Strategies to optimise nutritional practice for patients at nutritional risk – With special emphasis on hospital food and individual dietary counselling

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Strategies to optimise nutritional practice for patients at nutritional risk

With special emphasis on hospital food and individual dietary counselling

PhD thesis by Tina Munk

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Strategies to optimise nutritional practice for patients at nutritional risk

With special emphasis on hospital food and individual dietary counselling

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CV Tina Munk

I am a registered clinical dietitian, hold a Master's degree in Clinical Nutrition, and started my Ph.D.-fellowship at Aalborg University in 2012.
For 6 years I have been Head of the Dietetic Unit at Herlev University Hospital and part of the research unit, EFFECT, of which I am also one of the founders. In my most recent job I was Head of the bachelors program for clinical dietitians at Metropolitan University College. Before that I worked as a clinical dietitian at Copenhagen University Hospital, Rigshospital, and Glostrup Hospital.
I am experienced in evidence-based practice, supervision, conducting and, managing clinical trials, and developing study protocols. I have extensive experience in teaching, oral presentations and implementing new strategies to improve nutritional practice in hospitals. I also have substantial managerial experience.
In 2013 I was the only nominee from Herlev University Hospital for the "manager prize" of the Capital Region of Denmark. My main research areas include optimisation of nutritional intake in patients at nutritional risk and quality improvement of nutritional practice in the hospital setting.

Preface

The PhD project presented in this thesis was conducted at the Faculty of Medicine at Aalborg University and was supported by Herlev University Hospital (HUH). The research was conducted at HUH at the Departments of Internal Medicine, Gynaecology, Oncology, Orthopaedic Surgery and Urology in collaboration with the Central Kitchen.

The PhD thesis includes the following three papers:

Paper I:
Munk T, Seidelin W, Rosenbom E, Nielsen AL, Klausen TW, Nielsen MA, Thomsen T. A 24-h a la carte food service as support for patients at nutritional risk: a pilot study. J Hum. Nutr. Diet. 2013;26(3):268-75. (Published)

Paper II:
Munk T, Beck AM, Holst M, Rosenbom E, Rasmussen HH, Nielsen MA, Thomsen T. Positive effect of protein-supplemented hospital food on protein intake in patients at nutritional risk: a randomised controlled trial. J. Hum. Nutr. Diet. 2014;27(2):122-32. (Published)

Paper III:
Munk T, Tolstrup U, Beck AM, Holst M, Rasmussen HH, Hovhannisyan K, Thomsen T. Individualised dietary counselling for nutritionally at-risk older patients following discharge from acute hospital to home: a systematic review and meta-analysis (Submitted to J. Hum. Nutr. Diet. and resubmitted following second revision)

English Summary

Background

Many hospitalised patients are at nutritional risk on admission and at hospital discharge. Being at nutritional risk impacts negatively on physical function, diminishes quality of life (QoL), and increases the risk of a complicated clinical course. Lack of appetite in combination with inadequate clinical nutritional practice is associated with becoming at nutritional risk. The aims of this Ph.D.-thesis were to investigate strategies that may be able to improve nutritional practice and thereby possibly improve the nutritional status of patients at nutritional risk.

Aims

Study I: To develop a novel hospital food concept for patients at nutritional risk and to examine whether this hospital food concept would increase energy and protein intake in nutritionally at-risk hospitalised patients.

Study II: To examine the effect of a protein-fortified hospital food concept on energy and protein intake in nutritionally at-risk patients.

Study III: To evaluate the evidence for an effect of individualised dietary counselling following discharge from hospital to home on physical function in nutritionally at-risk older patients.

Methods

Study I: A historically controlled intervention pilot study. Forty patients at nutritional risk were offered a novel hospital food concept as a supplement to the standard hospital food service. The novel hospital food concept consisted of 36 naturally energy-enriched small dishes served on demand 24 h a day. Participating patients were recruited from the Departments of Gynaecology, Orthopaedic Surgery and Internal Medicine. The primary outcome was the number of patients achieving ≥75% of energy and protein requirements.

Study II: Results and experiences from *Study I* were used to adjust the intervention and the study design. A single-blinded block-randomised RCT was conducted. Eighty-four participants at nutritional risk were recruited from the Departments of Oncology, Orthopaedics and Urology. The intervention group (IG) received a supplementary protein-fortified hospital food concept served on demand from 7AM to 8PM. The control group (CG) received the standard hospital food service. The primary outcome was the number of patients achieving ≥75% of energy and protein requirements. Secondary outcomes were: mean difference between energy and protein intake, weight adjusted energy and protein intake, change in body weight (BW), handgrip strength (HGS) and length of hospital stay (LOS).

Study III: A systematic review of RCTs. Risk of bias was assessed in the included studies using The Cochrane Collaboration's Risk of Bias Tool. The Grading of Recommendations Assessment, Development and Evaluation system (GRADE) was used to assess the quality of evidence across outcomes. Participants were older nutritionally at-risk hospitalised patients discharged to home. The primary outcome was physical function. Secondary outcomes were readmissions, mortality, nutritional status, nutritional intake and QoL.

Results

Study I: No significant difference in energy and protein intake was observed between the groups; however, a significant (P = 0.001) time gradient in total energy intake was observed in the IG. Moreover, a significant (P = 0.03) time gradient in energy intake received from the novel hospital food concept was observed. A significant time gradient was not seen in protein intake. The dishes from the novel hospital food concept were mainly ordered from 11.00 AM to 2.00 PM and from 5.00 PM to 6.00 PM.

Study II: In the IG, 76% versus 70% CG patients reached ≥75% of their energy requirements (P = 0.57); 66% IG patients versus 30% CG patients reached ≥75% of their protein requirements (P = 0.001). The risk ratio (RR) for achieving ≥75% of protein requirements was 2.2 (95% Confidence Interval (CI):1.3–3.7); number needed to treat (NNT) was 3 (95% CI 2–6). IG had a higher mean intake of energy and protein when adjusted for BW (CG: 82 kJ kg^{-1} versus IG: 103 kJ kg^{-1}, P = 0.013; CG: 0.7 g protein kg^{-1} versus IG: 0.9 g protein kg^{-1}, P = 0.003). BW, HGS and LOS stay did not differ between groups.

Study III: Four RCTs (n = 729) were included. Overall, the evidence was of moderate quality. Clinical dietitians (RDs) provided counselling in all studies. Meta-analyses showed a significant increase in energy intake: mean difference (MD) 1.10 MJ/d, (95% CI: 0.66-1.54, p < 0.001), protein intake: MD 10.13 g/d, (95% CI: 5.14-15.13, p < 0.001) and BW: MD: 1.01 kg, (95% CI: 0.08-1.95, p = 0.03). Meta-analyses revealed no significant effect on physical function assessed using HGS, and likewise on mortality. Narrative summation of effects on physical function using other instruments revealed inconsistent effects. Meta-analysis was not conducted on QoL and readmissions due to lack of data.

Conclusions
The provision of a supplementary protein-fortified hospital food concept increased dietary intake (protein and weight adjusted energy intake) in hospitalised nutritionally at-risk patients. Further research is needed to confirm these results and also to establish the effect on clinically relevant outcomes. Individualised dietary counselling provided after hospitalisation improved energy and protein intake and BW in older nutritionally at-risk patients, however, without clearly improving physical function. No effect was observed on mortality and lack of data prevented pooling of data for QoL and readmissions. The effect of the “follow-home strategy” after hospital discharge therefore also warrants further investigation.

Dansk resume

Baggrund
Mange patienter er i ernæringsrisiko under og efter hospitalsindlæggelse. At være i ernæringsrisiko er associeret med nedsat fysisk funktion, forringet livskvalitet og et dårligere klinisk forløb. Manglende appetit i kombination med mangelfuld klinisk ernæringspraksis er associeret med øget risiko for at komme i ernæringsrisiko. Formålet med nærværende ph.d.-afhandling var at undersøge strategier, der formentlig ville kunne forbedre den kliniske ernæringspraksis og herved potentielt forbedre ernæringsstatus hos patienter i ernæringsrisiko.

Formål
Studie I: Formålet med studiet var at undersøge effekten at et ny-udviklet madkoncept på energi- og proteinindtaget hos indlagte patienter i ernæringsrisiko.

Studie II: Formålet med studiet var at undersøge effekten af et proteinberiget madkoncept på energi- og proteinindtaget hos indlagte patienter i ernæringsrisiko.

Studie III: Formålet med studiet var at evaluere evidensen for en effekt på fysiske funktion ved at udføre individualiseret diætvejledning hjemme hos ældre patienter, der var i ernæringsrisiko efter hospitalsindlæggelse.

Metoder
Studie I: Der blev udført et historisk kontrolleret interventions pilot studie. 40 patienter i ernæringsrisiko fik tilbudt det ny-udviklede madkoncept som et supplement til det ordinære madtilbud. Den historiske kontrolgruppe havde tidligere modtaget hospitalets ordinære madtilbud. Det ny-udviklede madkoncept bestod af 36 små energitætte retter, som kunne bestilles døgnets 24 timer. Studiet inkluderede patienter fra hhv. gynækologisk-, ortopædkirurgisk-, og medicinsk afdeling. Det primære effektmål var antallet af patienter, der opnåede ≥ 75 % af energi- og proteinbehov.

Studie II: Resultater og erfaringer fra *Studie I* blev brugt til at justere madkonceptet og studiedesign. *Studie II* var et single-blindet blok-randomiseret kontrol forsøg. 84 patienter i ernæringsrisiko blev rekrutteret fra hhv. onkologisk-, ortopædkirurgisk- og urologisk- afdeling. Interventionsgruppen (IG) blev tilbud et protein-beriget madkoncept som supplement til hospitalets ordinære madtilbud. Madkonceptet kunne bestilles fra kl. 07:00 til 20:00. Kontrolgruppen (KG) modtog hospitalets ordinære madtilbud. Primære effektmål var antallet af patienter, der opnåede ≥ 75 % af energi- og proteinbehov. Sekundære effektmål omfattede energi- og proteinindtag, kropsvægt, håndgribe styrke og indlæggelsestid.

Studie III: En systematisk gennemgang af randomiserede kontrollerede undersøgelser (RCT'er).
”The Cochrane Collaboration's Risk of Bias Tool” blev benyttet til at vurdere risiko for bias. ”The Grading of Recommendations Assessment, Development and Evaluation system” (GRADE) blev benyttet til at vurdere evidensen på tværs af effektmål. Deltagerne var ældre patienter vurderet til at være i ernæringsrisiko og som var udskrevet til eget hjem.
Det primære effektmål var fysisk funktion og de sekundære effektmål var genindlæggelser, dødelighed, ernæringsstatus, ernæringsindtag og livskvalitet.

Resultater

Studie I: Der blev ikke observeret en signifikant forskel i energi- og proteinindtag mellem grupperne, dog sås en signifikant (P = 0,001) stigning i energiindtag over tid i IG. Desuden sås også en signifikant stigning i energiindtag over tid fra det nye madkoncept (P = 0,03). En lignende stigning blev ikke set i proteinindtaget. Retterne fra madkonceptet blev hovedsageligt bestilt i tidsrummet 11.00 -14:00 og fra 17:00 – 18:00.

Studie II: I IG opnåede 76 % af patienterne versus 70 % i CG ≥ 75 % dækning af deres energibehov (P = 0,57); 66 % i IG versus 30 % i KG fik dækket ≥75 % af deres protein behov (p = 0,001). Den relative risiko for at opnå ≥ 75 % af proteinbehov var 2,2 (95 % CI = 1,3-3,7) og NNT var = 3 (95 % CI = 2-6). IG havde et højere gennemsnitlig indtag af energi og protein, når der blev korrigeret for legemsvægt (KG: 82 kJ kg^{-1} versus IG: 103 kJ kg^{-1}, P = 0,013; KG: 0,7 g protein kg^{-1} versus 0,9 g protein kg^{-1}, P = 0,003). Der var ingen forskel på kropsvægt, håndgribe styrke og indlæggelsestid mellem grupperne.

Studie III: Fire RCT’er (n = 729) blev inkluderet og samlet set var evidensen af moderat kvalitet. Kliniske diætister foretog den individuelle diætvejledning i alle studierne. Meta-analyser viste en signifikant stigning i energiindtag (MD: 1,10 MJ/d, 95 % CI: 0,66; 1,54, p <0,001), proteinindtag (MD: 10,13 g / d, 95 % CI: 5,14; 15,13, p <0,001) og kropsvægt (MD: 1,01 kg, 95 % CI 0,08; 1,95, p = 0,03). Meta-analyse viste ingen signifikant effekt på den fysiske funktion vurderet ved håndgribestyrke og ligeledes ej på mortalitet. Den narrative opsummering af effekten på fysisk funktion ved brug af andre instrumenter var inkonsistent. Meta-analyse blev ikke udført på livskvalitet og genindlæggelser på grund af manglende data.

Konklusion

Tilgængeligheden af et proteinberiget hospitalsmadskoncept til patienter i ernæringsrisiko øgede kostindtaget (proteinindtaget og det kropsvægt justeret energiindtag [kJ/kg]). Yderligere forskning er nødvendig for at bekræfte disse resultater samt for også at undersøge effekten på klinisk relevante effektmål. Individuel diætvejledning udført hjemme hos ældre patienter i ernæringsrisiko efter hospitals indlæggelse, forbedrede energi- og proteinindtaget og kropsvægten. Effekten på den fysiske funktion var dog ikke overbevisende. Metaanalyse viste ingen effekt på mortalitet og mangel på data forhindrede metaanalyse af livskvalitet og genindlæggelser. Effekten af sidstnævnte ”følge-hjem strategi” efter hospitalsindlæggelse kræver derfor også yderligere forskning.

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- Also, a special thanks to the many patients that participated in the studies.

- Last but not least, I wish to thank my lovely family and friends for their ongoing support, faith and understanding.

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List of abbreviations

HUH	Herlev University Hospital
GNP	Good Nutritional Practice
ESPEN	European Society for clinical Nutrition and Metabolism
A.S.P.E.N.	American Society of Parenteral and Enteral Nutrition
NRS-2002	Nutritional Risk Screening tool
ONS	Oral Ntritional Supplements
RCT	Randomised Controlled Trial
IG	Intervention group
HCG	Historical control Group
CG	Control Group
LOS	Length Of hospital Stay
QoL	Quality of Life
HGS	Hand Grip Strength
BW	Body Weight
ADL	Activity of Daily Living
NA	Not Available data
COPD	Chronic Obstructive Pulmonary Disease
GRADE	Grading of Recommendations Assessment, Development and Evaluation system
MD	Mean Difference
CI	Confidence Interval
NNT	Number Needed to Treat
RR	Risk Ratio
RD	Registered Dietitian
GP	General Practitioners

1. Introduction

The prevalence of patients at nutritional risk in European hospitals is reported to be around 30 % (1). A large proportion of these patients are at nutritional risk on admission (1–3), and, due to insufficient coverage of nutritional requirements, most of them experience further deterioration in nutritional status during hospitalisation (2,4,5). Being at nutritional risk is associated with a wide range of adverse effects e.g. increased morbidity, prolonged hospital stays, increased healthcare costs, poorer quality of life (QoL), and higher mortality rates (1,6–10).

To optimise nutritional status of hospitalised patients, The European Society for Clinical Nutrition and Metabolism (ESPEN) has developed a set of clinical guidelines for Good Nutritional Practice (GNP) to use in the hospital setting. GNP includes screening for nutritional risk using the validated screening tool Nutritional Risk Screening tool (NRS-2002), individual nutritional planning, including continuous monitoring and adjustment of nutritional plans throughout the hospital admission and following discharge (Figure 2.1-1) (11–13)

Danish hospitals have initiated different in-hospital strategies at the organisational level to implement GNP. These include efforts to involve general managers of the hospitals, involve “fiery nutritional souls” among nursing staff, nutritional education and development of guidelines on how to perform nutritional screening and nutritional therapy(14). Furthermore, nutritional screening is now mandatory at hospital admission and part of the accreditation criteria in Danish hospitals (15,16). Data indicate that a relatively high rate (~ 70 %) of nutritional screenings are now performed in Denmark (15). However, data from Danish hospitals still reveal a poor intake of energy and protein in patients at nutritional risk (17,18), indicating that sufficient action is not taken after screening. An observational study and a period prevalence study showed that only around 50 % of patients at nutritional risk reached their energy target (minimum 75 % of requirements) and only around 30 % reached both their energy and protein target (17,18). This indicates that reaching the protein target is more difficult than reaching the energy target.
Reasons for the very low intake of energy and protein in nutritionally at-risk hospitalised patients can be due both to lack of appetite and to poor GNP (e.g. lack of knowledge, time, interest, guidelines and lack of quality, appropriate hospital food) within the hospital (14,19).

As previously mentioned, strategies to improve GNP have predominantly focused on the organisational level whereby an important issue within the GNP has been overlooked, namely the development of appropriate hospital food for patients at nutritional risk. Hospital food represents a very important strategy since around 85 % of patients in hospitals depend solely on hospital food (20–22). However, a review of the literature within this important area revealed a huge knowledge gap.

Another important aspect of GNP which appears overlooked is ‘nutritional follow-up after hospital discharge’. This aspect of GNP is important given the increased fast-track nature of hospital treatment today. Increasingly, hospital stays are too short to allow nutritional repletion to occur, rendering many patients still at nutritional risk after discharge (1,8). Older patients appear particularly vulnerable to inadequate nutritional follow-up after discharge (e.g. increased risk of readmissions and functional decline) (23–26).
Only one systematic review exists with regard to provision of nutritional support at home after hospital discharge (27). The review assessed the benefits of oral nutritional supplements (ONS) without dietary counselling in older nutritionally at-risk patients.
A limited effect on the patient relevant outcome, physical function was found; possibly due to a relatively low level of compliance to ONS (27). Individualised dietary counselling in combination with ONS might have been able to give additional benefits, since this approach represent an opportunity to personalise the nutritional plan, thereby potentially overcoming problems with low compliance. However, no systematic review has yet evaluated the evidence for an effect of individualised nutritional counselling following hospital discharge in older patients at nutritional risk.

In conclusion, Denmark has quite successfully implemented early nutritional risk screening, despite this, low nutritional intake in hospitalised patients at nutritional risk still persists. There are undoubtedly multiple reasons for the failure to sufficiently address the screening results.
The development of appropriate hospital food may, however, be an important strategy to increase energy and protein intake. Nevertheless, this area has only scarcely been investigated.
Recognising that repletion and recovery after illness takes time, GNP also recommends nutritional planning after hospital discharge. Nutritional follow-up after hospital discharge is found to be especially important for older patients, since being older and at nutritional risk is associated with increased risk of adverse outcomes after hospital discharge (24,25,28,29).
Individualised dietary counselling after hospital

discharge may be superior to using ONS as a single intervention. However, the effect of individualised dietary counselling following hospital discharge for older nutritionally at-risk patients remains to be examined.

It is within this context the current PhD project was initiated.

1.1 Aims of the thesis

The overall aim of this PhD project was to investigate whether strategies within the GNP (Figure 2.1-1) would impact positively on energy and protein intake and patient-relevant outcomes in patients at nutritional risk. The PhD project aimed to evaluate the effect of a novel hospital food concept using two different approaches to increase energy and protein intake in hospitalised nutritionally at-risk patients. Further, the PhD project aimed to evaluate the evidence for an effect of individualised dietary counselling following hospital discharge on physical function in nutritionally at-risk older patients.

To accomplish these aims, the project comprised the following three studies.

Study I
The aim was to develop a novel hospital food concept for patients at nutritional risk and to examine whether this concept would increase energy and protein intake in nutritionally at-risk patients.

Intervention: The intervention group (IG) was offered a novel hospital food concept (36 small dishes enriched with ingredients naturally high in energy and served a la carte 24 h a day). The historical control group (HCG) was offered standard food service

Outcome: The primary outcome was the number of patients reaching a minimum of 75 % of their energy and protein requirements

Target population: Hospitalised patients at nutritional risk.

Design: A historically controlled intervention study.

Study II
The aim of this study was to examine the effect of a protein-fortified hospital food concept on energy and protein intake in nutritionally at-risk patients. The intervention was adjusted in accordance to the findings and experiences obtained in *Study I*.

Intervention: The IG was offered a protein-fortified hospital food concept (23 small dishes enriched with ingredients naturally high in energy and fortified with a high quality protein powder and served a la carte from 7 AM to 8 PM). The control group (CG) was offered standard food service.

Outcome: The primary outcome was the number of patients reaching a minimum of 75 % of their energy and protein requirements. Secondary outcomes were: mean difference between energy and protein intake, weight adjusted energy and protein intake, weight

change, handgrip strength (HGS) and length of hospital stay (LOS).

Target population: Hospitalised patients at nutritional risk.

Design: A randomised controlled study.

Study III

The aim of the study was to evaluate the evidence for an effect on physical function of individualised dietary counselling for nutritionally at-risk older patients following discharge from hospital to home.

Intervention: Individualised dietary counselling following discharge from hospital to home +/- ONS vs. standard care (i.e. no nutritional follow-up, or prescribed ONS without individualised dietary counselling after hospital discharge).

Outcome: The primary outcome was physical function and secondary outcomes were readmissions, mortality, nutritional status, energy and protein intake, and QoL.

Target population: Older hospitalised patients at nutritional risk following discharge from hospital to home.

Design: A systematic review and meta-analysis.

2. Definitions

Basic terminology used in this thesis includes definition of *good nutritional practice,* and definition of the *malnutrition syndrome* and *being at nutritional risk.*

2.1 Good Nutritional Practice (GNP)

The guidelines for GNP were developed based on recommendations from The Council of Europe. In 2001 The Council of Europe reviewed current nutritional practice in European hospitals. They found a need for standards for assessing and monitoring nutritional risk and status in patients, as well as a need for nutritional education of all staff involved in nutritional care.

Further, they recommended that the responsibility of hospitals with regard to nutritional care and support of patients should not be limited to the hospital stay (30,31). The Council of Europe also emphasised that hospital food, including the provision of meals, should be regarded as an essential element of treating patients, rather than just as a hotel service. It was further recommended that hospital food should be the first choice to correct or prevent undernutrition in patients (30).

A detailed overview of the recommended pathway of GNP by ESPEN can be seen in Figure 2.1-1.

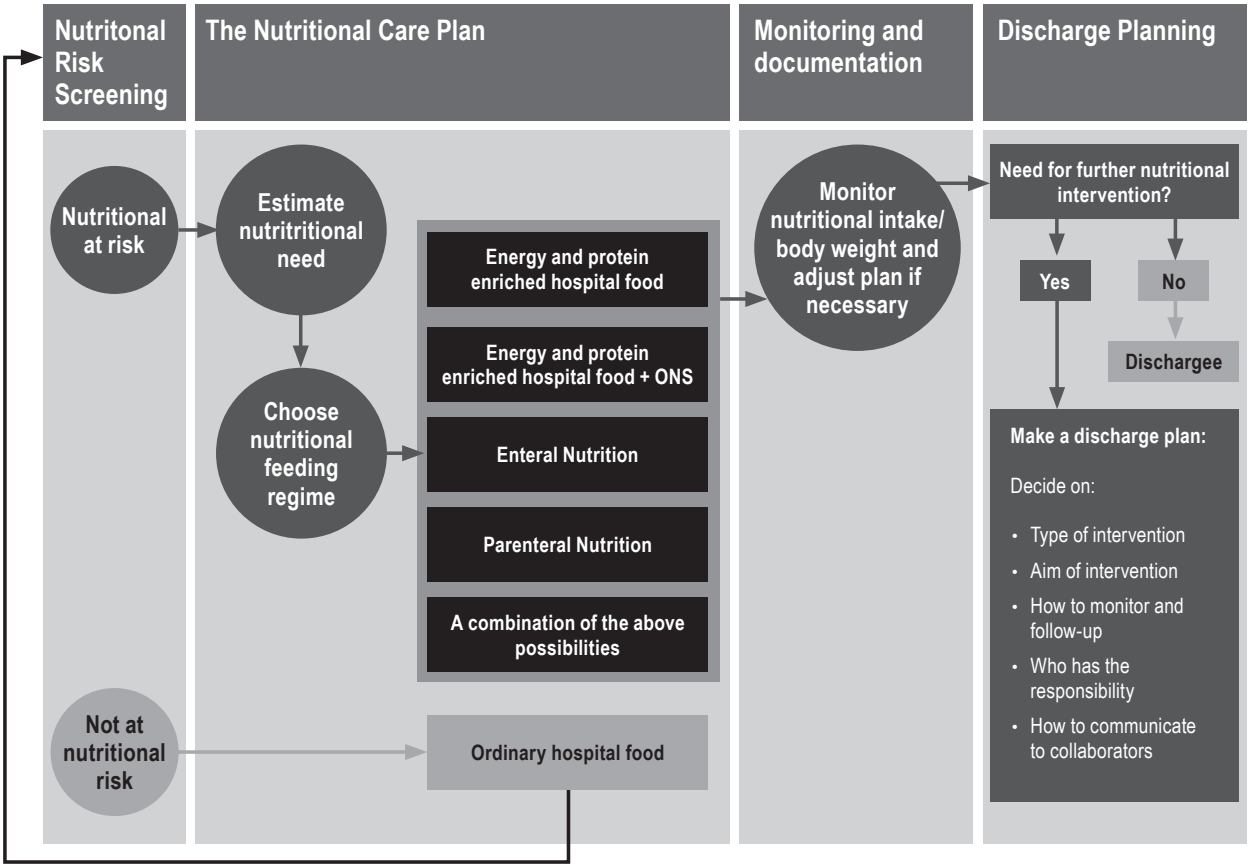

Figure 2.1-1 the pathway of GNP (15,32,33).

2.2 The malnutrition syndrome: Being at nutritional risk

No internationally accepted definition of the malnutrition syndrome exists, resulting in widespread confusion (34,35). It has however become increasingly evident that nutritional intake in adults may be compromised not only by chronic starvation (without inflammation) but also because of chronic diseases that impose sustained inflammation of a mild to moderate degree, or because of acute disease/injury with a marked inflammatory response resulting in catabolism (34).

In 2009 an aetiology-based consensus within the ESPEN Society and the American Society of Parenteral and Enteral Nutrition (A.S.P.E.N.) was reached (34). They proposed the following nomenclature for the "nutritionally at-risk diagnosis" in adults in the clinical practice setting. ''Starvation-related malnutrition'', where there is chronic starvation without inflammation, ''chronic disease-related malnutrition'', where inflammation is chronic and of a mild to moderate degree, and ''acute disease or injury-related malnutrition'', where inflammation is acute and of a severe degree (Figure 2.2-1) (34,36).

Danish hospitals have indirectly worked with these criteria since 2003 due to the implementation of the nutritional screening tool, the NRS-2002. The NRS-2002 includes both an assessment of nutritional status (intake, weight loss and BMI) and severity of disease (degree of inflammation). It also includes old age (> 70 years of age) to correct for age-related frailty (Appendix A) (11).
Patients found to be at nutritional risk by NRS-2002 can therefore be undernourished determined by a low BMI. Additionally, as the NRS-2002 also includes recent food intake and weight loss, it will also identify those patients who have lost weight/eaten less than normal unintentionally but still have a body composition of relative excess in terms of BMI. This is important since unintentional weight loss and low food intake per se are predictors for adverse outcomes (2,9).

Patients can, however, also be at nutritional risk "just" by being severely ill, e.g. patients in intensive care units with multi-organ failure. Most often, nutritional risk is due to a combination of 2 or 3 of the factors, being old and/or having a decreased nutritional status and/or having a moderate degree of inflammation due to disease.

