary care setting may help reduce COPD costs significantly.

PRS6
HEALTH AND ECONOMIC BURDEN OF TOBACCO USE IN SEVEN LATIN AMERICAN COUNTRIES: RESULTS FROM A MICROSIMULATION HEALTH ECONOMIC MODEL (HEM)

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OBJECTIVES: Smoking is the single most preventable cause of disease and death all around the world. Our objective was to quantify the disease burden associated with smoking in Argentina, Bolivia, Brazil, Chile, Colombia, Mexico and Peru. **METHODS:** The project began with a survey to health Decision Makers (DM) to explore country-specific information needs. The development stage involved the harmonization of a methodology to retrieve local relevant parameters and develop the model structure. A microsimulation HEM was built considering the availability and quality of epidemiological data and relevant outcomes were conceived to suit the identified information needs of DMs . It considers all tobacco-related diseases: heart, cerebrovascular and chronic obstructive pulmonary disease, pneumonia/influenza, lung cancer and nine other neoplasms. A systematic search on effectiveness, local epidemiology and costs studies was undertaken to populate the model. Calibration and validation was performed for each country. Predicted event rates were compared to the published rates used as model inputs. External validation was undertaken against epidemiological studies not used to provide input data. **RESULTS:** The calibrated model showed all simulated event rates falling within ±10% of the sources and a high correlation between published data and model results. In these seven LA countries, tobacco is responsible of 259,126 deaths each year. The diseases attributable to smoking cause a total of 1·90 million years of life lost due to premature death, 0·64 million years of life lost due to disability and at least 27 billion dollars (USD dollars 2013) in direct medical costs each year. **CONCLUSIONS:** Tobacco use is

responsible for an enormous burden of disease in the region. This evidence-based, internally and externally valid HEM showed to be an adequate tool for the assessment of the effects of smoking and could be a useful policy-making tool to estimate the cost-effectiveness of tobacco control interventions.

PRS7

CUSTOS DE PNEUMONIAS HOSPITALIZADAS NO BRASIL: ANÁLISE COMPARATIVA POR DIFERENTES MÉTODOS DE CUSTEIO

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OBJETIVOS: Comparar os custos do tratamento de crianças hospitalizadas por pneumonia bacteriana adquirida na comunidade, considerando diferentes metodologias de custeio. **MÉTODOS:** Estudo prospectivo realizado em Goiânia, Goiás/Brasil. Crianças com 28 dias a 35 meses internadas em 2 hospitais foram avaliadas. Três metodologias de custeio foram consideradas na perspectiva do Sistema Único de Saúde: (i) *bottom-up/micro-costing* através da revisão de prontuários; (ii) *top-down/micro-costing* através de diretriz terapêutica; e (iii) *top-down/gross-costing* através de ressarcimento pago pelo SUS. Casos foram pacientes internados com suspeita clínica de pneumonia, receberam antibioticoterapia durante a internação e não tiveram diagnóstico final de pneumonia viral. Casos graves foram aqueles internados em enfermaria enquanto os internados em unidade de terapia intensiva foram considerados muito graves. Foram considerados custos diretos (medicamentos, honorários médicos e de fisioterapia respiratória, exames e diárias hospitalares em UTI e enfermaria) e não-médicos (diárias de acompanhantes). Os custos foram estimados em dólares americanos (USD) e reais (R$) considerando a taxa de câmbio oficial (1 USD = R$ 1,875) em dezembro de 2011. O teste de Friedman foi utilizado para comparar os resultados. **RESULTADOS:** Foram analisados 59 casos (52 graves e 7 muito graves). Os custos de casos graves foram R$ 781 (USD 416) por *bottom-up/micro-costing*, R$ 641 (USD 342) por *top-down/micro-costing* e R$ 597 (USD 318) por *top-down/gross-costing (p=0,015)*. Para os casos muito graves, os custos foram R$ 3.539 (USD 1.887) por *bottom-up/micro-costing*, R$ 3.369 (USD 1.796) por *top-down/micro-costing* e R$ 3.175 (USD 1.693) por *top-down/gross-costing* (p=0,018). Para ambos os grupos, houve diferença significativa apenas entre *bottom-up/microcosting e top-down/gross-costing*. **CONCLUSÕES:** Nossos resultados sugerem a estimativa de custos por *top-down/micro-costing* através de diretriz terapêutica pode ser uma alternativa que se aproxima à estimativa considerando o *bottom-up/microcosting* através de revisão de prontuários, considerado o padrão ouro para estimativa de custos de doença.

PRS8

EFFECTIVENESS AND COST ANALYSIS OF THE SMOKING CESSATION PROGRAM IN THE PUBLIC HEALTH SYSTEM IN BRAZIL

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OBJECTIVES: To assess the effectiveness and costs of the Smoking Cessation Program (SCP) in the Public Unified Health System (SUS) and to estimate the cost for its full implementation in the city of Goiânia, Brazil. **METHODS:** The SCP intervention targets group of smokers, and includes medical visits, cognitive-behavioral group therapy, and medication use, lasting six months. Costs for SCP intervention and management were estimated. The SCP full implementation was defined as the program's expansion to meet the demand of all smokers motivated to quit smoking in the city of Goiânia. Direct medical and non-medical direct costs were considered, including staff, medications, consumables, general expenses, transportation, travel, events and capital costs. Microcosting and activity-based costing methods were used. Cost for the federal, state and municipal levels were estimated. The SUS perspective was considered. Two-way sensitivity analysis was conducted. Data sources included a convenience sample of primary health facilities, municipal and state health departments, and the Ministry of Health. Costs were estimated in Reais (R$) and U.S. Dollars (USD), considering the exchange rate of December/2010, which was 1.67. Quitting rates were estimated as the percentage of patients who reported not smoking at the end of the intervention. Costs of the SCP are presented as total cost of the intervention; costs stratified by component and level of funding source; cost per patient; and cost per quitter. **RESULTS:** The average quitting rate was 37.2%. The cost of SCP in Goiânia was R$428,580 (US$257,220), of which 23% were program management costs. Cost per patient was R$534 (US$320) and cost per quitter was R$1,433 (US$860). The SCP's full implementation reaching the estimated 37,455 smokers in Goiânia motivated to quit would cost R$21.5 million (US$13). **CONCLUSIONS:** The SCP is highly effective. Additional efficiency could be gained by expanding patient's access to the program.

