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BMJ Open Cost-effectiveness of telehealthcare to patients with chronic obstructive pulmonary disease: results from the Danish 'TeleCare North' clusterrandomised trial

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ABSTRACT

Objectives To investigate the cost-effectiveness of a telehealthcare solution in addition to usual care compared with usual care.

Design A 12-month cost-utility analysis conducted alongside a cluster-randomised trial.

Setting Community-based setting in the geographical area of North Denmark Region in Denmark.

Participants 26 municipality districts define randomisation clusters with 13 districts in each arm. 1225 patients with chronic obstructive pulmonary disease were enrolled, of which 578 patients were randomised to telehealthcare and 647 to usual care.

Interventions In addition to usual care, patients in the intervention group received a set of telehealthcare equipment and were monitored by a municipality-based healthcare team. Patients in the control group received usual care.

Main outcome measure Incremental costs per qualityadjusted life-years gained from baseline up to 12 months follow-up.

Results From a healthcare and social sector perspective, the adjusted mean difference in total costs between telehealthcare and usual care was €728 (95% CI -754 to 2211) and the adjusted mean difference in guality-adjusted life-years gained was 0.0132 (95% CI -0.0083 to 0.0346). The incremental costeffectiveness ratio was €55 327 per quality-adjusted life-year gained. Decision-makers should be willing to pay more than €55 000 to achieve a probability of cost-effectiveness >50%. This conclusion is robust to changes in the definition of hospital contacts and reduced intervention costs. Only in the most optimistic scenario combining the effects of all sensitivity analyses, does the incremental cost-effectiveness ratio fall below the UK thresholds values (€21 068 per quality-adjusted life-year).

Conclusions Telehealthcare is unlikely to be a costeffective addition to usual care, if it is offered to all patients with chronic obstructive pulmonary disease and if the willingness-to-pay threshold values from the National Institute for Health and Care Excellence are applied.

Trial registration Clinicaltrials.gov, NCT01984840, 14 November 2013.

Strengths and limitations of this study

- This study reports the within-trial cost-effectiveness of a pragmatic large-scale asynchronous telehealthcare initiative in order to improve the international evidence base of the economic effects of telehealthcare for patients with chronic obstructive pulmonary disease.
- A relatively broad healthcare and social sector perspective was chosen and the cost analyses of resource use are based on register data.
- A limitation of the study is that only 61% of the participants had complete registrations of all cost categories and outcomes.
- The way telehealthcare was implemented may have affected cost-effectiveness, since the involved organisations and healthcare professionals underwent a steep learning curve after implementation of the telehealthcare solution, where they had to find new ways of working together and adapt to new work procedures.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease.¹ The main symptoms of COPD are dyspnoea, recurrent lung infections, abnormal sputum, wheezing, decreased exercise tolerance and 'smoker's cough'.² Depending on the severity of COPD, patients can experience a number of exacerbations, where symptoms become more severe than normal, which are often associated with a further progression of the disease² and anxiety.³ COPD is one of the most prevalent and deadly diseases in the world.⁴ The global prevalence of COPD is high (11.7%).⁵ COPD is associated with high mortality,⁶ presence of comorbidities^{7 8} and reduced health-related quality of life.9 10 COPD poses a substantial financial burden on healthcare systems, for example, the annual direct costs for COPD has been estimated to be US\$20–26 billion in the USA with hospital admissions representing 52%–70% of all direct costs.¹¹ A recent Danish study has estimated that COPD is responsible for 8300 years of life lost and €174 million in annual direct cost for treatment and care.¹²

Telehealthcare has been suggested as a possible effective intervention to patients with COPD on especially health-related quality of life.¹³ Telehealthcare is a technology that contains data from a patient which is transferred electronically over a physical distance and healthcare professionals exercise their judgement in providing personalised feedback to the patient based on these data.¹⁴ Some feasibility studies including cost analyses have previously suggested an added value of telehealthcare compared with usual practise and some of these studies show that telehealthcare may lower hospital or healthcare costs.^{15–19} But most recent systematic reviews have questioned the quality of this evidence and have requested more cost-effectiveness evaluations,^{20–24} preferably with broader cost-perspectives.²⁵

The objective of this paper is to add to this international evidence base on the cost-effectiveness of telehealthcare by presenting the results of a cost-utility analysis of a telehealthcare intervention to patients with COPD compared with usual practise. The analysis was nested within a 12-month cluster-randomised trial (called 'TeleCare North') that were conducted in the geographic area of North Denmark Region in Denmark from 2013 to 2014.

METHODS

A more detailed trial protocol has been published elsewhere,²⁶ but a brief summary is provided in table 1. Twenty-six municipality districts in North Denmark Region define the randomisation clusters with 13 districts in each arm. In addition to usual care, patients in the intervention group received a set of telehealthcare equipment and were monitored by a community-based healthcare team. Patients in the control received usual care.

The primary outcome measure for the cost-effectiveness analysis was the incremental cost-effectiveness ratio (ICER) expressed as the total cost per quality-adjusted life-year (QALY) gained measured from baseline to follow-up at 12 months. In defining the total costs, this trial adopted a healthcare and social care sector perspective (including hospital services, primary care, medicine, home care services and rehabilitation).

Healthcare service use and healthcare costs

Healthcare and social care service use were all estimated based on register data by applying a unique civil registration number that all Danish citizens have and that makes precise linkage between registers possible. National patient-level data for all hospital contacts were collected from the Danish National Patient Register,²⁷ which contains all inpatient, outpatient and emergency ward visits in Denmark. The total costs for each contact is a variable in these datasets and are valued based on the diagnose-related group, the actual procedures conducted and the duration of the contact.²⁸ The included admissions, outpatient and emergency ward visits were in the main analysis restricted to those defined as COPD-specific in the Danish Register for COPD.²⁹

All contacts between patients and the primary care sector were collected from the National Health Insurance Service Register.³⁰ The costs for each contact is part of the dataset and are valued based on fees negotiated in a collective agreement.³¹ At present, it is not possible to identify the cause of contact to the primary care sector, so all contacts are included.