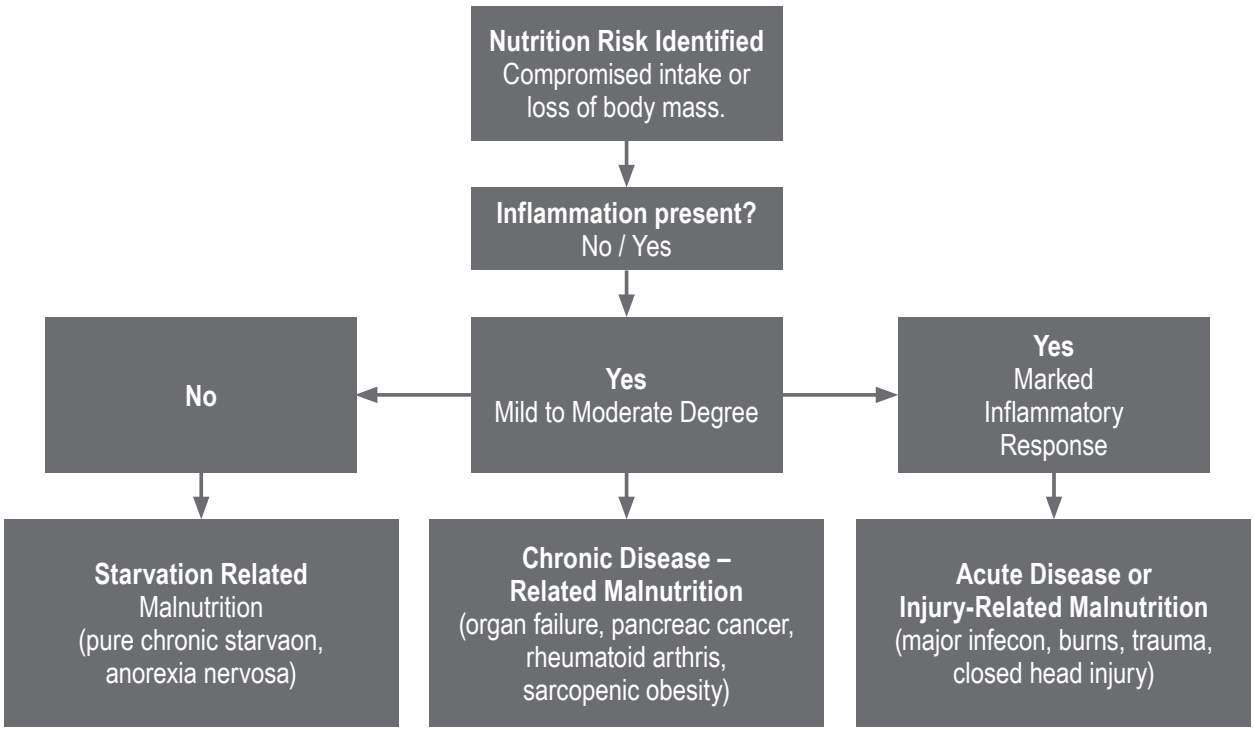

Figure 2.2-1. The aetiology-based malnutrition definitions. Reprinted from: Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition), with permission from Elsevier(36).

The NRS-2002 is endorsed by ESPEN for use in hospitals, since it is the best validated tool for identifying adult hospitalised patients who are likely to benefit from nutritional therapy in hospitals (11,33,37).
In Danish hospitals, the preferred term for classifying patients in need of nutritional support is therefore “at nutritional risk”. This is due to the fact that the NRS-2002 seems to captor all the relevant factors, which affect nutritional status and due to the tool’s ability to identify patients who are likely to benefit from a nutritional intervention.

In this Ph.D. thesis the term *“nutritionally at-risk”* will therefore be used instead of the previously mentioned nomenclatures (34,36), since this term encompasses all three nomenclatures.

3. Background

3.1 Prevalence of patients at nutritional risk

The prevalence of being at nutritional risk in European Hospitals is found to be around 30 % (range: 18-52 %). (Table 3.1-1)(8,38–43). The prevalence is most often measured at hospital admission. A large Spanish (n= 1707) cross-sectional, observational, multicentre study found that approximately 10 % (118/1225) of patients who were not at nutritional risk at hospital admission (using NRS-2002) developed malnutrition during hospitalisation (8). In contrast, data from a report based on a conference held in the United States reported a considerably higher rate, with 38 % of patients becoming at nutritional risk during hospital stay (44). Furthermore, it is worth mentioning that the Spanish study reported that 72 % (252/351) of the patients assessed to be at nutritional risk at hospital admission remained at nutritional risk at discharge (8).

Being at nutritional risk is common across hospital wards, with a particularly high prevalence found in older patients. A large international retrospective study (n =1385) showed that the prevalence of older patients at nutritional risk in hospitals was on average 47 % (45). In fact, the risk of being at nutritional risk was found to be 30 % greater in hospital patients aged ≥ 65 years compared to patients < 65 years (45). This increased risk is also reflected in the community. A pooled analysis of previously published datasets of community-dwelling older people (n = 964, > 65 years of age) revealed that 32 % (range: 29-52.6 %) were at nutritional risk (45).
In the developed countries, being at nutritional risk is highly related to disease (46). Specifically, the risk is high in patients with gastrointestinal, respiratory and malignant diseases (43). Indeed, rates of being at nutritional risk is found to be twice as high in cancer patients compared to patients without cancer (47).

The variations in the prevalence of being at nutritional risk both within hospitals and community settings are due to the use of different screening tools/assessment methods, age and difference in diseases and stage of disease (38). However, it seems clear that all studies point toward the same conclusion. Being at nutritional risk is very common in hospitals and communities and is of particular concern in older patients.

Table 3.1-1 Prevalence of hospitalised patients at nutritional risk in a random sample of studies published within the last 5 years.

Country	Author (year)	Study population	Patients (n)	Healthcare setting (timing)	Prevalence %	Method of assessment/screening
Europe and Island	Schindler et al. 2010 (38)	> 18 years of age	21007	Hospital (point prevalence on a single day)	52	Variety of tool used: NRS-2002[1], 'MUST'[2] and local/national tools
Italy	Lucchin et al. 2009 (39)	> 18 years of age	1284	Hospital (within 36 hours of admission)	29	NRS-2002
Portugal	Amaral et al. 2010 (40)	> 18 years of age	1144	Hospital (on admission)	36	NRS-2002
Republic of Ireland	Russel & Elia. 2012 (41)	> 18 years of age	1102	Hospital (within 72 hours of admission)	27	MUST'
Sweden	Westergren et al. 2009 (42)	> 18 years of age	1197	Hospital (point prevalence on a single day)	34	Involuntary weight loss and low BMI (BMI < 20 kg/m^2 if ≤ 69 years, BMI < 22 kg/m2 if ≥ 70 years)
Switzerland	Imoberdorf et al. 2010 (48)	> 18 years of age, medical patients	32837	Hospital (on admission)	18	NRS-2002
UK	Russel & Elia. 2012 (41)	> 18 years of age	7541	Hospital (within 72 hours of admission)	25	MUST'
Spain	Álvarez-Hernández et al. 2012 (8)	> 18 years of age	1707	Hospital (Within 48 hours of admission)	37	NRS-2002
The Netherlands	Meijers et al. 2009 (43)	> 18 years of age	8028	Hospital (point prevalence on a single day)	24	Malnutrition defined according to one of the 3 following criteria: BMI < 18.5 kg/m^2; unintentional weight loss (6 kg in previous 6 months or 3 kg in the previous month) or BMI 18.5–20 kg/m^2 in combination with no nutritional intake for 3 days or reduced intake for > 10 days

Table 3.1-1 illustrates an average of 30 % of hospitalised patients are at nutritional risk.
[1] NRS-2002: Nutritional Risk screening Tool
[2] MUST: The malnutrition Universal Screening Tool.

3.2 Consequences of being at nutritional risk

Patients at nutritional risk are at increased risk of complications during hospitalisation and delayed recovery after hospital discharge (Figure 3.2-1).
The increased risk is associated with impairment at a cellular, physical and psychological level (49).
At the cellular level, being at nutritional risk impairs the immune response, thereby increasing the risk of infection and delayed wound healing.Immunosuppression may also make an infection difficult to detect and more aggressive, rendering the infection difficult to treat (49). Physically, being at nutritional risk, i.e. having a low intake of energy and protein in combination with being sick, will promote catabolism and decrease anabolism, resulting in depletion of muscle and fat mass. The depletion of muscle mass will impact negatively on the function and recovery of all organ systems, for example gut integrity, and muscle strength and function (50). Psychologically, being at nutritional risk is associated with fatigue, depression and apathy, all of which may delay recovery due to difficulties in motivating the patient to increase nutritional intake and to be physically active in order to regain physical strength and function (49,51).

It is therefore not surprising that the rate of complications is found to be 30 % in hospitalised patients at nutritional risk compared to only 11 % in patients not at nutritional risk (1). Nor is it surprising that patients at nutritional risk experience significantly longer hospital stays than patients not at nutritional risk (1,52,53). Moreover, patients at nutritional risk also have a higher mortality rate than patients not at nutritional risk (6).

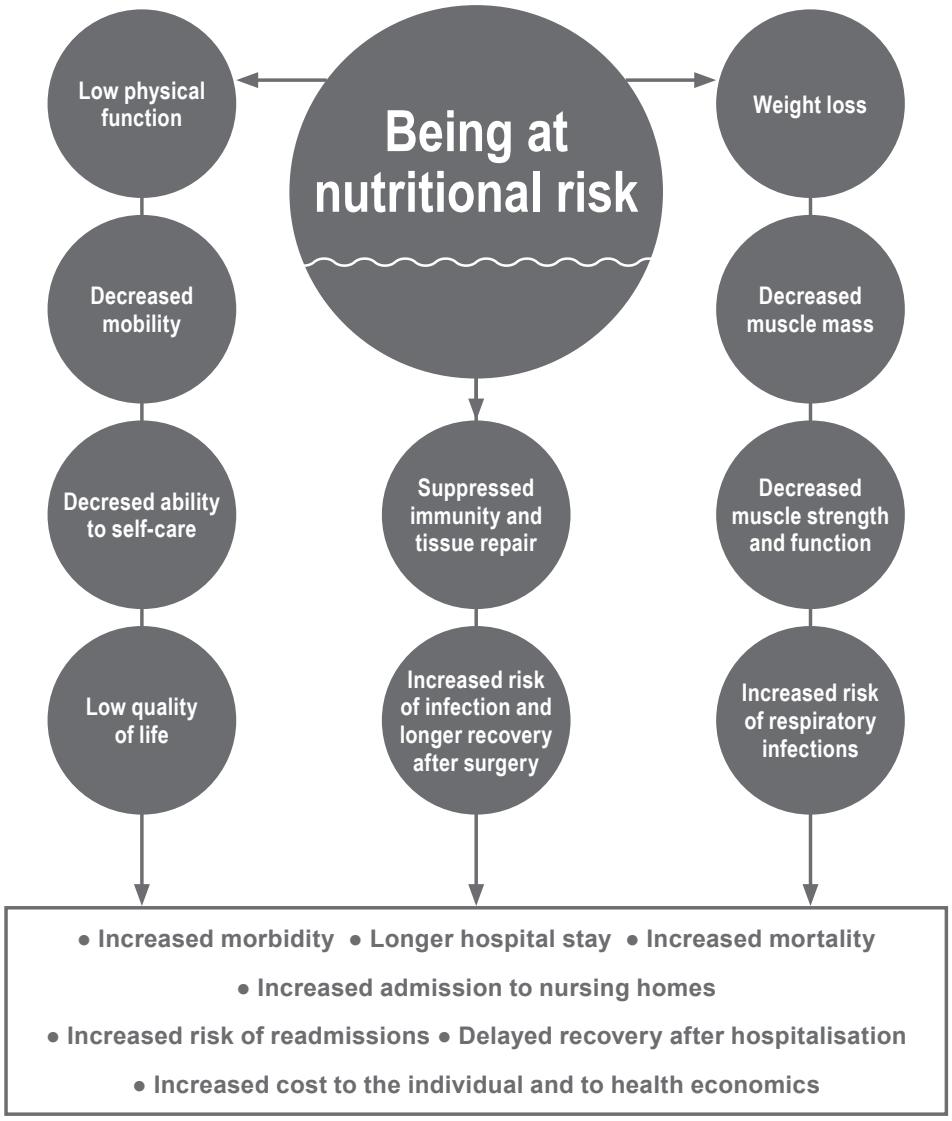

Figure 3.2-1 Consequences of being at nutritional risk(1,6,23,24,29,49,50,54)

The increased mortality is shown across a wide variety of patient groups, in medical and surgical patients, in older patients, in patients with chronic obstructive lung disease and in patients with gastrointestinal, neurological, cardiovascular and malignant diseases (6).

A large (n = 5051) multi-centre study including 26 hospitals departments (internal medicine, oncology, surgery, intensive care, gastroenterology and geriatrics) confirmed the higher risk in nutritionally at-risk patients. This study revealed a 12 % higher risk of death (12 % [189/1609] vs. 1 % [34/3374], $p < 0.001$) in patients at nutritional risk compared to well-nourished patients (1).

The increased risk of mortality appears linked to nutritional intake (9,38). Studies found that an intake below 50 % of energy and protein requirement was associated with an increased risk of dying, even after adjusting for potential confounders such as severity of disease, age and length of hospital stay (LOS) (38). In comparison, a nutritional intervention study reported a decreased risk of complications and LOS in patients at nutritional risk reaching ≥ 75 % of energy and protein requirement (22).

Older patients are particularly vulnerable to being at nutritional risk because in case of infection or trauma, rapid deterioration will occur delaying recovery of the insult (50).
Older patients also often suffer from co-morbidities which further increase the risk of complications and prolong recovery. In turn, this again leads to further deterioration in nutritional status (50). Indeed, hospitalisation *per se* is associated with loss of muscle mass in older patients, particularly if brought on by underfeeding of protein (54,55). Muscle function declines before changes in muscle mass occur (50). Decreased muscle mass therefore poses a potential threat to the ability to self-care after hospital discharge (50). In fact, thirty to sixty percentage of older patients experience functional decline, increased hospital readmissions or institutionalisation and thereby reduced QoL and autonomy after hospitalisation (6,24,25,29). In fact, a decrease in physical function in older patients, measured by daily steps after hospital discharge, was found to be the strongest predictor for readmission among known readmission risk factors (26).

Further, a prospective cohort study showed reduced ADL three months after discharge and an increased need for admissions to nursing homes during the first year after hospital discharge in older medical nutritionally at-risk patients(23). Further more, being at nutritional risk tripled mortality in older patients in hospital and after discharge(28). Therefore, sufficient nutritional treatment seems necessary not only in hospitals, but also after hospitalisation.

Being at nutritional risk is also costly for society. The estimated cost of managing patients at nutritional risk in the EU is found to be €120 billion (56).

In Germany, UK, Ireland and the Netherlands, the annual cost of patients being at nutritional risk on a national level, was estimated to be € 9 billion (2006), € 15 billion (2007), € 1.5 billion (2009) and 1.9 billion (2013) respectively (10). In Denmark, no reliable and accurate estimates of the total cost of being at nutritional at-risk in all healthcare setting are yet available.

Many studies have tried to calculate the additional cost of being at nutritional risk compared to not being at risk. A systematic review found up to a 3-fold increase in treatment costs associated with being at nutritional risk (57). An economic study from 2003 reported a mean daily expense of $228 per patient at nutritional risk compared to a mean daily expense of $138 per well-nourished patient (58). Another study conducted in 2000 illustrated that regardless of nutritional status at hospital admission, patients who deteriorated in nutritional status while hospitalised generated increased mean hospital expenses ($45,762) compared to patients who remained well-nourished ($28,631) (59).

3.3 Causes of becoming at nutritional risk

In the developed countries, the main cause of becoming at nutritional risk is disease (7). Deterioration in nutritional status during hospitalisation is of course also disease-related. However, factors within the hospital food chain unquestionably also influence patients' nutritional intake *(Figure 3.3-2) (19,60)*, including the prevailing practice for nutritional care *(Figure 2.1-1) (19)*. These factors are all interrelated *(Figure 3.3-1)*.

For example, when a disease induces catabolism and anorexia, it is imperative that nursing staff have relevant nutritional knowledge to develop and apply a targeted nutritional care plan with continuous monitoring of intake and nutritional status. Furthermore, that they reflect on these data to ensure sufficient intake of energy and protein during hospitalisation. Patients who are capable of eating orally, which the majority of hospitalised patients are, also require 'suitable' hospital food e.g. hospital food which meets patients' preferences for taste, texture and palatability, and has sufficient nutritional content.

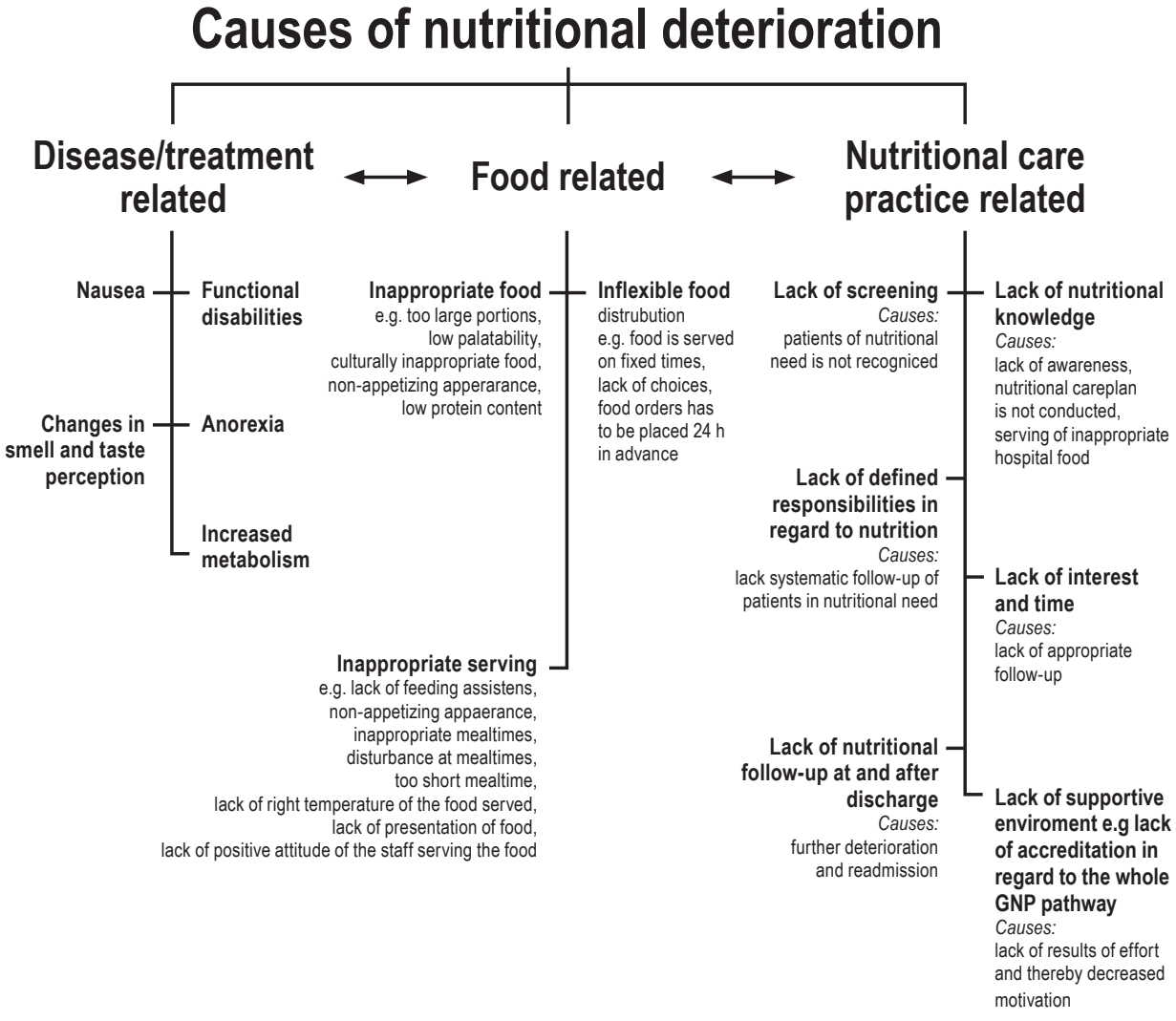

Figure 3.3-1 Causes of deterioration in nutritional status during hospitalisation (7,14,15,17,19,30,38,44,54,57,61–71).

3.3.1. Disease-related factors

Deterioration in nutritional status in hospitalised patients is closely linked to decreased appetite (19). In fact, a recent study, the NutritionDay survey (n=151666), showed that decreased appetite was the main reason for low dietary intake in hospitalised patients (72). Decreased appetite may be related to different issues within the hospital setting, e.g. feeling of insecurity and anxiety, loneliness and the offering of unpalatable food. However, in the hospital setting, lack of appetite and low dietary intake is also related to disease and treatment (7).

In situations with infection or inflammation, release of immunological factors such as appetite suppressing cytokines occurs(7). This is part of the immunological defence; yet, in regard to nutritional status it is an unfortunate pathophysiological reaction since these cytokines both decrease appetite and promotes catabolism. In turn, this may increase the nutritional requirements(7). Disease or treatment can however also affect nutritional intake in other ways. Patients with cancer may have altered taste, nausea and anorexia due to treatment whilst patients with stroke or other neurological conditions may have swallowing difficulties or problems with self-feeding (Figure 3.3-1) (7).

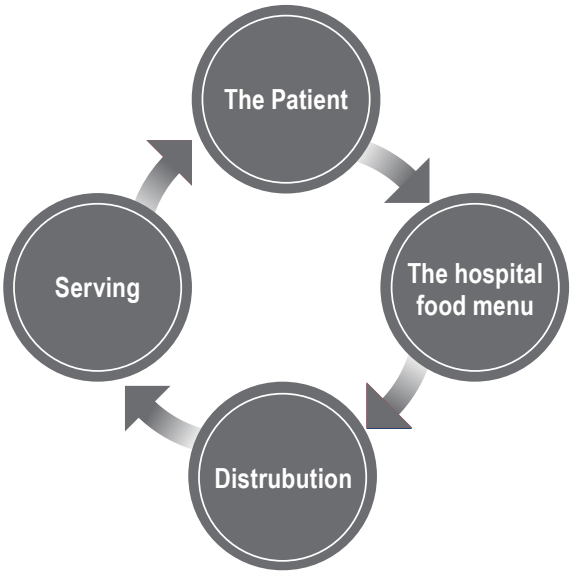

Figure 3.3-2 illustrates the food chain within hospitals. The term 'food chain' describes the whole process of catering for patients. This cycle is developed to emphasise the need to address not only the quality and palatability of food but the whole process or chain, from patient assessment, through ordering meals, to the preparation, transport, serving, and presentation of hospital food in a way which invites its consumption (75).

3.3.2. Food-related factors

Although disease may adversely impact appetite, factors related to the hospital food are also closely related to decreased appetite and low dietary intake in hospitalised patients (38). In fact, a large prospective survey (n = 975) showed that disease and treatment had little or no influence on food intake in the majority of patients who failed to reach their nutritional requirements, suggesting a potential for increasing intake of hospital food in many of these patients (62). Insufficient nutritional intake does not appear to be due to insufficient quantities of food from hospital kitchens. Rather, hospitals are often faced with a very large proportion of (up to 76%) plate waste (62,73,74). This indicates that the food served or factors within the food chain (Figure 3.3-2) may not be appropriate for promoting sufficient dietary intake in hospitalised patients.

Indeed, several factors within the hospital food chain (the hospital food menu, the distribution of the food and how the food is served) impact on dietary intake in hospitalised patients (57).

'The hospital food menu'

A review revealed that large portion sizes, culturally inappropriate food, low palatability, and non-appetising appearance, were all factors associated with decreased dietary intake (57). A comprehensive hospital survey (n=1707), found that inadequate taste and absence of choice were the most cited reasons for insufficient dietary intake (62). Appearance appears especially important for older patients because loss of taste and olfaction are common age-related functional changes (76). Disease and medication may also affect taste, making appearance even more important in the hospital setting (57).

Moreover, it seems that further efforts are needed to increase the protein content in hospital foods. Studies reveal that it is more difficult to cover protein requirements than energy requirements, suggesting that patients lack a desire for foods which are high in protein (17,19,62,63). Finding solutions to this problem is of great importance, since protein requirements are often higher in hospitalised patients' compared to healthy individuals. This is due to either old age, disease-related anabolic resistance or an increase in catabolic hormones (54,55,71,77).

'The distribution of the hospital food'

The review and comprehensive hospital survey, previously mentioned, found that lack of flexibility and lack of timing to patients' nutritional needs had an adverse effect on dietary intake (57,62). Specifically, the time-lap between the evening meal and breakfast was a cause for concern (78). A large (n=1771) cross-sectorial study revealed that an overnight fast of > 11 hours increased the risk of becoming at nutritional risk (78). Probably because this allows insufficient time between main meals to permit in-between snacks

during the daytime (78). This is also why an overnight fast of less than 11 hours is a quality indicator of GNP in municipalities in Sweden (78). Further, in the hospital setting, food often has to be ordered 24 hours in advance. This is problematic, since rapid changes in medical conditions may easily occur, rendering the food chosen unsuitable and often wasted (30).

'The serving part'

A review revealed factors such as length and timing of mealtimes, disturbance during mealtimes and lack of feeding assistants to be closely linked to low dietary intake (57). Furthermore, a large (n=309) questionnaire-based study revealed that the temperature and presentation of the food were important for increasing dietary intake (79). Similarly, the attitudes of the staff serving the food were of great importance for patients' desire to eat (80).

3.3.3. Nutritional practice-related factors

Within the hospital, insufficient implementation of a well-structured GNP (Figure 2.1-1) contributes to patients either becoming at nutritional risk or to further deterioration in nutritional status.

In many countries, nutritional risk screening is not systematically performed on admission and during hospitalisation (38). The nutritional condition of the patient is therefore unknown, and hence may be inappropriately addressed. Research further showed that even though patients were identified as being at nutritional risk, adequate nutritional care including monitoring of nutritional intake was seldom instigated (15,38).

One reason for the persistent high prevalence of patients at nutritional risk in hospitals may be lack of nutritional follow-up after discharge, the final step of the GNP. No data exist on the number of patients in need of nutritional follow-up after discharge. Two Danish studies reported that health care staff in hospitals, general practice and care homes believed that too few patients are discharged with nutritional therapy compared to the number they believed could benefit from nutritional therapy after discharge (15,65).

In Danish hospitals, factors at the organisational level have been reported to negatively affect the implementation of GNP (14,15,65–68). Among the main factors were lack of a clear description of responsibility, lack of interest, lack of nutritional knowledge, lack of patient involvement, lack of quality and choice of menus and lack of access to clinical dietitians (67–70). On a European level, reasons such as difficulties in defining individual nutritional goals and monitoring of individual nutritional intake within the daily clinical care comprised barriers to implementation (38). Moreover, within hospitals, staff advocate for an 'enabling environment' in which healthcare professionals are encouraged to translate education into clinical practice (44). A good example of the effectiveness of the latter suggestion is seen both in Denmark and the Netherlands where the rates of nutritional screening have increased after the governments made nutritional risk screening mandatory at hospital admission and a part of the accreditation criteria for hospitals (15,44).