PRS11

CLINICAL AND ECONOMIC ANALYSIS OF MOMETASONE FUROATE NASAL SPRAY IN THE TREATMENT OF RHINOSINUSITIS IN MEXICO

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OBJECTIVES: Little information exists on the acute treatment provided for rhinosinusitis and its associated costs. We hypothesize that introducing the administration of mometasone furoate (MFNS) as a treatment for rhinosinusitis will have a substantial impact on medical resource costs, outcomes and possibly cost-effectiveness. The goal of this paper is to estimate the cost-effectiveness of treating patients with rhinosinusitis with MFNS versus amoxicillin. **METHODS:** A decision-analytic model was developed to estimate lifetime costs and outcomes associated with MFNS 200µg twice daily and amoxicillin 500mg three times daily in treating rhinosinusitis from the Mexican health care perspective. This study further do not included MFNS 200µg once daily as a treatment arm because it was not found to be superior to amoxicillin. Data sources included published literature, clinical trials, official price/tariff lists, and Delphi panel data. The time horizon was 2 weeks. The effectiveness outcomes of the study were modeled as changes in the Major Symptom Score (MSS). MSS consists of five questions concerning rhinorrhoea, post-nasal drip, nasal congestion, sinus headache, and facial pain. Costs were valued in US dollar, year 2012 values. Multiple 1-way sensitivity analyses and a probabilistic sensitivity analysis using Monte Carlo simulation were performed to handle uncertainty. **RESULTS:** The projected costs were US$ 258 with MFNS and $US 272 with. The benefits (changes in the MSS) were 0.52 with MFNS 0.45 with Amoxicilin. MFNS was associated with a cost savings per patient of US$ 14 versus amoxicillin over a period of 2 weeks from a health care perspective. The incremental cost-effectiveness ratio for MFNS dominated Amoxicilin. Sensitivity analysis confirmed the overall cost savings and gains in effectiveness. **CONCLUSIONS:** Our analysis suggests MFNS improves health outcomes in a cost-effective manner compared with Amoxicilin. The economic value of Amoxicillin is influenced by difficulties involved in diagnosing the condition, effectiveness, resistance, patient compliance with treatment, and treatment failure associated with antibiotics.

RESPIRATORY-RELATED DISORDERS – Health Care Use & Policy Studies

PRS12

THE IMPACT OF PUBLIC FORMULARIES & GUIDELINES ON COMMUNITY ACQUIRED PNEUMONIA (CAP) DRUGS IN MEXICO

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OBJECTIVES: Pharmaceutical spending in Mexico represents approximately 25% of total health expenditures, with this number expected to grow by 14% from 2009-2014. 90% of Mexico's population receives health care from the public health system or Popular Health Insurance (PHI). A private insurance market has begun to take root. This study looks at how the increase in price controls and guidelines may impact access to newly approved Community Acquired Pneumonia (CAP) drugs. **METHODS:** An array of published data such as pricing process, current policies, sector-specific research articles contributed towards a framework to understand the key factors affecting access to CAPs drugs, were gathered. The data then informed a telephone survey of national and regional health care stakeholders (N=6). **RESULTS:** Findings show that in Mexico: 1) New pressures through price negotiations are occurring due to economic challenges facing PHI; 2) Private purchasing of pharmaceutical products represents 56% of sold units worth 79% of total spend versus public purchase representing 44% of sold units and 21% of total spend; 3) Formularies used by public coverage schemes require newly approved drugs for CAP to achieve marketing authorization, meet safety requirements and be cost effective versus comparator agents; and 4) International reference price serves as a benchmark for establishing a price threshold. **CONCLUSIONS:** Drugs used to treat CAP are compared to comparator agents based on cost effectiveness. This will determine placement in the public formulary. The private pharmaceutical market may use data from the public formulary system when making a determination on price. Existing clinical guidelines in the public sector are non-binding, leaving the final decision on use to physicians. However, patient access to drugs for CAP may be impacted based on price negotiations and cost effectiveness analysis.

PRS13

ASSESSMENT OF THE PERCEPTION AND PRACTICES WITH RESPECT TO ANTIBIOTIC USAGE IN PUBLIC THROUGH SOCIAL MEDIA

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OBJECTIVES: To assess the knowledge, perception and practices with respect to antibiotic usage amongst the Indian population with an aim to sensitize the survey participants about the consequences of misuse of antibiotics. **METHODS:** A questionnaire was designed around the use, misuse and consequences of antibiotic resistance based on latest National Policy for Antimicrobial Resistance of India. The survey was conducted using social media sites like facebook, twitter etc. The responses collected were classified as geographical locations, gender, age and occupation. Survey is designed in such a way that all the prevailing practices and views of the general public with respect to antibiotic usage are covered. **RESULTS:** The prescription for antibiotic was 25% for common cold. Empirical antibiotic prescription was reported for 61% of the respondents. 14% preferred for a diagnostic test for guiding antibiotic prescription by doctors. 50% of the respondents preferred to purchase antibiotics directly from the chemist shops without the prescription of a doctor. Almost half of the respondents were not aware about the antibiotic resistance development due to environmental contamination. 35% of the respondents affirmed to stopping the antibiotic regimen as soon as their symptoms subsided. **CONCLUSIONS:** The antibiotic resistance is a global phenomenon requiring the immediate reforms to curb as the danger of multi-drug resistant bacteria is a ticking time bomb. Our results have clearly indicated the misuse of antibiotics by public and practitioners which needs to be monitored and corrected immediately to prevent the catastrophe of epidemics by MDR bacteria as the new antibiotics are not invented and old drugs are becoming ineffective.

PRS14

LEVEL OF ASTHMA CONTROL AND HEALTH CARE UTILIZATION IN LATIN AMERICA

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OBJECTIVES: Data on the impact of asthma in Latin American countries is limited. The purpose of this study was to examine the association between partly- and uncontrolled asthma and asthma-related health care outcomes among patients residing in Argentina, Brazil, Mexico, Venezuela and the Common wealth of Puerto Rico. **METHODS:** Adults and parents of adolescents (12-17 years) with physician diagnosed asthma and asthma medication use or asthma attacks in the past year were surveyed as part of the 2011 Latin America Asthma Insights and Management (AIM) survey. Using Global Initiative for Asthma (GINA) guidelines as a reference, respondents were categorized into three levels of asthma control: well-controlled, partly- controlled, and uncontrolled. Chi-square tests and adjusted logistic regression were used to determine odds ratios (ORs) to assess the relation of degree of asthma control with utilization of asthma medications, health care outcomes, and productivity. **RESULTS:** Data was available for 2169 completed surveys. Overall, 7% of the patients surveyed had asthma that was classified as well-controlled, with the highest proportion in Mexico (9.4%) and the lowest in Venezuela (3.0%). Patients whose asthma was not well-controlled were significantly more likely to report use of asthma medications (ORs ranging from 1.5-42) and to have had emergency health care visits or hospitalizations for their asthma in the previous year (ORs ranging from 2.1-5.9). Respondents with uncontrolled asthma also reported significant decreases in productivity due to asthma compared to patients with well-controlled asthma. **CONCLUSIONS:** Patients who did not have well-controlled asthma had greater utilization rates of asthma medications and emergency health care services compared to patients whose asthma was well-controlled. These associations strongly suggest that emphasis on improving asthma control could have substantial effects on patient productivity and utilization of health care resources.

