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**Is telehealth effective in managing malnutrition in community-dwelling older adults? A systematic review and meta-analysis**

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**Abbreviations:**

MD, Mean Difference

OR, Odds Ratio

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

SMD, Standardised Mean Difference

## **Abstract**

Telehealth offers a feasible method to provide nutrition support to malnourished older adults. This systematic review and meta-analysis aims to determine the efficacy of telehealth methods in delivering malnutrition-related interventions to community-dwelling older adults. Studies in any language were searched in five electronic databases from inception to 2<sup>nd</sup> November 2017. Quality of the evidence was assessed using the Cochrane Risk of Bias tool and the GRADE approach. Nine studies were identified with results published across 13 included publications, which had mostly low to unclear risk of bias. Participants were patients following hospital discharge (n=7 studies), with kidney disease (n=1 study), or cancer (n=1 study). Seven studies delivered telehealth via telephone consultations and two used internet-enabled telemedicine devices. Ten meta-analyses were performed. Malnutrition-focussed telehealth interventions were found to improve protein intake in older adults by 0.13g/kg body weight per day ([95%CI: 0.01-0.25]; P=0.03; n=2 studies; n=200 participants; I<sup>2</sup>=41%; GRADE level: low) and improve quality of life (standardised mean difference: 0.55 [95%CI: 0.11-0.99]; P=0.01; n=4 studies with n=9 quality of life tools; n=248 participants; I<sup>2</sup>=84%; GRADE level: very low). There were also trends towards improved nutrition status, physical function, energy intake, hospital readmission rates and mortality in the intervention groups. Overall, this review found telehealth is an effective method to deliver malnutrition-related interventions to older adults living at home, and is likely to result in clinical improvements compared to usual care or no intervention. However, further research with larger samples and stronger study designs are required to strengthen the body of evidence.

## **Introduction**

Despite being preventable and treatable, malnutrition is highly prevalent and a strong independent contributor to poor health in the older adult population [1-4]. Malnutrition is defined as the unintentional and preventable loss of lean tissues such as muscle, with or without fat loss, due to prolonged inadequate dietary intake of protein and energy, increased requirements and/or excessive losses [1, 5]. A sufficient increase in dietary protein and energy intake to meet individualised requirements and cease the loss of lean tissues will reverse malnutrition [3, 5]. However, encouraging malnourished patients to consume appropriate types and quantities of foods to meet their nutritional requirements encounters many diverse barriers due to its complex physiological, socio-economic, and environmental risk factors, as well as unique presentation in each individual [5]. Individualised and long-term nutrition support is required to overcome these barriers and enable the older adult to meet their energy and protein requirements; thus, the current usual care of short term treatment during a health care admission is insufficient to properly treat malnutrition in many cases [5, 6]. Therefore, it is now essential to look to alternative methods of healthcare delivery which facilitate patient-centred care across the continuum and reduce barriers patients face, while also maximising current healthcare resources.

For this reason, healthcare providers have increasingly been using telehealth, which enhances patient access to long-term care. With the use of technology growing rapidly around the world, [7], telehealth methods have demonstrated a credibility in overcoming typical logistical challenges in modern healthcare delivery [8]. Telehealth can be defined as the delivery of healthcare services from a distance using telecommunication techniques synchronously (i.e. same time, different location) and/or asynchronously (i.e. different time, different location) [8].

As such, telehealth may allow for specialised nutrition care to be delivered more cost-effectively and to more patients in need.

Telehealth strategies have been shown to be effective at improving dietary behaviour in chronic disease [9, 10] and in primary care [11, 12]. Older adults suffering from chronic conditions have also shown improvements in areas of their self-management and confidence in using telehealth modalities [13]. Therefore, telehealth offers a feasible method to provide regular and long-term nutrition support to malnourished older adults living at home; a population group who may find it difficult to access health services, particularly in rural areas [6, 14-16]. However, this age group may also have limitations related to lack of internet accessibility, hearing difficulties, and familiarity and acceptance of technology, which may limit the effectiveness of telehealth interventions. Consequently, the effectiveness of telehealth with older adults to improve malnutrition warrants examination so that healthcare resources may be directed appropriately. This study aims to determine the efficacy of telehealth methods in delivering malnutrition-related interventions to community-dwelling older adults.

## **Methods**

A systematic review and meta-analysis of the literature was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17] and was registered with the International Prospective Register of Systematic Reviews (PROSPERO number: CRD42017080922).

### Search strategy

Studies in any language were searched for in the electronic databases CENTRAL, CINAHL (via Ebscohost), EMBASE, PubMed and Web of Science from database inception to 2<sup>nd</sup> November 2017 using a combination of keywords and controlled vocabulary (Appendix I). The search strategy was designed in PubMed and translated to the other databases using Polyglot [18]; and was further supported by snowball searching of the literature.