Knowledge of reasons for not providing nutritional follow-up after discharge is limited. A Danish study found that factors such as lack of guidelines, lack of time, lack of transparency regarding economy and workflow and lack of assistance from experts were barriers for implementing nutritional discharge planning in Danish hospitals (65). A questionnaire-based study conducted in the USA, reported that insufficient knowledge of community services among discharge case managers was a barrier for nutritional discharge planning (61).

3.4 Evidence for an effect of nutritional care after hospital discharge

The last step of GNP, nutritional follow-up after discharge, is considered important for securing recovery after hospitalisation, particularly in older patients. However, there is limited knowledge of the effect of this interventional part of GNP. (27). One review examined the evidence for an effect of intervening after hospital discharge. The review included 6 randomised controlled studies assessing the benefits of ONS given after hospital discharge to older patients at nutritional risk. A narrative summary indicated a positive effect on energy intake and protein intake. Further, in compliant patients, BW increased. The effect on clinical outcomes was however limited. Physical function increased in two studies investigating this outcome, however the clinical relevance of the observed changes was not discussed. Moreover, meta-analysis was not possible due to different measures for assessing physical function (HGS and Bartel Index). No effects were found on other relevant clinical outcomes (re-admissions, survival, QoL and morbidity). Further, two studies reported adverse-effects in the form of gastrointestinal disturbances (27).

The limited effect on clinical outcomes may have been due to inadequate statistical power to detect an effect. The included studies all had high drop-out rates (up to 44%). Further, in five of the studies, the duration of the nutritional intervention was only four to eight weeks, which may have been too short an intervention to induce an effect (27). In comparison, young healthy subjects exposed to 24 weeks of semi-starvation took more than six months to recover physical function (51). Further, in two of the six studies, being at nutritional risk was not an inclusion criteria; thus the effect of the intervention might have been diluted (27).

Last but not least, the relatively low level (38-67 %) of compliance to ONS may have compromised the nutritional intervention. It could be speculated whether individualised dietary counselling (including: individual goal setting, advice on energy- and protein rich food or fortification of food) in combination with ONS might have produced additional benefits. This approach may represent an opportunity to personalise the nutritional plan and offer greater variety and therefore in turn help to overcome problems of low compliance and taste fatigue, which often arise when using ONS as a single nutritional intervention (20,81–83).

Apparently, there are no systematic reviews of the effect of individual dietary counselling (+/- ONS) after hospital discharge. A Cochrane review has however, examined the effect of dietary advice for adults at nutritional risk in general (84). The review compared dietary advice to no advice (usual diet), to prescription of ONS, to dietary advice plus ONS and dietary advice plus supplements if required to no advice or supplements(84). The authors concluded that there was evidence of variable quality suggesting that dietary advice, given with or without ONS, improves BW and body composition. Meta-analyses also revealed a significant effect on HGS, however, no evidence for a beneficial effect was found on other relevant outcomes (morbidity, QoL and mortality)(84). Unfortunately they did not compare dietary advice plus ONS to ONS alone which may be a more realistic comparison in relation to daily nutritional practice in Danish hospitals.

Based on the evidence presented, dietary counselling may represent a superior strategy for nutritional intervention after hospital discharge, especially if individualised dietary counselling is provided (85). Individual dietary counselling given post discharge also poses the possibility to be able to follow-up on the patients' in-hospital nutritional plan. This would make the patient's nutritional pathway more coherent and, potentially, the in-hospital efforts more worthwhile (86).

3.5 Effect of food-based interventions in hospitalised patients

Hospital food is applicable to the majority (85 %) (20–22) of hospitalised patients and is recommended as “the first line of defence”, whenever possible, for treating patients with low nutritional intake (31). This is due to the associated safety and low cost compared to the use of enteral and parenteral nutrition. Moreover, it is also related to social and psychological aspects of maintaining aspects of daily life (87–89). However, hospitalised patients often have insufficient dietary intake (17,38). Many studies have explored reasons for low food intake (Chapter 3.3). Interestingly, only a small number of controlled studies have investigated whether hospital food alone can improve energy and protein intake in hospitalised patients in general (Table 3.5-1) (90–93).

The main approach investigated has been to increase the energy density of the hospital food using ingredients naturally high in fat, e.g. butter, crème and oil (90,92,93), with only one study using skimmed milk powder (91). Overall, these interventions led to increased energy intake, however, in all but one small study (n=10) (92), no significant increase in protein intake (90,91,93).

Importantly, only one study investigated the effect on clinically relevant outcomes. Olin et al. reported significantly increased BW and a significant association between increased physical activity and increased energy intake (93). However no overall difference in functional condition was found between groups (93). It should be noted that three of the four studies were non-randomised (90,92,93) and none of the studies reported blinding of outcome and data assessors, which limits the internal validity of the studies. The results of three of the studies (90,92,93) could also be biased due to the risk of small study effects (94). Additionally, the studies did not differentiate between well-nourished patients and patients at nutritional risk, making it difficult to interpret the clinical benefits for patients at nutritional risk.

In conclusion, the results of the hospital food intervention trials seem promising for increasing energy intake in hospitalised patients. However, bearing in mind that the studies were not stratified for nutritionally at-risk patients and three out of four studies exclusively included patients from geriatric or rehabilitation wards, the evidence base appears insufficient to draw firm conclusions, particularly in regard to nutritionally at-risk patients in general. Further, the results revealed a need for an increased focus on increasing protein intake as well as energy intake. There is also a need for research that examines the effects of flexible access to ordering food, palatable and appetising food for nutritionally at-risk patients, securing the right temperature of the food and other factors of importance for promoting appetite in hospitalised patients (Chapter 3.3.2). Finally, no of studies involved the target group in the development of special hospital food menus and this seems rather crucial for success.

Table 3.5-1 Controlled food-based interventions within the hospital setting

First author (year)	N	Mean age (year)	Setting, country	Study design	Intervention (duration)	Nutritional at-risk	Outcome	Significant effects
Olin et al. 1995 (93)	36	82 (±1)[3]	Long-term geriatric care hospital, SE	Cross-over study, non-randomised	Energy-enriched hospital food using natural energy rich ingredients (duration: 6 weeks)	Not assessed	Volume of food, energy intake, body weight, physical function	Increased energy intake, increased body weight Increased physical activity
Gall et al. 1998 (91)	143[1]	Female: 74 (±1.5)[3] Male: 61 (± 2)[3]	Hospital, UK	Non-randomised control study	standard hospital diet + supplement of dishes fortified with skimmed milk powder (duration: 3 days)	Not assessed	Energy and protein intake	Energy deficit lower, increased energy intake
Barton et al. 2000 (90)	35	NA[2]	Elderly hospital rehabilitation ward, UK	Cross-over study, randomised	Reduced portion size fortified menu (duration: 14 days)	Not assessed	Food waste, food intake	Lower food waste, Increase energy intake
Lorefält et al. 2005 (92)	10	Mean: NA[2] (77-87 years of age)	Elderly hospital rehabilitation ward, SE	Cross-over study, non-randomised	Energy-and protein using natural energy rich ingredients (duration: 3 days)	Both well-nourished (n=3) and at risk (n=7)	Energy and nutrients	Increased energy, protein and fat intake and some nutrients

[1] *62 patients in the IG*
[2] *Data not available*
[3] *SEM*

3.6 The missing gaps

GNP is recommended to optimise hospitalised patients' nutritional status. In Denmark, there are improvements in nutritional practice. However, patients at nutritional risk still lack sufficient energy and protein intake and the high rate of patients being or becoming at nutritional risk seems to persist, indicating that further work during hospitalisation is necessary to improve implementation of GNP (15,17,95). Specifically, the final step of the GNP process, nutritional care after hospital discharge, has so far been an overlooked area. This step is important, particularly for older patients, since a high number of patients remain at nutritional risk at discharge (8). If action is not taken after discharge, older patients are at increased risk of adverse effects (8).

Furthermore, in order for the GNP-procedure to achieve significant clinical benefits, there is a need for further development of appropriate 'tools' within the GNP to overcome for example low appetite. In other words, a successful nutritional plan cannot be achieved if the food available does not match the patient's food requirements and preferences. Currently, there is, however, little research into the development of appropriate hospital food for patients at nutritional risk.

4.Presentations of studies

This PhD-thesis comprises three studies which investigated two different aspects of GNP. *Study I* and *II* investigated how to increase dietary intake using hospital food. *Study I* was a pilot study preceding *Study II*. Therefore the methods of these two studies are similar. The third study *(Study III)* investigated the effect of individualised dietary counselling following hospital discharge on physical function. All three studies exclusively included patients at nutritional risk.

Table 4-0 gives an overview of the methods used in the three studies.
A more detailed description of methods, results, and discussions are presented separately in the following chapter and in full in the articles in appendix B *(study I)*, C *(study II)*, D *(study III)*.

Table 4.0-1 Overview of study participants, designs, settings, outcomes and interventions in *Study I, II* and *III*

Study	Participants	Design	Setting	Outcome	Intervention
I.	Patients at nutritional risk assessed by NRS-2002 (N = 79)	Historical controlled study	Hospital	Primary: Number of patients reaching ≥ 75 % of energy and protein	IG received a novel hospital food concept: 36 energy dense small dishes, served a la carte 24 h a day by the ward staff. The menu was a supplemental offer to the standard hospital food service. CG received the standard hospital food service (buffet style serving system: 3 main meals + 2-3 in-between meals e.g. snacks or ONS)
II.	Patients at nutritional risk assessed by NRS-2002 (N = 81)	Randomised controlled study	Hospital	Primary: Number of patients reaching ≥ 75 % of energy and protein Secondary: Mean energy, protein intake, changes in BW, physical function measured by HGS, LOS	IG received a protein-fortified hospital food concept: 23 energy and protein dense small dishes (minimum 6 grams of protein per dish), served a la carte from 7 AM to 8 PM by the kitchen staff. The menu was a supplemental offer to the standard hospital food service. CG received the standard hospital food service (buffet style serving system: 3 main meals + 2-3 in-between meals e.g. snacks or ONS)
III.	Older (> 60 y) patients at nutritional risk (N = 729)	Systematic review and meta-analysis	Following hospital discharge	Primary: Physical function as assessed in the included study Secondary: Energy and protein intake, nutritional status, QoL, hospital readmissions and mortality	Individualised dietary counselling following hospital discharge vs. standard care

Table 4.0-1 gives an overview over the three studies.

Study II differs from Study I in study design, the use of a high quality protein powder, the use of kitchen staff instead of ward staff to serve the dishes, the time frame in which the dishes could be ordered, the use of a run-in period in which hospitalised nutritionally at-risk patients participated in taste-sessions to secure the quality of taste and appearance of the protein-fortified menu. A more detailed description of Study I, II and III is shown in chapters 4.1, 4.2, 4.3 and appendix B, C and D.

IG: intervention group, HCG: historical control group, CG: control group, ONS: oral nutritional supplements, HGS: hand grip strength, LOS: length of hospital stay, QoL: quality of life.

4.1 Study I

Aim

To develop a novel hospital food concept for patients at nutritional risk and to examine whether this hospital food concept would increase energy and protein intake in nutritionally at-risk patients.

Methods

Design
A historically controlled intervention study.

Setting
Department of Gynaecology, Orthopaedic Surgery and Internal Medicine at HUH, Denmark.

Inclusion criteria
Nutritionally at-risk patients according to NRS-2002, aged 18 years or more, proficient in Danish, sufficient cognitive functioning, well-functioning gastrointestinal tract and an anticipated length of hospitalisation of 3 days or more.

Exclusion criteria
Terminal patients, dysphagia, food allergy or intolerance, and patients who exclusively received enteral or parenteral nutrition.

Outcomes
The primary outcome was the number of patients reaching a minimum of 75 % of their energy and protein requirements.

The intervention group (IG)
The IG received a novel hospital food concept which was developed in collaboration with RDs, chefs and former patients. The menu consisted of 36 small energy dense dishes with soft texture and prepared as a supplemental offer to the standard hospital food service. The dishes were served a la carte 24 h a day and could be ordered by telephone either by patients themselves or by ward staff. The dishes were appetisingly served (topped with different kinds of garnish) and delivered ready to eat within 20 min. after an order was placed. The dishes were served by the ward staff. No individualised nutritional planning occurred, and patients did not receive dietary counselling during the intervention.

Energy and protein intake were calculated as the mean intake of 3 days from inclusion.

Historical control group (HCG)
Historical nutritional data was obtained from an observational study of nutritionally at-risk patients (assessed by the NRS-2002) (17).
The HCG patients had been admitted to the same departments as those participating in the present study. The HCG had received the standard hospital food service.

Nutritional intake was quantified as in the present study.

Power calculation
A previous observational study conducted at HUH was used to calculate sample size (17). In this study 44 % of patients at nutritional risk achieved an energy intake ≥ 75 % of requirement. For 70 % of the patients to reach ≥ 75 % of energy requirement in the IG and to reach a power of 90%, 39 patients were required for the lower limit of the confidence interval to be above 44%.

Results

Sixty-nine patients matched the inclusion criteria and were invited to participate, 17 refused to participate.

Twelve patients withdrew from the study after inclusion, 40 patients (72.5% women), above 70 years of age (on average) completed the study (11 orthopaedic patients, 7 gynaecological patients and 22 medical patients).

A comparison of patient characteristics between groups revealed that the two groups were similar except for an uneven representation of the number of patients recruited from the participating wards (Appendix B, Table 2).

No significant difference between groups was seen in regard to percentage of patients achieving at least 75% of their energy and protein requirements (Table 4.1-1).

Table 4.1-1 Number of patients achieving ≥ 75 % of energy requirements

Outcome	IG	HCG	P- value
Number of patients (%) receiving ≥ 75 % of energy requirements	55 %	44 %	P = 0.18
Number of patients (%) receiving ≥ 75 % of protein requirements	17,5 %	28 %	P = 0.17

IG: intervention group, HCG: Historical intervention group

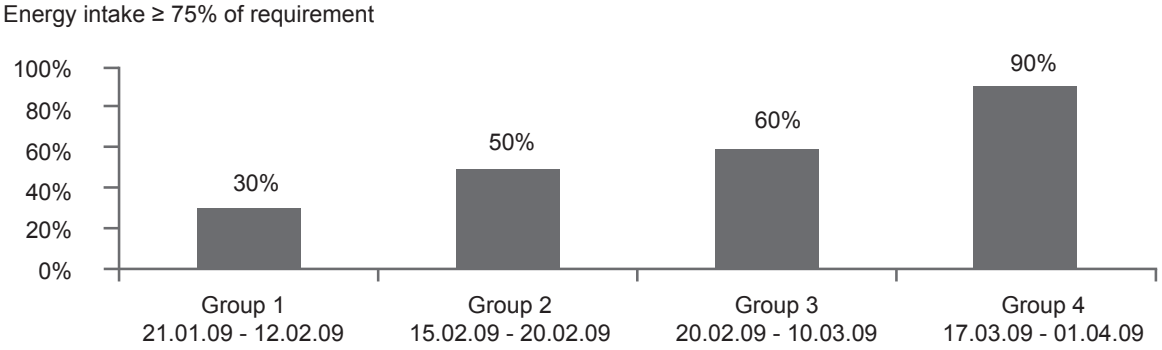

Figure 4.1-1 reveals a significant time gradient in energy intake (p = 0.001). Patients who were included later on in the study had a higher energy intake compared to those who were included earlier. Figure 4.1-1 shows energy intake when patients are divided in groups of 10, according to their time of enrolment in the study. In group 1, 30 % of the patients reached ≥ 75 % of energy requirements, in group 2, 50 % reached ≥ 75 % of energy requirements etc.

The mean (SD) energy and protein intake contributed by the intervention menu was 26.6% (10%) and 19.5% (8%) of the intervention patients' total mean energy and protein intake.
A significant time gradient in energy intake ($P < 0.001$, $r = 0.53$) was present (Figure 4.1-1).
When adjusting for BMI, age, total nutritional risk score and type of ward, the time point of inclusion remained significantly associated with energy intake ($P = 0.001$).
The intervention menu contributed significantly to the increase in energy intake ($P < 0.03$).
No significant time gradient was seen in protein intake.
The dishes were mainly ordered at lunch time (from 11.00 AM to 02.00 PM) and around dinner (from 05.00 PM to 06.00 PM). The dishes were only ordered 4 times after 10.00 PM.

Discussion

No significant difference between groups was seen in regard to percentage of patients achieving at least 75% of their energy and protein requirements. However, a significant upward trend in overall energy intake from the intervention menu during the course of the study was found. This may be explained by the so-called 'learning curve', according to which the ability to perform a given task increases over time (96). The significant time gradient suggests that nursing staff became more aware of the possibility of ordering (and how to order) during the course of the study. In future hospital food-intervention studies, a run-in period should therefore be considered.

Another reason for not reaching the target of success may be that ward staff was engaged in competing responsibilities and therefore not able to serve the food when ready, resulting in the food being served at an inappropriate temperature.

Only 17.5% of patients reached their minimum requirements for protein. Reasons for this low protein intake may have been a too large variation in protein content in the dishes. Further, all the patients' favourite dishes, with the exception of one, were relatively low in protein content (1.4 to 4.6 grams of protein per dish). Additionally, on average, the patients only ordered 2 dishes per meal and not as expected 3 dishes, implying that the protein density of each dish needed to be much higher to be able to meet the protein requirements of the target group.

Furthermore, the supplemental intervention menu was on demand 24 h a day, since this has been shown to increase energy and protein intake (97). However, a 24 h access appears to be unnecessary as orders after 10.00 PM occurred only 4 times during the study period.

Finally, and in agreement with previous studies (90,91), energy dense hospital food increases energy intake but not protein intake. Protein fortification may be necessary to increase both energy and protein intake.

Internal and external validity

The study suffered from risk of bias and to some extent also risk of confounding. In regard to external validity some limitations were also present.

Selection bias

The use of a HCG increased the risk of selection bias in the present study. There was a significant difference in the number of patients included from the participating departments, implying that there may have been differences in diseases between groups.
A borderline significant difference in baseline nutritional status was also observed. This could have affected the results negatively since low nutritional status is a known risk factor for decreased appetite. An imbalance between known risk factors between the groups increases the risk of unknown factors influencing the results of the study (98). Therefore the risk of

potentially important factors influencing the results of this study is deemed at least moderate; however it is not possible to make any conclusions in relation to under or over estimation of the results.

Performance bias
Performance bias refers to systematic differences between groups in the care that is provided (98). Blinding of study participants and personnel reduces this risk (98). It is however very difficult to mask a food-intervention as conducted in the present study and this increases the risk of performance bias.

Detection bias
Detection bias refers to systematic differences between groups in how outcomes are determined. Blinding of outcome assessors and data assessors reduces this risk (98). However in the present study we only investigated food intake as an outcome, making it difficult to blind the outcome assessor. Furthermore, the data assessor was not blinded. Therefore, the present study is at risk of detection bias.

Attrition bias
Attrition bias refers to systematic differences between groups in withdrawals from a study (98). Twelve patients (23 %) withdrew from the study after inclusion (four died, three were discharged before sufficient data were collected and five decided to withdraw as they did not wish to continue participation). This poses a potential risk of attrition bias and thereby limits the strength of the conclusions of the study.

Selective outcome reporting
Selective outcome reporting occurs if analyses with statistically significant differences between groups are reported and analyses with non-significant differences are not (98). All pre-specified outcomes, non-significant as well as significant is reported in the present study. Therefore we do not consider the present study to be at risk of selective outcome reporting.

Confounding
The present study is at risk of confounding due to lack of randomisation. Confounding may occur if exposures in two groups differ, making it difficult to determine whether any differences in outcomes are due to confounding factors rather than the interventions. Lack of randomisation may increase the risk of overestimation of results (98), however in the present study it is not possible to make any conclusions in relation to under or over estimation of results.

External validity
External validity may be limited in the present study due to a relatively small sample size and the high frequency of patients declining participation (24.5%) (99). Further, a higher percentage of women were included (72.5%); probably due to recruitment of patients from the department of Gynaecology. This may limit the extent to which results can be extrapolated to male patients. Furthermore, included patients were generally older, and the degree to which our results may be generalised to a younger patient population may therefore be questioned. Nevertheless, considering that the eligibility criteria were not highly selective, we believe the results of this study can be transferred to older nutritionally at-risk hospitalised patients in DK as well as in other countries (99).

The exact dishes of the concept may not be transferrable to other cultures since the dishes were developed in collaboration with ethnic Danish patients. Regardless, the underlying principle of the supplementary novel hospital food concept, the use of small, soft, appetising, and energy dense dishes served a la carte, is transferrable.

Key points
The study suffered from limitations to internal and external validity. However, bearing these limitations in mind, we conclude that the supplemental novel hospital food concept seemed able to increase energy intake in nutritionally at-risk patients. However, to secure sufficient protein intake in nutritionally at-risk patients, the protein content of the menu needs to be optimised, possibly by using protein powder fortification. Further, to secure right timing and temperature when serving the dishes, the use of kitchen staff instead of ward staff may also be considered. Moreover to address start-up difficulties, a run-in period may be necessary. Finally, a 24 h a la carte service appears unnecessary. The results of the hospital food concept also needs confirmation in a randomised controlled trial.

4.2 Study II

Aim

To investigate the effect of a protein-fortified hospital food concept on energy and protein intake in nutritionally at-risk patients. The intervention was adjusted in accordance with the findings and experiences obtained in *Study I*.

Methods

The methods of *Study I* and *Study II* are similar and overview of the differences between the studies is apparent from Table 4.0-1.

Design

A stratified block-randomised controlled trial. After a run-in period of 5 weeks, eligible patients were randomly assigned to the intervention or control group using stratified block randomisation according to hospital wards. Patients were randomised using sealed, opaque envelopes with a total of nine blocks each consisting of 10 envelopes.

Setting

Departments of Oncology, Orthopaedics Surgery and Urology at HUH, Copenhagen, Denmark.

Inclusion and exclusion criteria

As in *Study I*.

Intervention

Intervention group (IG)

The IG received a hospital food concept which was adjusted according to the findings in *Study I*. The favourite dishes were selected from *Study I* and fortified with a high quality protein powder. RDs, chefs and nurses invested considerable time and effort into achieving the right flavour, texture, volume and a minimum content of 6 g of protein in each dish. Further, to incorporate the preferences for taste and appearance of the target population, a convenience sample of patients meeting the inclusion criteria for the RCT pre-tested the protein-fortified intervention menu in a 5-week run-in period. The dishes were on order from 07.00 AM to 08.00 PM and served by a trained group of kitchen staff. The protein-fortified hospital food concept was served a la carte within 20 minutes from an order was placed and was supplemental to the standard food service.

Control group (CG)

The CG received the standard hospital food service. The standard hospital food service offers three main meals (breakfast, lunch, and dinner) served from a buffet. Two main diet types are available: the 'hospital diet' for nutritionally at-risk patients and the 'normal diet' for well-nourished patients. The 'hospital diet' has a higher energy and protein density than the 'normal diet'. The CG received the 'hospital diet'. The three main meals are intended to provide 50–75% of nutritional requirements. The remaining requirements are to be covered by three in-between meals (e.g. microwaveable meals, snacks [e.g. cakes], biscuits with cheese, ice cream and/ or beverages [e.g. ONS]). In-between meals are served either by the buffet-staff or nursing staff.

Outcomes

Primary outcome: the percentage of patients reaching ≥75% of their protein and energy requirements. Secondary outcomes: mean difference between energy and protein intake, weight adjusted energy and protein intake, change in BW, HGS and LOS.

Nutritional intake was quantified as in *Study I*.

Power calculation

Power calculations suggested that 40 patients in each group were required to detect a significant difference in the percentage of patients achieving ≥75% of their energy and protein needs with a power of 80% and a 5% two-sided significance level.

Results

84 patients were randomly assigned to the supplemental protein-fortified hospital food concept (n = 44) or standard food service (n = 40). Of these, 81 patients completed the trial, 41 intervention and 40 control patients (a completion rate of 96%).

Baseline characteristics were comparable in intervention and control patients (Appendix C, Table 2). Also the number of patients diagnosed with malignant diseases requiring medical treatment known for reducing appetite, was balanced between groups (25 in each group) (100).

Table 4.2-1 shows the results for the primary and secondary outcomes. Overall the protein-fortified hospital food concept had a significant positive impact on protein intake and on weight-adjusted energy intake compared to the standard hospital food service. No significant differences between groups were found with respect to BW, HGS and LOS. The supplemental protein-fortified menu accounted for 30% of the energy intake and 40% of the protein intake.

An exploratory analysis revealed a significant positive effect of achieving ≥75% of energy requirement on stability or increase in HGS (P = 0.015). Another explorative analysis showed a highly significant association (P< 0.0001) between reaching ≥ 75 % of protein target and reaching ≥ 75 % of the energy target, indicating that if the protein target is met, so is the energy target. It should be noted that the explorative analyses were performed on non-randomised material.

The most frequently ordered dishes were sweet or soft dishes such as soup, buttermilk dessert, mild fromage, confections of marzipan and mashed potatoes (Table 4.2-2). Patient preferences did not appear dependent on whether protein powder was added as the preferred dishes all contained protein powder.