PRS15

CARACTERÍSTICAS SOCIOECONÓMICAS DE PACIENTES CON ENFERMEDAD VASCULAR CEREBRAL Y ANTECEDENTES DE TABAQUISMO TRATADOS EN UN HOSPITAL DE TERCER NIVEL DE MÉXICO

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OBJECTIVOS: Determinar las variables socioeconómicas asociadas a pacientes con enfermedad vascular cerebral (EVC) y antecedentes de tabaquismo, tratados en un centro neurológico de tercer nivel en México. **METODOLOGÍAS:** Es un estudio cuantitativo, descriptivo, transversal y retrospectivo. Los pacientes debían tener edades ≥ 35 años, antecedentes de tabaquismo y diagnóstico de EVC; clasificados por el sistema CIE-10 (I60-I69). Se revisaron 174 expedientes del 2011. Se utilizó el análisis de componentes principales para estimar los pesos de las variables socioeconómicas. La adecuación del modelo se realizó mediante la medida de Kaiser-Meyer-Oklin (KMO), la prueba de Bartlett y la consistencia interna mediante el alpha de Crombach (α). **RESULTADOS:** De los 174 pacientes 78(45%) presentaron antecedentes de tabaquismo y de estos 49(63%) fueron hombres, con 58±14 (media, DE) años de edad y 9.4±5.3 de escolaridad, nivel socioeconómico de 2.3±1.1, 71(91%) habita en departamentos populares y 37(47%) se dedicaron al hogar o fueron trabajadores no calificados. Se obtuvo un α =0.80, KMO= 0.78 y Bartlett (p=0.000). Dos componentes explicaron 58.3% de la varianza total. El primero; (42.02%), se integró por las variables servicio intra-domiciliario (Ponderación;0.763), estatus socioeconómico (0.749), escolaridad (0.748), zona de ubicación (0.673), material de construcción (0.707), ubicación de la vivienda (0.673) y ocupación (0.437). el segundo; (16.24%), con el tipo de vivienda (0.564) y número de habitaciones (0.460). **CONCLUSIONES:** Los pacientes atendidos por EVC se caracterizaron por niveles bajos de escolaridad y clasificación socioeconómica, ocupaciones poco remunerables y edad avanzada; que los hace vulnerables a la enfermedad.

SYSTEMIC DISORDERS/CONDITIONS – Clinical Outcomes Studies

PSY1

AGRANULOCYTOSIS DETECTION OUTCOME BY CLOZAPINE TREATMENT (ADOC STUDY) IN PSYCHIATRY: A COST-EFFECTIVENESS STUDY

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OBJECTIVES: White Blood Cell (WBC) monitoring in schizophrenic patients treated by Clozapine aims to prevent agranulocytosis. We assess the cost-effectiveness of WBC monitoring strategies based on three national regulations and an additional weekly short-run monitoring compared to the absence of monitoring. **METHODS:** A decision analytic model was built to perform a cost-utility analysis comparing distinct monitoring strategies from a health care perspective with a 3-year time horizon. Clinical and resources used parameters were based on national Clozapine patients' registries, cohorts, and pharmacovigilance data; health-related quality of life and mortality estimates were derived from literature reviews. Robustness of results was challenged with one-way and probabilistic sensitivity analyses. **RESULTS:** Compared to the absence of monitoring, the number needed to treat of all strategies to avoid one death was 5,000. The gains in survival time adjusted on quality of life were less than 1 day, resulting in prohibitive incremental cost-effectiveness ratios (ICER) of at least 1 million USD per QALY gained,. The ICER increased with higher frequency and longer monitoring duration. The results remain robust in the one-way sensibility analyses and the probabilistic sensitivity analysis indicating that the absence of monitoring strategy has the highest probability of cost-effectiveness **CONCLUSIONS:** Long-run WBC monitoring based on current national detection guidelines is not cost-effective, even by unrealistically high agranulocytosis prevalence. New guidelines are needed to improve WBC monitoring in schizophrenic patients receiving Clozapine.

PSY2

OSTEOTOMIA DE ACORTAMIENTO RADIAL EN LA ENFERMEDAD DE KIENBOCK (SEGUIMIENTO DE 5 AÑOS)

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OBJECTIVOS: evaluar los resultados clinicos y funcionales (grado de satisfacción) de paciente con enfermedad de kienbock ttratados con osteotomia de acortamiento radial. **METODOLOGÍAS:** estudio realizado en la umae de traumatologia y ortopedia lomas verdes del imss, en el servicio de cirugia de mano, en un periodo comprendido entre 2000 al 2003, con seguimiento de 5 años.estudio retrospectivo, observacional, transversal. se estudiaron ´18 pacientes de ambos sexos con diagnostico de enfermedad de kienbock utilizando la clasificacion de litchman, evaluados con las escala de wrist mayo score y QDash. pba estadistica de wiscolson **RESULTADOS:** se obtuviero 18 paciente 9 mujeres y 9 hombres, el 84% obreros 16% al hogar, de acuerdo al resultados de la escla funcional wrist mayo score fueron 56% buenos, 33% excelentes, 5.5% malo, 5% regulares, con 25 puntos de grado de satifaccion de acuerdo al QDash. un paciente fue reintervenido 2 años posteriores al cual se le realizo una artrodesis delas cuatro esquinas. **CONCLUSIONES:** la evaluacion clinica y funcional, sugiere una eficacia aceptable de la osteotomia de acortamiento radial y provee datos alentadorespara continuar con este tipo de tratamiento.

PSY3

THE RELATIONSHIP BETWEEN SPECIFIC ANNUAL BLEED RATES AND HEALTH OUTCOMES AMONG CHILDREN WITH SEVERE HEMOPHILIA A IN LATIN AMERICA

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OBJECTIVES: Recurrent bleeding among severe hemophilia A children can lead to disability and lower health-related quality of life (HRQOL). Little is known about how many bleeds can be endured before patients report an impact on health outcomes. The objective was to assess health outcomes of pediatric patients reporting a zero annual bleed rate (ABR) to identify the impact of higher ABRs on outcomes. **METHODS:** This cross-sectional survey of parents of severe hemophilia A patients aged 2-17 was conducted in Argentina, Chile, Colombia, Mexico and Panama. Eligible, consenting patients completed a questionnaire: from October-November 2009 (Argentina), June-August 2011 (Chile, Colombia, Mexico) and September-October 2012 (Panama). HRQOL was measured by the Pediatric Quality of Life Inventory (PedsQL). ABR, target joints and school days missed were also assessed. **RESULTS:** A total of 211 parents of severe hemophilia A children completed the survey. Compared to patients with a 0 ABR who reported a mean PedsQL Total score of 76.6, patients with ABR categories of: 3-4, 5-10, 11-20, 21-30, 31-50, 51 or more showed significantly worse mean PedsQL Total scores of: 66.4, 63.5, 67.4, 62.5, 62.4 and 59.9 respectively (all $p<0.05$). Similarly, compared to patients with 0 ABR who reported a mean number of target joints of 0.69, patients with higher ABR categories showed significantly higher mean target joints: 1.49, 2.57, 3.42, 3.47, 3.74, 4.67 (all $p<.05$). Differences in missed days from school showed the same significant trend when comparing 0 ABR to ABR categories of 3-4 and beyond. There were no significant differences between patients with zero compared to 1-2 ABR on these health outcomes. **CONCLUSIONS:** This analysis suggests that even 3-4 bleeds/year may have a negative impact on a patient's joint health, missed school days and HRQOL. Efforts to maintain a 0 ABR among pediatric patients with severe hemophilia A may help ensure optimal outcomes.