Inclusion criteria were older adult samples with a mean age of  $\geq 65$  years living independently in their own homes (including post-hospital discharge and outpatients) who received intervention for managing risk or progression of protein-energy malnutrition. Participants in residential aged care or assisted living facilities were excluded. Studies where the intervention was delivered in both inpatient and community settings (e.g. during admission and then follow-up post-discharge) were included only if the intervention delivered in the community setting was of equal or greater duration than that delivered in the inpatient setting. Telehealth was considered as: 1) a synchronistic consultation with a health professional with point-of-contact via any telephone or internet-based method, or 2) an asynchronistic telephone- or internet-based intervention system. Studies were included only where community-based interventions were delivered with at least 50% of the intervention contacts (frequency or duration) were from telehealth methods, and at least two points-of-contact made via telehealth. If an intervention was multidisciplinary and focussed on more than just nutrition (e.g. support for dementia or stroke patients), studies were included only where there were at least two malnutrition-specific



telehealth contacts within the larger intervention program. Studies were included if the telehealth intervention was given directly to the patient or to their family carer.

Any original research intervention study was included. Excluded study and publication types were abstracts, observational studies, conference papers, qualitative studies, study protocols, opinions, commentaries, and review papers.

#### Selection of studies and data extraction

After citations were identified from all databases, duplicates were removed using Systematic Review Assistant-Deduplication [19]. Two authors (MC and HM) scanned the titles and abstracts of studies identified by the search for their potential eligibility. Full-text articles were assessed for eligibility independently by two authors (DC and MC); with disagreements managed by consensus between the two authors and eligibility confirmed by the senior author (SM). Data were extracted into standardised tables by one author (WM) and checked for accuracy by a second (SM).

Outcomes of interest were nutrition status according to any tool validated for use in older adults [20], energy and protein intake, body composition, physical function, quality of life, admission to residential aged care, hospitalisation, pressure wounds, falls, cost-efficacy and all-cause mortality. Feasibility was of interest and was assessed by attrition rate (reflecting participant engagement) and participant satisfaction. In addition to outcomes, data describing the study intervention and participant sample were extracted.

#### Review of study strength and quality

The Cochrane Risk of Bias tool [21], which assesses selection, performance, detection, attrition and reporting bias, was applied to each included study by two independent authors (DC, JC or SM) and consensus reached via discussion. Regarding performance bias, due to the nature of nutrition support interventions, it is not possible to implement participant and researcher blinding. Therefore, acknowledging some bias may be introduced by the lack of intervention

blinding but that it is an accepted and necessary approach in these study designs, “unclear risk of bias” was allocated to all studies for this item.

The certainty in the body of evidence for each outcome of interest for which there was sufficient data reported was classified using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach [22]. GRADE assessment provides four levels of certainty for the estimated effect: high (very confident), moderate (moderately confident), low (limited confidence) and very low (very little confidence). The GRADE assessment was completed using GRADEpro [23] and was determined during discussion by three authors (SM, WM and JK).

### Meta-analysis

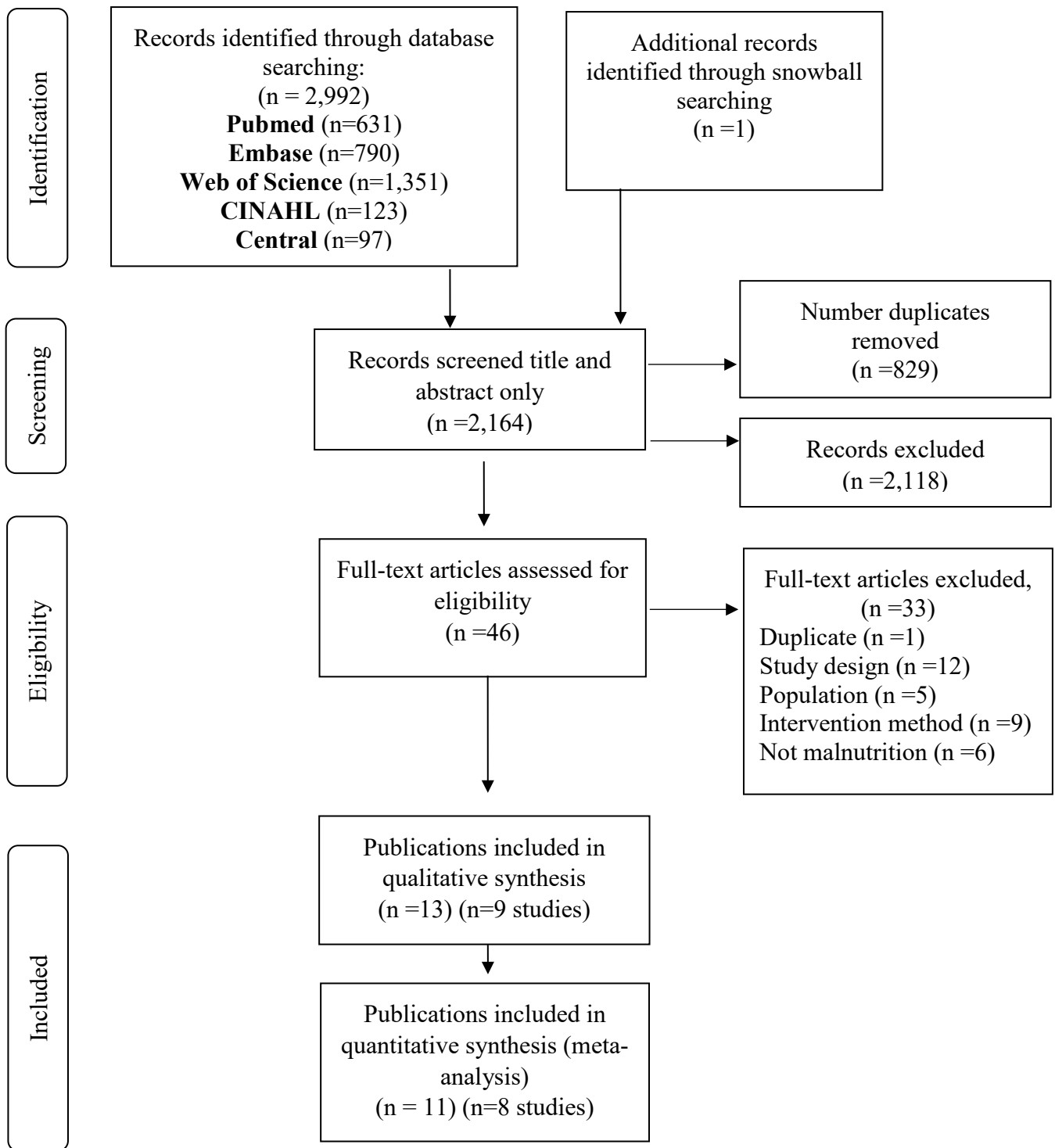
Outcomes were pooled where studies reported sufficient outcome and variance data on categorical or normal continuous variables using Revman [Review Manager 5, Version 5.3, 2014, Cochrane Informatics & Knowledge Management Department]. Dichotomous outcome data was expressed as odds ratios (OR) with 95% confidence intervals, using the Mantel-Haenszel test. Continuous outcome data were calculated as mean differences (MD) for studies which used the same measurement, or standardised mean differences (SMD) for studies which used different assessment tools for the same construct; where SMD effect sizes of  $<0.4$  were considered small,  $0.4 - 0.7$  moderate, and  $>0.7$  large [24]. Additionally, where SMD was reported, the effect size was re-expressed into the scale of one of the included instruments by multiplying the SMD by the standard deviation of that tool reported in the total sample [25]. Where continuous outcomes were measured on scales with opposite directions, one of the directions was multiplied by -1 [26]. Due to the complex presentation of malnutrition between individuals, a random effects model was used for all meta-analyses. Heterogeneity between studies was assessed using the  $I^2$  statistic, where  $>50\%$  was considered substantial heterogeneity. Where sensitivity analysis was required, analysis was repeated excluding studies