Table 4.2-1 Primary and secondary outcomes

	Intervention Group (n = 41)	Control Group (n = 40)	Risk Ratio (95 % CI)	Mean Difference between IG/CG (95 % CI)	P-value
Primary Outcome					
Coverage of > = 75 % of nutritional requirements					
Energy [n(%)]	31 (76)	28 (70)	1.1 (0.8;1.4)		0.57[A]
Protein [n (%)]	27 (66)	12 (30)	2.2 (1.3;3.7)		0.001[A]
Secondary Outcome					
Mean energy and protein intake					
Energy [kJ (SD)]	5843 (1660)	5149 (1832)		693 (-80;1466)	0.08[B]
Protein [g (SD)]	53 (16)	43 (17)		9.6 (2;16)	0.011[B]
Mean intake kJ/kg					
Energy [kJ/kg (SD)]	103 (39)	82 (33)		20 (5;36)	0.013[B]
Protein [g/kg (SD)]	0.9 (0.4)	0.7 (0.3)		0.2 (0.1; 0.4)	0.003[B]
Mean difference in Body Weight (BW)[C]					
BW[kg(SD)][D]	0.4 (2.6)	-0.4 (1.8)		- 0.8 (-1.9;0.3)	0.17[B]/G0.33[G]
Mean difference in Hand Grip Strength (HGS)[E]					
HGS [kg(SD)][F]	-0.1 (2.9)	-0.4 (4.3)		-0.3 (-1.9;-1.4)	0.76[B]/0.95[G]
Length Of hospital Stay (LOS)[H]					
LOS1[I] [d (SD)]	15(10)	14 (8)		1.8 (-2;6)	0.38[B]
LOS2[J] [d (SD)]	10(8)	10 (8)		0.6 (-3;4)	0.73[B]

[A] Pearsons Chi²- test
[B] T-test
[C] n= 66 (IG: 37)
[D] Mean difference from baseline to day 3. Later follow-up data (> 3 days) is not presented because of many missing data
[E] n = 76 (IG = 41)
[F] Mean difference from baseline to day 3. Later follow-up data (> 3 days) are not presented because of many missing data
[G] Result adjusted for baseline using Univariate Analysis of Variances
[H] n = 79 (death: IG = 1 and CG = 1)
[I] LOS1 = days from admission to discharge
[J] LOS2 = days from inclusion to discharge

Table 4.2-2 The menu of the protein-fortified hospital food concept and a ranking of the most frequently ordered dishes

Menu	Portion size	Energy	Energy density	Protein	Orders
	g	kJ	kJ/g	g	Ranked[1]
Breakfast dishes					
Omelette with bacon	60	699	11.7	9.1	4
Breakfast muffin with butter, cheese and jam	100	1518	15.2	11.5	5
Ryebread porridge with fresh vanilla cream	90	371	4.1	7.4	6
Soups					
Clear soup with vegetables, meatballs and dumplings	79	195	2.5	6.9	1
Classical mushroom soup	75	468	6.2	8.2	5
Fish dishes					
Terrine of smoked eel	60	555	9.3	7.6	4
Baked salmon with egg coleslaw, hazelnuts and olive tapenade	70	763	10.9	8.9	4
Slightly smoked trout seasoned with egg salad and fresh chervil	55	540	9.8	8.0	5
Meat dishes					
Meat loaf with game sauce and cranberries	73	448	6.1	7.6	4
Meat balls of veal with stewed cabbage and bechamel sauce	55	451	8.2	6.5	4
Crispy fried fish crépine with Jerusalem artichokes in cream sauce	75	720	9.6	7.5	5
Chicken sticks with peanut butter	55	739	13.4	7.9	5
Side dishes					
Mashed sweet potatoes with onion and bacon	68	658	9.7	6.4	3
Torta di risotto with fried mushrooms, herbs and lemon peel	47	412	8.8	7.7	5
Warm potato omelette with a compote of pickled red onions	50	537	10.7	6.1	5
Baked cauliflower cream with roasted nuts and pickled cucumbers	60	389	6.5	7.1	5
Mashed root vegetables with browned butter	75	628	8.4	6.1	5
Desserts					
Chocolate confection of marzipan and nougat	52	1028	19.8	6.3	2
Crunchy apple cake with peel of orange	90	815	9.1	7.3	2
Mild fromage with cream and chocolate	68	623	9.2	7.6	3
Buttermilk dessert with lemon and small cookies	100	835	8.4	6.9	3
Hot chocolate with whipped cream	110	801	7.3	6.2	4
Ice cream of avocado with fresh fruit	70	772	11.0	7.1	5

Table 4.2-2 gives an overview of the menu including, portion size, energy density, protein and energy content of all dishes.
[1]The dishes are ranked according to how often the dishes were ordered. Ranking order: 1 = dishes ordered > 50 times, 2 = dishes ordered ≥ 40 - < 50 times, 3 = dishes ordered ≥ 30 - < 40 times, 4 = dishes ordered ≥ 20 - < 30 times, 5 = dishes ordered ≥ 20 - < 30 times, 6 = dishes ordered < 10 times.

Discussion

The supplemental protein-fortified hospital food concept significantly increased the number of intervention patients achieving ≥75% of their protein requirements. With a NNT of three for one patient to achieve ≥75% of their protein requirements, and considering that the protein-fortified intervention menu accounted for 40% of the protein intake, we consider the protein-fortified hospital food concept a relevant and feasible intervention for hospitalised patients at nutritional risk.

The percentage of patients achieving an energy intake ≥75% of energy requirements did not differ between groups. It is possible, that the increased focus on nutritional intake in the control group, as a result of the registration of nutritional intake, may have influenced the awareness of food intake in control patients and thereby increased their energy intake. This is commonly referred to as 'The Hawthorne effect' or "the observer effect". This is a phenomenon where individuals shortly improve or modify an aspect of their behaviour in response to their awareness of being observed (101). It is argued that "the observer effect" on average can cause a 50–63% increased effect (102). It will however decrease over time, but it can take up to eight weeks; indicating that the present intervention (maximum seven days) was too short to control for this effect (102).

The increase in protein intake in nutritionally at-risk hospitalised patients in our study points towards the value of protein fortification. Previous studies in similar settings using only energy dense hospital food have only been able to increase energy intake (90,91,93).

No differences between groups were found in regard to BW, HGS and LOS primarily due to lack of power. Indeed, the explorative analyses indicated that the intervention might have affected HGS positively if more patients had been included. An increase in BW in the IG was not to be expected due to the short-term intervention and also due to an average intake of around 100 kJ/kg-1. A factor of around 1.3 multiplied with basic metabolic rate, including an activity factor i.e. around 140-150 kJ/kg-1 is reported necessary to increase BW (60).

Other reasons for the lack of effect on HGS and LOS could be the short-term intervention (3-7 days) and, possibly, an insufficient average intake of protein ($0.9g\ kg^{-1}$) to counteract the anabolic resistance often present in older and sick patients (55,71,77,103). Finally, lack of physical training (104) and low level of vitamin D (105–108) may have diluted the effect of the nutritional intervention.

Even though the results of the present trial are promising, we need to continue to set even higher standards so that more hospitalised patients achieve at least their minimum energy and protein requirements. ONS is reported to be effective in increasing energy and protein intake in hospitalised patients (6). Surprisingly, in the present study, only seven patients received ONS. By supplementing the protein-fortified hospital food concept tested in the present study with two cans of protein and energy rich ONS a day, a further increase in the percentage of patients reaching ≥ 75% of their energy and protein requirements may be reached. ONS may however alone be insufficient or inappropriate for some patients as compliance in the hospital setting is found to be as low as 37 % (109). Another approach could be to supplement the protein-fortified hospital concept with dietary counselling by a RD including individual goal setting and tailored advice, on symptoms and lifestyle and motivational conversations to reach the nutritional goal. Using dietary counselling may offer patients greater variety and flexibility than using ONS alone. This could possibly increase patient compliance. In a study of COPD patients, compliance with dietary advice was 86 % (81). Further, dietary counselling may also allow for change in dietary habits that may persist beyond discharge and thus result in maintenance of any benefits achieved in hospital. Involving RDs in the in-hospital strategy may also, if they are included in discharge planning, facilitate identification of patients in need of nutritional intervention after hospital discharge. Further, if food fortification is to be part of a nutritional follow-up home plan, dietary counselling by a RD appears important. A leaflet alone on "how to fortify food" has been shown to be insufficient (81).
It is however, important to recognise that causes of becoming at nutritional risk often are multifactorial (76). Therefore to increase the rate of patients reaching ≥ 75 % energy and protein requirement a multidisciplinary (e.g. doctors, nurses, occupational therapists, physiotherapists and RDs) approach may be necessary (110).

Internal and external validity

The study suffered from some risks of bias and limitations to the external validity.

Selection bias
Stratified block randomisation was used to allocate the interventions. Block randomisation is a commonly used technique in clinical trials to achieve balance in the allocation of participants to treatment arms, especially when the sample size is small (98).
A disadvantage of block randomisation is that the allocation of participants may be predictable and result in selection bias. Selection bias may be reduced by the use of random block sizes, which increases the likelihood of the person randomising participants, remain blinded to the next allocation. There were no systematic differences between the intervention and

control groups in baseline characteristics, suggesting that successful randomisation was achieved. The possibility of the influence of unknown factors affecting the results due to selection bias is therefore deemed to be low, but can, however, not be completely ruled out.

Performance bias
The study is at risk of performance bias due lack of blinding of participants and ward staff (98). Indeed, the increased energy intake seen in the control group indicates that performance bias may be present and may have diluted the effect of the protein-fortified hospital food concept on energy intake.

Detection bias
The study also suffers from risk of detection bias since the outcome assessors for the primary and secondary outcomes were not blinded (98). The data analysis was blinded, which to some degree minimised the risk of detection bias, thereby increasing the strengths of the conclusions of the study.

Attrition bias
Three patients from the IG were lost to follow up post-randomisation and before receiving the intervention; two due to early discharge and one died. This may pose a small risk of attrition bias, however overall the risk is deemed low due the balanced baseline characteristics of the remaining included patients and due to the small number of patients lost to follow-up (98). We do therefore not consider the study to be at risk of attrition bias.

Selective outcome reporting
The risk of selective outcome reporting is not present in this study as we have reported all pre-specified outcomes, non-significant as well as significant (98).

External validity
The external validity of *Studies I* and *II* is comparable. Therefore, we believe the results of this study can be transferred to older (> 60 year) nutritionally at-risk hospitalised patients in Denmark as well as in other countries.

Key points
The supplementary protein-fortified hospital food concept had a significant positive impact on overall protein intake and on weight-adjusted energy intake compared to the standard hospital service. This indicates that the protein-fortified hospital food concept can be used as a relatively simple and effective strategy for increasing protein and energy intake in hospitalised patients at nutritional risk. The underlying principle of the protein-fortified hospital food concept is transferable to other cultures. However, which dishes will promote appetite and be tasteful in other cultures needs to be explored locally. Further, the long-term impact of the intervention on relevant treatment outcomes (e.g. physical function, LOS and QoL) should be studied in larger RCTs. Moreover, the economic implications of the intervention also warrant investigation.

4.3 Study III

Aim

To evaluate and collate the evidence for an effect of individualised dietary counselling following discharge from hospital to home on physical function in nutritionally at-risk older patients.

Methods

Study design

A systematic review and meta-analysis of RCTs, conducted according to the Cochrane methodology (98).

In- and exclusion criteria

Studies including older patients (> 60 years of age) who were undernourished or assessed to be at nutritional risk, and which evaluated individualised dietary counselling following discharge from hospital to home. Studies evaluating the effect of ONS without individualised dietary counselling were excluded.

Definition of individual dietary counselling

Dietary counselling was defined as advice on how to increase energy and protein intake using dietary fortification to optimise the energy and protein density of the diet and/or adding extra snacks or drinks (homemade or ONS)

Outcome

Primary: physical function as assessed in included studies.
Secondary: energy and protein intake, nutritional status, QoL, hospital readmissions and mortality as assessed in the included studies.

Search strategy and selection

The databases Medline Ovid, EMBASE and Central were searched. No restrictions on date of publication or language were applied. Additional studies were searched by reference lists of included trials and reviews. Relevant ongoing or unpublished trials were sought by contacting experts in the field and by searching http://www.clinicaltrials.gov.

Quality assessment

Two authors independently assessed risk of bias using The Cochrane Collaboration's Risk of Bias Tool (98). The Grading of Recommendations Assessment, Development and Evaluation system (GRADE) was used to assess the quality of the evidence across outcomes (98).

Synthesis of data

Review Manager 5.2 was used for data analysis (98). MD were used for continuous data and RR for dichotomous data; both with 95% CIs. Data were analysed according to the intention-to-treat principle. Heterogeneity was assessed using the I^2-test and the chi-squared test. When data were not comparable, data were summarised narratively.

Results

The searches yielded 1857 citations (Appendix D, Figure 1). Thirty potentially eligible studies were retrieved in full text. Of these, 4 RCTs (6 articles) were included involving initial recruitment of 729 patients.

Characteristics of studies

The included studies originated from Holland, Sweden, Israel and Denmark and were published from 2007 to 2012 (111–114). Participants included medical and surgical patients with a mean age varying from 74-85 years of age. Further characteristics of the included studies are shown in Table 2 in appendix D.

Risk of bias

Overall, the studies were assessed to be at high risk of bias, mainly due to lack of adequate blinding of patients, personnel and outcome assessors and high drop-out rates. Sequence generation and allocation concealment was judged to be at low risk of bias (Appendix D, Figure 2).
The overall quality of the evidence for HGS and mortality was assessed to be moderate. In regard to HGS the moderate quality of evidence was mainly due to lack of blinding and high rate of drop-outs and in regard to mortality it was due to high rates of drop-outs (Appendix D, Table 3).

Primary outcome

Data on physical function was summarised narratively except for data on HGS. The narrative summary revealed some positive effects (Table 4.3-1). The pooled effect estimate on HGS was non-significant (Appendix D, Figure 3).

Secondary outcomes

Meta-analyses were conducted on BW, energy and protein intake and mortality. All studies (N= 525) revealed a significant effect on BW (Appendix D, Figure 4); two studies(111,114) (N = 272) evaluated energy and protein intake and found a significant increase in both (Appendix D, Figure 5); no significant effect was found on mortality (N=729) (Appendix D, Figure 6). Lack of data prevented pooling of data in regard to QoL and hospital readmissions.

Discussion

This systematic review revealed a positive effect of individualised dietary counselling following hospital discharge to home on protein and energy intake and BW in nutritionally at-risk older patients, however, without revealing a convincing positive effect on physical function. No conclusions can be made in regard to QoL and hospital readmissions due to too few studies assessing these outcomes. Meta-analysis found no effect

Table 4.3-1 The effect of dietary counselling following discharge from hospital to home on physical function measured by different instruments

Study	Measurement instrument [scale]	IG: Improved, N (%)	CG: Improved, N (%)	IG: MD (SD)	CG: MD (SD)	P-value/ Difference (95 % CI)
Beck (2013)(114)	Chair Stand test [30-Seconds]	35 (56)	32 (53)	-	-	P = 0.75
	The de Morton Mobility Index [0-100]	-	-	6 (11)	3 (12)	P = 0.09
	The de Morton Mobility Index [0-100]	34 (54)	28 (46)	-	-	P = 0.03
	The mobility-tiredness scale [0-6]	-	-	-1.11 (2.2)	-0.96 (2.8)	P = 0.90
	The mobility-tiredness scale [0-6]	27 (48)	27 (52)	-	-	P = 0.39
	Functional Recovery Score [0-100%]	-	-	3 (14)	5 (15)	P = 0.50
	Functional Recovery Score [0-100%]	30 (48)	34 (59)	-	-	P = 0.51
	Hand grip strength [kg]	-	-	0.6 (3)	0.5 (3)	P = 0.65
	Hand grip strength [kg]	31 (50)	27 (45)	-	-	P = 0.84
Feldblum (2011)(113)	Barthel index [0-100]	na	Na	-2.6 (18.3)	-3.6 (18.9)	P = 0.76
Neelemaat (2011)(111)	Functional Limitation score [0-6]	na	Na	-2.6 (18.3)	-3.6 (18.9)	P = 0.76
	Physical activity score [0-6]	na	Na	-0.3 (1.2)	0.2 (1.5)	-0.5 (-1.0;0.1)
	Physical performance [0-16]	na	Na	0.5 (1.5)	0.6 (1.5)	-0.1 (-0.7; 0.5)
	Hand grip strength [kg]	na	Na	3.0 (4.2)	2.1 (5.4)	0.8 (-1.0; 2.6)
	Functional limitations score [0-6]	na	Na	0.2 (5.6)	1.0 (6.7)	-0.8 (-3.0; 1.5)
Neelemaat (2012)(115)	Functional limitations score [0-6]	na	Na	-0.47 (0.15)	0.24 (0.15)	-0.72(-1.15;-0.28)
	Physical activity score [0-6]	na	Na	0.52 (0.17)	0.4 (0.26)	0.1 (-0.53; 0.73)
Persson (2007)(112)	Katz ADL index [A-H]	na	Na	na	na	P < 0.05
	Hand grip strength [kg]	na	Na	1.81 (4.1)	0.1 (5.5)	P = 0.20

Table 4.3-1 gives an overview of the effect on physical function measured by different instruments. Positive results are highlighted with dark grey
N = number of patients, MD = Mean Difference, IG = Intervention group, CG = Control group, na = not available, Neelemaat 2011 + 2012: same trial but different statistical methods to analyse outcome, Chair stand = manual counting of the number of sit-stand-sit cycles completed within 30 seconds, The de Morton Mobility Index is a validated tool to assess mobility, The mobility-tiredness scale measure tiredness using the validated Mob-T scale, Functional Recovery Score measured restoration of function, Hand grip strength was measured in kg using a Jamar Hydraulic Hand Dynanometer, Barthel index was used to measure performance in activities of daily living, Functional Limitation score and Physical activity score (two validated questionnaires) were used to assess physical function. Physical performance, was measured by examining walking speed, ability to rise from a chair, to put on and take off a cardigan and standing balance, Katz ADL index measured activities of daily living.

on mortality. Reasons for the lack of a convincing effect on physical function may be lack of power and too short duration of intervention and follow-up.

We probably also need a deeper understanding of the mechanisms behind the recovery of physical function in older patients (116). In this regard, we also need consensus regarding the use of valid instruments to measure physical function and identify minimal clinically relevant changes in regard to these instruments. Another reason for the lack of effect on clinically relevant outcomes such as physical function may be due to lack sufficient understanding of the aetiology of why older people become at nutritional risk (i.e. multi comorbidities, reduced level of function, and the excessive use of medication). A comprehensive multidisciplinary nutritional approach involving doctors, nurses, physiotherapist and RDs in post-discharge interventions may therefore be necessary to achieve a positive effect on clinically relevant outcomes (61,117).

Current evidence does not indicate a convincing effect of dietary counselling (including ONS), provided by RDs, compared to the use of ONS alone for nutritionally at-risk patients after hospital discharge. To increase weight and nutritional intake in medical and surgical patients, the prescription of ONS at hospital discharge should therefore be the first line of choice. However, if patients express dislike of the ONS, dietary counselling following discharge should be considered.

More research within this field is, however, needed to enable evidence-based recommendations for clinical practice.

Limitations and strengths

This systematic review suffered from limitations to both internal and external validity. Inadequate blinding and high dropout rates pose a substantial threat to the internal validity, and the small number of studies limits the external validity.
Furthermore, all studies potentially lack sufficient statistical power. Additionally, the use of a range of different instruments to assess physical function prevented meaningful meta-analysis.
A strength of the systematic review is the comprehensive attempt to collate and evaluate the evidence for an effect of individualised dietetic counselling in the management of older nutritional at-risk patients after hospital stay. The review also provides useful information for the design of future studies in this area.

Key points

Four studies investigating the effect of individualised dietary counselling following hospital discharge were included. We found moderate-quality evidence that provision of individualised dietary counselling by a RD following hospital discharge improves weight, energy and protein intake in older nutritionally at-risk patients, however without clearly improving physical function. Furthermore, the evidence indicated no effect on mortality. Lack of data prevented pooling of data on QoL and hospital readmissions. In further trials, power calculations should use clinically relevant outcomes, for example physical function. In this regard, it is important to strive for agreement regarding which instruments are to be used when measuring physical function in older patients. Furthermore, it should be examined what constitutes a minimal clinically relevant change in physical function in older patients. Finally, to increase the quality of evidence regarding effects of individualised dietary counselling following hospital discharge, we recommend randomised controlled trials with blinded outcome assessment and data analysis.

4.4 Conclusions

Study I

A supplementary novel hospital food concept, consisting of energy dense, small, soft dishes which were nicely presented and served a la carte 24 h a day revealed no significant overall difference in the coverage ≥ 75 % of energy and protein requirements between IG and the HCG. However, a significant upward trend in the number of IG patients reaching ≥ 75 % of their energy requirement during the course of the study was observed. This indicates that a run-in period of 4-6 weeks should be considered in future hospital food intervention trials. No significant upward trend was found in the IG in regard to reaching protein requirements, indicating a need for optimising the protein content of the intervention menu.

Study II

A supplementary protein-fortified hospital food concept, consisting of protein fortified energy dense, small, soft, dishes, nicely presented and served a la carte from 7 AM – 8 PM, had a significant positive impact on overall protein intake and on weight-adjusted energy intake compared to the standard hospital food service. The supplemental protein-fortified menu accounted for 30% of energy intake and 40% of protein intake. No significant differences were found with respect to BW, HGS and LOS between groups.

Study III

The evidence indicates that individualised dietary counselling provided by a RD to nutritionally at-risk older patients at home after hospital discharge does not clearly improve physical function. However, meta-analyses revealed significant improvements in BW, energy intake and protein intake. The evidence indicated no effect on mortality and lack of data prevented pooling of data in regard to hospital readmissions and QoL.

Overall conclusion

Implementation of the strategies studied in this PhD-thesis may optimise the clinical nutritional practice and thus be able to improve nutritional status of patients at nutritional risk. The provision of a protein-fortified hospital food concept increased dietary intake (protein and weight-adjusted energy intake) in hospitalised nutritionally at-risk patients. This suggests that the protein-fortified hospital food concept can be used as a relatively simple and effective strategy for increasing protein and energy intake in hospitalised patients at nutritional risk. However, further research is needed to confirm these results and also to establish the effect on clinically relevant outcomes. Individualised dietary counselling provided after hospitalisation, improved energy and protein intake and BW in older nutritionally at-risk patients, however, without clearly improving physical function. No effect was observed on mortality and lack of data prevented pooling of data for QoL and readmissions. More research within this field is therefore still needed to facilitate evidence-based recommendations for clinical practice.

5. Perspectives

5.1 Implications for further research

This Ph.D. thesis investigated two different aspects of GNP; how to increase dietary intake using hospital food and the effect of providing individualised dietary counselling at home following hospital discharge on physical function. Both aspects were investigated in older nutritionally at-risk patients.

Quality Of Evidence

In regard to these two aspects, further high quality research (RCTs) is necessary to generate high level evidence for the effect of these strategies on clinically relevant outcomes.

In particular, patient-reported outcome measures and cost effectiveness are recommended as important outcomes for future nutritional trials (118). Furthermore, future trials should consider not only statistical significance but also the clinical relevance of outcomes. There is a need for studies investigating clinically meaningful changes in different outcomes in the target population. Future randomised controlled trials of nutritional interventions need to calculate power based on considerations of clinical relevance.

To allow for an effect on relevant clinical outcomes, longer duration of both nutritional intervention and follow-up needs to be considered. Longer duration of both will also decrease the risk of "the observer effect". In regard to nutritional follow-up after hospital discharge, further research should also seek to identify the patients most in need of nutritional follow-up after hospital discharge.

Physical Function

In the systematic review, patients increased their BW without clearly experiencing improved physical function. Research into molecular and cellular mechanisms associated with recovery of physical function is therefore warranted, especially in older patients. Measuring body composition might be relevant for increasing knowledge in this field, even though physical function is found to improve more rapidly with nutritional support compared to replacement of muscle mass alone (50). Further, vitamin D is important for physical functioning in older people. Therefore, future studies may need to consider vitamin D supplementation in case of low vitamin D status (119).

Future studies should also examine the effect of physical training in addition to nutritional interventions to counteract the anabolic resistance found in older people (55,71,77). Also, more research in regard to the dose-response effect of protein on physical function is needed (71).

Multi-Factorial Strategies

The causes of becoming at nutritional risk in older patients are often multifactorial (76). Strategies including multimodal intervention and/or multidisciplinary interventions may have a better potential to target the underlying causes and therefore be more successful in regard to relevant clinical outcomes (61). Studies within this field of research are therefore warranted (110).

Compliance

Compliance also deserves further investigation. Compliance could potentially have a major impact on the effect of a nutritional intervention but it is often reported inadequately, probably due to practical difficulties involved in its measurements (85,120). Measuring compliance to ONS may be fairly easy but how should it be done in individualised dietary counselling. Different questions also arise, for example what influences compliance? Does the environment in which a nutritional intervention is provided influence compliance, e.g. should dietary counselling following hospital discharge be provided at home or in the hospital? Does the length of each session and frequency of follow-up affect compliance? Should individualised dietary counselling be followed up by a personalised nutritional plan to be successful? There are many unanswered questions within this complex issue and qualitative studies of patients' perspectives are needed.

External Validity

In all three studies *(Study I, II, III)* high percentages of patients declined participation, decreasing the external validity of the studies. Future studies investigating the experiences and perspectives of the patients who decline to participate are therefore needed to identify if there is a need for developing specific strategies for reaching these patients.
The nutritional interventions in the studies included in *Study III* were insufficiently described in regard to the training, experiences and techniques of the RDs providing the interventions. Lack of these details makes it difficult to translate the research into practice and it also makes it impossible to replicate the individual studies. Lack of a detailed description of nutritional interventions is however not unusual and needs to be addressed in future studies (85). One cannot expect that all RDs work exactly alike. Indeed the provision of detailed protocols on how to provide individual dietary counselling may be necessary to secure a systematic performance. This will also help us gain knowledge

within this field in relation to how the dietary counselling should be performed to be effective and it will allow for sufficient insight to be able to decide if pooling of data from studies is reasonable.

Assessment Of Food Intake

Researchers within the nutritional field often face the challenge of assessing food intake accurately, the biggest challenge being time constraints. There is a great need for "easy to use" technology that can assess food intake validly. For example iPads presenting food options that can be wiped away when consumed. The validity of using such approaches needs to be examined.

The Most Important Implications For Future Research

The most important implication for future research in the nutritional field is the need for sufficiently powered RCTs with an adequate duration of intervention and follow-up to identify a possible effect on clinically relevant outcomes. Finally, economic studies within the nutritional research area are also warranted.

5.2 Implications for Practice

The Protein-Fortied Hospital Food Concept

The protein-fortified hospital food concept increased dietary intake in hospitalised patients *(Study II)*. However, which components were most effective remains to be identified. Therefore, the complete food concept needs to be implemented to reach the same results as in our study *(Study II)*. The concept can fairly easily be implemented in other Danish hospitals to ethnic Danish patients at nutritional risk, since the recipes are not classified. In other countries and cultures, the overall concept can also be implemented. However, identification of taste preferences in the target population is necessary for deciding which dishes to include in the menu.

A barrier to implementation may be the lack of economic evaluation of the intervention *(Study II)*.
An unpublished cost analysis of *study II* has estimated that one dish costs an average of 0.3 EUR which equals 4 EUR a day if a patient's energy and protein requirements are covered by the protein-fortified hospital food concept alone. The cost of implementing the whole concept for 150 nutritionally at-risk Danish patients, including food production, RDs instead of kitchen staff for serving and provision of individualised dietary counselling and nutritional plans, is estimated to reach 400.000 EUR annually. In HUH we have decided to use RDs instead of kitchen staff to serve the food during week days, because we anticipate that this will increase the number of patients reaching their nutritional requirements. This approach has also been chosen to enable translation of the food concept following hospital discharge. We further believe that RDs will have better access to ward staff and thereby increase overall awareness of the importance of nutrition. In regard to the cost of this protein-fortified hospital food concept, it is worth noticing that studies have reported that sufficient nutrition seems able to decrease LOS by around 3 days (22,121).

Individualised Dietary Counselling Following Hospital Discharge

Nutritional care after hospital discharge is an important part of GNP. Especially, nutritionally at-risk older patients appear to be at risk of adverse events after hospital discharge (24,25,29,122).

There are several barriers to the implementation of nutritional care following hospital discharge in clinical practice. Firstly, nutrition is not included systematically in discharge planning; secondly, there is a lack of guidelines on who will benefit from a nutritional intervention following hospital discharge; thirdly, the evidence for an effect of follow-up is weak.

In regard to the latter, this thesis indicates that, at present, available evidence favours the prescription of ONS rather than systematic provision of individualised dietary counselling by a RD for increasing energy/ protein intake and BW after hospital discharge in older patients at nutritional risk. However, if a patient expresses dislike of ONS, individualised dietary counselling following discharge should be considered.