Medication use was taken from The Danish Register of Medicinal Product Statistics that contains information about what prescribed medicine citizens purchase in Denmark.³² For this analysis, these are restricted to patient-level medicine associated with COPD (R03 ATC codes), specific antibiotics, antifungals and medicine for anxiety, all associated with the treatment of COPD exacerbations, as well as medicine for smoking cessation. The costs for each product is given in this dataset and is valued based on a standardised pharmacy consumer price.³³

Patient-level community care service use was collected from individual care systems in each of the 26 included municipality districts. The type and duration of standard care activities such as personal care, practical help, home nursing care and rehabilitation activities are routinely recorded for each contact. Each municipality district values contacts differently based on an internal calculated mean hourly cost. It was pragmatically decided to value time consumption in municipality districts as an average of the reported hourly costs from municipality districts. Four of the 26 municipality districts in the trial were implementing a different information technology (IT) system at the time of data collection, which meant that rehabilitation costs for these four municipality districts were unavailable (2 municipality districts in the telehealthcare group and 2 in the usual care group).

Healthcare service use was collected for 12 months to allow for within-trial costs to be calculated. In addition, patient-level health service use was also collected 12 months prior to randomisation, because it was suspected that baseline differences in costs could occur that would not be explained by differences in health status or sociodemographic characteristics by patients, for example, due to variations in referral and visitation practises across municipality districts.

Intervention costs

Costs associated only with the clinical trial, preparing the organisation and developing the telehealthcare solution were excluded. Intervention costs were costs of hardware and peripherals, installation and deinstallation costs, maintenance and support costs, training costs for healthcare professionals, patient-specific training, monitoring costs and project management costs.

Per person costs of the 'package' of telehealthcare equipment (the so-called 'Telekits' consisting of a tablet

Table 1 Descript	ion of the Danish TeleCare North cluster-randomised trial
Eligible criteria for clusters	All municipalities in North Denmark Region except one (a small island off the coast), 10 municipalities in all. Each municipality consisted of between 2 and 5 municipality districts and these districts were randomisation units, 26 municipality districts in total (13 in each arm).
Eligible criteria for patients	COPD as primary disease, diagnosis by spirometry, in treatment according to guidelines recommended by 'The Global Initiative for Chronic Obstructive Lung Disease', ¹ at least two exacerbations within the past 12 months, motivated for treatment, fixed residence in North Denmark Region, The Modified Medical Research Council scale (mMRC) \geq 2 or mMRC \geq 3 and COPD Assessment Test \geq 10. Exclusion criteria were: no phone line or Global System for Mobile communications coverage, unable to understand Danish sufficiently to complete the study questionnaires or diagnosed with a cognitive impairment
Intervention group: cluster- level intervention	Municipality district healthcare personnel (primarily nurses and health assistants) were trained in two separate sessions. One session focused on the technical aspects of the tablet and physical measurements. Another session focuses on general disease awareness and communication with patients. The training was performed by members of the trial administration office. General practitioners were responsible for establishing threshold values for physical measurements. Nurses in the patient's residing municipality were responsible for monitoring the data obtained and should incorporate monitoring time duties with their existing job responsibilities. Exemptions were patients with COPD receiving oxygen therapy and patients with COPD with open hospital admissions who were monitored at their hospital as usual. Patients were monitored asynchronously by a nurse on a daily basis. Measurements were classified with either a green, yellow or red code (green code: no threshold values were exceeded; yellow code: one or more values exceeded the threshold values; red code: one or more values exceeded the threshold values and had not previously been recorded). The nurse had the option to contact the patient by telephone and/or the patient's general practitioner and/or dispatch an ambulance. Installation, swopping of defects, deinstallation and technical support and maintenance of the equipment was handled by information technology specialists
Intervention group: patient- level intervention	Telephone contact to each patient from municipality healthcare personnel no later than 10 days after randomisation, and a 45 min appointment scheduled for patients who wanted to receive the tablet at home. For those who wished to receive the tablet at a municipality health centre, a 75 min appointment was scheduled with 3–4 patients in each group. At both appointments, a nurse from the patients' municipalities demonstrated the use of the tablet and instructed patients in how to conduct physical measurement. Patients were asked to measure their vital signs daily during the first 2 weeks (both weekdays and weekends) and 1–2 times weekly after the first 2 weeks. A 45 min follow-up visit was scheduled 3–4 weeks after the first appointment to check if the patient used the device appropriately and if the threshold values of the physical measurements needed to be adjusted
Intervention group: device	All patients received the same device and peripherals. It consisted of a standard tablet (Samsung Galaxy) containing information on handling COPD in general and software (two apps) that automatically instructs the patient in handling COPD during exacerbations. The tablet can collect and wirelessly transmit data on blood pressure, pulse, blood oxygen saturation and weight via an attached Fingertip Pulse Oximeter, a digital blood pressure monitor, and a scale
Control group: usual care	Usual practise for caring for patients with COPD is the responsibility of the patient's general practitioner (treatment and monitoring) and the municipalities (practical help and home nursing care). Patients with COPD can make appointments with their general practitioner or call the emergency contact number without copayment in order to get treatment or advice in managing COPD, but this advice is not personalised. Community care administered by municipality district personnel comes at regular intervals based on a clinically based estimate of the patients' needs, but these personnel are not necessarily certified nurses and often not fully educated in COPD and not on call

COPD, chronic obstructive pulmonary disease.

and peripherals) were calculated. The 'Telekits' supplied were exactly the same for all patients and was purchased to each patient ahead of the trial and valued as prices paid. The per person costs of installation/deinstallation and swopping any defects in the equipment was negotiated with an external supplier prior to the trial and valued as prices paid. Per patient maintenance and support costs consisted of software licenses and data charges, technical support to patients and healthcare professionals as well as IT infrastructure and application maintenance and valued as prices paid. Costs associated with IT infrastructure and application maintenance was not dependent on the number of patients in the trial but the software and hardware configuration employed by the telehealthcare solution which in principle could include all patients with COPD and patients with chronic heart failure. It was decided to allocate these costs on the estimated number of patients with COPD and chronic heart failure in North Denmark Region (10500 patients).^{34 35} The per patient costs of training healthcare professionals were based on planned time spent conducting education workshops in COPD disease awareness and the telehealthcare solution, the number of conducted workshops and the average hourly wage for a community district nurse. Per

patient costs of patient-specific training were based on planned time and valued based on a mean hourly wage for a community district nurse. Time spent per patient on monitoring were estimated by time registries in the municipality districts and valued based on a mean hourly wage for a community district nurse. Based on the experiences gained with the implementation in the trial period, it was estimated that it would be necessary to have an administrative officer employed to 'run' the telehealthcare solution, should it be implemented in routine practise (coordinating activities, contract supervision, etc). Project management costs were valued as mean yearly salary for an administrative officer including all standardly available pensions and pay supplements.³ As with IT infrastructure and application maintenance, these costs could be allocated on more patients than in the trial and they were therefore also allocated on the estimated number of patients with COPD and chronic heart failure in North Denmark Region (10500 patients).³⁴³⁵

Equipment costs (the Telekits), installation/deinstallation costs, costs associated with training healthcare professionals and patient-specific training were annuitised over a period of 5 years with a discount rate of 3% per annum and presented as equivalent annual cost. Five years and 3% can be used as standard lifetime and discount rate for 'other IT equipment' in Danish capital accounting.³⁷

All costs are reported in 2014 prices. Costs were obtained in Danish kroner (DKK) and exchanged to \in using the average 2014 exchange rate (1 \in =7.4547 DKK). All healthcare service use and costs are reported as means and standard errors and where descriptive statistics are presented, differences between intervention and control group means are reported as raw differences and, to allow for future meta-analysis, as standardised differences (the raw difference between group means, divided by the SD of the total sample) presented as a percentage.