with low study quality/high risk of bias, timeframe of the reported outcome, study design or participant characteristics.

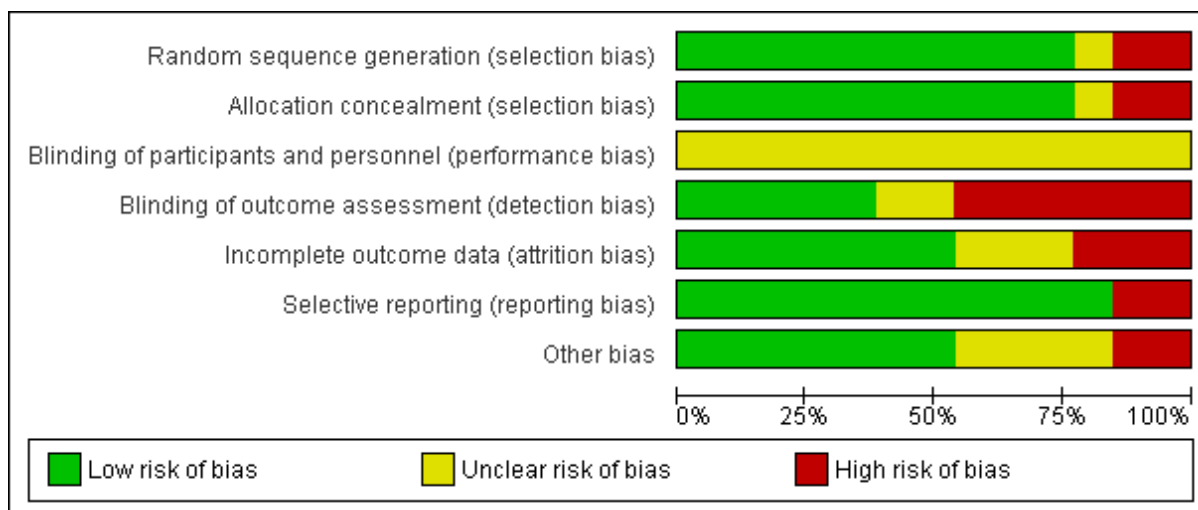
## **Results**

### Search results and study quality

The search identified 2,993 records, with 2,164 remaining after deduplication (Figure 1). Forty-six publications were assessed for eligibility via full text, and 13 were included. Of these 13 publications, six papers were used to report outcomes from two studies, leading to nine intervention studies included (Table 1). Seven studies were randomised controlled trials (RCTs), where the study by Lim et al. [27] was pre-test post-test, and the study by Lindhardt et al. [28] was a non-randomised controlled trial. Eleven of the included publications provided data which contributed to ten meta-analyses. Figure 2 reveals risk of bias across all studies was mostly low, excepting bias introduced by a lack of blinding of subjective outcome assessments (justifications are presented in the Online Supplementary Material). No included studies blinded participants or researchers to the intervention; however, as described previously this is not possible due to the nature of nutrition interventions. Using funnel plots, there appeared to be no publication bias in all-cause mortality (n=10 studies included). No other outcomes could be assessed for publication bias due to a small number of studies contributing data. All study funding appeared to be from independent sources, and no authors declared conflict of interest (Table 1).