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Appendices

Appendix A

Nutritional Risk Screening (NRS-2002)

Nutritional Risk Screening (NRS 2002)

Table 1 Initial screening			
1	Is BMI <20.5?	Yes	No
2	Has the patient lost weight within the last 3 months?		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill ? (e.g. in intensive therapy)		
Yes: If the answer is 'Yes' to any question, the screening in Table 2 is performed. **No**: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

Table 2 Final screening			
Impaired nutritional status		**Severity of disease (≈ increase in requirements)**	
Absent **Score 0**	Normal nutritional status	Absent **Score 0**	Normal nutritional requirements
Mild **Score 1**	Wt loss >5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild **Score 1**	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. *Chronic hemodialysis, diabetes, oncology*
Moderate **Score 2**	Wt loss >5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate **Score 2**	Major abdominal surgery* Stroke* *Severe pneumonia, hematologic malignancy*
Severe **Score 3**	Wt loss >5% in 1 mth (>15% in 3 mths) or BMI <18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe **Score 3**	Head injury* Bone marrow transplantation* *Intensive care patients (APACHE>10).*
Score:	+	**Score**:	**=Total score**
Age	if ≥70 years: add 1 to total score above	**=age-adjusted total score**	
Score ≥3: the patient is nutritionally at-risk and a nutritional care plan is initiated **Score <3**: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

NRS-2002 is based on an interpre-tation of available randomized clinical trials.
*indicates that a trial directly supports the categorization of patients with that diagnosis. Diagnoses shown in *italics* are based on the prototypes given below.
Nutritional risk is defined by the present **nutritional status** and risk of impairment of present status, due to **increased requirements** caused by stress metabolism of the clinical condition.

A nutritional care plan is indicated in all patients who are

(1) severely undernourished (score=3), or (2) severely ill (score=3), or (3) moderately undernourished + mildly ill (score 2 +1), or (4) mildly undernourished + moderately ill (score 1 + 2).

Prototypes for severity of disease
Score=1: a patient with chronic disease, admitted to hospital due to complications. The patient is weak but out of bed regularly. Protein requirement is increased, but can be covered by oral diet or supplements in most cases.
Score=2: a patient confined to bed due to illness, e.g. following major abdominal surgery. Protein requirement is substantially increased, but can be covered, although artificial feeding is required in many cases.
Score=3: a patient in intensive care with assisted ventilation etc. Protein requirement is increased and cannot be covered even by artificial feeding. Protein breakdown and nitrogen loss can be significantly attenuated.

(11)

Appendix B

THE OFFICIAL JOURNAL OF THE BRITISH DIETETIC ASSOCIATION

Journal of Human Nutrition and Dietetics

Journal of Human Nutrition and Dietetics

CLINICAL NUTRITION

A 24-h a la carte food service as support for patients at nutritional risk: a pilot study

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Keywords
energy intake, energy-dense meals, hospital food, implementation, malnutrition, nutritional risk.

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Abstract

Background: Undernutrition and insufficient energy and protein intake is a common problem in hospitalised patients. The aim of this pilot study was to investigate whether a novel hospital menu would be an effective strategy for increasing nutritional intake in patients at nutritional risk.
Methods: A historically controlled intervention pilot study was conducted. Forty patients at nutritional risk were offered a novel hospital menu as a supplement to the ordinary hospital menu. The menu consisted of 36 naturally energy-enriched small dishes served on demand 24 h a day. Energy and protein intake were calculated as the mean over a period of 3 days.
Results: No significant difference in energy and protein intake was observed between the groups; however, a significant ($P = 0.001$) time gradient in total energy intake was observed in the intervention group. Moreover, a significant ($P = 0.03$) time gradient in energy intake received from the novel menu was observed. The dishes from the novel menu were mainly ordered from 11.00 h to 14.00 h and from 17.00 h to 18.00 h.
Conclusions: No overall significant differences in energy and protein intake between the groups were found. However, the present pilot study revealed a significant time gradient in total energy intake ($P = 0.001$) and in energy intake from the novel menu ($P = 0.03$). This indicates the need to include a run-in period when investigating novel hospital menus as a support for patients at nutritional risk. Additionally, food service, available 24 h a day, appears to be unnecessary.

Introduction

Undernutrition is a common problem in hospitalised patients, with a prevalence of approximately 40% (Rasmussen *et al.*, 2004; Stratton & Elia, 2006). Undernutrition is related to increased morbidity, mortality (Stratton *et al.*, 2003) and a decreased quality of life in several populations (Norman *et al.*, 2006). Results from a meta-analysis suggest that nutritional support reduces complication rates, infection rates, mortality, length of hospital stay and improves quality of life (Stratton & Elia, 2007b).

The reasons for undernutrition in hospitalised patients are multiple. Some are disease- and treatment-related, whereas others are related to a lack of help in eating, appetising foods, snacks or special meals and services tailored to patients with a low appetite (Kondrup & Ovesen, 1997; Kondrup *et al.*, 2002).

The catering system at Herlev University Hospital (HUH) is a buffet style. We have previously reported that this catering system improves food intake at the hot evening meal and that patients' overall satisfaction with the buffet style is very high (Nielsen *et al.*, 2004; Freil *et al.*,

2006). However, undernourished patients at HUH still lack both sufficient energy (E) and protein (P) intake. A retrospective observational study conducted at HUH in 2006 revealed that only 44% of the patients at nutritional risk achieved their minimum E requirements and only 28% achieved their minimum requirements for P (Hansen *et al.*, 2008). Furthermore, the Nutrition Day Survey 2010 disclosed that only 53% of patients admitted to hospitals in Europe received their E requirements. The survey also revealed that patients classified as being at nutritional risk had a significantly lower E intake than patients who were not at risk ($P = 0.0001$) (Schindler *et al.*, 2010).

Oral nutritional supplements (ONS) are the most thoroughly studied strategy for treating undernutrition (Stratton *et al.*, 2003). Systematic reviews and meta-analyses of studies investigating the effects of ONS in undernourished patients report improved clinical outcomes, including reduced mortality and fewer complications (Stratton *et al.*, 2003; Stratton & Elia, 2007a,b; Milne *et al.*, 2009). However, lack of compliance with intake of ONS has been highlighted as a problem in hospitalised patients (Bruce *et al.*, 2003; Lad *et al.*, 2005; Starke *et al.*, 2011). A newly-systematic review carried out by Hubbard *et al.* (2012) reported an overall good compliance to ONS across different healthcare settings, although a high variation in compliance to ONS was found in the hospital setting (37–94%) and, furthermore, the review revealed a lower compliance to ONS in the hospital settings compared to community settings (67% versus 78%). Therefore, additional strategies with respect to optimising the nutritional treatment of hospitalised patients at nutritional risk appear to be relevant. The present study aimed to assess whether a novel hospital menu supplemental to standard hospital food service would be an effective strategy for improving nutritional intake in patients at nutritional risk.

Materials and methods

Study design and population

The study comprised a historically controlled intervention study with the consecutive inclusion of 40 patients at nutritional risk over a period of 10 weeks (from the 21 January to 1 April 2009). Intervention patients were recruited from Gynaecology, Orthopaedic Surgery and Internal Medicine wards from HUH. Patient data from a previous observational study (Hansen *et al.*, 2008) were used as a historical control group (CG). Characteristics of the CG are presented below.

Exclusion criteria were terminal patients, dysphagia, food allergy or intolerance, patients who exclusively received enteral or parenteral nutrition. Inclusion criteria were sufficient cognitive functioning, a well-functioning gastrointestinal tract, anticipated length of hospitalisation of ≥ 3 days, ability to understand and speak Danish and a nutritional risk score (NRS) ≥ 3 according to the NRS-2002 criteria.

Nutritional risk score-2002

The NRS-2002 is a validated tool for identifying patients who are likely to benefit from nutritional support (Kondrup *et al.*, 2003). Evaluation of nutritional risk is based on two components: nutritional status and severity of disease. Nutritional status depends on three variables: body mass index (BMI), recent weight loss and dietary intake during the last week before admission. A score of 3 is given for severe undernutrion: BMI < 18.5 kg m^{-2}, weight loss >5% during the last month, or 0–25% of required dietary intake. A score of 2 is given for moderate undernutrition: $18.5 <$ BMI < 20.5 kg m^{-2}, weight loss >5% during the last 2 months, or 25–50% of required dietary intake. A score of 1 is given for mild undernutrition: weight loss >5% during the last 3 months, or 50–75% of required dietary intake. For severity of disease, as an indicator of stress metabolism and increased nutritional requirement, a score of 3 is given for severe illness (e.g. intensive care or sepsis), a score of 2 is given for moderate illness (e.g. colectomy) and a score of 1 is given for mild illness (e.g. fractured neck of femur). The score for nutritional status is added to the score for severity of disease to give a total score, which can range from 0 to 6. Finally, if the patient is aged ≥ 70 years, a score of 1 is added to the total score to correct for age-related frailty. If the age-corrected total score is ≥ 3, nutritional support is indicated (Kondrup *et al.*, 2003).

Information of staff in the participating wards

The staff of the participating wards were informed about the study and their role in the study (their role is described in detail below) approximately 1 week before study initiation. Additionally, posters were put up in the wards so both patients and staff could read about the study and patients reflect on whether they were interested in participating.

Recruitment of participants

Nursing staff scored the nutritional status of all patients within 24 h of their admission to the wards. If a patient was identified as being at nutritional risk according to NRS-2002, the responsible research manager (a registered clinical dietitian) was informed. Patients, who were eligible for inclusion in the study according to the inclusion criteria were subsequently invited to participate in the

study by the research manager. At inclusion, the baseline data recorded were: age, sex, BMI and total NRS according to the NRS-2002 criteria.

Outcome

Data on food intake were collected for 3 days after initiation of the intervention. E and P intake were calculated as the mean of these 3 days. Patients were free to use the novel hospital food menu until discharge.

Food intake was registered by the nursing staff alone or in collaboration with the patient. A detailed nutritional registration form was used to distinguish between different meal components in the present study. For example, one portion (= 3 potatoes) of potatoes amounts to 300 kJ and zero protein, and one portion of fish including sauce amounts to 650 kJ and 10 g of protein. The amounts consumed of each portion of food/beverage were eye-measured and recorded in quartiles (0%, 25%, 50%, 75% and 100%). The accuracy of assessing food intake using this method has been validated previously (Olin *et al.*, 1996). The research manager collected the forms daily and also conducted a dietary recall interview with the patient to secure and verify the content of dietary records.

The novel hospital menu

The menu was developed in collaboration with dietitians, chefs and former patients hospitalised at HUH $\geq$ 5 days within the previous 6 months. The former patients (n = 11) participated in a focus group interview and two taste sessions to allow us to gain knowledge of the patient perspectives on food and flavour preferences. The novel menu was named 'Delights of Herlev Hospital' (DHH) and was prepared as a supplemental offer to the standard hospital food service.

The final DHH menu consisted of 36 small (portion size ranged from 28 to 109 g per dish) dishes (Table 1). The dishes were fortified with natural E dense ingredients (e.g. butter, cream and oil). MASTER CATER SYSTEM, version 3.055 (Anova Data A/S, Holte, Denmark) was used as the food composition database to analyse the E and P content of the dishes. The patients were allowed to order as many dishes as they liked from DHH, 24 h a day. The dishes could be ordered by telephone either by patients themselves or by ward staff. The DHH dishes were delivered ready to eat on a tray in the wards by kitchen staff within 20 min after an order was placed. The dishes were subsequently served to the patient by ward staff or the kitchen staff.

Standard hospital food service offers three main meals (breakfast, lunch, dinner) from a served buffet. Two main diet types are available: the 'hospital diet' with higher energy and protein density than the 'normal diet'. For breakfast, patients could choose between hot porridge (e.g. oatmeal) and bread with butter, jam and cheese. For lunch, five small slices of rye bread with various toppings such as sliced boiled eggs, ham, shrimps and pate and, also, a hot soup of the day. For dinner, two different kinds of starters, two different kinds of hot meals and two different kinds of desserts are available. The main three meals are intended to fulfil two-thirds of nutritional requirements. The remaining third is to be covered by microwaveable meals, snacks (e.g. cakes, biscuits with cheese, ice cream) and beverages (e.g. ONS), prepared in small kitchens on the units and served on demand of the ward staff. Patients could choose freely whether they wished to eat in the dining room or in bed. If a patient was bedridden or disabled, their food was served in bed by the nursing staff. Furthermore, according to Danish guidelines, standard care for patients at nutritional risk includes a multi-vitamin supplement administered by the ward staff to ensure sufficient micronutrient intake (Danish Veterinary & Food Administration, 2009).

At inclusion, all patients received detailed information about the standard hospital food service as well as the dishes of DHH from the daily research manager. Patients were also informed about the importance of achieving a sufficient intake of E and P. No individualised nutritional planning occurred, and patients did not receive dietary counselling during the intervention.

The historical control group

The patients who comprised the historical CG were recruited at HUH in 2006 from the same wards as those participating in the present study. Similar to the patients in the present study, patients of the CG all had a NRS score $\geq$3. The same method to quantify nutritional intake was used, including verification of the dietary record through dietary recall interviews. Also, E and P intake was calculated identically. To the best of our knowledge, routines surrounding meal services have not changed. Neither has the standard hospital food service for patients.

Outcome variable

The primary outcome of the study was for 70% of patients in the intervention group (IG) to reach 75% of their P and E requirements. The level of intake was set at this target because a previous study disclosed that weight stability could be achieved with this level of intake (Kondrup, 2001).

Table 1 The 36 dishes of the novel hospital food menu

Dish	Portion size (g)	Energy (kJ)	Energy density (kJ g^{-1})	Protein (g)
Marinated duck with roasted hazelnuts and lemon	60	1084	18.1	5.3
Long-cooked lamb with cream of white beans and sour cream	50	740	14.1	6.1
Mashed sweet potatoes with onion and bacon	68	498	7.3	2.4
Baked salmon with olive	47	534	11.3	5.3
Terrine of smoked eel*	40	349	8.7	4.6
Long-cooked pork in orange juice	50	533	10.7	6.7
Spicy chicken stick with peanut butter	40	557	14.0	5.0
Meatballs of chicken with soya sauce	37	409	11.1	4.9
Smoked salmon with eggs and capers	55	540	9.8	8.0
Meatballs of veal with stewed cabbage	55	451	8.2	6.5
Glazed salmon with sauce of Jerusalem artichoke	55	364	6.6	6.0
Falafel with humus	35	629	18.0	2.9
Meatloaf with bacon	53	448	8.5	6.3
Soup of beetroot with sour cream	50	203	4.1	1.4
Soup of mushrooms	50	274	5.5	1.1
Soup of beans with cream cheese	50	125	2.5	1.6
Cold fresh-tasting cucumber soup	50	357	7.1	1.4
Risotto with onions and roasted mushrooms	40	233	5.8	1.4
Crispy fried potato mash with ham and parmesan	60	593	9.9	5.1
Pumpkin pie with bacon	43	475	11.1	2.1
Baked mashed potatoes with parmesan and ham	43	335	7.8	5.3
Creamed cauliflower	45	266	5.9	2.7
Italian bread with rosemary and olives	28	316	11.3	1.4
Omelet of potatoes	35	236	6.7	1.1
French toast with cinnamon and blueberries	57	740	13.0	2.9
Omelet with bacon and parmesan	50	530	10.6	4.4
Breakfast muffin with butter and jam	90	1319	14.7	7.5
Smoothie with nuts and berries	50	278	5.6	1.5
Yogurt with fresh berries and muesli	75	504	6.7	4.3
Ice cream of avocado with lemon and vanilla*	40	384	9.6	1.4
Crunchy apple cake*	109	1060	9.7	1.9
Baked Marzipan tart with berries	54	732	13.6	2.2
Blackcurrant mousse with white chocolate*	34	514	15.1	1.4
Tiramisu*	44	595	13.5	2.6
Cake with berries and chocolate	86	884	10.3	3.1
Tart meringue with lemon flavor and white chocolate	54	877	16.2	2.0

*Favourite dishes of the novel hospital food menu.

Estimation of energy and protein requirements

At inclusion, the patients' E requirements were estimated according to Danish guidelines for hospitalised patients; the basal metabolic rate (BMR) multiplied by an estimated activity factor[1] and by an arbitrary stress factor in case of fever or a factor for weight gain[2] (Danish Veterinary & Food Administration, 2009). The BMR was calculated in two different ways: by the Harris–Benedict equation[3] and by setting BMR to 100 kJ $kg^{-1}day^{-1}$. The first method is a worldwide recommended equation (Raimondo & Scolapio, 2006) where sex, age and height are taken into account when estimating the E requirement. The latter method is an easy and recommended Danish bedside method, which was also used to estimate the E requirement of the historical CG (Danish Veterinary & Food Administration, 2009). P requirements were set at 18 E% of the E requirement (Danish Veterinary & Food Administration, 2009).

Statistical analysis

Statistical analyses were carried out using SPSS, version 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics are presented as the mean (SD) because data were normally distributed. Pearson correlations and linear regression models were used to assess the degree of correlation between variables: E intake and study time, age, total NRS, BMI. Chi-squared tests were used for categorical data, the Mann–Whitney *U*-test for ordinal data and

[1]($\times$1.1 if bedridden and $\times$1.3 if being able to walk a bit around on the ward).

[2]($\times$1.3).

[3]Harris–Benedict equation for calculating BMR: men: BMR = 66.5 + 13.8 weight + 5.0 height − 6.8 age; women: BMR = 655 + 9.6 weight + 1.8 height − 4.7 age).

t-tests for interval scale variables to assess potential differences in patient characteristics between the groups. Subsequently, the mean E intake in% in the groups was compared by a *t*-test. Spearmans correlation was used to determine whether the time gradient in E intake was significant. All statistical tests and *P*-values were two-sided and $P < 0.05$ was considered statistically significant.

The previous observational study conducted at HUH (Hansen *et al.*, 2008) found that 44% of patients in the historical CG, all of whom were at nutritional risk, achieved an E intake above 75% of their nutritional requirement. In this study, our primary outcome was for 70% of the patients in the IG to achieve a nutritional intake of 75% of their nutritional requirement. With a power of 90%, 39 patients were required for the lower limit of the confidence interval for this outcome to be above 44%. The calculation was performed using a permutation technique and exact binomial confidence intervals were used.

Ethics

The protocol was approved by the Danish Regional Committee on Biomedical Research Ethics and registered at http://www.ClinicalTrial.gov (ID nr: H-D-2008-125). Written informed consent was obtained from patients before inclusion in the study.

Results

Study population

Sixty-nine patients matched the inclusion criteria and were invited to participate. Seventeen refused to participate, either because of lack of desire to engage in additional activities immediately after their admission to hospital ($n = 12$) or because they were satisfied with the existing food concept ($n = 5$). Twelve patients withdrew from the study after inclusion (four died and three were discharged before sufficient data were collected; five decided to withdraw as a result of a lack of desire to continue participation). Forty patients (72.5% women), aged 48–92 years, completed the study: 11 orthopaedic, seven gynaecological and 22 internal medicine patients. The primary diagnoses were osteoarthritis of the knees or hip (orthopaedic surgery), chronic obstructive lung disease (internal medicine) and ovarian/uterine cancer (gynaecology). According to the baseline characteristics (Table 2), 30% were assessed to be severely undernourished, 30% moderately undernourished and 37.5% mildly undernourished. In total, 55% of intervention patients were bedridden.

A comparison of patient characteristics in the present study and patient characteristics in the historical CG is presented in Table 2. The two groups were similar with respect to age, sex and nutritional status at admission.

Table 2 Baseline characteristics of the subject in the intervention and historical control groups

Variables	Intervention group	Historical control group	*P*
Sex, *n* (%)			
Male	11 (27.5)	9 (23.0)	0.7‡
Female	29 (72.5)	30 (77.0)	
Age (years)*	74 ± 12	71 ± 12	0.4§
Anthropometric data*			
Weight (kg)	59 ± 16	57 ± 11	0.5§
Body mass index (kg m^{-2})	22 ± 6	21 ± 4	0.6§
Departments, *n* (%)			
Gynaecology	7 (17.5)	8 (20)	0.01¶
Orthopaedic surgery	11 (27.5)	1 (2.5)	
Internal medicine	22 (55)	31 (77.5)	
Nutritional risk assessment, *n* (%)			
Nutritional status			0.08**
0	1 (2.5)	4 (10)	
1	15 (37.5)	18 (46)	
2	12 (30)	10 (26)	
3	12 (30)	7 (18)	
Severity of disease			
0	2 (5)	1 (2.5)	0.15**
1	32 (80)	27 (69)	
2	5 (12.5)	10 (26)	
3	1 (2.5)	1 (2.5)	
Total†			
3	23 (57.5)	23 (57.5)	0.7**
4	9 (22.5)	11 (27.5)	
5	7 (17.5)	4 (10)	
6	1.0 (2.5)	0	
7	0	1.0 (2.5)	

*Mean (SD).
†Adjusted for age.
‡Chi-squared test.
§*t*-test.
¶Fisher's exact test.
**Mann–Whitney *U*-test.

However, a tendency ($P = 0.08$) towards a poorer nutritional status in the IG should be noted. As a result of the recruitment of patients from the same wards in the CG and IG, the overall primary diagnoses were similar in the groups; however, there was a significant difference between CG and IG with respect to the number of patients recruited in the participating wards.

A la carte 24 h a day

The dishes from DHH were mainly ordered at lunch time (from 11.00 h to 14.00 h) and around dinner (from 17.00 h to 18.00 h). Registration of the time point for ordering the dishes from DHH revealed that orders after 22.00 h only occurred four times. The mean number of dishes ordered together was 2.3 [median 2 (range 1–5) in one order].

The registration revealed that some of the dishes were more popular than others. The most frequently ordered dishes were smoked eel and various desserts (Table 1).

Nutritional intake versus requirement

Approximately sixty percent of patients in the IG received 75% of their E requirements. A nonsignificant increase in the percentage of patients achieving 75% of their E requirements was observed in the IG compared to the historical CG (55% versus 44%). There was no significant interaction between total NRS, age, BMI and mean E intake ($P = 0.56$, 0.17 and 0.69, respectively). Mean (SD) E and P intake from the dishes of DHH contributed 26.6% (10%) and 19.5% (8%) of the total mean E and P intake.

A significant time gradient in energy intake ($P = 0.0005$, $r = 0.53$) was present. In other words, E intake appeared to be positively affected by late entry into the study (Figure 1). In a model adjusting for BMI, age, total NRS and type of ward, the time point of inclusion remained significantly associated with E intake ($P = 0.001$). No other variables had $P < 0.05$. When examining the increase in E intake over the course of the study, we found a significant time gradient ($P < 0.03$) in the E intake contributed by the dishes of DHH.

In total, 17.5% of the patients in the IG reached their minimum P requirements. A significant increase over the course of the study was not seen in P intake, nor was a significant time gradient observed in the P intake contributed by the dishes of DHH ($P = 0.17$).

Discussion

The target in the present study was for 70% of patients in the IG to reach 75% of their E and P requirements. This requirement was reached by 60% and 17.5% of patients, respectively. The result is in accordance with a previous Danish study, which similarly examined the effect of a hospital menu, designed from patients' favourite dishes, as nutritional support for patients at nutritional risk. In that study, energy requirement was also reached by 60%. P intake was not presented (Kondrup, 2001).

The data revealed a clearly significant upward trend in E intake over the course of the study. After statistically correcting for potential confounding variables, such as BMI, age and total NRS, the time point of entry to the study appeared to be the primary determinant of this increase in E intake. The time gradient could be explained by the so-called 'learning curve' (Drew, 2010), according to which the ability to solve or perform a given task increases over time. The significant time gradient in E intake coming from the dishes of DHH suggests that staff of the wards became more aware of the possibility of ordering (and how to order) from DHH during the course of the study. In future studies, a run-in period should therefore be considered. A run-in period enabling dishes to be ordered by patients before study initiation and data collection would allow staff to acquire the necessary study-related knowledge and skills for the study.

The lack of a significant increase in overall E intake compared to the historical IG may be related to the factors described above. However, it is also important to note that the results may have been influenced by the poorer nutritional status in the IG ($P = 0.08$) compared to the historical CG, which could have negatively affected the desire for food in the present study. The significant difference between the distributions of patients from the participating departments could also have affected the results. Nevertheless, statistical analysis did not reveal any significant ward interaction.

Only 17.5% of patients reached their minimum requirements for P. The reasons for this low P intake may be diverse. Variation in P content in the 36 dishes

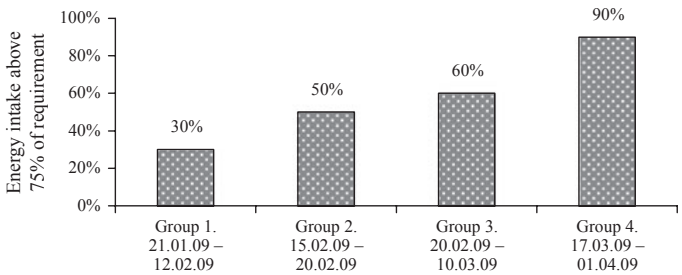

Figure 1 Energy (E) intake. A significant time gradient in energy ($P = 0.001$) was observed. Patients who were included later on in the study had a higher E intake compared to those who were included earlier. The energy intake of the patients is shown when divided into groups of 10, according to their time of enrolment in the study. In total, 30% reached their minimum energy requirement in group 1, 50% in group 2, 60% in group 3 and 90% in group 4.

was large. It ranged from 1.1 to 8.0 g of P per dish, with a median value of 2.9 g. We accepted the varied P content in the dishes before initiation of the pilot study because the dishes were to be supplementary to the standard hospital menu. We considered that patients would order at least three dishes a day, which, however, was not the case. Individualised nutritional planning by a clinical dietitian might have been able to compensate for the large P variation. The intervention investigated in the present study was, however, solely the novel hospital menu. The low intake of P was further exacerbated by the fact that the patients' favourite dishes, with the exception of one dish, were low in P. The P content of the favourite dishes ranged from 1.4 to 4.6 g per dish.

In accordance with our findings, similar results using naturally fortified hospital foods to improve food intake in hospitalised patients have been reported (Gall *et al.*, 1998; Barton *et al.*, 2000). Gall *et al.* (1998) and Barton *et al.* (2000) were able to improve E but not P intake in patients at nutritional risk.

Our ambition was to develop a novel menu comprised of small dishes with great taste and enriched with natural ingredients only. Unfortunately, we were unable to achieve a stable high protein content in all the dishes. Therefore, P fortification using high-quality protein powder should be considered if hospital food is to be an additional intervention to ONS for increasing E and P intake in undernourished hospitalised patients. P fortification would also make it possible to establish the minimum content of grams of P per dish of DHH and thereby enable patients to choose freely among dishes without their P intake being negatively affected.

However, adding artificial P to the dishes may change the texture, taste and smell of the dishes, which in turn could influence the intake of artificially P-enriched dishes negatively. Close collaboration with chefs would be essential to minimise the risk of such side-effects.

The present study was inspired by another study previously conducted in Denmark. The results obtained in that study showed an increased E and P intake when foods were served on demand, 24 h a day (Pedersen & Laursen, 2008). However, according to our findings, access to the dishes from DHH 24 h a day appeared to be an unnecessary operating expense for the hospital kitchen because orders were only made four times after 22.00 h. A possible explanation could be lack of knowledge of the possibility for ordering foods after the 'office hours' among hospital staff. In addition, patients might have been hesitant to impose on the ward staff or the dishes from DHH might have not been applicable at this late time of the day.

Twenty-five percent of eligible patients declined to participate in the study. A similar nonparticipation rate (26%) was seen in a nutritional study by Johansen *et al.* (2004). The nonparticipation rate may have affected the results of the study. If decliners were in a worse clinical condition than participants, the significant upward trend in E intake over the course of the study might have been smaller. The drop-out rate after inclusion was 23%; <10% as a result of a lack of interest in the intervention dishes, and >13% as a result of death or early discharge. Drop-out after inclusion into the study poses a potential limitation to the strength of the conclusions of the study.