Effectiveness

Information of mortalities were obtained from the Danish Register of Causes of Death,³⁸ which contain mortality statistics on all deaths in Denmark. Utility scores stem from the EQ5D-3L health-related quality-of-life questionnaire with Danish societal weights.³⁹ QALYs were calculated by linear interpolation of utility scores. The health-related quality-of-life items and relevant demographic data were collected at baseline by help from the patients' general practitioners who distributed the questionnaires to all patients but with a prepaid return envelope to the trial administration office. At follow-up, a questionnaire consisting of the health-related quality-of-life items were sent from the trial administration office to the patients' home addresses with a prepaid return envelope.

ANALYSIS

Statistical analyses were all performed in STATA V.12.1 except the probabilistic sensitivity analysis that was developed in Microsoft Excel 2010.

Missing data

A total of 1225 patients were randomised in the study (578 patients in the telehealthcare group and 647 in the control group). At baseline, missing data for the EQ5D summary score were present for 8% of the participants (48 in the telehealthcare group; 53 in the control group). One hundred and three patients died during the trial period (8%; 50 in telehealthcare group; 53 in control group) and they were assigned an EQ5D summary score of 0 at follow-up that were used in the QALY calculation.⁴⁰ In addition, 27% had missing data on the EQ5D summary score at follow-up (199 in the telehealthcare group; 133 in the control group) either due to non-response or to incomplete registration of EQ5D questionnaire items. Twelve percent had missing values on rehabilitation costs (79 in the telehealthcare group; 73 in the control group). Complete data for both total costs (ie, all cost categories), baseline EQ5D score and EQ5D score at follow-up were available for 751 patients (61%; 325 in telehealthcare group; 426 in control group).

Current good practise for trial-based economic evaluation recommends that analyses should account for missing data by imputation, especially when there is a large amount of missing data.⁴¹ The applied imputation procedure followed the principles recommended by Faria et al.⁴² Missing data were assumed missing at random (MAR), which can be a plausible assumption if a wide range of variables, and variables that are predictive of missingness, are included in the imputation model.⁴³ Therefore, missing data on EQ5D scores, rehabilitation costs and baseline characteristics were imputed using the mi impute chained command in STATA12.1 and 30 complete datasets were created. Continuous variables were imputed by predictive mean matching and categorical variables by multinomial logistic or logistic regression. Imputation models included outcome variables, predictors for the outcomes at both time points and predictors for missing observations in the individual variables. The imputation models were estimated separately by treatment group and included the clustering variable, measures of health-related quality-of-life (EQ5D scores), costs at baseline or at 12 months follow-up (in the categories presented in table 4), measures of disease status (forced expiratory volume in one second (FEV1%), forced vital capacity (FVC%), diastolic and systolic blood pressure), smoking status, presence of comorbidities (diabetes, cancer, cardiovascular disease, mental illness or musculoskeletal disorders) and sociodemographic variables (age, gender, marital status, education and employment status).

Cost-effectiveness analysis

The cost-effectiveness analysis followed an intention-to-treat principle. The statistical analysis applied multilevel modelling for continuous variables that rely on near-normality,⁴⁴ which has been suggested as an analysis strategy for cost-effectiveness research of cluster-randomised trials.⁴⁵ To allow for different sets of covariates, estimation of incremental total costs and

Table 2 Baseline characteristics				
	All 1225 participants at baseline			
	Telehealthcare	Usual care	Difference	
	n=578	n=647	Raw	
Age (years)*	69.55 (9.36)	70.33 (9.11)	-0.78	
Men (%)*	48.27 (n=279)	43.74 (n=283)	4.53	
Marital status (%)				
Married/in a relationship	55.88 (n=323)	54.25 (n=351)	1.63	
Single	20.42 (n=118)	22.10 (n=143)	-1.68	
Widow/widower	16.78 (n=97)	16.54 (n=107)	0.24	
Missing (%)	6.92 (n=40)	7.11 (n=46)	-0.19	
Smoking status (%)				
Non-smokers	59.34 (n=343)	63.06 (n=408)	-3.72	
Smokers	33.91 (n=196)	29.21 (n=189)	4.70	
Missing (%)	6.75 (n=39)	7.73 (n=50)	-0.98	
Duration of COPD (years)	7.80 (6.23)	7.70 (5.79)	0.10	
Missing (%)	14.01 (n=81)	15.14 (n=98)	-1.13	
FEV1 (%)	47.70 (18.05)	48.37 (18.94)	-0.67	
Missing (%)	18.51 (n=107)	19.78 (n=128)	-1.27	
FVC(%)	70.38 (20.02)	74.34 (22.33)	-3.96	
Missing (%)	34.43 (n=199)	39.41 (n=255)	-4.98	
Comorbidities (%)				
Diabetes	10.21 (n=59)	9.89 (n=64)	0.32	
Coronary heart disease	32.70 (n=189)	31.84 (n=206)	0.86	
Mental health problem	4.84 (n=28)	4.79 (n=31)	0.05	
Musculoskeletal disorder	24.91 (n=144)	29.37 (n=190)	-4.46	
Cancer	6.06 (n=35)	4.79 (n=31)	1.27	
Missing (%)	8.13 (n=47)	7.88 (n=51)	0.25	
Baseline total costs (€)†	6492 (14 150)	4900 (7149)	1.592	
Missing (%)	13.66 (n=79)	11.28 (n=73)	2.38	
Baseline EQ5D	0.706 (0.202)	0.716 (0.185)	-0.01	
Missing (%)	8.30 (n=48)	8.19 (n=53)	0.11	

Data are mean (SD) or proportion (number of patients).

*Variable has no missing values.

+Baseline total costs are missing for three cost categories (help and care at home, community or district nurse and rehabilitation, see table 4) in four municipality districts.