PSY4

EFFICACY AND SAFETY OF BELIMUMAB FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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OBJECTIVES: To evaluate the efficacy, safety and tolerability of 1 and 10 mg/kg belimumab, a biologic drug, for the treatment of Systemic Lupus Erythematosus (SLE) through a meta-analysis, comparing these treatments with placebo. **METHODS:** A systematic review and meta-analysis of randomized, placebo-controlled trials of belimumab was conducted. Data were collected from several databases until August 2012. Efficacy outcomes included the SELENA-SLEDAI score (Safety of Estrogens in Lupus Erythematosus National Assessment version of the SLE Disease Activity Index), SRI (Systemic Lupus Erythematosus Responder Index), normalization of low C3 (<90 mg/kg), and anti-dsDNA positive to negative. Data on safety included any adverse events, serious adverse events, severe adverse events, death, malignancy, infections, and infusion reactions. We also evaluated withdrawals from treatment due to lack of efficacy or adverse events. **RESULTS:** Fours studies were included in this study. Anti-dsDNA positive to negative was the most significant efficacy outcome in our meta-analysis for both of the evaluated concentrations. No significant differences in the safety data were observed between the belimumab (1 and 10 mg/kg) and placebo groups. Tolerability results revealed no significant differences in withdrawals due to lack of efficacy and adverse events between the belimumab and placebo groups. **CONCLUSIONS:** Belimumab exhibited good efficacy results, especially at 10 mg/kg, a good safety profile, and adequate tolerability, which indicates that this biologic drug is a promising therapy

for the treatment of SLE. Additional randomized placebo-controlled trials should be conducted to establish the efficacy and safety of belimumab.

SYSTEMIC DISORDERS/CONDITIONS – Cost Studies

PSY5
IMPACTO FINANCIERO DEL TRATAMIENTO FARMACOLÓGICO EN PACIENTES ADULTOS CON ENFERMEDAD DE GAUCHER TIPO 1 EN MÉXICO

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OBJECTIVOS: La enfermedad de Gaucher (EG) es una enfermedad de baja prevalencia caracterizada por deficiencia de la enzima glucocerebrosidasa ácida, que promueve la acumulación del sustrato glucocerebrósido en lisosomas de monocitos-macrófagos, lo que conduce a hipertrofia del sistema lisosomal celular, infiltrando tejido esquelético, medula ósea, bazo, hígado, pulmones y cerebro, causando disfunción orgánica. El uso de la terapia de remplazo enzimático (TRE) revierte la organomegalia, previene complicaciones e incrementa la calidad de vida. El propósito del estudio fue evaluar el impacto económico de la TRE en pacientes con EG tipo 1 desde la perspectiva institucional Mexicana. **METODOLOGÍAS:** La prevalencia en México de pacientes con EG se extrajo de fuentes publicadas. Se estimaron los costos promedio del tratamiento de las TRE disponibles en México en pacientes de alto riesgo (60UI/Kg cada 2 semanas durante 6 meses, posteriormente 30UI/Kg durante 6 meses) y de bajo riesgo (30UI/Kg cada 2 semanas durante 6 meses, posteriormente 20UI/Kg durante 6 meses). Los costos de adquisición de las TRE se extrajeron de fuentes gubernamentales y se expresan en US$ de 2012. Se estimó el impacto presupuestal del uso de TRE a nivel institucional en base al Presupuesto de Egresos de la Federación (2012). **RESULTADOS:** El número de pacientes con EG tipo 1 fue de 22 para bajo riesgo y 8 para alto riesgo. El costo promedio anual de la TRE por paciente de bajo riesgo fue de US$153,265, para pacientes de alto riesgo fue de $260,551, un 70% más. La carga financiera para las instituciones de salud pública fue aproximadamente US$338,000 para pacientes de bajo riesgo y US$575,000 para pacientes de alto riesgo, lo que agregado representa el 0.016% del gasto público en salud de México. **CONCLUSIONES:** La estimación del impacto presupuestal de la TRE en México es relevante para la planeación de los recursos financieros necesarios.

PSY6
ANÁLISIS DE LA CARGA FINANCIERA DE LAS PRINCIPALES ENFERMEDADES REUMATOLÓGICAS

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OBJECTIVOS: Realizar un análisis de la carga financiera desde la perspectiva del paciente de las principales enfermedades reumatológicas y qué impacto tiene en el gasto de las familias en el estado de Oaxaca, México. **METODOLOGÍAS:** Se evaluó el gasto catastrófico de las enfermedades reumáticas. En 2011 se encuestó a nueve pacientes diagnosticados con enfermedades reumatológicas del hospital de especialidades de la SSA y hospitales privados (tres de artritis reumatoide (AR), cuatro de Lupus eritomatoso sistémico (LES), uno de Dermatomiositis y uno de Espondilitis Anquilosante (EA)). El instrumento de recolección de datos se centró en la carga financiera del manejo de la enfermedad. Se evaluaron los costos médicos directos (fisioterapia, estudios de laboratorio y tratamiento farmacológico), intervenciones quirúrgicas y costos de transporte. Se estimó el costo anual del tratamiento con rituximab (2 infusiones de 1000mg por año) y qué impacto representaría para el ingreso familiar. **RESULTADOS:** El costo médico promedio anual ascendió a $43,271.00, el costo promedio anual con gasto en transporte ascendió a $55,537.78, montos que representan el 61% y 79% del ingreso promedio de las familias. El 83% de los gastos médicos son causados por gasto en medicamentos. Las enfermedades que generaron mayores gastos médicos fueron LES ($7,339.44 promedio mensual), Dermatomiositis $4,800 y AR con $1,405.56 promedio mensual. Los gastos inesperados como intervenciones quirúrgicas causadas por la enfermedad $9,000 promedio y las hospitalizaciones por complicaciones $8,500. El costo anual del tratamiento con rituximab asciende a $117,66.60 monto que representa el 167% del ingreso de las familias. **CONCLUSIONES:** El costo de las enfermedades reumatológicas genera una carga financiera importante, los pacientes diagnosticados por una causa reumatológica ven mermada su situación financiera, es decir, incurren en gastos catastróficos en salud. El uso de tratamientos biológicos sobrepasa los ingresos anuales de las familias.