**Figure 1:** PRISMA flowchart of the search results and the included studies



**Figure 2:** Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included publications (n=13).

### Intervention characteristics

There were two interventions delivered to disease-specific groups, one with kidney disease [29] and one with cancer [30]. The remaining seven interventions were delivered to patients with mixed morbidities following discharge from an inpatient facility [27, 28, 31-35]. Only one study included the participants' carers [36]. The most common method used to deliver telehealth was via telephone consultations with a dietitian or dietetic assistant, which ranged widely in intensity and duration (2x30 minute consultations reported by Sharma et al. [35] to 18x15-30 minute consultations reported by Silvers et al. [30]). In addition to the telephone consultations, Silvers et al. [30], Andersson et al. [31] and Lim et al. [27] provided some face-to-face support, either through additional outpatient or home visits. Two studies used a telehealth device to deliver the interventions. Kraft et al. [32] provided participants with a telemonitoring device, in which they input health-related data and answered nutrition-related questions that would then trigger a-priori interventions, depending on the input data. Lindhardt et al [28] provided participants with an internet-enabled tablet, preloaded with an application which allowed them to order meals three times per week, and provided automated feedback on how intake corresponded with individual energy and protein requirements. Only one

intervention, reported across four publications by Neelemaat et al [34, 37-39], provided all participants with oral nutritional supplements; whereas five other studies provided them on a case-by-case basis to align with an individualised plan [27, 30, 32, 33, 35, 36].

All nine studies were designed to have true control groups receiving standard care and/or no follow-up. However, Lim et al. [27] described a historical control group in which attrition was so large that no data were reported, and instead the intervention group was analysed as a pre-test post-test study. Additionally, the control group described by Silvers et al [30] received usual care of greater intensity compared to other studies, where face-to-face consultations were provided starting at a later timepoint (6-10 weeks after cancer diagnosis) than the telehealth consultations (starting at the time of cancer diagnosis).

**Table 1:** Characteristics and outcomes of the included 13 publications (9 studies) which reported malnutrition-related telehealth interventions to community-dwelling older adults.