COPD, chronic obstructive pulmonary disease; FEV1(%), forced expiratory volume in one second of predicted normal; FVC(%), forced vital capacity.

incremental QALYs gained was based on two separate linear mixed effects models; one for total costs and one for QALYs. Total costs were controlled for treatment arm, baseline EQ5D score, baseline costs (total costs 12 months prior to randomisation), age, baseline FEV1%, presence of musculoskeletal disease (a significant cost driver in municipality districts) and clustering. QALYs gained were controlled for treatment group, baseline EQ5D score, age, gender, baseline FEV1%, marital status, presence of diabetes, presence of cancer and clustering. These estimations were facilitated by the *mi estimate: xtmixed* command with robust standard errors. A deterministic ICER estimate was calculated using the treatment beta-coefficients from these two models. In order to explore the uncertainty surrounding cost-effectiveness, the output from the *mi estimate: xtmixed* was exported to Microsoft Excel 2010 along with Cholesky's decomposition matrix to allow for a potential correlation between all the parameters in the analyses models. By redrawing new parameter estimates from the estimated treatment effect with its SE, 5000 simulations were calculated to obtain new estimates of incremental QALYs and incremental total costs which were used to construct cost-effectiveness acceptability curves.

Table 3 Service use at 12 months across treatment groups and applied unit costs							
		Mean (SE) contacts		Between-group difference		Unit	Unit cost
ę	Service use	Telehealthcare (n=578)	Usual care (n=647)	Raw	Standardised (%)*		
ł	Hospital contacts						
	Admissions	0.5 (0.05)	0.45 (0.49)	0.046	3.70	Per contact	DRG value of contact ²⁸
	Inpatient bed days	2.69 (0.31)	2.60 (0.31)	0.09	1.18	Per contact	Included in DRG value of contact ²⁸
	Outpatient/emergency department visits	0.87 (0.08)	0.74 (0.07)	0.13	7.16	Per contact	DRG value of contact ²⁸
Primary care contacts							
	General practitioner	10.72 (0.35)	9.92 (0.33)	0.80	9.35	Per contact	Tariffs from collective agreement ³¹
ſ	Municipality care (time sp	pent)					
	Help and care at home	2137.32 (275.17)	1614.09 (207.76)	523.24	8.79	Per hour	Average hourly cost across municipalities (€57)
	Community or district nurse	607.29 (100.95)	438.59 (73.00)	168.69	7.86	Per hour	Average hourly cost across municipalities (€75)
	Rehabilitation ⁺	77.75 (14.34)	53.00 (13.21)	24.75	7.77	Per hour	Average hourly cost across municipalities (€75)
ſ	Vedicines						
	No. of antibiotics	2.41 (0.13)	1.89 (0.11)	0.52	17.28	Various	Pharmacy consumer price ³³
	No. of R03 ATC codes (COPD medicine)	25.08 (0.68)	23.92 (0.65)	1.16	7.08	Various	Pharmacy consumer price ³³

*Standardised difference: difference between randomisation group averages divided by the SD of the total sample.

†Incomplete register-data. Data unavailable for four municipality districts (two in the control group and two in the intervention group, respectively).

COPD, chronic obstructive pulmonary disease; DRG, diagnose-related group; SE, SE of the mean.

Sensitivity analysis 1: all-cause hospital contacts

In the base-case analysis, we have sought to limit hospital contacts to COPD-specific contacts because the hypothesis were that telehealthcare could prevent a proportion of admissions and emergency ward visits associated with exacerbations and make most COPD-specific outpatient control visits redundant. However, it became apparent that the included patients suffer from a variety of diseases concomitant with COPD (see table 2). As part of the intervention, it is therefore plausible that a more integrated care and monitoring approach assisted by the telehealthcare technology could also prevent some hospital contacts due to comorbidities. Some of the measurements facilitated by the Telekits could be indicative of cardiovascular disease and especially chronic heart failure. The effect on incremental costs of including all hospital contacts was therefore explored.

Sensitivity analysis 2: reduced procurement prices and larger scale

Potential discounts on procurement prices could be achieved when contemplating to implement technologies on a larger scale and increased capacity of the telehealthcare solution could also drastically reduce intervention cost, thereby affecting the cost-effectiveness conclusion. Therefore, an effect of a 30% discount on Telekit equipment, installation, support and maintenance was explored. Thirty percent is an estimate stemming from experiences with negotiating procurement prices subject to large-scale implementation of telehealthcare in the Danish healthcare sector.⁴⁶ In addition, suppliers have stated that the costs of maintenance (IT infrastructure and applications) and support costs does not depend on the number of patients included, but the complexity of the hardware and software configuration. The effects of making these costs negligible due to very large-scale implementation were therefore also explored.

Sensitivity analysis 3: reduced monitoring time

Municipality healthcare personnel had a steep learning curve for their new monitoring tasks and the patients' need for monitoring was uncertain at the outset. This resulted in approximately 5 min of average monitoring time per patient per week in the trial. After 12 months, personnel had become more efficient at monitoring and responding to vital values, so a new average target

Table 4Average costs per patient across treatment groups at 12 months follow-up (€)				
	Mean (SE) costs	Between-group difference		
Service use	Telehealthcare (n=578)	Usual care (n=647)	Raw (€)	Standardised (%)*
Hospital contacts				
Admissions	2756.1 (463.8)	2753.1 (458.9)	3.0	0.02
Outpatient/emergency department visits	343.4 (24.8)	278.3 (21.5)	65.1	11.37
Primary care contacts	602.9 (17.8)	629.4 (20.3)	-26.5	-5.55
Municipality care contacts				
Help and care at home	1936.7 (249.3)	1462.6 (188.2)	474.1	8.79
Community or district nurse	733.4 (121.9)	529.7 (88.1)	203.7	7.86
Rehabilitation†	93.4 (11.01)	61.0 (10.57)	32.4	8.56
Medicine	1610.1 (45.2)	1525.7 (37.7)	84.4	8.26
Service costs (excluding intervention costs)	8076.0 (417.6)	7239.8 (411.5)	836.2	5.76
Project management	7.4	0	7.4	-
Computer hardware and peripherals	200.5	0	200.5	-
Installation	38.6	0	38.6	-
Maintenance and support	94.6	0	94.6	-
Training healthcare professionals	12.4	0	12.4	-
Patient-specific training	20.6	0	20.6	-
Monitoring vital signs	330.0 (12.76)	0	330.0	123.43
Total costs (including intervention costs)	8780.2 (417.2)	7239.8 (411.5)	1540.4	10.61

*Standardised difference: difference between randomisation group averages divided by the SD of the total sample.