PSY7
ANÁLISIS ECONOMICO DE LA PROFILAXIS SECUNDARIA VERSUS EL TRATAMIENTO A DEMANDA DE UNA COHORTE DE PACIENTES COLOMBIANOS CON HEMOFILIA A Y B SEVERA

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OBJECTIVOS: Evaluar las diferencias en efectividad y costos de la profilaxis secundaria vs el tratamiento a demanda en pacientes con hemofilia severa. **METODOLOGÍAS:** Pacientes: Seguimiento retrospectivo durante 30 meses a una cohorte de 52 pacientes con diagnóstico confirmado de Hemofilia A y B severa, atendidos por una institución prestadora de servicios de alta complejidad a nivel nacional. La permanencia minina dentro de la cohorte fue de 12 meses. Perspectiva: Asegurador. Desenlaces en salud: promedio de sangrado articular/pacientes/mes. Costos: Se evaluaron los costos médicos directos (atención hospitalaria, atención ambulatoria, urgencias, medicamentos), tomados del sistema de información del asegurador y del prestador a precios de 2012, en COP. **RESULTADOS:** Desenlaces en Salud: Los 52 pacientes aportaron 847 meses de tratamiento en demanda con 154 sangrados y 539 meses en profilaxis con 93 sangrados. La tasa de sangrado paciente/mes fue de 0,18 para demanda y de 0,17 para profilaxis (p=0,627), con un RR de 0,949 (IC95% 0,78 - 1,15). Costos: Si se toma en cuenta la administración de antinhibidores, el costo promedio por paciente/mes en demanda es de $ 26,427,616 y el costo promedio paciente/mes en profilaxis secundaria es de $ 23,032,817 (p=0,456). Sin contabilizar los medicamentos antinhibidores el costo promedio por paciente/mes en demanda es de $ 4,143,308 y el costo promedio paciente/mes en profilaxis secundaria es de $ 19,113,948 (p<0,0001). **CONCLUSIONES:** No se observa diferencia significativa en la tasa de sangrados en los grupos de profilaxis secundaria y demanda. El grupo de pacientes con inhibidores experimenta el mayor costo dentro de la población observada. Al excluir los inhibidores el costo promedio/paciente/mes en profilaxis secundaria es 4,6 veces mayor que el costo en tratamiento a demanda.

PSY8
BIOLOGICAL AGENTS IN THE TREATMENT OF MODERATE TO SEVERE PSORIASIS: A PHARMACOECONOMIC ANALYSIS

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OBJECTIVES: To evaluate the cost-effectiveness of biologic agents in the treatment of moderate to severe psoriasis. **METHODS:** Four biologics were assessed: adalimumab, etanercept, infliximab and ustekinumab. Direct costs were obtained from the perspective of Brazilian Public Health Service (SUS). Probabilities and efficacy were extrapolated from literature. Unit costs is the Brazilian currency – Real (R$) – and the outcomes considered were PASI90 and PASI75 response (rPASI90 and rPASI75, respectively). For each outcome one Markov Model was created with 12 cycles of 3 months (3 years). Annual discounting of 5% was applied for costs and outcomes. The model considered patients with moderate to severe psoriasis who had *Psoriasis Severity Index* or *Dermatology Quality of Life Index* greater than 10 or were unable to take standard systemic therapies. Univariate and probabilistic sensitivity analysis was applied to evaluate parametric uncertainties. **RESULTS:** Results were expressed as the financial resources demanded for each patient that have achieved and kept rPASI90 or rPASI75. Regarding rPASI90, adalimumab showed to be dominant against the other biologics with a total cost of R$ 64,588.79 (U$ 32,714.78) and 33,7% of patients with rPASI90 after 3 years of treatment (R$ 191,658.13/rPASI90, U$ 97,076.50/rPASI90). When rPASI75 is considered as the measure of outcome, adalimumab and ustekinumab were dominant against infliximab and etanercept, with R$ 124,200.41/rPASI75 (U$ 62,908.58/rPASI75) and R$ 114,230.59/rPASI75 (U$ 57,858.78/rPASI75), respectively. Univariate sensitivity analysis pointed acquisition cost of biologics as the main critical variable. Probabilistic sensitivity analysis shows robustness of our findings. **CONCLUSIONS:** From the perspective of SUS, adalimumab is the most cost-effective biological agent for rPASI90. Threshold up to R$ 124,000/rPASI75 (U$ 62,807.07/rPASI75) favors ustekinumab as the most cost-effective drug, while threshold greater than that point to adalimumab. Is being conducted a new Markov modelling to evaluate which sequence of biologic agents is the most cost-effective when failure of initial biological treatment occurs.

PSY9
A COST-EFFECTIVENESS MODEL COMPARING SUB-CUTANEOUS BIOLOGIC TREATMENT FOR SEVERE PLAQUE PSORIASIS IN MEXICO

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OBJECTIVES: To evaluate the cost-effectiveness of different sub-cutaneous biologic treatments for severe plaque psoriatic patients in public institutions in Mexico. **METHODS:** A Markov model was developed to simulate patients with moderate-to-severe plaque psoriasis. Biologic therapies compared were ustekinumab 45mg every 12 weeks, adalimumab 40mg every two weeks, and etanercept 50mg twice a week. Measured by the Psoriasis Area and Severity Index (PASI), clinical response was derived from the latest published meta-analysis. PASI response was translated into QALYs in two steps: (1) defining the correlation between PASI levels and the Dermatology Life Quality Index (DLQI); and (2) using a formula to predict utility from DLQI score derived from a mapping exercise of the DLQI with the EQ-5D. The model considered expenditure on drugs, monitoring visits, adverse events and inpatient stays. Costs were obtained from Mexican public institutions. Health and economic outcomes were estimated over a 10-year time horizon with cycle length of 12 weeks. Cost and QALYs were discounted at 5% annually. **RESULTS:** Etanercept is the least costly treatment in Mexican public institutions followed closely by adalimumab and ustekinumab. Cost-effectiveness analysis shows that adalimumab was an extended dominated strategy by ustekinumab. The incremental cost-per-QALY of ustekinumab versus etanercept was US$19,542. **CONCLUSIONS:** Considering the GDP per-capita of Mexico in 2010 (US$9,123), and according to the WHO Commission on Macroeconomics and Health, ustekinumab is a cost-effective strategy (≤3xGDP per-capita /QALY gained) versus etanercept, and a more cost-effective strategy vs adalimumab by extended dominance. Probabilistic sensitivity analysis results did not change the conclusions.