The accuracy of assessing food intake in individual patients naturally depends on the extent to which different food components on the plate are consumed by the patient. We used a detailed nutritional registration form discriminating between different meal components and a validated method for estimating energy and protein intake in the present study. Therefore, we consider the method used to calculate energy and protein intake reliable.

Finally, it should be noted that the small sample size, the use of a historical control group and a lack of randomisation limits the internal validity and generalisability of the present study. Randomised controlled trials with sufficient power are warranted to explore if a special target hospital menu can be an effective strategy for improving nutritional intake in patients at nutritional risk, leading to improved clinical outcomes that are cost-effective.

In conclusion, no overall significant differences in E and P intake between the IG and the CG were found. However, the present pilot study revealed a significant time gradient in total E intake ($P < 0.001$) and intake of E from DHH ($P < 0.03$). No increase in P intake was observed. Furthermore, a 24-h a la carte service appears to be unnecessary because the food was seldom ordered after 22.00 h. In future studies, a run-in period and protein fortification should be considered.

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Conflict of interests, source of funding and authorship

All authors declare that there are no conflicts of interest. ER and MAN primarily contributed to the study design and data collection. ALN and WS primarily contributed to the study design and revision of the manuscript. TT primarily contributed to the revision of the manuscript. TWK primarily contributed to statistical analyses. TM

contributed to the study design, data analyses and the drafting of the manuscript. All of the authors contributed to the study design, data analysis, and revision of the manuscript for important intellectual content. All authors have read and approved the final manuscript submitted for final publication. The study was self-funded by the Hospital Kitchen.

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Appendix C

THE OFFICIAL JOURNAL OF THE BRITISH DIETETIC ASSOCIATION

Journal of Human Nutrition and Dietetics

Journal of Human Nutrition and Dietetics

CLINICAL NUTRITION

Positive effect of protein-supplemented hospital food on protein intake in patients at nutritional risk: a randomised controlled trial

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Keywords
food fortification, hospital food, nutritional support, protein, room service, undernutrition.

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Abstract

Background: New evidence indicates that increased dietary protein ingestion promotes health and recovery from illness, and also maintains functionality in older adults. The present study aimed to investigate whether a novel food service concept with protein-supplementation would increase protein and energy intake in hospitalised patients at nutritional risk.
Methods: A single-blinded randomised controlled trial was conducted. Eighty-four participants at nutritional risk, recruited from the departments of Oncology, Orthopaedics and Urology, were included. The intervention group (IG) received the protein-supplemented food service concept. The control group (CG) received the standard hospital menu. Primary outcome comprised the number of patients achieving ≥75% of energy and protein requirements. Secondary outcomes comprised mean energy and protein intake, body weight, handgrip strength and length of hospital stay.
Results: In IG, 76% versus 70% CG patients reached ≥75% of their energy requirements ($P = 0.57$); 66% IG versus 30% CG patients reached ≥75% of their protein requirements ($P = 0.001$). The risk ratio for achieving ≥75% of protein requirements: 2.2 (95% confidence interval = 1.3–3.7); number needed to treat = 3 (95% confidence interval = 2–6). IG had a higher mean intake of energy and protein when adjusted for body weight (CG: 82 kJ kg^{-1} versus IG: 103 kJ kg^{-1}, $P = 0.013$; CG: 0.7 g protein kg^{-1} versus 0.9 g protein kg^{-1}, $P = 0.003$). Body weight, handgrip strength and length of hospital stay did not differ between groups.
Conclusions: The novel food service concept had a significant positive impact on overall protein intake and on weight-adjusted energy intake in hospitalised patients at nutritional risk.

Introduction

Undernutrition remains a considerable problem in hospitalised patients despite evidence describing both its clinical and economic consequences. The prevalence of hospital undernutrition is reported to range between 20% and 50%, depending on the methods used to measure undernutrition (Norman *et al.*, 2008). Furthermore, there is evidence that 75% of patients at nutritional risk, who remain hospitalised for more than 1 week, lose weight (McWhirter & Pennington, 1994).

If nutritional therapy is not adequately provided, undernourished patients are at risk of increased morbidity, an increased length of hospital stay, a decreased quality of life and increased mortality (Edington *et al.*, 2000; Stratton *et al.*, 2003; Norman *et al.*, 2006).

Food is traditionally recommended as the first choice for treating undernutrition and, subsequently, approximately 75% of hospitalised patients rely solely on the hospital food service menu for nutrition (Mahoney *et al.*, 2009). Hospital food therefore constitutes an important strategy for treating undernutrition within the hospital setting.

Energy-enriched hospital food has been shown to be effective in increasing energy intake in hospitalised patients at nutritional risk (Olin *et al.*, 1996; Gall *et al.*, 1998; Barton *et al.*, 2000). However, none of these studies demonstrated an increase in protein intake.

In 2009, we conducted a historically controlled pilot study aiming to investigate whether a novel food service concept would increase both energy and protein intake in patients at nutritional risk. The food concept was a novel menu of small energy-enriched dishes, on order a la carte 24 h a day (Munk *et al.*, 2013). The study showed a significant time gradient in total energy intake but protein intake did not increase accordingly. Only approximately 20% of the included patients reached 75% of their protein requirements.

The general recommendation for protein requirements during illness is 1.3–2 g kg body weight $(BW)^{-1}$ (Kudsk & Sacks, 2006; Braga *et al.*, 2009). This amount is higher than the 0.8 g kg^{-1} per day recommended for healthy individuals because hospitalised patients are at risk of increased gluconeogenesis, muscle catabolism and, in some cases, decreased absorption of nutrients, as often mediated by the cytokine response to illness or injury (Kudsk & Sacks, 2006; Braga *et al.*, 2009).

This indicates that hospital food intervention trials need to focus more on increasing the protein content of the food at the same time as maintaining focus on energy intake.

The present study aimed to determine whether protein fortification of the novel menu used in the pilot study and subsequent testing of the menu in a randomised controlled trial (RCT) would impact positively on both energy and protein intake in patients at nutritional risk. To date, there have been no published RCTs employing a similar intervention.

Materials and methods

Study design and participants

The trial was conducted in 2011–2012, as a single-blinded block RCT. We included patients over a period of 18 weeks from October 2011 to February 2012.

Study participants were recruited from the departments of Oncology, Orthopaedics and Urology at Herlev University Hospital, Copenhagen, Denmark.

We included a run-in period of 5 weeks (29 August 2011 to 30 September 2011) before randomisation of patients and initiation of data collection. During the run-in period, a convenience sample of patients meeting the inclusion criteria for the RCT pretested the novel food service concept. The aim of the run-in period was to ensure optimal training of staff with regard to screening for eligible patients and ordering of food from the novel menu. The need for a run-in period was identified in a previous pilot study (Munk *et al.*, 2013). After the run-in period, eligible patients were randomly assigned to the intervention (IG) or control group (CG) using stratified block randomisation according to hospital wards. Patients were randomised using sealed, opaque envelopes with a total of nine blocks each consisting of 10 envelopes. The allocation sequence was generated by a secretary who was not otherwise involved in the trial. One of three research assistants (all registered clinical dietitians) recruited and enrolled patients.

Blinding of participants and data assessors was not possible; the latter because patients revealed their group allocation when interviewed about their food intake. Data analysis was blinded by allocating the letters A and B to the two groups. The analysis was undertaken by the principal investigator who was blinded to the randomisation.

Inclusion criteria were:

- newly-admitted patients ≥18 years old who were at nutritional risk according to the validated Nutritional Risk Screening-2002 (NRS-2002) tool (≥3) (Kondrup *et al.*, 2003),
- patients who were able to eat orally,
- an anticipated length of hospitalisation of ≥3 days,
- sufficient language proficiency.

Exclusion criteria were:

- dysphagia,
- food allergy or intolerance,
- anatomical obstructions preventing oral food intake,
- patients who exclusively received enteral or parenteral nutrition,
- terminal patients.

Nursing staff performed the nutritional risk screening and one of the three research assistants screened patients for the remaining inclusion criteria before enrolment.

Nutritional Risk Screening tool

The NRS-2002 is a validated tool for identifying patients who are likely to benefit from nutritional support. Evaluation of nutritional risk is based on two components: nutritional status and severity of disease. Nutritional status depends on three variables: body mass index (BMI), recent weight loss and dietary intake during the last week before admission. A score of 1–3 is given depending on severity of undernutrition, where 3 is given for severe undernutrition. For severity of disease, as an indicator of

stress metabolism and increased nutritional requirement, a score of 1–3 is also given. A score of 3 is given for severe disease (e.g. intensive care). The score for nutritional status is added to the score for severity of disease to give a total score, which can range from 0 to 6. Finally, if the patient is aged ≥70 years, a score of 1 is added to the total score to correct for age-related frailty. If the age-corrected total score is ≥3, nutritional support is indicated and assumed beneficial (Kondrup *et al.*, 2003).

The intervention

The IG received a targeted food concept consisting of an a la carte menu of small dishes enriched with natural energy-dense ingredients and supplemented with a high-quality protein powder (Fig. 1). The dishes were on order by telephone. Patients, ward staff or research assistants could order the dishes, which were presented and served by kitchen staff using a 'room service' approach. We chose this solution because it was anticipated that nursing staff would not always be able to serve the dishes as a result of competing ward responsibilities.

Nursing staff were responsible for preparing patients for eating and for assisting patients who were unable to eat by themselves. Moreover, the dishes were specifically designed so that they were easy to eat with only a fork or a spoon. The novel menu was supplemental to the standard hospital food service. Patients could order as many dishes as they liked between 07.00 and 20.00 h Monday to Sunday. After an order was placed, kitchen staff delivered the dishes within 20 min. To secure nutritional intake during weekends, patients were also able to place orders 48 h in advance so that reductions in ward staff during weekends would not compromise the intervention. If a patient remained hospitalised after completion of data collection (7 days), he/she was free to continue to use the novel hospital food menu until discharge.

We selected the most popular dishes from the original menu tested in our previous pilot study (Munk *et al.*, 2013) and fortified them with a high-quality protein powder (a milk protein, 'GlanPro'; Toft Care System, Copenhagen, Denmark). The amino acid profile of the protein powder was in accordance with the recommendations of the World Health Organisation's technical report from 2007 (WHO, 2007). The final energy and protein fortified novel menu consisted of 23 small dishes (Table 1). All dishes contained a minimum (range) of 6 g (6.1–11.5 g) of protein. The mean (range) energy density was 9.4 kJ/g (2.5 kJ/g to 19.8 kJ/g). All but three dishes (baked salmon, meat loaf, meat balls of veal) contained protein powder. Portion sizes ranged from 52 to 110 g per dish. We used the MASTER CATER SYSTEM, version 3.055 (ANOVA Data A/S, Holte, Denmark) to analyse the energy and protein content of the dishes.

Dietitians, chefs and nurses from the participating departments invested considerable time and effort into achieving the right flavour, texture, volume and a minimum content of 6 g of protein in each dish.

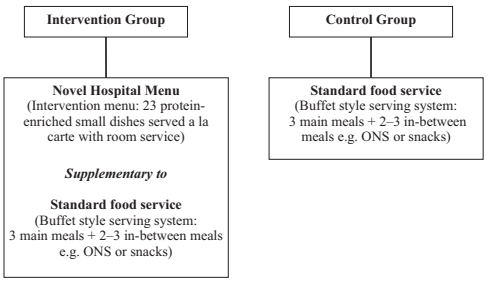

Figure 1 Food concept in the control group compared to the intervention group. ONS, oral nutritional supplements.

Standard hospital food service

The CG received the standard hospital food service (Fig. 1). The standard hospital food service offers three main meals (breakfast, lunch, dinner) served from a buffet. Two main diet types are available: the 'hospital diet' for nutritionally at risk patients and the 'normal diet' for well-nourished patients. The 'hospital diet' has a higher energy and protein density than the 'normal diet'. The CG received the 'hospital diet'.

For breakfast, the CG patients could choose between hot porridge (e.g. oatmeal) and bread with butter, jam and cheese. For lunch, CG patients could choose between, five small slices of rye bread with butter and various toppings such as sliced boiled eggs, ham, shrimps and paté and, also, a hot soup of the day. For dinner, two different kinds of starters, two different kinds of hot meals and two different kinds of dessert were available. The three main meals served from the buffet are intended to provide 50–75% of nutritional requirements. The remaining requirements are covered by three in-between meals [e.g. microwaveable meals, snacks (e.g. cakes), biscuits with cheese, ice cream and/or beverages (e.g. oral nutritional supplements)]. In-between meals are served either by the buffet-staff or by nursing staff.

The national nutritional guidelines for the 'hospital diet', energy and protein rich beverage included, recommend that the hospital diet on average contains 9000 kJ, 95 g of protein (15–20% of energy), 100 g of fat (40–50% of energy) and 225 g of carbohydrate (40–45% of energy) (Danish Veterinary & Food Administration, 2009).

Table 1 The novel food service concept menu*

Menu	Portion size g	Energy kJ	Energy density kJ g^{-1}	Protein g	Orders Ranked†
Breakfast dishes					
Omelette with bacon	60	699	11.7	9.1	4
Breakfast muffin with butter, cheese and jam	100	1518	15.2	11.5	5
Ryebread porridge with fresh vanilla cream	90	371	4.1	7.4	6
Soups					
Clear soup with vegetables, meatballs and dumplings	79	195	2.5	6.9	1
Classical mushroom soup	75	468	6.2	8.2	5
Fish dishes					
Terrine of smoked eel	60	555	9.3	7.6	4
Baked salmon with egg coleslaw, hazelnuts and olive tapenade	70	763	10.9	8.9	4
Slightly smoked trout seasoned with egg salad and fresh chervil	55	540	9.8	8.0	5
Meat dishes					
Meat loaf with game sauce and cranberries	73	448	6.1	7.6	4
Meat balls of veal with stewed cabbage and bechamel sauce	55	451	8.2	6.5	4
Crispy fried fish crépine with Jerusalem artichokes in cream sauce	75	720	9.6	7.5	5
Chicken sticks with peanut butter	55	739	13.4	7.9	5
Side dishes					
Mashed sweet potatoes with onion and bacon	68	658	9.7	6.4	3
Torta di risotto with fried mushrooms, herbs and lemon peel	47	412	8.8	7.7	5
Warm potato omelette with a compote of pickled red onions	50	537	10.7	6.1	5
Baked cauliflower cream with roasted nuts and pickled cucumbers	60	389	6.5	7.1	5
Mashed root vegetables with browned butter	75	628	8.4	6.1	5
Desserts					
Chocolate confection of marzipan and nougat	52	1028	19.8	6.3	2
Crunchy apple cake with peel of orange	90	815	9.1	7.3	2
Mild fromage with cream and chocolate	68	623	9.2	7.6	3
Buttermilk dessert with lemon and small cookies	100	835	8.4	6.9	3
Hot chocolate with whipped cream	110	801	7.3	6.2	4
Ice cream of avocado with fresh fruit	70	772	11.0	7.1	5

*Reflects portion size, the energy density, energy and protein content of all 23 dishes of the novel menu.
†The dishes are ranked according to how often the dishes were ordered. Ranking order: 1 = dishes ordered >50 times; 2 = dishes ordered ≥40 to <50 times; 3 = dishes ordered ≥30 to <40 times; 4 = dishes ordered ≥20 to <30 times; 5 = dishes ordered ≥20 to <30 times; 6 = dishes ordered <10 times.

Nutritional content of the novel food service concept compared to the 'hospital diet'

The novel food service concept was designed to fulfill, as a minimum, the same criteria for energy and protein content as described above. To reach daily nutritional requirements solely from the novel menu, patients needed to consume two dishes of the novel menu six times daily and drink two glasses of whole milk. This would on average provide patients with 8700 kJ and 102 g of protein. As noted earlier, the intention of the novel menu was to comprise a supplementary offer to the standard hospital food menu (Fig. 1).

Outcomes

The primary outcome was the percentage of patients reaching ≥75% of their protein and energy requirements. This nutritional target was based on a previous trial reporting that weight stability is achieved with this level of intake (Kondrup, 2001).

Secondary outcomes were mean energy and protein intake, changes in body weight (BW), hand grip strength (HGS) and length of hospital stay (LOS). BW and HGS were recorded at baseline and every second or third day.

Body weight was measured with patients wearing underwear and immediately after they had urinated. Values were rounded to the nearest 0.1 kg.

Hand grip strength was measured in the patients' right hand using the Jamar 5030J1 hydraulic hand dynamometer (SAEHAN Corporation, Changwon, Korea). This dynanometer is reported to produce the most accurate measurement of HGS (Mathiowetz *et al.*, 1984).

We standardised the measurement of HGS in each patient by using the same position in individual patients for repeated measurements. HGS was only measured in the right hand because this is a valid method to use in

both right- and left-handed people (Petersen *et al.*, 1989; Incel *et al.*, 2002). We demonstrated the technique once to patients and then encouraged them to squeeze the hand dynamometer quickly and with maximum strength three times within 15-s intervals. The highest of three consecutive measurements was used in the data analysis.

We included the baseline data: age, sex and self-reported height, with the data being collected by research assistants.

Energy and protein intake

We calculated energy and protein intake as a mean intake over 3, 4, 5, 6 or 7 days, depending on the patient's LOS after inclusion. A detailed nutritional registration form was used to distinguish between different meal components. The amounts consumed of each portion of food/beverage were visually assessed and recorded in quartiles (0%, 25%, 50%, 75% and 100%) by nursing staff or patients. This is a validated method to assess food intake (Olin *et al.*, 1996). To ensure and verify the content of patients' dietary records, the research assistants collected records daily and conducted short daily dietary recall interviews with both IG and CG patients.

Estimation of energy and protein requirements

Patients' energy requirements were estimated according to Danish guidelines for hospitalised patients; the basic metabolic rate (BMR) multiplied by an estimated activity factor[1] (i.e. and by a stress factor in case of fever[2] [i.e. or, if BMI < 18.5, a factor for weight gain[3] (i.e. (Danish Veterinary & Food Administration, 2009). The BMR was calculated by Harris–Benedict equation[4]. Protein requirements were set at 18% of the energy requirement as recommended in Danish institutional diets guidelines (Danish Veterinary & Food Administration, 2009).

Statistical analysis

Statistical analyses were carried out using SPSS, version 18.0 (SPSS Inc., Chicago, IL, USA) . Descriptive statistics were used to calculate the mean (SD). We used Pearson's chi-squared tests and Fisher's exact test, as appropriate, to test differences between categorical data. Independent *t*-tests were used for interval scale variables. Mean energy and protein intake according to BW was calculated. Mean difference in HGS and BW was adjusted for baseline using univariate analysis of variance. For categorical outcomes, we calculated risk ratios (RR) with 95% confidence intervals (CI) and, for significant results, numbers needed to treat (NNT); for continuous outcomes, we calculated mean differences with 95% CIs. Data were analysed according to intention-to-treat.

In an exploratory analysis using the chi-squared test, we examined the effect of reaching ≥75% of energy and protein requirements on stability/increase in HGS.

Power

In a previous pilot study, 75% of the last 20 enrolled patients consumed ≥75% of their energy needs (Munk *et al.*, 2013). With a run-in period before initiation of the present trial, it was considered realistic to expect that 75% of IG patients would be able to cover ≥75% of their energy. Based on results from an earlier observational study (Hansen *et al.*, 2008), we further expected that 44% of the CG would be able to consume ≥75% of their energy and protein needs. With these expectations, 40 patients in each group were required to detect a significant difference in the percentage of patients achieving ≥75% of their energy and protein needs (from 44% to 75%) with a power of 80% and a 5% two-sided significance level. To take a potential 20% drop-out into account, we planned to include an additional 16 patients.

Ethical aspects

The Danish Regional Committee on Biomedical Research Ethics and the Danish Data Protection Agency approved the protocol, as well as the safety of the protein enrichment powder. The trial was registered at http://clinicaltrials.gov (ID nr: H-1-2011-048).

Before inclusion, patients received both oral and written information about the project from the research assistants. Before inclusion in the trial, patients were asked to provide their written informed consent.

Results

Study population

Overall, 105 patients were eligible for inclusion (Fig. 2). Twenty-one patients refused to participate.

The reasons for not wanting to participate were lack of resources to engage (n = 11), no interest in trial participation (n = 2), anticipation of short LOS (n = 1), dissatisfaction with hospital treatment (n = 1) and no reason given (n = 6).

Eighty-four patients were randomised and 81 patients completed the trial, giving a completion rate of 96%.

[1](×1.1 if bedridden and ×1.3 if being able to walk around on the ward)

[2](×1.2 (38 °C), 1.3 (39 °C), 1.4 (40 °C)]

[3](×1.3)

[4]Harris-Benedict equation for calculating BMR: men: BMR = 66.5 + 13.8 weight + 5.0 height − 6.8 age; women: BMR = 655 + 9.6 weight + 1.8 height − 4.7 age)

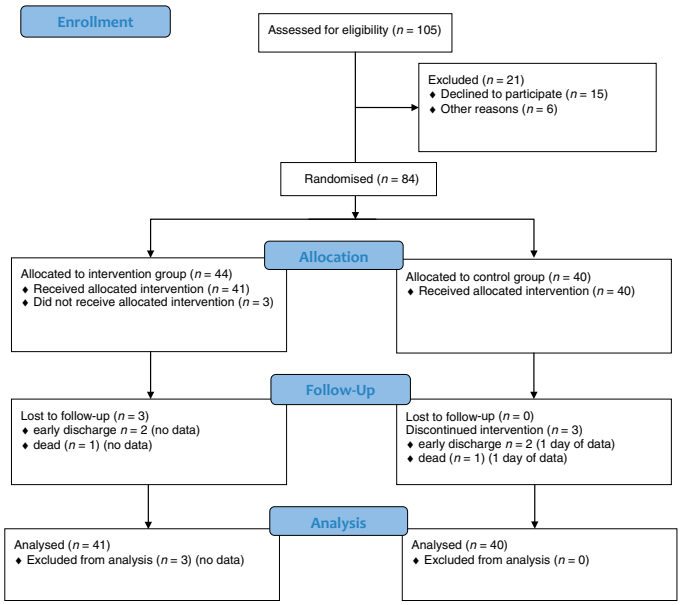

Figure 2 Consolidated Standards of Reporting Trials flowchart of patient enrolment, random assignment and follow-up.

Demographic data are shown in Table 2. IG and CG patients were similar with respect to age, sex, anthropometry and nutritional status at baseline. All patients were moderately undernourished [mean (SD) nutritional score of 1.9 (0.8)] and, overall, had a mild severity of disease score [mean (SD) severity of disease score of 1.1 (0.5)]. The distribution of cancer diagnoses was similar in the groups.

Outcome

Primary outcome

Significantly more IG patients compared to CG patients achieved an intake of ≥75% of their protein requirements ($P = 0.001$) (Table 3). The RR for reaching ≥75% of their protein requirements was 2.20 (95% CI = 1.3–3.70), with NNT = 3 (95% CI = 2–6) (Table 3).

The IG and CG did not differ with respect to achieving ≥75% of energy requirements, with a RR of 1.1 (95% CI = 0.8–1.4) (Table 3).

Secondary outcomes

The difference in mean energy intake was 693 kJ between IG and CG, with the IG achieving the highest energy intake. However, the difference did not reach significance ($P = 0.08$) (Table 3). Calculating energy intake according to BW, the energy intake was significantly higher in the IG (mean difference: 20 kJ kg^{-1}, $P = 0.013$) (Table 3).

Table 2 Baseline data for intervention and control group

	Intervention	Control
N	41	40
Sex (*n*)		
Male	16	18
Female	25	22
Age (years)*	75 (10)	74 (11)
Anthropometric data*		
Weight (kg)	60 (14)	65 (13)
Body mass index (kg m^{-2})	21 (4)	22 (4)
Departments (*n*)		
Urology	15	15
Orthopaedic surgery	12	10
Oncology	14	15
Nutritional risk assessment (*n*)		
Score for nutritional status (0–3)		
0	1	0
1	10	15
2	18	17
3	12	8
Score for severity of disease		
0	2	3
1	30	34
2	8	3
3	1	0
Total score		
3	18	27
4	13	9
5	7	4
6	3	0

*Mean (SD).

Table 3 Results of primary and secondary outcomes of intervention group versus control group

	Intervention group (IG) (n = 41)	Control group (CG) (n = 40)	Risk ratio (95% confidence interval)	Mean difference between IG/CG (95% confidence interval)	P-value
Primary outcome					
Coverage of ≥75% of nutritional requirements					
Energy, n (%)	31 (76)	28 (70)	1.1 (0.8–1.4)		0.57*
Protein, n (%)	27 (66)	12 (30)	2.2 (1.3–3.7)		0.001*
Secondary outcome					
Mean energy and protein intake					
Energy, kJ (SD)	5843 (1660)	5149 (1832)		693 (−80 to 1466)	0.08†
Protein, g (SD)	53 (16)	43 (17)		9.6 (2–16)	0.011†
Mean intake (kJ kg^{-1})					
Energy, kJ kg^{-1} (SD)	103 (39)	82 (33)		20 (5–36)	0.013†
Protein, g kg^{-1} (SD)	0.9 (0.4)	0.7 (0.3)		0.2 (0.1–0.4)	0.003†
Mean difference in body weight (BW)‡					
BW, kg (SD)§	0.4 (2.6)	−0.4 (1.8)		−0.8 (−1.9 to 0.3)	0.17†/††0.33
Mean difference in hand grip strength (HGS)¶					
HGS, kg (SD) **	−0.1 (2.9)	−0.4 (4.3)		−0.3 (−1.9 to −1.4)	0.76†/0.95††
Length of hospital stay (LOS)‡‡					
LOS1§§, day (SD)	15 (10)	14 (8)		1.8 (−2 to 6)	0.38†
LOS2¶¶, day (SD)	10 (8)	10 (8)		0.6 (−3 to 4)	0.73†

*Pearsons chi-squared test.
†t-test.
‡n = 66 (IG: 37).
§Mean difference from baseline to day 3. Subsequent follow-up data (>3 days) are not presented because of many missing data.
¶n = 76 (IG = 41).
**Mean difference from baseline to day 3. Subsequent follow-up data (>3 days) are not presented because of many missing data.
††Result adjusted for baseline using an univariate analysis of variance.
‡‡n = 79 (death: IG = 1 and CG = 1).
§§LOS1 = days from admission to discharge.
¶¶LOS2 = days from inclusion to discharge.

Mean protein intake was significantly higher (mean difference: 9.6 g day^{-1}; P = 0.011) in the IG, also according to BW (mean difference: 0.2 g kg^{-1}; P = 0.003) (Table 3). No significant differences were found with respect to BW, HGS and LOS between groups (Table 3). Adjusting mean differences in HGS and BW for baseline values did not change the results.

Seven patients received oral nutritional supplements (ONS) (IG: two patients). We did not observe any significant difference between the groups in consumption of ONS (P = 0.26). The ONS used were products from Fresenius Kabi (Bad Homburg, Germany) or Nutricia (Schiphol, The Netherlands). The ONS contained 1260 kJ, with protein varying from 8 to 12 g. The seven patients received a maximum of one ONS per day during the intervention period. No patients received enteral or parenteral nutrition during the study period.

Data revealed no significant differences in energy intake between the groups according to the distribution of quartiles. The distribution showed that 6% of CG and 2% of IG patients achieved an energy intake below 50% of requirements; 20% of CG and 10% of IG patients had a protein intake below 50% of requirements (Table 4). There was a significant difference between quartiles with respect to protein intake. The majority of CG patients (81%) achieved a protein intake ≥50% of requirements. The main difference between the groups was that significantly more IG patients achieved ≥75 of their protein requirement.