†Imputed data.

SE, Standard error of the mean.

of 2min/week/patient (ie, 110min annually) have been discussed by the North Denmark Region and the municipality districts⁴⁷ and the effects of this target on cost-effectiveness is investigated.

Finally, a most optimistic scenario exploring the combined effect of sensitivity analyses 1, 2 and 3 was investigated. The effect on total costs and/or QALYs was explored using the same models and covariates as the base-case analysis.

RESULTS

Baseline characteristics of all the included patients are presented in table 2. Baseline characteristics are fairly balanced across treatment groups. The FVC(%) is lower in the telehealthcare group and there is an overall tendency for patients in the telehealthcare group to have slightly worse health (lower average lung function, lower average health-related quality of life, higher average proportion of comorbidities (except musculoskeletal disorders)). The number of smokers is higher in the intervention arm and baseline costs were also higher in the telehealthcare group.

The unadjusted healthcare service use over the trial period with unit costs sources is summarised in table 3. Average values for healthcare service use were not imputed (ie, values are based on non-missing cases unadjusted for patient case mix). Table 3 reveals that resource use is consistently higher in the telehealthcare group.

The unadjusted within-trial costs are summarised in table 4. The annual per patient healthcare service costs (excluding intervention costs) were higher in the telehealthcare group (by €836) driven primarily by higher costs in the municipality districts on practical help and home care as well as costs to community or district nurses. table 4 also reveals that COPD-specific hospital admissions costs are roughly the same in the telehealthcare and usual care group. Excluding intervention costs, the three largest healthcare service cost drivers in telehealthcare were COPD-specific hospital admissions (34%), costs associated with practical help and care in municipality districts (24%) and medicine (20%). By adding intervention costs (also elaborated in table 4), the raw mean difference in annual per patient total costs between telehealthcare and usual care was $\in 1540$.

Table 5 presents the results of the incremental analyses. The base-case unadjusted average difference in QALYs was 0.0062 (not statistically significant) and the unadjusted difference in total costs was \in 1219 per patient. The base-case adjusted average difference in QALYs was 0.0132 (not statistically significant) with an adjusted average difference in annual total costs of \in 728 per patient. Based on these estimates, the ICER is \in 55327 per QALY. This telehealthcare solution is therefore only

Table 5 Incremental costs (€) and incremental QALYs at 12 months follow-up		
Between-group difference (95% CI) or ICER	Intraclass coefficient	
0.0062 (–0.0307; 0.0431)	0.007	
1219 (–937; 3376)	0.014	
0.0132 (–0.0083; 0.0346)	0.000	
728 (–754; 2211)	0.014	
55 327		
Sensitivity analysis 1: all-cause hospital contacts		
583 (–1397; 2563)	0.005	
44 301		
618 (–865; 2100)	0.014	
46 931		
525 (–969; 2018)	0.012	
39 854		
277 (–1700; 2255)	0.014	
21 068		
	etween-group difference (95% Cl) r ICER .0062 (-0.0307; 0.0431) 219 (-937; 3376) .0132 (-0.0083; 0.0346) 28 (-754; 2211) 5 327 83 (-1397; 2563) 4 301 18 (-865; 2100) 6 931 25 (-969; 2018) 9 854 77 (-1700; 2255) 1 068	

*Linear mixed model with treatment arm as only covariate.

†Linear mixed model adjusted for treatment arm, baseline EQ5D score, age, gender, baseline FEV1%, marital status, presence of diabetes, presence of cancer and clustering.

‡Linear mixed model adjusted for treatment arm, baseline EQ5D score, baseline costs, age, baseline FEV1%, presence of musculoskeletal and clustering.

QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio.

cost-effective, if the willingness-to-pay threshold exceeds the ICER estimate. Figure 1 presents the cost-effectiveness acceptability curve (CEAC) and it can be seen that decision-makers should be willing to pay more than €55000 to achieve a probability of cost-effectiveness >50%.

Sensitivity analyses

Results from sensitivity analyses are also presented in table 5 and CEACs for all scenarios are presented in figure 2. In sensitivity analysis 1, all-cause hospital contacts were included in the analysis. Incremental total costs remain higher in the telehealthcare groups (€583) with an ICER of €44301 per QALY. From figure 2, it can be seen that the willingness-to-pay threshold falls to €45000 per QALY to achieve a probability of cost-effectiveness >50%.

By reducing procurement prices and operating on a larger scale (sensitivity analysis 2), incremental total costs falls to \in 618 (ICER= \in 46931 per QALY). The willingness-to-pay threshold is \in 49000 per QALY, if a probability of cost-effectiveness >50% should be achieved.

Sensitivity analysis 3 (reducing average per patient monitoring time from 5 to 2min) would reduce incremental total costs to \in 525 and the ICER to \in 39 854. The

willingness-to-pay threshold falls to \in 40 000 per QALY, if a probability of cost-effectiveness >50% should be achieved.

In the most optimistic scenario combining the results from all sensitivity analyses (1+2+3), the adjusted incremental costs of telehealthcare were \in 277 giving rise to an ICER of \in 21068 per QALY and a willingness-to-pay threshold of \in 21000 per QALY to achieve a probability of cost-effectiveness >50%.

DISCUSSION

The adjusted mean difference in QALYs was 0.0132 (-0.0083; 0.0346) and the adjusted mean difference in costs were \in 728 (-754; 2211) leading to an ICER of \in 55327 per QALY. This ICER is higher than any explicit threshold values employed by countries today, for example, those recommended in the UK.⁴⁸ The cost-effectiveness conclusion is robust to changes in the definition of hospital contacts and reduced intervention costs. Only in the most optimistic scenario combining the effects of all sensitivity analyses, does the ICER fall below the UK thresholds. The telehealthcare solution is therefore unlikely to be cost-effective for all included patients with COPD.



Figure 1 Cost-effectiveness acceptability curve in the base-case analysis. QALY, quality-adjusted life-year.

Strengths and limitations

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This study is the largest trial-based cost-utility study of telehealthcare to patients with COPD in Denmark so far. A relatively broad range of cost categories from contacts with healthcare and social services are included and these contacts are all based on register data routinely registered in Denmark. A healthcare and social sector perspective was chosen that excludes transportation costs, time spent by patients and relatives and productivity loss to society. But travel distances in Denmark are relatively short compared with other larger countries (the longest distance to a university hospital is 160 km) and only 11% of the patients enrolled in the trial stated that they are employed (5% are full-time; 6% part-time).