PSY10
ANÁLISIS COSTO-EFECTIVIDAD DEL TRATAMIENTO FARMACOLÓGICO PARA LAS MANIFESTACIONES CLÍNICAS MUCOCUTÁNEAS DE LA ENFERMEDAD DE BEHCET

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OBJECTIVOS: Determinar la efectividad de la intervenciones farmacológicas disponibles en Chile para tratar las manifestaciones clínicas de tipo mucocutáneas, esto es úlceras orales (UO) y genitales (UG), en la Enfermedad de Behcet (EB). Conducir un análisis de costo-efectividad para determinar la alternativa superior entre los dos tratamientos que resulten más efectivos. **METODOLOGÍAS:** Se efectuó una revisión de la literatura de los trabajos publicados entre 1980-2010, disponibles en las bases de dados MEDLINE y Cochrane Library. Se incluyeron en los criterios de selección todos los estudios clínicos controlados, aleatorizados, además de revisiones sistemáticas y meta-análisis disponibles bajo las palabras claves enfermedad

de Behcet y tratamiento farmacológico. La evaluación farmacoeconómica se llevó a cabo, utilizando un modelo de efecto fijo, desde la perspectiva de un paciente adulto, con sistema previsional de salud público, EB activa y las manifestaciones clínicas seleccionadas, diagnosticado según el criterio del International Study Group, en un horizonte temporal de un año. El análisis de decisión para las dos alternativas más efectivas se llevó a cabo a través de DATA 3.5. **RESULTADOS:** De los 38 estudios encontrados en cada una de las bases de datos, 15 cumplieron los criterios de selección, con los cuales se calculó el efecto de la intervención. Las alternativas más efectivas resultaron ser talidomida de 100 y 300 mg y la suspensión de sucralfato. Una vez realizado el análisis costo-efectividad, la suspensión de sucralfato fue dominada por talidomida de 100 mg. **CONCLUSIONES:** A pesar de la falta de evidencia en enfermedades raras y eficacia de tratamientos clásicos, fue posible proponer una alternativa costo-efectiva para la EB. No obstante, dada la heterogeneidad de las manifestaciones clínicas en enfermedades raras y los costos de los tratamientos, resulta necesario proponer análisis alternativos a la costo-efectividad, que permitan apoyar a toma de decisiones para estos grupos de pacientes.

PSY11

ANÁLISIS DE COSTO-EFECTIVIDAD PARA EL MANEJO FARMACOLÓGICO DE LA HEMOFILIA A SEVERA EN 5 ENTIDADES DE ASEGURAMIENTO EN COLOMBIA

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INTRODUCTION: La Federación Mundial de la Hemofilia indica que existen registrados 137.352 pacientes hemofílicos en 77 países, sin embargo se estima que deben existir cerca de 400.000 personas en todo el mundo. Un reciente estudio de carga de enfermedad genética estima que existirían 2931 colombianos con hemofilia, considerando el período de 1996 a 2025. **OBJECTIVOS:** Evaluar la costo-efectividad de tres tratamientos: Kogenate, Advate y Recombinate para el tratamiento de Hemofilia tipo A Severa en una población de 1 a 78 años. Describir los resultados de pacientes con Hemofilia Severa que reciben profilaxis con distintos productos del Factor VIII. **METODOLOGÍAS:** Se adaptó un modelo de Markov que describe la historia natural y los resultados de la Hemofilia A Severa. El modelo considera siete estados de salud caracterizados por el estado del inhibidor (3 niveles: HR, LR, Ninguno), daño articular (Si o no) y la muerte (estado absorbente). **RESULTADOS:** Um total de 1.186 pacientes con Hemofilia A, lo que representaría una prevalencia del 0,009% dentro de la población afiliada. La ganancia en términos de AVACs es similar para los tres tratamientos. Los componentes con el mayor impacto en los costos son profilaxis y control de sangrado. Del análisis de sensibilidad determinístico, el parámetro con el mayor impacto es la dosis de Advate con profilaxis. Del análisis de sensibilidad probabilísticos, Kogenate es una alternativa dominante respecto a Advate en 45% de las simulaciones, y en 70.4% de las simulaciones respecto a Recombinate. **CONCLUSIONES:** Se encontró que los costos de Kogenate y Recombinate son en su mayoría atribuidos a la profilaxis y aquellos a Advate al tratamiento de sangrado. Aunque la eficacia clínica de los productos es similar, las diferencias en la incidencia del desarrollo del inhibidor significan menores costos y mejor calidad de vida para los pacientes que son tratados con Kogenate.

SYSTEMIC DISORDERS/CONDITIONS – Patient-Reported Outcomes & Patient Preference Studies

PSY12

BETA-THALASSEMIA PATIENTS SURVEY ON DEFERRIZATION THERAPY

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OBJECTIVES: To investigate family burden, awareness and treatment status of ß-thalassemia patients in China. **METHODS:** The families with major ß-thalassemia received investigation. The questionnaire involved medical management of ß-thalassemia, economic burden, life quality and recognition, attitude and behavior of the relatives to the disease. **RESULTS:** Currently, the mainstay treatment of major thalassemia remains transfusion and deferrization therapy, so that the treatment cost is about 60,000 to 70,000 RMB per year for a 10-year-old-child and this number even rises with the increasing of the age. Therefore, the family burden and life quality of the patients is significantly involved during the treatment of this disease. Among different diferrization treatment, deferasirox was first choice of the patients concerning the cost-effect factors and lower incidence of adverse events, exemplified as local injection reactions which are commonly occurred in the patients receiving desferrioxamine. Most of the patients chose the convenience as the most important factor for the compliance to the treatment. And in addition to disease related factors and symptoms as discussed below, convenience was also considered as important issue for life quality. Although until now, 70.7% of the patients received intravenous desferrioxamine treatment, over half of the patients would like to change to a more convenient oral deferrization treatment, and deferasirox was considered as the first choice due to the low price of this medicine in China. **CONCLUSIONS:** ß-thalassemia as a hereditary disease severely influenced the life quality of the patients, increased economic and social burden to the family. The medical utility and society should pay more care to the patients and their families, especially the grass-root ones. The government should take the responsibility to improve the medical reimbursement system for this disease.