Study	Study design, setting and participants	Intervention Group	Comparator Group	Results	Financial and other conflicts of interest
<b>Sample: Older adults with chronic kidney disease</b>					
Campbell et al. 2008 [29]	<ul style="list-style-type: none"> <li>• RCT</li> <li>• Brisbane, Australia</li> <li>• N=56</li> <li>• Attrition: 11%; IG n=5; CG n=1</li> <li>• Age: <math>\mu</math>70.7<math>\pm</math>14 years</li> <li>• Female: 38%</li> <li>• All patients had an eGFR &lt;30ml/min.</li> </ul>	<ul style="list-style-type: none"> <li>• n=29</li> <li>• Delivery: up to 1hr baseline consultation, 0.25-0.5hr telephone consultation every fortnight for first month, then monthly for an unclear amount of time (possibly 12 weeks).</li> <li>• Content: Individually tailored nutrition counselling delivered which involved adjusting diet to include energy (125-146kJ/kg/day) and protein intake (0.75 - 1.0g/kg/day) in line with K/DOQI recommendations. Consultation involved goal setting, menu planning, label reading and identification of foods relevant nutrients, depending on requirements.</li> <li>• Supplements: not described</li> </ul>	<ul style="list-style-type: none"> <li>• n=27</li> <li>• Delivery: Written information</li> <li>• Content: Generic nutrition information tailored for CKD</li> <li>• Supplements: not described</li> </ul>	<p>At 12 weeks post-baseline:</p> <p><u>Malnutrition</u>  <i>SGA rating (rated A, B or C, where B and C indicate malnutrition);</i></p> <ul style="list-style-type: none"> <li>• IG: 5/7 malnourished improved nutrition status; none worsened. CG:4/26 participants became malnourished; none improved. P&lt;0.01 between groups.</li> </ul> <p><u>Dietary intake</u>  <i>Energy intake (kJ/kg; mean change (95% CI))</i></p> <ul style="list-style-type: none"> <li>• IG: Unadjusted: 11.4 (4.7-18.0); Adjusted: 14.2 (7.6-20.8); CG: Unadjusted: -6.3 (-13.0-0.4); Adjusted: -7.9 (-14.3 - -1.6); P&lt;0.01 between groups.</li> </ul> <p><i>Protein (g/kg mean change (95% CI))</i></p> <ul style="list-style-type: none"> <li>• IG: Unadjusted: -0.07 (-0.15 to 0.02); Adjusted: -0.05 (-0.13 to -0.03); CG: Unadjusted: -0.11 (-0.19 to -0.03); Adjusted: -0.13 (-0.21 to -0.05); No difference between groups.</li> </ul> <p><u>Mortality (incidence)</u></p> <ul style="list-style-type: none"> <li>• IG: n= 4/29; CG: n=0/27; groups not compared.</li> </ul>	The study was funded in part by a Royal Brisbane and Women's Hospital Foundation Seeding grant, Queensland University of Technology Postgraduate Research Award (PhD scholarship) and an Institute of Health and Biomedical Innovation Research Scholarship. The authors declare no COI
<b>Sample: Older adults with cancer</b>					
Silvers et al. 2014 [30]	<ul style="list-style-type: none"> <li>• RCT</li> <li>• Australia</li> <li>• N=21</li> <li>• Attrition: 19%; IG n=1; CG n=5</li> <li>• Age: <math>\mu</math>68 years</li> <li>• Female: 43%</li> <li>• All patients had histologically proven diagnosis of primary esophageal or stomach cancer</li> </ul>	<ul style="list-style-type: none"> <li>• n=10</li> <li>• Delivery: Commenced immediately after the time of diagnosis, weekly telephone calls by a research dietitian. Patients were consulted weekly for 18 weeks (15–30 min per contact), and then at week 26 to monitor progress. Face-to-face support was provided if patient attended the hospital for treatment-related appointments. Additional contacts made if patient requested.</li> <li>• Content: The intervention adopted a tailored, symptom-directed approach. Weight, nutrition impact symptoms and oral intake were monitored. A number of behaviour change techniques were drawn upon as a part of this intervention.</li> <li>• Supplements: Oral nutritional supplement samples were supplied if indicated.</li> </ul>	<ul style="list-style-type: none"> <li>• n=11</li> <li>• Delivery: no planned dietetic input until the patient was admitted for surgery or chemotherapy (a delay of 6-10 weeks after diagnosis), and only if referred by nursing staff.</li> <li>• Content: Face-to-face dietetic assessment and intervention were conducted at time of treatment-related visits to hospital.</li> <li>• Supplements: Oral nutritional supplement samples were supplied if indicated.</li> </ul>	<p>After 6 months post-baseline</p> <p><u>Malnutrition</u>  <i>PG-SGA, score (range 0 to 35, higher scores indicate more nutritional risk, mean<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>• IG: 7<math>\pm</math>2; CG: 19<math>\pm</math>5; P-value not reported</li> </ul> <p><i>PG-SGA, rating (A, B or C, B and C indicating malnutrition)</i></p> <ul style="list-style-type: none"> <li>• IG: n=6/9 B or C; CG: 4/6; P-value not reported</li> </ul> <p><u>Anthropometry</u>  <i>Weight (kg; mean<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>• IG: 81<math>\pm</math>14; CG: 61<math>\pm</math>20; P=0.002 between groups</li> </ul> <p><u>Quality of life</u>  <i>EORTC QLQ-C30 global health scale (rated 0-100; higher scores indicate better health)</i></p> <ul style="list-style-type: none"> <li>• IG: 83<math>\pm</math>12; CG: 41<math>\pm</math>24; P&lt;0.001 between groups</li> </ul> <p><i>EQ-5D index (range 1 to -0.59, higher scores indicate better health, mean<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>• IG: 0.72<math>\pm</math>0.3; CG: 0.21<math>\pm</math>0.3; P&lt;0.001 between groups</li> </ul> <p><i>EQ-5D VAS score (range 0 to 100, higher scores indicate better health, mean<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>• IG: 74<math>\pm</math>4; CG: 43<math>\pm</math>15; P&lt;0.001 between groups</li> </ul>	Funded by the Southern Melbourne Integrated Cancer Service. The authors declare no COI.