Data on each monitoring contact was available for 21 of the 26 municipality districts included (the remaining



Figure 2 Cost-effectiveness acceptability curves for sensitivity analyses. QALY, quality-adjusted life-year.

5 districts has reported aggregated time spent monitoring each participant during the trial period). The median number of monitoring encounters within these 21 districts was 53 out of 64 planned contacts.²⁶ Although monitoring does not represent all facets of adherence and we do not have complete data for each individual encounter, it does suggest that participants in general were willing to engage with the TeleCare North initiative.

A limitation of the study is that single-level multiple imputation with clustering as a fixed effect was performed. Gomes et al has found that an imputation approach that accounts for clustering as a random effect performs better than single-level imputation.⁴⁹ More specifically, Andridge have in a simulation study found that including clustering as a fixed effect in the imputation model could overestimate the uncertainty of the estimates, especially if the number of clusters are small and the ICC is low as in this case.⁵⁰ However, a barrier to the adoption of multilevel multiple imputation is that these techniques are not part of conventional statistical software. Furthermore, separate modelling of costs and effects were performed in the analyses of incremental QALYs and costs, which could be less statistically efficient than joint modelling,⁵¹ although a multiway sensitivity analysis in a simulated cost-effectiveness study of bivariate multilevel models set to small correlations between costs and outcomes also perform reasonably well under the circumstances of this trial (eg, a small number of clusters and unequal cluster sizes).

Smoking status is an important risk factor for COPD⁵³ and the proportion of non-smokers was lower in the intervention arm, which was not accounted for in the randomisation (eg, through minimisation). However, the difference in smoking status between intervention and control group is not statistically significant (Fisher's exact test, p=0.103) and including smoking status as an additional covariate in the QALY and cost models have little impact on treatment effects (ie, incremental QALYs is reduced from 0.01316 to 0.01288 with smoking status included and incremental costs is changed from €728 to €705).

The way telehealthcare was implemented may have affected cost-effectiveness. The involved organisations and healthcare professionals underwent a steep learning curve after implementation of the telehealthcare solution, where they had to find new ways of working together and adapt to new work procedures. Monitoring is one example and personnel became more efficient at the end of the trial, when the needs and reactions of patients as well as work tasks were more familiar to municipality healthcare personnel. Other implementation effects such as how care-coordination across municipality districts, hospitals and general practitioners actually occurred or the engagement of health professionals and involved organisations could also have affected cost-effectiveness, but is hard to quantify post hoc.

Comparison with other studies

To our knowledge, three other studies have recently published cost-effectiveness results for telehealthcare involving patients with COPD and they all demonstrated a low probability of cost-effectiveness by the standards of their countries.⁵⁴⁻⁵⁶ A British study (Whole System Demonstrator) concludes that telehealth as a supplement to usual care is not likely to be cost-effective for patients with COPD, diabetes and chronic heart failure primarily due to a 'similar' QALY-gain and high intervention costs,⁵⁴ although this does not exclude that the COPD subgroup is cost-effective. The Telescot initiative for patients with COPD concludes that their telehealth initiative was associated with a non-significant QALY-gain and higher costs.⁵⁵ A study based in Northern Ireland also concludes that telehealthcare is not cost-effective.⁵⁶ Our findings are similar (non-significant QALY-gain and higher costs), but contrary to the UK experiences, it is not the intervention costs alone that have a considerable effect on the cost-effectiveness of telehealthcare, but rather differences in community care costs and the failure to save costs on COPD-related hospital contacts.

Implications for clinicians and decision-makers

When interpreting small differences in effectiveness, it is important to be aware that results can be highly sensitive to between-group differences in death. Even though, it is standard practise to assign an EQ5D summary score of 0 to deceased patients⁴⁰ in order to calculate incremental QALYs, this practise could potentially have a drastic effect on estimated cost-effectiveness. However, in this case the estimated between-arm QALY difference from the imputed dataset and an analysis where this EQ5D scoring is not done, is similar (QALY difference reduced from 0.01316 to 0.01004).

With regard to cost differences, it was suspected that baseline differences in costs could occur that would not necessarily be explained by differences in health or sociodemographic characteristics, for example, due to variations in visitation practise across municipality districts. The results demonstrate a big difference between adjusted and unadjusted costs and this raises the issue of the relevance of adjusting for baseline cost, if it makes such a large difference in a randomised study design. If baseline cost is removed as a covariate in the analysis of adjusted total costs, incremental costs rise from €728 to €1334. Recent guidance for trial-based cost-effectiveness evaluation suggest that baseline resource use should be collected and that the analysis of both costs and effects could include baseline measures of costs,⁴¹ which is also recommended by van Asselt et al.57 However, guidance is not as explicit as including baseline utility in the analysis of QALYs.⁵⁸ In our opinion, the baseline difference in cost reported in this study underlines the importance of requesting information on institutional context, such as variations in existing resource patterns, when interpreting cost-effectiveness research.

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Danish decision-makers has determined that if the telehealthcare solution in this trial proves cost-effective, it can serve as a national Danish standard for a technological platform as well as an implementation model for telehealthcare to this patient group.⁵⁹ However, the results suggest that the target COPD population in this study may have proven to be too broad. An implication could be that decision-makers should await further research, at least into sources of heterogeneity or explanations of the results from this trial, for example, there was a 10%difference in service cost before inclusion of intervention-related costs and plausible explanations could be that patients randomised to telehealthcare became more aware of their disease and hence used more resources or it could be that especially municipalities discovered patients with an unmet need for home care when telehealthcare was introduced. Future research planned within this trial would seek to tap into explanations for this difference. It is unknown whether the telehealthcare solution has released its full potential for cost-effectiveness. It is therefore important for healthcare professionals and decision-makers to spend time learning from the experiences gained within the trial in order to investigate if any best practises could be implemented that would increase effectiveness and/or reduce cost without compromising safety and effectiveness.

Future studies

This study indicates that telehealthcare could potentially assist in hindering some COPD-related hospital contacts and hospital contacts associated with other diseases (incremental costs were reduced by applying all-cause hospital contacts). It could be a coincidence but also due to closer collaboration between healthcare delivery organisations or more frequent monitoring of physical measurements that may also be indicative of other diseases. Future studies should therefore investigate the link between telehealthcare, patients with COPD with well-defined comorbidities and hospital contacts.

Average cost-effectiveness estimates applied in this and other studies could in general hide important sources of heterogeneity. Not much is known on prognostic criteria (eg, sociodemographic, geographic, lifestyle or health characteristics of the patients) for cost-effectiveness of telehealthcare to chronically ill patients, so further heterogeneity studies should be conducted and are also planned within this trial.