An exploratory analysis of the data revealed a significant effect of achieving ≥75% of energy requirement on stability or increase in HGS. In the group achieving >75% of energy requirements, 68% (27/40) either increased or stabilised HGS versus only 43% (16/37) of those not reaching >75% of energy requirements (P = 0.015). It should be noted that this analysis was performed on nonrandomised material.

The novel menu

The dishes from the novel menu accounted for 30% [mean (SD) 1691 (1225) kJ day^{-1}] of the energy intake

Table 4 Coverage of energy and protein requirements in quartiles in intervention group (IG) versus control group (CG)

Quartiles	0–24%	25–49%	50–74%	≥75%	Total
Energy intake*					
CG, *n* (%)	1 (2.5)	1 (2.5)	10 (25)	28 (70)	40
IG, *n* (%)	0 (0)	1 (2.4)	9 (22)	31 (75.6)	41
Total	1	2	19	59	81
Protein intake†					
CG, *n* (%)	2 (5)	6 (15)	19 (47.5)	13 (32.5)	40
IG, *n* (%)	0 (0)	4 (9.7)	10 (24.4)	27 (65.9)	41
Total	2	10	29	40	81

*Fisher's exact test, $P = 0.846$.
†Fisher's exact test, $P = 0.013$.

and 40% [mean (SD) 35 (22) g day^{-1}] of the protein intake in the IG.

A varied distribution of dishes was ordered. However, patients appeared to prefer sweet and/or soft dishes such as: soup, buttermilk dessert, mild fromage, confections of marzipan and mashed potatoes (Table 1). Patient preferences did not appear dependent on whether protein powder was added because the preferred dishes all contained protein powder.

Discussion

Primary outcome

The novel menu significantly increased the number of IG patients achieving ≥75% of their protein requirements, although without increasing the number of patients achieving ≥75% of their energy requirements accordingly. Indeed, the menu doubled the number of patients achieving ≥75% of their protein requirements. With a NNT of three for one patient to achieve ≥75% of their protein requirements, and considering that the novel menu accounted for 40% of the protein intake in the IG, we consider the novel menu a relevant and feasible intervention for hospitalised patients at nutritional risk.

Surprisingly, the percentage of patients achieving an energy intake ≥75% of energy requirements, did not differ between groups. It is possible that the increased focus on nutritional intake in the CG as a result of the registration of nutritional intake may have influenced the awareness of food intake in CG patients and thereby increased their energy intake.

Previous RCTs report similar results. However, the interventions tested in these studies were considerably more time consuming, requiring daily attention from a dietitian or nurse to motivate patient and staff, daily adjustments of individualised nutritional plans, ordering of food in collaboration with patients, and securing the supply of food ordered (Johansen *et al.*, 2004; Starke *et al.*, 2011). The present study, in comparison, demonstrated that a relatively simple and feasible nutritional intervention was as effective.

To this date, we have not identified other RCTs of similar interventions using the same primary outcome as in the present study. This is unfortunate because comparing mean values for energy and protein intake alone between intervention and control groups may mask the proportion of severely underfed patients in either of the groups.

Our results point towards the value of protein enrichment. Previous studies with similar settings, interventions and primary outcome (i.e. increasing energy and protein intake) have demonstrated increased mean energy intakes but, in contrast to the present study, did not increase protein intake (Gall *et al.*, 1998; Barton *et al.*, 2000; Munk *et al.*, 2013). This is not surprising because these studies primarily enriched the food with naturally energy-dense ingredients. In our experience, it is easier to increase energy content without compromising taste, texture and volume. Increasing protein content, on the other hand, is more difficult, especially when using high-quality protein powder becauase aromatic amino acids can alter taste negatively.

However, it is definitely possible to develop a delicious menu using high-quality protein powder. Three key issues need to be taken into consideration: (i) a chef should be responsible for developing the menu because of his/her professional knowledge of producing foods with excellent taste; (ii) experienced clinical dietitians are vital for supplying the chef with knowledge about the taste preferences of hospitalised patients at nutritional risk, as well as for securing the energy and protein content of the menu; and (iii) sufficient time should be allocated for taste testing sessions in the development phase, including test sessions where patients are included.

Energy and protein intake <50% of requirement has been shown to be associated with increased 6-month mortality (Holst *et al.*, 2010). A minority of patients in the present study had a protein intake below this level. The effect of the novel food service concept tested in the present study was rather that patients consuming 50–74% of protein target further increased their protein intake, thus moving up to the ≥75% of protein target.

Secondary outcomes

We observed no differences in weight change between groups. We did not take oedema, ascites or degree of hydration into account. Registration of food intake over a maximum of 7 days might also have been too brief to detect a significant difference between groups. The high energy intake in both the IG and CG may also have contributed.

Muscle function is a clinically relevant outcome parameter that responds rapidly to insufficient nutritional intake, making HGS a popular surrogate outcome for changes in nutritional status (Norman *et al.*, 2011). We did not identify a difference between groups in HGS. The present study was not powered to detect differences between groups in HGS. The high mean age in the included patients could also have contributed, especially because, in elderly patients, HGS may not consistently reflect nutritional therapy (Norman *et al.*, 2011). Indeed, a meta-analysis found no positive effect of nutritional intervention on HGS in older people (Milne *et al.*, 2009).

Length of hospital stay did not differ between groups. The primary reason was a lack of power. However, a supplemental reason could be that the difference between energy and protein intake in the groups was too small. Some studies argue that a minimum difference is required to influence LOS (Johansen *et al.*, 2004; Starke *et al.*, 2011). An energy intake of 155 (8) kJ kg^{-1} and a protein intake of 1.4 (0.1) g kg^{-1} may lead to reduced LOS (Johansen *et al.*, 2004). LOS furthermore depends on a plethora of patient-related, treatment-related and organisational factors, all of which may be unrelated to nutritional intake.

Even though the results of the present trial are promising, we need to continue to set even higher standards so that more patients achieve at least their minimum energy and protein requirements when hospitalised. ONS are effective for increasing energy and protein intake in hospitalised patients (Stratton *et al.*, 2003). Surprisingly, in the present study, only seven patients received ONS.

By supplementing the novel food service concept tested in the present study with two ONS a day, we might further increase the percentage of patients reaching 75% of their minimum energy and protein requirements. Another approach could be to supplement the novel food service concept with dietary counselling. However, this should be investigated in further RCTs including the economic implications of such an intervention.

Furthermore, to increase the level of evidence in future food interventions studies, we emphasise the value of conducting RCTs using relevant and comparable outcomes. Koller *et al.* (2013) recommend the use of biomedical outcomes in combination with patient-reported outcomes (e.g. quality of life and health economic outcomes to assess the effect of nutritional therapies).

Strengths and limitations of the study

The use of a randomised controlled design and the low drop-out rate increases the strength of the results of the present study. Blinding of ward staff and data assessors would have been preferable to minimise the risk of performance and detection bias. However, blinding of patients and staff was not possible and, because of the way in which nutritional intake was monitored, only a single-blinded design with blinded data analysis was possible.

The use of a validated method to estimate energy and protein intake is also a strength. We calculated mean energy and protein intake over as many days as possible for each patient (maximum 7 days). This may have inflated the overall mean energy and protein intake as a result of an expected increase in nutritional intake over time. Patients who were followed for 7 days, however, did not have an increased intake compared to those followed for <7 days (data not shown).

Furthermore, we attempted to use a standardised protocol for measuring HGS. This protocol proved to be difficult to apply in a hospital setting. Many patients were unable to get out of bed or sit up in a chair, a position that is part of the standardisation. Instead, we chose to use the same position in individual patients for repeated measurements. This may influence the comparability of our study with other similar studies.

If this novel food service concept is to be implemented, economic implications should be considered. We did not conduct an economic evaluation of the costs associated with our approach.

Future studies should include this aspect. The risk of increasing costs might limit the translation and subsequent implementation of the novel menu model. However, given the major economic consequences of undernutrition, individually and for society (Ljungqvist & de Man, 2009), translation of the novel menu could potentially constitute a relatively low-cost intervention for addressing undernutrition in hospitalised patients.

Although time-consuming at the start, we argue that adaptation of the novel menu to local food cultures and hospital menus, as carried out in the present study, is feasible.

Conclusions

The intervention had a significant positive impact on overall protein intake and on weight-adjusted energy intake compared to the standard hospital menu, indicating that the novel food service concept can be a simple and effective strategy for increasing protein and energy intake in hospitalised patients at nutritional risk.

However, the impact of the food concept on relevant treatments outcomes (i.e. physical function, LOS and quality of life) needs to be studied further in larger RCTs. Finally, the economic implications of the intervention also require additional investigation.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.

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TM, MAN and TT designed the research. ER and AMB conducted the research. TM performed the statistical analysis. TM, TT, HHR, MH and AMB interpreted the data. TM and TT wrote the manuscript. TT and TM have primary responsibility for the final content. All authors critically read and approved the final version submitted for publication.

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Appendix D

Study III

Individualised dietary counselling for nutritionally at-risk older patients following discharge from acute hospital to home: a systematic review and meta-analysis

Abstract

Background
Many older patients are undernourished after hospitalisation. Undernutrition impacts negatively on physical function and the ability of older patients to perform activities of daily living at home after discharge from acute hospital. The objective was therefore to evaluate the evidence for an effect of individualised dietary counselling following discharge from acute hospital to home on physical function, and, secondly, readmissions, mortality, nutritional status, nutritional intake and quality of life (QoL) in nutritionally at-risk older patients.

Methods
A systematic review of randomised controlled trials. The overall quality of the evidence was assessed according to the GRADE criteria.

Results
Four RCTs (n = 729) were included. Overall, the evidence was of moderate quality. Dietitians provided counselling in all studies. Meta-analyses showed a significant increase in energy intake (MD: 1.10 MJ/d, 95% CI: 0.66; 1.54, $p < 0.001$), protein intake (MD: 10.13 g/d, 95% CI: 5.14; 15.13, $p < 0.001$) and body weight (BW) (MD: 1.01 kg, 95% CI 0.08; 1.95, $p = 0.03$). Meta-analyses revealed no significant effect on physical function assessed using Hand Grip Strength, and likewise on mortality. Narrative summation of effects on physical function using other instruments revealed inconsistent effects. Meta-analysis were not conducted on QoL and readmissions due to lack of data.

Conclusion
Individualised dietary counselling by dietitians following discharge from acute hospital to home improved BW, and energy and protein intake in older nutritionally at-risk patients, however without clearly improving physical function. The effect of this strategy on physical function and other relevant clinical outcomes warrants further investigation.

Introduction

Undernutrition is common in older hospitalised patients and nutritional state often deteriorates further during hospital stay; leaving a high percentage of older patients undernourished or at nutritional risk at discharge (The Danish National Quality Database for Geriatrics., 2012; Vanderwee et al., 2010; Holst et al., 2013; Cansado et al., 2009; Kyle et al. 2005; McWhirter& Pennington., 1994). Deterioration in nutritional status results in decreased muscle mass and function which in turn may lead to loss of autonomy (Hoogerduijn et al., 2012, Alley et al. 2010). Loss of autonomy in older patients may require discharge to nursing homes rather than to home after hospitalisation (Sorensen et al., 2008, Charlton et al,. 2012). Reduced muscle-mass and function in older patients is also associated with prolonged recovery post-discharge and a higher risk of readmissions to hospital (Charlton et al., 2010; Boumendjel et al., 2000; Boyd et al,. 2008). In fact, thirty to sixty percent of older patients experience functional decline, hospital readmissions, reduced QoL and loss of autonomy after hospitalization (Hoogerduijn et al., 2012). This affects the individual patient and places an economic burden on the health system and society as a whole (Rosen et al., 2013).

Therefore, the transition across sectors (from hospital to home) may comprise a unique window of opportunity for targeted nutritional interventions for older patients at nutritional risk.
Indeed, according to the Resolution of the Council of Europe, patients in need of nutritional support should receive such nutritional treatment at the earliest opportunity during hospital stay and after discharge (Council of Europe., 2003).

Currently, only one systematic review has examined the effect of nutritional support for nutritionally at-risk older patients following discharge from acute hospital to home (Beck *et al.,* 2013). The review included 6 studies assessing the benefits of oral nutritional supplements (ONS) without dietary counselling. A positive effect on BW and energy and protein intake was identified while the effect on physical function was weak. No effect was found on survival and the risk of hospital readmission. One explanation for the weak effect on physical function and no effect on survival and hospital readmission could be the relatively low level of compliance to ONS in the included studies. Individualised dietary counselling in combination with ONS might be able to give additional benefits, since this approach may represent an opportunity to

personalise the nutritional plan, thereby potentially overcoming problems with low compliance. (Lad *et al.,* 2013; Bruce *et al.,* 2003; Starke *et al.,* 2011). Individualised dietary counselling provided at home following hospital discharge also enables continuous monitoring of the in-hospital nutritional plan. This furthermore confers continuity across sectors.

To our knowledge, there are no systematic reviews of the effect of individualised dietary counselling after discharge from an acute hospital to nutritionally at-risk older patients.
Thus, the aim of this systematic review was to collate and evaluate the evidence for an effect of individualised dietary counselling following discharge from an acute hospital to home, on physical function, and, secondly, on energy and protein intake, nutritional status, quality of life, hospital readmissions and mortality in nutritionally at-risk older patients.

Methods

A systematic review and meta-analysis conducted according to the method of Cochrane (Higgins & Green., 2011).

Eligibility of studies

The inclusion criteria of the review were: Studies which included older patients (> 60 years of age) who were assessed to be at nutritional risk, and studies which evaluated individualised dietary counselling following discharge from an acute hospital to home regardless of any previous in-hospital individualised dietary counselling. To provide the highest level of evidence only randomised controlled trials (RCTs) were included.

Exclusion criteria were: Studies that included patients suffering from chronic medical conditions requiring repeated ambulatory visits or planned hospital readmissions (e.g. dialysis, chemotherapy), studies using artificial nutritional support as nutritional source (i.e. enteral tube feeding and parenteral nutrition), studies which evaluated the effect of oral nutritional supplements without individualised dietary counselling and, finally, studies evaluating multifactorial interventions e.g. physical training and individualised dietary counselling compared to standard care.

Individualised dietary counselling could include advice on how to increase energy and protein intake, such as using dietary fortification to optimise the energy and protein density of the diet without increasing quantity; and/or adding extra snacks or drinks e.g. homemade or ONS. Individualised dietary counselling should be initiated directly after hospital discharge and could be given either by personal visits or telephone or using both methods.

Search strategy and selection

Medline Ovid, EMBASE and Cochrane Central Register of Controlled Trials were searched in March 2013 and updated in May 2014 using the PICO(S) framework (Patients, Interventions, Comparison, Outcomes, Studies) (Table 1).

No restrictions on date of publication or language were applied to the search. Reference lists of included trials and related reviews were searched to identify additional studies. Relevant ongoing or unpublished trials were sought by contacting experts in the field and by searching www.clinicaltrials.gov. The search strategy is provided as additional material.

Two authors (TM, UT) independently assessed abstracts and titles according to the inclusion and exclusion criteria. Full text articles retrieved for potential inclusion were assessed by the same two authors independently. Differences of opinion were discussed among the two authors and decisions reached through consensus. A PRISMA flow-chart of study selection is described in Figure 1.

Table 1. The PICO(S)

Patient	Nutritional at-risk patients
Intervention	Individualised dietary counselling following discharge from acute hospital to home +/- ONS
Comparison	Standard care (i.e. no nutritional follow-up, or prescribed oral nutritional supplements but without any post-discharge individualised dietary counseling)
Outcomes	Physical function (i.e. activity of daily living, gait speed) as primary outcome. Secondary outcomes were energy and protein intake, nutritional status, Quality of Life, hospital readmissions and mortality
Study	Randomised controlled trials

PICOS (Patients, Interventions, Comparison, Outcomes, Studies), ONS = oral nutritional supplements

Quality assessment

Two authors (TM, UT) independently assessed risk of bias (internal validity) in included studies using The Cochrane Collaboration's Risk of Bias Tool (Higgins & Green., 2011). Differences of opinion were discussed among the two authors and decisions reached through consensus.
The tool includes six domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective reporting. Biases not addressed in these six domains were evaluated in the last domain named “other bias”. Each domain was assessed to be at “Low risk’, ‘High risk’ or at ‘Unclear risk’ of bias (Figure 2).

The Grading of Recommendations Assessment, Development and Evaluation system (GRADE) was used to assess the quality of the evidence across outcomes in the included studies. The quality of evidence was assessed for physical function (measured by hand grip strength) and mortality (Higgins & Green., 2011). Grade was not used to assess the quality for energy intake, protein intake and BW since these outcomes were not considered to be ‘important’ clinical outcomes. The quality of the evidence was graded from very low to high quality based on study design, risk of bias, inconsistency, indirectness, imprecision and risk of publication bias (Higgins & Green., 2011).

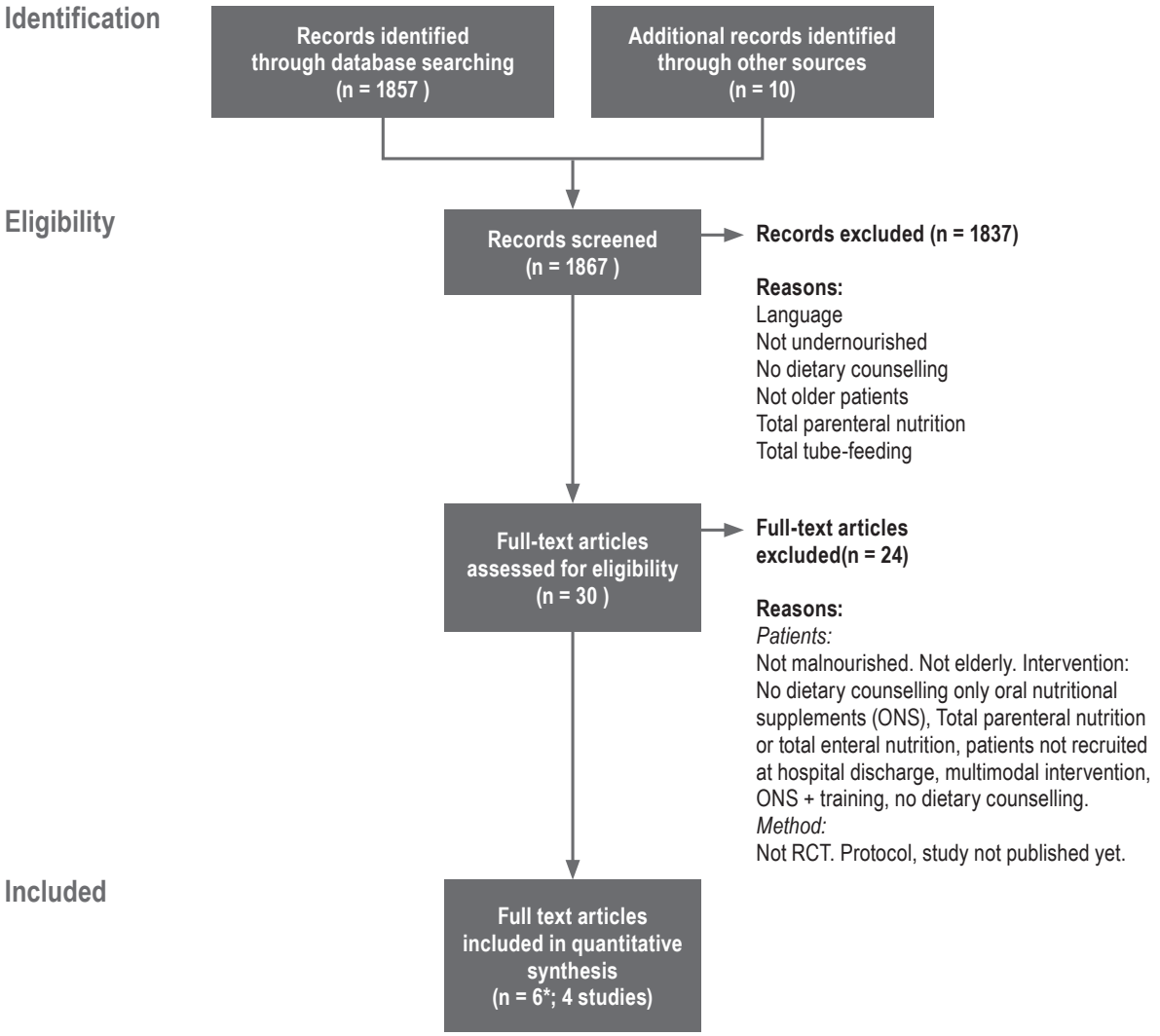


*Figure 1. Flow chart of study selection process. *4 RCTs published in 6 articles.*

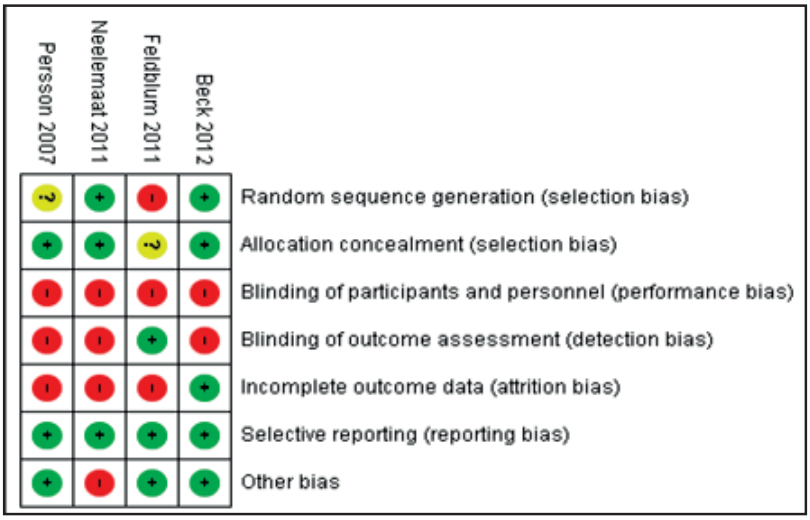


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. Yellow = unclear risk, red = high risk, green = low risk

It is important to note that in dietary interventions it is difficult to blind patients and staff. This inevitably results in a judgement of high risk of bias in this domain and subsequent downgrading of the quality of the evidence according to the recommendations of The Cochrane Collaboration's Risk of Bias Tool and GRADE (Higgins & Green., 2011). In the blinding domain, the quality of evidence was, however, downgraded by only 1 if at least 50 % of the included studies had either blinded outcome assessment or blinded data analysis. Furthermore, mortality was not considered to be at risk of detection bias and was therefore not downgraded due to lack of blinding.

Synthesis of data and statistical analysis

The Review Manager 5.2 (The Cochrane Collaboration, Oxford, England) was used for data analysis (Higgins & Green., 2011) and when appropriate, pooled effects were estimated using meta-analyses. Mean Differences (MD) were used for continuous data and Risk Ratios (RR) for dichotomous data; both with 95% confidence intervals (CIs). Data were analysed according to the intention-to-treat principle.
Heterogeneity was assessed using the I^2-test and the chi-squared test (Higgins & Green., 2011). To account for the inclusion of only a few numbers of studies in the meta-analysis, a P-value of 0.10 was chosen when assessing whether heterogeneity was statistically significant (Higgins & Green., 2011). When I^2 values were between 0 and 40% and the chi-squared test was non-significant, heterogeneity was not considered important (Higgins & Green., 2011). Given the potential clinical heterogeneity across studies, a conservative approach to meta-analysis using the random effects model was chosen as the default method to summarise the pooled effect. However, the fixed effect model was chosen if the above criteria for heterogeneity were fulfilled, and if it did not significantly change the pooled effect estimate of the random effects approach. When data were not available or not comparable (e.g. physical function assessed with different instruments across studies) results were summarised narratively.

Authors were contacted in case of missing data. Data on weight change (MD) in the control group were provided by Neelemat et al. as the authors did not report these data in the original article (Neelemaat *et al.,* 2011). Data on weight change (MD) in Perssons et al. were obtained from a meta-analysis (Baldwin & Weeks., 2012). Finally, Beck et al. provided additional, detailed data on weight change and energy and protein intake (Beck *et al.,* 2011).
Sensitivity analyses were planned excluding studies at high risk of bias. Furthermore, investigation of publication bias was planned using a funnel plot. Finally, we intended to conduct subgroup analyses of

a) interventions applied both during and after hospitalisation versus exclusively post-discharge interventions, and
b) prolonged interventions (≥ 3 months duration) versus brief interventions (<3 months).

Results

The searches yielded 1857 citations (Figure 1).
Thirty potentially eligible studies were retrieved in full text. Of these, 24 were excluded in accordance with the inclusion and exclusion criteria. This resulted in inclusion of four RCTs (six articles) involving initial recruitment of 729 patients.

Characteristics of included studies

Table 2 shows the main characteristics of the included studies. The percentage of eligible patients accepting participation in the trials ranged from 55%-81%, with an average of 70%. Completion rates ranged from 50-78%. The interventions lasted from 8 to 12 weeks (Neelemaat *et al.,* 2011; Persson *et al.,* 2007; Feldblum *et al.,* 2011; Beck *et al.,* 2012), however, in one study the intervention period was not clearly described (Feldblum *et al.,* 2011). In all studies the individualised dietary counselling was performed by a registered dietitian (RD). The individualised dietary counselling was performed either by visiting the patient's home (Feldblum *et al.,* 2011) or by telephone (Neelemaat *et al.,* 2011) or as a combination of both (Persson *et al.,* 2007, Beck *et al.,* 2012) (Table 2).
Neelemaat et al. published 3 articles originating from the same trial (Neelemaat *et al.,* 2011; Neelemaat et al., 2012; Neelemaat *et al.,* 2012 B). In the first article, results on physical function and weight change were reported (Neelemaat *et al.,* 2011).
In the second article, data on energy and protein intake were reported (Neelemaat *et al.,* 2012) and, finally, in the third article, results on physical function were updated using multiple imputation of missing data in the data analysis (Neelemaat *et al.,* 2012 B).

Risk of bias

Overall, the studies were assessed to be at high risk of bias, mainly due to lack of adequate blinding of patients, personnel and outcome assessors and high drop-out rates (Figure 2). Sequence generation and allocation concealment was judged to be at low risk of bias.

The overall quality of the evidence for physical function assessed using HGS and mortality was moderate, mainly due to lack of blinding and high drop-outs (Table 3).