PSY13

EFFICACY AND TOLERABILITY OF CT-GUIDED EPIDURAL STEROID INJECTIONS AND PHARMACOTHERAPY FOR MANAGING CHRONIC LOW BACK ACHE WITH RADICULOPATHY

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OBJECTIVES: Substantial number of patients with persistent low back pain (LBP) are treated with multimodal spectrum of conservative and invasive therapies. Few have investigated the utility of pharmacotherapy and epidural steroid injections (ESI) in large practice setting. We sought to gather comprehensive data about the characteristics, efficacy, tolerability and quality of life (QoL) of patients with LBP with these therapies. **METHODS:** Information was collected on a standardized form. Information included patient characteristics, type and duration of therapies, adverse events, pain relief using visual analogue scale (VAS) and QoL by measuring disability using modified ODQ at each month of follow-up. **RESULTS:** Consecutive 81 patients were recruited and followed for 6 months. Average baseline pain duration was found to be 45.5 months. Combination of drugs and ESI was given in 75 (92%) patients. Anticonvulsants (75%) and Antidepressants (57%) were most commonly prescribed medications. Change in VAS & ODQ score from baseline to each follow-up at 3 months (VAS - 15), 6 months (VAS -25) was significantly ($P < 0.05$) improved. **CONCLUSIONS:** Pregabalin and amitriptyline were most commonly used drugs with maximum pain relief and improved Qol. Desired pain relief fluctuated with time. ESI can be promising choice when desirable pain relief is not achieved with medications.

SYSTEMIC DISORDERS/CONDITIONS – Health Care Use & Policy Studies

PSY14

MULTI-CRITERIA BENEFIT-RISK ASSESSMENT OF BIOLOGICAL AGENTS IN THE TREATMENT OF MODERATE TO SEVERE PSORIAIS: A STOCHASTICAL APPROACH

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OBJECTIVES: To evaluate the benefit-risk of biological agents (BA) in the treatment of moderate to severe psoriasis. **METHODS:** It was performed a mixed treatment comparison (MTC) based on all available clinical trials of psoriasis treated with BA. The common agent comparator was placebo and the time-horizon was up to 24 weeks of treatment. This indirect meta-analysis was followed by a stochastic multicriteria acceptability analysis (SMAA) to compare adalimumab, etanercept, infliximab and ustekinumab on two benefit and two risk criterias. Efficacy was evaluated by means of *Psoriasis Area Severity Index* 90 and 75 response (rPASI90 and rPASI75, respectively) and the risks corresponded to any adverse event (AAE) and serious adverse event (SAE). MTC/SMAA analysis was performed for two scenarios: one with missing outcome preference and the other with ordinal preference information established by experts in psoriasis (SAE > rPASI90 > rPASI75 > AAE). **RESULTS:** Results show the same tendency for both created scenarios. Infliximab 5 mg/kg had the highest probability of being the 1st-place in MTC/SMAA ranking (84% to 67%). It was followed by ustekinumab 90 mg for the 2nd-place (54% to 50%), ustekinumab 45 mg for the 3rd-place (51% - 50%), adalimumab 80 mg followed by 40 mg (51% - 47%), etanercept 50 mg TW (74% to 62%) and placebo in the 6th-place(97% - 94%). **CONCLUSIONS:** From all available evidence on treatment with BA for psoriasis, the designed method was enabled to point that infliximab 5 mg/kg is the BA with the highest probability of having the best benefit-risk ratio in the short-term follow up. It is followed by ustekinumab 90mg, ustekinumab 45 mg, adalimumab 80-->40 mg, etanercept 50 mg TW and placebo, respectively. Our findings can be useful to help on deciding which sequence of BA must be defined by guidelines and health services when therapy failure happens.

PSY15

DIRECT HEALTH CARE COSTS OF PATIENTS SWITCHING BIOLOGIC THERAPIES IN CHRONIC PLAQUE PSORIASIS

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OBJECTIVES: To describe patient characteristics and costs associated with first year biologic therapy use in psoriasis patients who switched or remained on biologic therapy. **METHODS:** Adult patients with psoriasis diagnosis (ICD-9 CM 696.1 or 696.8 codes, excluding psoriatic arthritis (ICD-9-CM 696.0), rheumatoid arthritis(ICD-9-CM 714.x), ankylosing spondylitis(ICD-9-CM 720.0), Crohn's disease(ICD-9-CM 555.x) or ulcerative colitis(ICD-9-CM 556.x)) with continuous insurance coverage for one year pre and post first biological therapy prescription, having at least one prescription of adalimumab, etanercept, infliximab or ustekinumab and no previous use of biologic were selected from a privately insured MarketScan® commercial and Medicare database, 2012 . Two patient cohorts of switchers and non-switchers were defined based on gap of 60 days of therapeutic benefit. Analyses included descriptive statistics and per member per year costs. **RESULTS:** Of the 2848 patients who met the study criteria, 8.32% (n=237) switched(S) to another biologic therapy, 1305 (45.82%) remained on initial biologic therapy (non-switched (NS)) and 1,306 (45.86%) discontinued their treatment within the first year of initiating biologic therapy. The mean age(SD) was 46.9(13.3) years with a higher percentage of males in the non-switched group than switched and discontinued groups (59.4% vs. 51.1% and 52.5%, respectively). One year post start of biologic therapy, total health care cost per patient (S: US$38,529(24,328), NS: US$32,822(15,913)), all cause hospitalization cost per patient (S: US$1713(12,528), NS: US$911(4663)) and all cause emergency room cost per patient (S: US$447 (1300), NS: US$266 (1000)) were higher among patients who switched to another biologic therapy than among patients who remained on their initial biologic therapy. **CONCLUSIONS:** Although few patients switched from their initial biologic therapy within first year of initiating treatment, higher direct health care costs were observed in this patient group compared to those who remained on their initial therapy. These results suggest an unmet need among patients that switch biologic therapies in psoriasis.

PSY16

ORPHAN DRUG ACCESS: RISK/REWARD ANALYSIS OF LOCAL CLINICAL DEVELOPMENT IN CHILE

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BACKGROUND: As many orphan drug (OD) manufacturers expand their businesses across emerging markets(EM) they are faced with restrictive and often non-existent funding pathways. As a result pricing and reimbursement (P&R) negotiations remain very challenging, pushing manufactures to explore the value of local clinical development in supporting access. **OBJECTIVES:** To a) understand the value of local clinical development for payers, to support reimbursement in Chile, and b) compare and contrast against four other emerging markets: Russia, Turkey, India and China. **METHODS:** In-depth interviews were conducted with 3 stakeholders per market including national payers, reimbursement committee advisors and rare diseases clinical specialists, to understand a) Current OD funding pathways; b) P&R decision drivers; and c) Impact of local development on reimbursement. Selected value drivers were used to develop a scale and qualitatively measure the risk/reward analysis of local clinical development on OD access. **RESULTS:** The impact of local development on OD reimbursement varies across markets. Respondents in Chile (n=3) highlighted that clinical development will have a strong influence on future willingness to pay, but the opportunity will remain small due to lack of clarity around long-term funding. In Turkey (n=3), providing access to patients through compassionate use schemes, prior to obtaining registration, positively impacts reimbursement.While in Russia, conducting a local clinical trial adds no value to the P&R decision process as cited by payers (n=3). As for India and China where price remains the overriding factor, respondents (n=6) stated that national reimbursement remains a distant prospect. **CONCLUSIONS:** High clinical experts' awareness, strong influence of advocacy groups and developing OD funding pathways renders Chile and Turkey the most attractive EM for local development. While in comparison, the generation of local patient data is also favoured across the remaining markets, price remains the overriding factors influencing access and reimbursement.