				Mortality (incidence at 6-months)	
<p><b>Sample: Older adults after discharge from inpatient facility</b></p>					
Andersson et al. 2017 [31]	<ul style="list-style-type: none"> <li>▪ RCT.</li> <li>▪ Oslo, Norway.</li> <li>▪ N=115</li> <li>▪ Attrition: 13%; IG n=12; CG n=18</li> <li>▪ At risk or malnourished at baseline according to NRS-2002</li> <li>▪ <math>\mu</math>75±8-9 years of age</li> <li>▪ Female: 72%</li> <li>▪ Mixed morbidities with average rehabilitation LOS 19 days.</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=52</li> <li>▪ During admission: Standard care given during rehabilitation. Individualised nutrition plan to meet EER and EPR given by clinical nutritionist at hospital discharge.</li> <li>▪ Delivery: 1/2hr telephone calls delivered during week 1, 7 and 10 after discharge + 1x1hr home visit week 4 after discharge.</li> <li>▪ Content: Individually tailored nutrition counselling delivered following discharge to maintain nutrition status, which focused on: supportive eating environment, increasing food/nutrient intake, improving appetite, motivation and support for self-management, simplifying food procurement, managing nutrition impact symptoms such as psychological, medical and environmental factors.</li> <li>▪ Supplements: none provided.</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=48</li> <li>▪ During admission: standard care given during rehabilitation. No individualized nutrition plan given at discharge.</li> <li>▪ Delivery: no contact made with patients either via telephone or other methods.</li> <li>▪ Content: no intervention of any kind was given following rehabilitation discharge.</li> <li>▪ Supplements: none provided.</li> </ul>	<p>At 12 weeks post-discharge:</p> <p><u>Anthropometry</u></p> <p><i>Body weight:</i></p> <ul style="list-style-type: none"> <li>• IG: 2/52 lost 5% since baseline. Weight increased since baseline (p=0.0026; data not provided). CG: 5/48 lost 5% since baseline. No change in weight since baseline (p&gt;0.05; data not provided). No difference in odds of 5% weight loss OR: 0.34 (95%CI: 0.064-1.86; p=0.22).</li> </ul> <p><u>Quality of life</u></p> <p><i>EQ-5D VAS (scale 0-100, higher score indicates worse quality of life)</i></p> <ul style="list-style-type: none"> <li>• IG: no change since baseline (data not provided). CG: no change since baseline (data not provided). No difference between groups</li> </ul> <p><u>Appetite</u></p> <p><i>DRAQ (scored 10 – 50, higher score indicating better appetite)</i></p> <ul style="list-style-type: none"> <li>• IG: no change since baseline (data not provided). CG: no change since baseline (data not provided). No difference between groups</li> </ul> <p><u>Mortality (incidence)</u></p> <ul style="list-style-type: none"> <li>• IG: n= 1/58; CG: n=0/57; groups not compared.</li> </ul>	Funding from Throne Holst Foundation and The Directorate of Health, Norway. Authors declare no COI.
Kraft et al. 2012 [32]	<ul style="list-style-type: none"> <li>▪ RCT</li> <li>▪ Greifswald, Germany</li> <li>▪ N=26</li> <li>▪ Attrition: 54%; IG n=8; CG n=4</li> <li>▪ Median age: 79.8 years</li> <li>▪ Female: 61%</li> <li>▪ Mixed morbidities. All patients included in the study were at high risk of malnutrition, reflected by an NRS-score of at least 3.</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=13</li> <li>▪ During admission: Standard care not described.</li> <li>▪ Delivery: Telemedical monitoring device in which participants recorded body weight and answered questions related to appetite, supplement use, wellbeing and fluid intake.</li> <li>▪ Content: Participants would be regularly screened via telemedical device. If responses indicated need for intervention, an a-priori defined intervention scheme was implemented to address the problem. This may include changes to supplements, referrals to health and medical professionals, or nutrition counselling.</li> <li>▪ Supplements: Modified or provided depending on individual patient needs.</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=13</li> <li>▪ During admission: Standard care not described.</li> <li>▪ Delivery: Standard care not described.</li> <li>▪ Content: Standard care not described.</li> <li>▪ Supplements: not described.</li> </ul>	<p>At 6 weeks post-baseline:</p> <p><u>Malnutrition</u></p> <p><i>NRS score</i></p> <ul style="list-style-type: none"> <li>▪ Data Not reported</li> </ul> <p><i>Geriatric Nutritional Risk Index</i></p> <ul style="list-style-type: none"> <li>▪ Data Not reported</li> </ul> <p><u>Anthropometry</u></p> <p><i>Weight (kg, mean±sd)</i></p> <ul style="list-style-type: none"> <li>▪ n=5, IG: 64.1±15.0 (-4.5±7.9 since baseline); n=9, CG: 60.6±13.2 (-3.0±6.2 since baseline); No significant difference (p value not reported)</li> </ul> <p><i>Body Mass Index (kg/m<sup>2</sup>, mean±sd)</i></p> <ul style="list-style-type: none"> <li>▪ n=5, IG: 23.0±4.2 (1.5 since baseline); n=9, CG: 22.8±4.3 (-1.1 since baseline); No significant difference (p value not reported)</li> </ul> <p><i>Phase angle: Bioelectrical Impedance Analysis</i></p> <ul style="list-style-type: none"> <li>▪ Data Not reported</li> </ul> <p><u>Mortality (incidence)</u></p> <ul style="list-style-type: none"> <li>• IG: n= 0/13; CG: n=0/13; groups not compared.</li> </ul>	The Ministry of Social Affairs and Health of the Federal State of Mecklenburg-Western Pomerania Telemedicine Programme, Future fund). The study was supported by Nutricia GmbH (Erlangen, Germany). The authors declare no COI.
Lim et al. 2013 [27]	<ul style="list-style-type: none"> <li>▪ Pre-Post study (on IG; CG no data reported as</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=163</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=261</li> </ul>	<p>At 5 months post-discharge:</p> <p><u>Malnutrition</u></p> <p><i>SGA; (scored 0-7, higher score indicating better nutrition status)</i></p>	Funded by the Healthcare Quality Initiative and Innovation