Table 2. Study characteristics of the included studies

Study (year published)	a. Number of patients *(treatment/control).* b. Drop-out *(treatment/control)*	Patient characteristics *(treatment/control):* mean age in year, sex, nutritional screening tool	Setting (recruitment)	Intervention	Dietary counselling in intervention group	Control group	Outcome measures and follow-up time (months)
Beck (2012)	a. N: 152 (73/79). b.Drop-out: 18% (14%/22%).	Age: (81 y/82 y) F: (74 % / 72%) Undernourished/nutritional risk assessed by NRS-2002, level 1.	Department of Geriatric Medicine, Herlev University Hospital, Denmark	• No in-hospital intervention. • 3 x RD counselling + 3 x GP visits at home after discharge Intervention time: 8 weeks	Individual plan including timing of meals, energy and protein dense meals/drinks, ONS	• 3 x GP home visits. • No RD counselling at home	Physical function (3), Physical strength (3), Nutritional status (3), Nutritional intake (3) Hospital readmission (6), Mortality (6).
Feldblum (2011)	a. N: 259 (78/181). b. Drop-out: 35% (15%/43%).	Age:(75 y / 75 y) F: (64 % / 64 %) Undernourished/nutritional risk assessed by MNA-SF or weight loss (> 10 % within 6 months before intervention)	Department of Internal Medicine, Soroka University Medical Center, Israel.	• In hospital: 1 x RD counselling • 3 x RD home visits after discharge Intervention time: 8 weeks	Individual nutritional plan including ONS and glucose fortification in hospital and post-discharge	• Standard care (no RD counselling in hospital or at home)	Physical function (6), Nutritional status(6), Mortality (6).
Neelemaat (2011)	a.N: 210 (105/105). b.Drop-out: 29% (29%/ 29%)	Age: (75 y / 74 y) F: (53 % / 57 %) Undernourished/nutritional risk assessed by BMI < 20 or unintentional weight loss (>5 % within the last month or > 10 % within the last 6 months)	Departments of general internal medicine, rheumatology, gastroenterology, dermatology, nephrology, orthopaedics, traumatology, and vascular surgery of the VU University Medical Center, Holland.	• Enriched diet in hospital • 6 x RD counselling by telephone at home after discharge Intervention time: 12 weeks	2 ONS/day + 400 IE vitamin D3 and 500 mg Calcium during hospitalisation and post-discharge Individual counselling to promote nutritional intake and stimulate compliance to ONS. Counselling was only given post-discharge.	• Standard care (no counselling in hospital or at home).	Physical function(3), Physical strength (3), Nutritional status(3), Nutritional intake (3).
Persson (2007)	a. N: 108 (51/57). b.Drop-out: 50% (56%/ 44%)	Age: (85 y / 85 y) F: (66 %/ 72%) Undernourished/nutritional risk assessed by MNA-SF	Department of Geriatric Medicine, Rosenlund Hospital, Sweden	• In hospital: 1 x RD counselling • 1 x RD counselling at home and 3 x RD telephone counselling at home after discharge Intervention time: 16 weeks	Fat fortification, prescription of 2 ONS/d, daily multivitamin supplement.	• No in hospital intervention • Brief written dietary advice at hospital discharge • Follow-up: 4 months	Physical function (4), Physical strength (4), Nutritional status (4), Quality of Life (4).

RD: Registreted Dietitian
ONS: Oral Nutritional Supplements
GP: General Practitioners

Primary outcome

Physical function

All studies evaluated physical function (Table 4). Three studies (N = 330) assessed physical function using HGS. The pooled effect of the intervention on HGS was non-significant (MD: -0.06, 95% CI: 1.03; 0.90, p = 0.50) and heterogeneity between studies was not important (I^2 = 31 %, p = 0.24) (Figure 3).

Other instruments used to measure physical function in the studies were too different to enable meaningful meta-analysis and results were therefore summarized narratively (Neelemaat et al., 2011; Persson *et al.,* 2007; Fleldblum *et al.,* 2011; Beck et al., 2012).
Beck et al. assessed physical function 3 months after discharge using five different instruments (Table 4). A significantly higher percentage of intervention (54 %) versus control patients (46 %) improved on the mobility score (p = 0.029). However, no significant difference between the intervention (MD: 6 ± 11) and control groups (MD: 3 ± 12) was identified in mobility at 12-weeks follow-up (p = 0.09). No significant effects between groups were identified by any of the other instruments used to assess physical function (Beck *et al.,* 2012).

Feldblum et al. assessed the effect on physical function 6 months after discharge using the Barthel Index and found no difference between groups (p = 0.76) (Feldblum *et al.,* 2011).

Neelemaat et al. assessed physical function 3 months after discharge using three different instruments (Table 4). In the original article, the intervention had no significant effect on physical function in any of the instrument used (Neelemaat et al., 2011), however, in a later paper, multiple imputation of missing data led to a significant improvement in the Functional Limitation Score (MD: -0.72, 95 % CI: -1.15;-0.28) (Neelemaat et al., 2012 B). Imputation of data targeted the number of patients required according to the original power calculation. Multiple imputations represented data for 17 % of patients lost to follow-up. Data on patients who died during the study were not included (Neelemaat et al., 2012 B). Further, it should be noted, that drop-out analysis showed that the drop-outs were significantly older, than those who completed the trial and that multiple imputation of missing data had no significant effects on physical function when assessed by other instruments (Neelemaat *et al.,* 2011; Neelemaat et al., 2012 B).

Persson et al. assessed physical function after a median of 4.3 months (3.6-6.9 months) using two different instruments (Table 4). Only the Katz Index showed a significant improvement in the intervention group (p <0.05) compared to the control group (Persson *et al.,* 2007). The Katz Index follows an ordinal scale and therefore no mean difference was available.

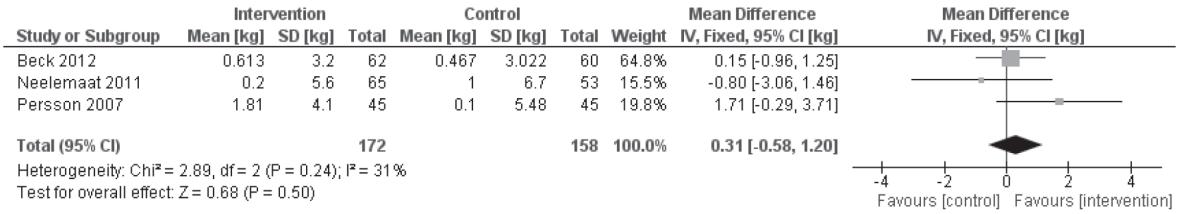


Figure 3 Meta-analysis of the effect of individualised dietary counselling given at home following discharge from an acute hospital compared to standard care on hand grip strength among older patients at nutritional risk

Table 3. GRADE Evidence profile for Hand Grip Strength and Mortality

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Follow home with nutritional counseling after discharge	Control	Relative (95% CI)	Absolute		
Hand Grip Strength (follow-up mean 3.3 months; better is indicated by higher values)												
3	randomised trials	serious[1]	no serious inconsistency[2]	no serious indirectness[3]	no serious imprecision	none[4]	172	158	-	MD 0.31 higher (0.58 lower to 1.2 higher)	⊗⊗⊗○ MODERATE	IMPORTANT
Mortality (follow-up mean 4.8 months)												
4	randomised trials	serious[5]	no serious inconsistency	Mortality (follow-up mean 4.8 months) no serious indirectness[3]	no serious imprecision	none	26/301 (8.6%)	47/337 (13.9%)	RR 0.64 (0.29 to 1.4)	50 fewer per 1000 (from 99 fewer to 56 more)	⊗⊗⊗○ MODERATE	CRITICAL
								15.5%		56 fewer per 1000 (from 110 fewer to 62 more)		

The Grading of Recommendations Assessment, Development and Evaluation system (GRADE) assess the quality of the evidence across outcomes in the included studies. The quality of evidence was assessed for physical function (measured by hand grip strength) and mortality. The quality of the evidence was graded from very low to high quality based on study design, risk of bias, inconsistency, indirectness, imprecision and risk of publication bias.

[1] No blinding of participants and treatment personnel (3 of 3 trials), and outcome was not analysed blinded (1 of 3 trials). High rate of drop-outs (2 of 3 trials: 29-50%)

[2] Heterogeneity was low (31%)

[3] No significant difference in populations, interventions and follow-up time

[4] Funnel plot shows no publication bias. No unpublished trials identified when searching protocol databases

[5] High rate of drop-outs (3 of 4 trials: 29-50%). One study had an unusual high mortality rate in the control group.

Table 4. The effect of dietary counselling following discharge from hospital to home on physical function measured by different instruments

Study	Measurement instrument [scale]	IG: Improved, N (%)	CG: Improved, N (%)	IG: MD (SD)	CG: MD (SD)	P-value/ Difference (95 % CI)
Beck (2013)(114)	Chair Stand test [30-Seconds]	35 (56)	32 (53)	-	-	P = 0.75
	The de Morton Mobility Index [0-100]	-	-	6 (11)	3 (12)	P = 0.09
	The de Morton Mobility Index [0-100]	34 (54)	28 (46)	-	-	P = 0.03
	The mobility-tiredness scale [0-6]	-	-	-1.11 (2.2)	-0.96 (2.8)	P = 0.90
	The mobility-tiredness scale [0-6]	27 (48)	27 (52)	-	-	P = 0.39
	Functional Recovery Score [0-100%]	-	-	3 (14)	5 (15)	P = 0.50
	Functional Recovery Score [0-100%]	30 (48)	34 (59)	-	-	P = 0.51
	Hand grip strength [kg]	-	-	0.6 (3)	0.5 (3)	P = 0.65
	Hand grip strength [kg]	31 (50)	27 (45)	-	-	P = 0.84
Feldblum (2011)(113)	Barthel index [0-100]	na	Na	-2.6 (18.3)	-3.6 (18.9)	P = 0.76
Neelemaat (2011)(111)	Functional Limitation score [0-6]	na	Na	-2.6 (18.3)	-3.6 (18.9)	P = 0.76
	Physical activity score [0-6]	na	Na	-0.3 (1.2)	0.2 (1.5)	-0.5 (-1.0;0.1)
	Physical performance [0-16]	na	Na	0.5 (1.5)	0.6 (1.5)	-0.1 (-0.7; 0.5)
	Hand grip strength [kg]	na	Na	3.0 (4.2)	2.1 (5.4)	0.8 (-1.0; 2.6)
	Functional limitations score [0-6]	na	Na	0.2 (5.6)	1.0 (6.7)	-0.8 (-3.0; 1.5)
Neelemaat (2012)(115)	Functional limitations score [0-6]	na	Na	-0.47 (0.15)	0.24 (0.15)	-0.72(-1.15;-0.28)
	Physical activity score [0-6]	na	Na	0.52 (0.17)	0.4 (0.26)	0.1 (-0.53; 0.73)
Persson (2007)(112)	Katz ADL index [A-H]	na	Na	na	na	P < 0.05
	Hand grip strength [kg]	na	Na	1.81 (4.1)	0.1 (5.5)	P = 0.20

Table 4.3-1 gives an overview of the effect on physical function measured by different instruments. Positive results are highlighted with dark grey
N = number of patients, MD = Mean Difference, IG = Intervention group, CG = Control group, na = not available, Neelemaat 2011 + 2012: same trial but different statistical methods to analyse outcome, Chair stand = manual counting of the number of sit-stand-sit cycles completed within 30 seconds, The de Morton Mobility Index is a validated tool to assess mobility, The mobility-tiredness scale measure tiredness using the validated Mob-T scale, Functional Recovery Score measured restoration of function, Hand grip strength was measured in kg using a Jamar Hydraulic Hand Dynanometer, Barthel index was used to measure performance in activities of daily living, Functional Limitation score and Physical activity score (two validated questionnaires) were used to assess physical function. Physical performance, was measured by examining walking speed, ability to rise from a chair, to put on and take off a cardigan and standing balance, Katz ADL index measured activities of daily living.

Secondary outcomes

Nutritional status

Change in body-weight

All studies (N = 525) evaluated the effect of individualised dietary counselling on weight change (Neelemaat *et al.,* 2011; Persson et al,. 2007; Feldblum *et al,.* 2011; Beck *et al.,* 2012). The follow-up times for weight change were 3 months (Neelemaat et al., 2011; Beck *et al.,* 2012), 4 months (Persson *et al.,* 2007) and 6 months (Feldblum *et al.,* 2011). The pooled effect estimate showed a significant increase in weight in intervention patients compared to control patients (MD: 1.80 kg, 95% CI: 0.29; 3.30, p = 0.02). It should, however, be noted, that there was important heterogeneity (I^2 = 80 %, p = 0.002) (Figure 4).

Mini Nutritional Assessment

Feldblum et al. examined the effect of intervening on nutritional status 6 months after discharge using the full Mini Nutritional Assessment (MNA) as published in 1999 by Vellas et al. (Guigoz & Vellas, 1999). A significant positive effect in favour of the intervention was identified in two specific domains of the MNA; dietary assessment (eight questions, related to number of meals, food and fluid intake, and autonomy of feeding) and subjective assessment (self-perception of health and nutrition). There were no significant differences between intervention versus control patients in the anthropometric and global assessments (six questions related to lifestyle, medication, and mobility). The improvements in dietary and subjective domains resulted in an overall improved MNA score in intervention versus control patients (total score change: 3.01±2.65 vs. 1.81 ± 2.97, p = 0.004).

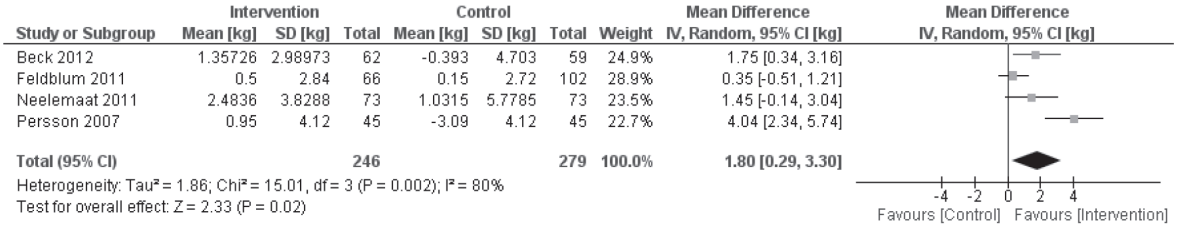
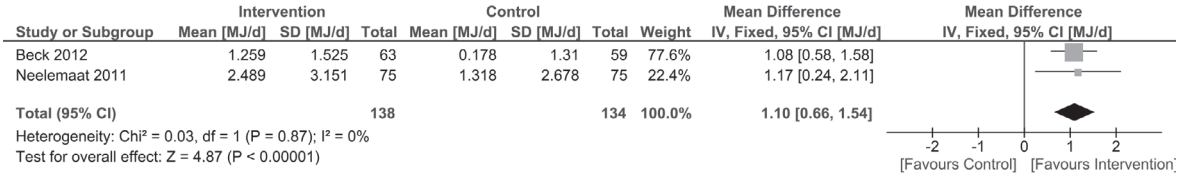


Figure 4. Meta-analysis of the effect of individualised dietary counselling given at home following discharge from an acute hospital compared to standard care on weight change among older patients at nutritional risk. In the study of Perssons et al. data of weight change (MD) was obtained from another meta-analysis (Baldwin & Weekes, 2011).

** In the study of Perssons et al. data of weight change (MD) was obtained from another meta-analysis[13].*

Energy



Protein

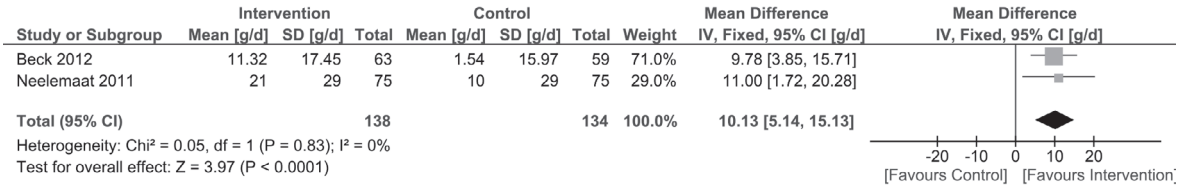


Figure 5. Meta-analyses of the effect of individualised dietary counselling given at home following discharge from an acute hospital compared to standard care on energy and protein intake among older patients at nutritional risk

Energy and protein intake

Two studies (N = 138) evaluated energy and protein intake 3 months after discharge (Beck et al., 2012; Neelemaat et al., 2012). Meta-analysis showed that individualised dietary counselling resulted in a significant mean difference in energy (MD: 1.10 MJ, 95% CI:0.66;1,54, p < 0.001) and protein (MD: 10.13g, 95% CI: 5.14;15.13, p < 0.001) per day in favour of the intervention (Figure 5). There was no heterogeneity between studies (I^2 = 0 %, p = 0.87/ p = 0.83) (Figure 5).

Mortality

None of the included studies assessed mortality as an outcome. However, information on mortality was available from all four studies (N= 729) enabling meta-analysis. Mortality was assessed at the longest follow-up time, 3 months (Neelemaat *et al.,* 2011), 4 months (Persson et al., 2007) and 6 months (Feldblum *et al.,* 2011; Beck *et al.,* 2012). Individualised dietary counselling following discharge from acute hospital to home did not influence mortality significantly (RR: 0.72, 95% CI: 0.45; 1.16, p = 0.18) and heterogeneity was not important (I^2 = 31 %, p = 0.23) (Figure 6).

Quality of life and hospital readmission

No meta-analyses of QoL and hospital readmissions were conducted due to few studies investigating these outcomes. Persson et al. evaluated QoL at four months follow-up using The Short Form Health Survey (SF-36). No data within the 'intention-to- treat' analysis were available. The per protocol analysis revealed no difference between groups in the physical or mental domains (SF-36 Physical, p = 0,19; SF-36 Mental, p = 0.91) (Persson *et al.,* 2007). Beck et al examined the effect on hospital readmissions and likewise found no difference between groups (intervention group: 53% readmitted; control group: 42% readmitted, p = 0.070) (Beck *et al.,* 2012).

Sensitivity and subgroup analyses and publication bias

The study by Persson et al. was assessed to be at high risk of bias due to attrition bias (drop-out 50%) (Perssons *et al.,* 2007). A sensitivity analysis excluding the study reduced the effect on change in BW. Nevertheless, the effect remained significant (MD: 1.01 kg, 95% CI: 0.08; 1.95, p = 0.03). The heterogeneity between the remaining studies was not important (I^2 = 41 %, p = 0.18)

Subgroup analyses were not conducted due to the similarity of interventions across studies. Furthermore, we did not do a funnel plot since a minimum of 10 studies are recommended for assessment of publication bias using a funnel plot (Higgins & Green., 2011).

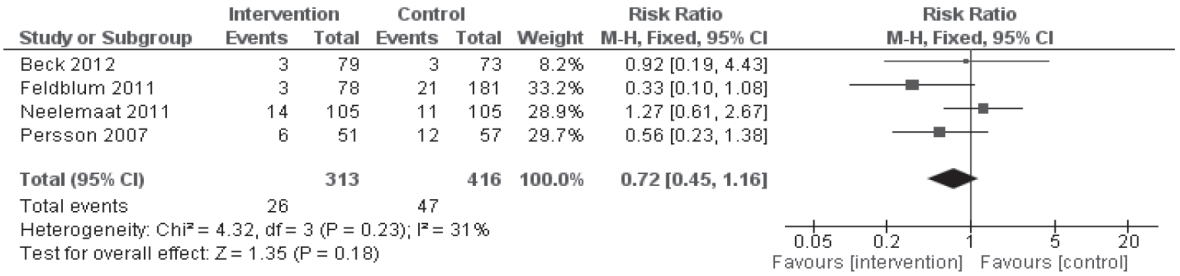


Figure 6. Meta-analyses of the effect of individualised dietary counselling given at home following discharge from an acute hospital compared to standard care on mortality among older patients at nutritional risk

Discussion

This systematic review revealed a positive effect of individualised post-discharge dietary counselling on protein and energy intake and weight gain in nutritionally at-risk older patients, however without revealing a convincing effect on physical function. Meta-analysis showed no effect on mortality. In regard to QoL and hospital readmission no conclusions could be drawn due to lack of data.

Our findings are in accordance with an earlier systematic review investigating the effect of dietary counselling (including the use of ONS) in all healthcare settings. This review revealed significant improvements in nutritional status and dietary intake. However, the evidence regarding other outcomes such as physical function was weak (Baldwin and Weeks, 2011).

We hypothesised that the order of effects would be increased energy and protein intake, weight gain and, subsequently, improved physical function. However, the effect on physical function was inconclusive despite significant increases in energy and protein intake and BW. A reason for this may be that we lack a deeper understanding of the molecular and cellular mechanisms behind the recovery of physical function in older patients.

Another reason for the lack of effect on physical function may be that interventions were too brief (8-12 weeks) to facilitate improvement in physical function. A seminal study from 1950 showed that young healthy people, exposed to semi-starvation for 24 weeks, suffered from decreased physical performance and required a recovery period of more than six months to regain habitual strength and physical function (Keys *et al.,* 1950).

The use of different screening tools for assessing nutritional risk (NRS-2002, MNA-SF, BMI, unintentional weight loss) could also have impacted on the results. It is paramount for a nutritional screening tool to have predictive validity in order to identify those who will benefit from a nutritional intervention. Of the different tools used in the included trials, only the NRS-2002 has been tested for its ability to predict the clinical effect of nutritional treatment in hospitalised, acutely ill patients (Kondrup *et al.,* 2003). The NRS-2002 is therefore recommended by ESPEN (The European Society for Clinical Nutrition and Metabolism) for use in hospital settings (Kondrup *et al.,* 2003). The NRS-2002 is, however, not specifically designed to screen aging subjects with chronic conditions. Nevertheless, the NRS-2002 has been found to be an important outcome predictor for older patients, probably because it includes correction for old age (Martins *et al.,* 2005). The MNA from which the MNA-SF originates was primarily developed to detect undernutrition and the risk of developing undernutrition among older community-dwelling persons. The predictive validity of MNA has been evaluated by demonstrating its association with adverse health outcomes i.e. increased mortality (Kondrup *et al.,* 2003). However, it has not yet been demonstrated to be able to identify those who would benefit from nutritional therapy among older community-dwelling persons or older hospitalised patients (Kondrup *et al.,* 2003).

Conclusively, none of the screening tools used have been validated for identifying older patients who would benefit from individualised dietary counselling following discharge from an acute hospital to home.

The included studies may also have been inadequately powered to detect a significant effect on physical function (a type 2 error). In fact only one study used physical function to calculate the required sample size (Neelemaat *et al.,* 2011). Regrettably, due to attrition bias, the calculated sample size was not reached. Another possible reason for the lack of a convincing effect on physical function could be insufficient protein intake. Existing evidence indicates that older patients require a high intake of dietary protein (i.e. > 1.2g/kg BW/d) in order to promote health, recovery from illness, and functionality (Bauer *et al.,* 2013). Moreover, a more positive effect on physical function might have been achieved by combining the nutritional intervention with physical training. A recent meta-analysis revealed that dietary protein supplementation during a period of resistance-type exercise training in healthy older adults resulted in an increase in fat free mass (+ 38 %) and muscle strength (+ 33 %) (Cermak *et al.,* 2012). Therefore, it could be speculated that frail older post-discharge patients could achieve the same or an even greater effect of protein supplementation during physical training. A recent randomised controlled trial showed that training of older persons impacted positively on physical function. Interestingly, due to what was hypothesised to be “post-training fatigue”, this effect was accompanied by reduced QoL (Tuunainen *et al.,* 2013). This indicates that training should be offered in combination with a nutritional intervention.

None of the studies defined the minimal clinically relevant change required to improve physical function in older nutritionally at-risk patients. Neither did they discuss how physical function ideally can be measured in this patient population. Older patients are a heterogeneous population and clinically meaningful improvements may depend on baseline function and health status. In a study of older patients (aged 70-89), a clinically meaningful effect on walking speed was identified at 0.1 m/s (Kwon *et al.,* 2009). In contrast, another study of older patients after hip fracture (aged 74-88) revealed a clinically meaningful effect of a walking speed at 0.26 m/s (Alley *et al.,* 2011).
Recently the Short Physical Performance Battery (SPPB) has been recommended for testing physical function in the older frail population (Cruz-Jentoft *et al.,* 2010). The SPPB combines gait speed, chair stand and balance tests. The SPPB is relevant since clinically meaningful changes in the SPPB have been defined (Cruz-Jentoft *et al.,* 2010).

Beck and colleagues for example reported a mean difference in physical function of 6±11 in the intervention versus 3±12 in the control group, however without discussing the potential clinical relevance of this difference (Beck *et al.,* 2012). Furthermore, they concluded that a positive effect was seen in physical function even though this effect was seen only when data were presented as percentages (Beck *et al.,* 2012). Presenting data as percentages can be misleading since the smallest change can count as an improvement without taking into account the clinical relevance of these changes.

However, until consensus has been reached, it is recommended that authors at least justify their choice of instrument, including descriptions of the psychometric properties of the chosen instruments.

Limitations and strengths

A limitation of this systematic review is the small number of studies included. This potentially limits the external validity of the review. Nevertheless, due to the inclusion of studies from both Europe and the Middle East, we believe the findings are transferable to older patients living in other countries with the same level of discharge system.

Overall, the included studies were assessed to be at high risk of bias, due to inadequate blinding (performance and detection bias) and high dropout rates (attrition bias). These limitations pose a substantial threat to the internal validity of the review. Another limitation is that only one study had physical function as a primary outcome. Moreover, all studies potentially lack sufficient statistical power. Finally the use of different instruments to assess physical function prevented meaningful meta-analysis.

A strength of this systematic review is the comprehensive attempt to collate and evaluate the evidence for an effect of individualised dietetic counselling in the management of older nutritional at-risk patients after hospital stay. The review also provides useful information for the design of future studies in this area.

Further research and health care implications

Given the power of physical function and QoL to reflect current and future health of older patients, future studies of dietary counselling must be adequately powered and include sufficiently long intervention and follow-up (probably at least 24 weeks) (Keys *et al.,* 1950) to enable assessment of these patient important outcomes. Further, to improve study quality in future studies, outcome assessors and data analysis should be blinded.
Future studies should explore the effect of combining dietary counselling and physical training. The dose-response effect of protein intake also warrants attention since specifically protein intake appears to have a positive effect on promoting anabolism in older patients (Bauer *et al.,* 2013). We also emphasise that the clinical relevance of changes in physical function should be critically evaluated and also the need for consensus concerning a gold standard to measure minimal clinically relevant changes in physical function in older patients.

In terms of heath care implications, individualised dietary counselling including use of ONS was found to increase nutritional parameters. However the effect on physical function was unclear and no effect was found on other clinical outcomes. These findings accord with a systematic review investigating the use ONS without dietary counseling, in older patients following discharge from acute hospital (Beck *et al.,* 2012). Therefore either approach (dietary counselling + ONS or ONS only) seems to lead to the same outcomes for patients. Providing ONS as a single intervention does however not incur the resource demands incurred by the health system (time and cost of a RD) associated with individualised dietary counselling provided at home after hospital discharge. Therefore, for the reason of health service efficiency (not lack of effect), ONS as a single intervention is an appropriate fist line of treatment. Individual dietary counselling without ONS following discharge can be considered if compliance or tolerance or costs of purchasing ONS are issues for the patient. It is however unclear whether individualised dietary counselling without ONS leads to improved nutritional parameters as all the studies in this review provided a combination of ONS and individual dietary counselling.
More research within this field is, though, needed to enable evidence-based recommendations for clinical practice.

Conclusions

We found moderate-quality evidence that individualised dietary counselling provided by a RD improved weight, energy and protein intake in older nutritionally at-risk patients, however without clearly improving physical function. No effect was found on mortality. Due to lack of data on hospital readmissions and QoL, meta-analyses of these outcomes were not possible.
Given the prevalence of undernutrition in older patients, valid evaluation of the effect of nutritional interventions on clinically relevant outcomes is prerequisite. Therefore, consensus regarding which instruments to use to measure outcomes and identification of minimal clinically relevant changes in these is needed.

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Conflict of interest

No conflict of interest was declared in the included studies. On the other hand it was only clearly described in the study of Beck *et al.,* and Feldblum *et al.,* (Beck *et al.,* 2012; Feldblum *et al.,* 2011)

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