PSY18

TOXOCARIASIS: A DISEASE OF HIGH PREVALENCE BUT FORGOTTEN

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OBJECTIVES: Toxocariasis is a anthropozoonosis that occurs in various regions of the world, often found in developing countries and in regions where sanitation conditions are poor. This disease affects dogs and cats, whose etiologic agents are, respectively, *Toxocara canis* and *cati*. These mammals are the definitive hosts of this geohelminth and a person it's a paratenic host. Infection in humans can cause acute clinical severity varied and eventually chronicity. The diagnosis is made by means of the ELISA and the classical treatment is done with benzimidazole anthelmintics. The toxocariasis, despite not being on the list of neglected diseases of WHO, has aroused little interest in academia and even less in health services, despite its prevalence in various regions of Brazil. Some studies have discussed the possible association between parasitic infections and allergic / atopic diseases and asthma, working with the hypothesis that exert immunomodulatory role. To review the literature on the current prevalence of toxocariasis in Brazil and its association with other diseases. **METHODS:** A search was performed in electronic databases, Medline, Lilacs, PubMed and Embase. The words were: "toxocariasis and Brazil", in the period from 2008 to 2013, and found 406 articles, with the inclusion criteria of studies done with humans and presenting epidemiological aspects. **RESULTS:** We selected 90 articles that prove the current high prevalence of toxocariasis in various regions, ranging from 11.1% to 65.4%. Several studies point to an association of toxocariasis with other diseases of high public health relevance. Despite this evidence the Brazilian Public Health System does not repayment diagnostic tests for the detection of anti-*Toxocara*, complicating the clinical and leading to no treatment. **CONCLUSIONS:** The review provides grants for the revision of public policies for prevention, diagnosis and treatment of toxocariasis.

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PMH7	Bralnc.om, Bilbao, Spain
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PMH11	Department of Mental Health, Bangkok, Thailand
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PMS13	Pfizer CIA.LTD.A, Quito, Ecuador
PMS14	None
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PMS20	CNPq, Brasília, Brazil; FAPEMIG, Belo Horizonte, Brazil
PMS21	Pfizer S.A.S., Bogota, Colombia
PMS22	None
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PMS24	Pfizer S.A. de C.V., México, Mexico; UCB de México S.A. de C.V., México, Mexico; Productos Roche S. A. de C.V, México, Mexico
PMS25	None
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PRM7	Novartis de Colombia S.A., Bogotá D.C., Colombia
PRM8	ORIZON, Barueri, Brazil
PRM9	None
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Reference Code	Financial Support
PRM15	None
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PRS4	None
PRS5	GlaxoSmithKline, Uxbridge,
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PRS7	CAPES-Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Convênio DINTER UFG/UEMA), Brasília, Brazil
PRS8	Instituto de Avaliação de Tecnologias em Saúde/Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq, Goiânia - Goiás, Brazil
PRS11	None
PRS12	None
PRS13	None
PRS14	Merck & Co., Inc., West Point, PA, USA
PRS15	None
PR1	None
PR2	Becton Dickinson de Mexico S.A. de C.V., Mexico, Mexico
PR3	Pfizer SAS, Bogotá DC, Colombia
PR4	None
PSS1	Ministerio de Salud, Santiago, Chile
PSS2	Janssen Cilag, Bogotá, Colombia
PSS3	None
PSS4	None
PSS5	Ministerio de Salud, Chile, Santiago, Chile
PSS6	Bayer Colombia, Bogota, Colombia
PSS7	Bayer Alemania, Bogotá, Colombia
PSY1	None
PSY2	None
PSY3	Baxter Healthcare Corporation, Westlake Village, CA, USA
PSY4	None
PSY5	Pfizer S.A. de C.V., Ciudad de México, Mexico
PSY6	None
PSY7	Audifarma, Bogota, Colombia
PSY8	Programa Pesquisa para Sistema Único de Saúde (PPSUS), Curitiba, Brazil; Ministério da Educação/Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (MEC/CAPES), Curitiba, Brazil
PSY9	Janssen de México, Mexico, Mexico
PSY10	None
PSY11	Bayer, Bogota, Colombia
PSY12	Beijing Novartis Pharma Co., Ltd.., Beijing, China
PSY13	None
PSY14	None
PSY15	Novartis Pharmaceutical Corporation, East Hanover, NJ, USA
PSY16	Double helix Consulting, London,
PSY18	None
PUK1	RTS Baxter, Bogota, Colombia
PUK2	NOVARTIS, Mexico City, Mexico
PUK3	Bristol-Myers Squibb Colombia, Bogota, Colombia
PUK4	Pfizer, Bogotá, Colombia
PUK5	Abbott Laboratórios do Brasil Ltd.a, São Paulo, Brazil
PUK6	None
PUK8	Baxter, Bogota, Colombia
PUK9	Colciencis, Bogotá, Colombia
PUK10	AMGEN, Brazil, Brazil
PUK11	Sanofi-aventis de Colombia S.A., Bogotá, Colombia
PUK12	NOVARTIS, Mexico City, Mexico
PUK13	Pfizer, Bogota, Colombia
PUK14	None
PUK15	None
RF1	None
RF2	Grupo de Investigación en Economía de la Salud, Universidad de Cartagena, Cartagena, Colombia
RF3	None
RF4	Roche Diagnostics, Sao Paulo, Brazil; Roche Molecular Diagnostics, Pleasanton, CA, USA
TR1	None
TR2	None
TR3	Baxter Healthcare Corporation, Westlake Village, CA, USA
TR4	None

ISPOR 4TH LATIN AMERICA CONFERENCE RESEARCH ABSTRACTS AUTHOR INDEX

GUIDE FOR AUTHORS

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Arocho R, McMillan CA. Discriminant and criterion evaluation of the U.S.-Spanish version of the SF-36 Health Survey in a Cuban-American population with benign hyperplasia. Med Care 1998;36:766-72.

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***Book*:** Surname and initials of author(s)/editor(s), title and subtitle, volume, edition (other than first), city, publisher, year.

Johnston J. Econometric Methods (3rd ed.). New York: McGraw-Hill, 1984.

Chapter in Book: Surname and initials of author(s), title of chapter, author(s)/editor(s) of book, title of book, volume, edition (other than first), city, publisher, year.

Luce BR, Manning WG, Siegel JE, et al. Estimating costs in cost-effectiveness analysis. In: Gold MR, Siegel JE, Russell LB, et al., eds., Cost-effectiveness in Health and Medicine. New York: Oxford University Press, 1996.

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