	<p>follow-up was very poor)</p> <ul style="list-style-type: none"> <li>Unclear location, possibly Singapore or Malaysia.</li> <li>N=424</li> <li>Attrition: 0% within IG. High attrition in CG, data not reported.</li> <li>Age: <math>\mu</math>70.8<math>\pm</math>16.1 years in IG, <math>\mu</math>72.5<math>\pm</math>15.8 years in CG</li> <li>Female: 51%.</li> <li>Mixed morbidities. All patients had malnutrition, reflected by score of <math>\leq</math>5/7 on the SGA.</li> </ul>	<ul style="list-style-type: none"> <li>During admission: Provided with inpatient nutrition counselling and support</li> <li>Delivery: 4-month ambulatory nutrition support. Telephone calls at 1 week, 2 and 4 months post-discharge. Provided by trained dietetic assistant supported by dietitian. Outpatient visits to follow if needed.</li> <li>Content: addressed dietary intake, supplement usage if prescribed, dietary/nutrition issues, weight monitoring, nutrition status monitoring.</li> <li>Supplements: As needed on individual basis, not described further.</li> </ul>	<ul style="list-style-type: none"> <li>During admission: Provided with inpatient nutrition counselling and support</li> <li>Delivery: Face-to-face dietetic outpatient clinic follow-up appointments</li> <li>Content: not specified. Very poor attendance leading to no outcomes available for CG.</li> <li>Supplements: not described</li> </ul>	<ul style="list-style-type: none"> <li>73% of patients had improvement in score (no P-value reported).</li> </ul> <p><u>Anthropometry</u></p> <p><i>Body weight (kg, mean<math>\pm</math>sd)</i></p> <ul style="list-style-type: none"> <li>n=162, IG: 46.3 <math>\pm</math> 9.6 (2.2<math>\pm</math>4.7 change since baseline); P&lt;0.001 improvement since baseline.</li> </ul> <p><i>Handgrip (kg force, mean<math>\pm</math>sd)</i></p> <ul style="list-style-type: none"> <li>n=105, IG: 17.5 <math>\pm</math> 8.5 (2.4<math>\pm</math>4.2 change since baseline); P&lt;0.001 improvement since baseline.</li> </ul> <p><i>Mid-arm circumference (cm, mean<math>\pm</math>sd)</i></p> <ul style="list-style-type: none"> <li>n=153, IG: 22.9 <math>\pm</math> 3.5 (0.4<math>\pm</math>2.3 change since baseline); P=0.048 improvement since baseline.</li> </ul> <p><i>Mid-arm muscle circumference (cm, mean<math>\pm</math>sd)</i></p> <ul style="list-style-type: none"> <li>n=153, 19.77 <math>\pm</math> 2.63; (-0.1<math>\pm</math>1.8 change since baseline); P=0.511 since baseline.</li> </ul> <p><i>Triceps skinfold thickness (mm, mean<math>\pm</math>sd)</i></p> <ul style="list-style-type: none"> <li>n=153, 9.9 <math>\pm</math> 5.1 (1.5<math>\pm</math>2.9 change since baseline); P&lt;0.001 improvement since baseline.</li> </ul> <p><u>Quality of Life</u></p> <p><i>EQ-5D VAS tool (mean<math>\pm</math>sd)</i></p> <ul style="list-style-type: none"> <li>n=81, IG: 71.6 <math>\pm</math> 17.4 (10.3 <math>\pm</math>22.2 change since baseline); P&lt;0.001 improvement since baseline.</li> </ul>	<p>Fund (HQI2F). The authors declare no COI.</p>
<p>Pedersen et al. 2016 [33]</p>	<ul style="list-style-type: none"> <li>RCT</li> <li>Aarhus, Denmark</li> <li>N=135</li> <li>Attrition: 33%; n=17 IG; n=13 CG</li> <li>Age: <math>\mu</math>86.1 years</li> <li>Female: 58%</li> <li>Mixed morbidities, mean hospital stay 8 days. All patients malnourished or risk of malnutrition as per MNA score &lt;24.</li> </ul>	<ul style="list-style-type: none"> <li>n=68</li> <li>During admission: Standard care which included individualized nutrition support including supplements, post-discharge planning, daily meals and snacks.</li> <li>Delivery: Telephone consultations with patient and carer one, two, and four-weeks after discharge, average 15 minute duration.</li> <li>Content: Individualized nutritional care post-discharge, by a clinical dietician. Primary focus was on nutritional and meal behavior to improve appetite and increase nutritional intake.</li> <li>Supplements: provided based on need during hospitalization (unclear if provided post-discharge).</li> </ul>	<ul style="list-style-type: none"> <li>n=67</li> <li>During admission: Standard care which included individualized nutrition support including supplements, post-discharge planning, daily meals and snacks.</li> <li>Delivery: N/A</li> <li>Content: No contact following discharge.</li> <li>Supplements: provided based on need during hospitalization (unclear if provided post-discharge).</li> </ul>	<p>At 8 weeks post-discharge:</p> <p><u>Malnutrition</u></p> <p><i>MNA score (mean change<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>IG: 4<math>\pm</math>3 change since baseline; CG: 3.5<math>\pm</math>3 change since baseline; P=0.30 between groups.</li> </ul> <p><u>Quality of life</u></p> <p><i>SF-36 (Physical Component Summary, higher scores indicate better health; mean change<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>IG: 5 <math>\pm</math>9 change since baseline; CG: 7<math>\pm</math>11 change since baseline; P=0.60 between groups</li> </ul> <p><i>SF-36 (Mental Component Summary, higher scores indicate better health; mean change<math>\pm</math>SD)</i></p> <ul style="list-style-type: none"> <li>IG: 1.5<math>\pm</math>8 change since baseline; CG: 0<math>\pm</math>10 change since baseline; P=0.60 between groups</li> </ul> <p><u>Physical function</u></p> <p><i>Total Modified Barthel-100 Index (scores range from 0-100, with a higher score indicating greater independence (change median [IQR]))</i></p> <ul style="list-style-type: none"> <li>IG: 6 (-1; 16) change since baseline; CG: 7 (-2; 15) change since baseline; P=0.30 between groups</li> </ul> <p><i>Chair to stand test (higher scores indicate better function; median change [IQR])</i></p> <ul style="list-style-type: none"> <li>IG: 0 [0-4] change since baseline; CG: 0 [0-0] change since baseline; P=0.9 between groups</li> </ul> <p><i>Handgrip strength (kg, mean change<math>\pm</math>SD)</i></p>	<p>No funding details reported. Authors declare no COI.</p>