Telehealthcare is a complex intervention involving a broad class of technologies and organisational infrastructures, actions of healthcare professionals and patients. Experimental evaluation research has been criticised for being atheoretical in nature in trying to understand why and under what circumstances complex interventions are (un)likely to lead to desired outcomes.⁶⁰ In this study, mechanisms leading to higher health-related quality of life and cost in the telehealthcare group has largely been treated as a black-box, where patient education, monitoring, emotional support, assisted planning,

etc could all have an effect.¹³ We would recommend that future cost-effectiveness studies are more informed by a programme theory, such as the TECH model⁶¹ that was used in the Healthlines cost-effectiveness studies.^{62 63} These studies explicitly sought to describe implementation context or account for the causation of the most important telehealthcare activities that were most likely to activate mechanisms that could lead to 'efficient' design and deployment of telehealthcare. However, context and mechanisms that specifically gave rise to between-arm differences in EQ5D in the Healthlines studies are difficult to identify, reflecting that programme theories are often focused on explaining trial-related aspects or outcomes (eg, smoking cessation or weight loss). In the future, context and mechanisms leading to between-arm differences in EQ5D and costs should receive more attention in programme theory development.

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Contributors OH is the principal investigator for the TeleCare North trial and LHE is lead investigator for the economic evaluation in the trial; LHE and OH planned the overall trial design and are guarantors of the statistical quality for the trial as a whole. FWU and PHL contributed to the detailed planning of the data collection of trial questionnaires. FWU planned and collected register data. FWU planned and conducted all analyses under the supervision of LHE and OH. FWU reported the analyses. All authors met regularly during and after the trial period and contributed as a whole to interpreting and the presentation of the data. All authors reviewed and approved the manuscript. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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REFERENCES

- Roisen RR, Vestbo J. Global initiative for chronic obstructive lung disease – Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease [Internet, 2013. Available from. http://www.goldcopd.org/uploads/users/files/GOLD_ Report_2013_Feb20.pdf
- McCance K, Huether S, Brashers V, et al; The biologic basis for disease in adults and children. 6th edition. Maryland Heights: Mosby Elsevier, 2010.
- Bailey PH. The dyspnea-anxiety-dyspnea cycle--COPD patients' stories of breathlessness: "It's scary /when you can't breathe". Qual Health Res 2004;14:760–78.
- Vos T, Barber RM, Bell B, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a

systematic analysis for the global burden of disease study 2013. *Lancet* 2015;386:743–800.

- Adeloye D, Chua S, Lee C, *et al.* Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. *J Glob Health* 2015;5:20415.
- Burney PG, Patel J, Newson R, et al. Global and regional trends in COPD mortality, 1990-2010. Eur Respir J 2015;45:1239–47.
- Divo M, Cote Ć, de Torres JP, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;186:155–61.
- Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *Eur Respir J* 2009;33:1165–85.
- Bentsen SB, Rokne B, Wahl AK. Comparison of health-related quality of life between patients with chronic obstructive pulmonary disease and the general population. *Scand J Caring Sci* 2013;27:905–12.
- DiBonaventura M, Paulose-Ram R, Su J, et al. The impact of COPD on quality of life, productivity loss, and resource use among the Elderly United States workforce. COPD 2012;9:46–57.
- Foster TS, Miller JD, Marton JP, et al. Assessment of the economic burden of COPD in the U.S.: a review and synthesis of the literature. COPD 2006;3:211–8.
- 12. Flachs EM, Eriksen L, Koch MBThe disease burden in Denmark. 2015.
- McLean S, Nurmatov U, Liu JL, et al. Telehealthcare for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2011;7:1–52.
- Miller EA. Solving the disjuncture between research and practice: telehealth trends in the 21st century. *Health Policy* 2007;82:133–41.
- Haesum LK, Soerensen N, Dinesen B, et al. Cost-utility analysis of a telerehabilitation program: a case study of COPD patients. *Telemed J E Health* 2012;18:688–92 http://www.scopus.com/ inward/record.url?eid=2-s2.0-84869057985&partnerID=40&md5= 87200bfb992018c29819b0f75c0d60cf
- Johnston B, Wheeler L, Deuser J, et al. Outcomes of the Kaiser Permanente Tele-Home Health Research Project. Arch Fam Med 2000;9:40–5.
- 17. Koff PB, Jones RH, Cashman JM, *et al.* Proactive integrated care improves quality of life in patients with COPD. *Eur Respir J* 2009;33:1031–8.
- Pare G, Poba-Nzaou P, Sicotte C, et al. Comparing the costs of home telemonitoring and usual care of chronic obstructive pulmonary disease patients: a randomized controlled trial. Eur Res Telemed [Internet]. 2013235–47 http://www.embase.com/search/ results?subaction=viewrecord&from=export&id=L52635611
- Vitacca M, Bianchi L, Guerra A, et al. Tele-assistance in chronic respiratory failure patients: a randomised clinical trial. Eur Respir J 2009;33:411–8.
- 20. Goldstein RS, O'Hoski S. Telemedicine in COPD: time to pause. Chest 2014;145:945–9.
- Jaana M, Paré G, Sicotte C, et al. Home telemonitoring for respiratory conditions: a systematic review. Am J Manag Care 2009;15:313–20 http://www.embase.com/search/results?subaction= viewrecord&from=export&id=L354710451
- Mistry H. Systematic review of studies of the cost-effectiveness of telemedicine and telecare. Changes in the economic evidence over twenty years. J Telemed Telecare 2012;18:1–6.
- 23. Polisena J, Coyle D, Coyle K, *et al*. Home telehealth for chronic disease management: a systematic review and an analysis of economic evaluations. *Int J Technol Assess Health Care* 2009;25:339–49.
- Polisena J, Tran K, Cimon K, et al. Home telehealth for chronic obstructive pulmonary disease: a systematic review and metaanalysis. J Telemed Telecare 2010;16:120–7.
- Udsen FW, Hejlesen O, Ehlers LH. A systematic review of the cost and cost-effectiveness of telehealth for patients suffering from chronic obstructive pulmonary disease. J Telemed Telecare 2014;20:212–20.
- Udsen F, Lilholt P, Hejlesen O, *et al.* Effectiveness and costeffectiveness of telehealthcare for chronic obstructive pulmonary disease: study protocol for the danish "TeleCare North" pragmatic cluster-randomized trial. *Trials* 2014.
- The State Serum Institute. The danish national patient register (Internet). 2014 http://www.ssi.dk/Sundhedsdataogit/ Registre%20og%20kliniske%20databaser/De%20nationale% 20sundhedsregistre/Sygdomme%20leagemidler%20behandlinger/ Landspatientregisteret.aspx
- Sundhedsdatastyrelsen (No English translation). Reimbursement And financing (DRG) (Internet).DRG tariffs. http://sundhedsdatastyrelsen. dk/da/afregning-og-finansiering
- 29. Danish register for COPD.Datadefinitions2015.

- National Health Insurance Service Register, 2014. Available from: http://www.ssi.dk/Sundhedsdataogit/Registre%20og% 20kliniske%20databaser/De%20nationale%20sundhedsregistre/ Sundhedsokonomi%20finansiering/Sygesikringsregister.aspx
- Danish Medical Association. Collective agreement between Danish Regions and general practice 2014 Current collective agreement. http://www.laeger.dk/portal/page/portal/LAEGERDK/Laegerdk/P_L_ O/Overenskomster/OK%20om%20almen%20praksis/OK%2001-09-2014
- 32. Register of Medicinal Product Statistics [Internet]. 2014. http://www. ssi.dk/English/HealthdataandICT/Health
- Danish Medicines Agency. Prices of medicines [Internet]. *Reimbursement and prices* https://laegemiddelstyrelsen.dk/en/ reimbursement/prices
- North Denmark Region Disease specific health agreement on COPD 2015-2018, 2011.
- 35. Rasmussen H. Number of patients with chronic heart failure in North Denmark Region, 2015.
- Average salary for administrative officer including pensions and pay supplements [Internet. 2014. SIRKA, 2014. Available from. http:// www.krl.dk/
- Agency for Modernisation at the Ministry of Finance. depreciation rates, other IT-equipment [Internet]. General accounting procedures 2015 http://www.modst.dk/OEAV/3-Bogfoering/33-Generellebogfoeringsbestemmelser/336-Levetider
- The State Serum Institute. The danish register of causes of death, 2014.
- Wittrup-Jensen KU, Lauridsen J, Gudex C, et al. Generation of a danish TTO value set for EQ-5D health states. Scand J Public Health 2009;37:459–66.
- 40. van Reenen M, Oppe M. EQ-5D-3L user Guide. *EuroQol Res Found* 2015;22.
- Ramsey SD, Willke RJ, Glick H, et al. Cost-effectiveness analysis alongside clinical trials II-An ISPOR good research Practices Task Force report. Value Health 2015;18:161–72 http://linkinghub.elsevier. com/retrieve/pii/S1098301515000169
- 42. Faria R, Gomes M, Epstein D, *et al.* A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. *Pharmacoeconomics* 2014;32:1157–70.
- Sterne JA, White IR, Carlin JB, *et al*. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393–60.
- Rabe-Hesketh S, Skrondal A. Multilevel and Longitudinal Modeling Using Stata. *Volume I: continouos responses*. Texas: Stata Press, 2012.
- Bachmann MO, Fairall L, Clark A, et al. Methods for analyzing cost effectiveness data from cluster randomized trials. Cost Eff Resour Alloc 2007;5:12.
- 46. Initial business case for the dissemination of telemedicine in Denmark.. 2015.
- 47. Region ND. Service catalogue for TeleCare North. 4th edition.2016.
- 48. Devlin N, Parkin D. Does NICE have a cost effectiveness threshold and what other factors influence its decisions ? A discrete choice analysis. by Nancy Devlin and David Parkin Department of Economics Discussion Paper Series does NICE have a cost effectiveness threshold and. *Health Econ* 2004;13:437–52.
- Gomes M, Díaz-ordaz K, Grieve R, et al. Missing Data in Costeffectiveness analyses an application to Cluster Randomized Trials.. 2013:15–17.
- Andridge RR. Quantifying the impact of fixed effects modeling of clusters in multiple imputation for cluster randomized trials. *Biom J* 2011;53:57–74.
- Nixon RM, Thompson SG. Methods for incorporating covariate adjustment, subgroup analysis and between-centre differences into cost-effectiveness evaluations. *Health Econ* 2005;14:1217–29.
- Gomes M, Ng ES, Grieve R, et al. Developing appropriate methods for cost-effectiveness analysis of cluster randomized trials. *Med Decis Making* 2012;32:350–61.
- Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007;370:765–73.
- Henderson C, Knapp M, Fernández JL, et al. Cost effectiveness of telehealth for patients with long term conditions (Whole Systems Demonstrator telehealth questionnaire study): nested economic evaluation in a pragmatic, cluster randomised controlled trial. BMJ 2013;346:f1035.
- Stoddart A, van der Pol M, Pinnock H, *et al.* Telemonitoring for chronic obstructive pulmonary disease: a cost and cost-utility analysis of a randomised controlled trial. *J Telemed Telecare* 2015;21:108–18.
- 56. McDowell JE, McClean S, FitzGibbon F, et al. A randomised clinical trial of the effectiveness of home-based health care

6

with telemonitoring in patients with COPD. *J Telemed Telecare* 2015;21:80–7.

- van Asselt AD, van Mastrigt GA, Dirksen CD, et al. How to deal with cost differences at baseline. *Pharmacoeconomics* 2009;27:519–28.
- Manca A, Hawkins N, Sculpher MJ. Estimating mean QALYs in trialbased cost-effectiveness analysis: the importance of controlling for baseline utility. *Health Econ* 2005;14:487–96.
- The Danish Agency for Digitilisation. The National Action Plan for Dissemination of Telemedicine [Internet] 2012 http://www.digst. dk/Servicemenu/English/Policy-and-Strategy/Strategy-for-Digital-Welfare/Telemedicine
- 60. Pawson R, Tilley N. Realistic Evaluation: Publications Sage, 1997.
- Salisbury C, Thomas C, O'Cathain A, et al. TElehealth in CHronic disease: mixed-methods study to develop the TECH conceptual model for intervention design and evaluation. BMJ Open 2015;5:e006448.
- Dixon P, Hollinghurst S, Ara R, et al. Cost-effectiveness modelling of telehealth for patients with raised cardiovascular disease risk: evidence from a cohort simulation conducted alongside the Healthlines randomised controlled trial. *BMJ Open* 2016;6:e012355.
- Dixon P, Hollinghurst S, Edwards L, et al. Cost-effectiveness of telehealth for patients with depression: evidence from the Healthlines randomised controlled trial. BJPsych Open 2016;2:262–9.



Cost-effectiveness of telehealthcare to patients with chronic obstructive pulmonary disease: results from the Danish 'TeleCare North' cluster-randomised trial

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