				<ul style="list-style-type: none"> <li>▪ IG: 0±4 change since baseline; CG: 0±3 change since baseline; P=0.60 between groups</li> </ul> <p><i>CAS Score (median change [IQR])</i></p> <ul style="list-style-type: none"> <li>▪ IG: 0 [0-0] change since baseline; CG: 0 [0-0] change since baseline; P=0.40 between groups</li> </ul> <p><u>Mortality (incidence)</u></p> <ul style="list-style-type: none"> <li>• IG: n= 2/68; CG: n=6/67; groups not compared.</li> </ul>	
Lindgaard Pedersen et al. 2017 [36]	Same as reported for Pedersen et al. 2016. 0% attrition for readmission outcomes.	Same as reported for Pedersen et al. 2016	Same as reported for Pedersen et al. 2016	<p><u>Hospital readmission (incidence and Hazard ratio [95% CI])</u></p> <p><i>30 days</i></p> <ul style="list-style-type: none"> <li>▪ IG: n=11/68 (HR: 0.6 [0.3-1.3]); CG: n=17/67 (HR: reference group); P=0.18 between groups</li> </ul> <p><i>90 days</i></p> <ul style="list-style-type: none"> <li>▪ IG: n=20/68 (HR: 0.7 [0.4-1.3]); CG: n=26/67 (HR: reference group); P=0.23 between groups</li> </ul>	No funding details reported. Authors declare no COI.
Lindhardt et al. 2017 [28]	<ul style="list-style-type: none"> <li>▪ Quasi-experimental, non-randomised, controlled trial</li> <li>▪ Herlev, Denmark</li> <li>▪ N=36</li> <li>▪ Attrition: 30%; IG n=9; CG n=2.</li> <li>▪ Age: <math>\mu</math>79.85 years</li> <li>▪ Female: 63.9%</li> <li>▪ Mixed morbidities. All patients risk of malnutrition as per <math>\geq 3</math> using the NRS-2002</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=18</li> <li>▪ Delivery: Application on tablet-computer operated by participants in their own homes. Training and technical support by research assistant.</li> <li>▪ Content: 1) App on tablet used to order meals enriched with energy and protein which were delivered three times a week for 12-weeks post-discharge (average 1730kJ/serve and 18g protein/serve) + mid-meals. Meals viewed by online photographs prior to ordering. Meals ordered were automatically calculated against EER and EPR, allowing goal setting and self-monitoring.</li> <li>▪ Supplements: None provided as part of intervention</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=18</li> <li>▪ Delivery: not reported</li> <li>▪ Content: usual care.</li> <li>▪ Supplements: not reported</li> </ul>	<p>After 12 weeks post-discharge.</p> <p><u>Anthropometry</u></p> <p><i>Body mass index (mean±SD)</i></p> <ul style="list-style-type: none"> <li>▪ IG: 19.7±3.3; -0.59±1.2 change since baseline; CG: 21.7±4.2; 0.23±2.2 change since baseline; P-values not reported</li> </ul> <p><i>Weight (kg, mean±SD)</i></p> <ul style="list-style-type: none"> <li>▪ IG: 52.4±9.6; -1.7±3.3 change since baseline; CG: 61.9±15.8; 1.0±6.8 change since baseline; P-values not reported</li> </ul> <p><u>Quality of life</u></p> <p><i>EQ-5D index (rated 0-100; higher scores indicate better health ; mean±SD)</i></p> <ul style="list-style-type: none"> <li>▪ IG: 0.74±0.12; 0.08±0.12 change since baseline; CG: 0.70±0.15; -0.03±0.16 change since baseline; P-values not reported</li> </ul> <p><u>Physical function</u></p> <p><i>Hand grip strength (kg force, mean±SD)</i></p> <ul style="list-style-type: none"> <li>▪ IG: 19.7±7.2; 2.5±3.4 change since baseline; CG: 20.5±7.9; 0.9±3.7 change since baseline; P-values not reported.</li> </ul> <p><i>Chair-to-stand test (mean±SD)</i></p> <ul style="list-style-type: none"> <li>▪ IG: 6.8±6.6; 3.3±5.2 change since baseline; CG: 5.7±5.4; 1.8±4.9 change since baseline; P-values not reported.</li> </ul> <p><i>CAS score (scored 0-6; higher scores indicating better function)</i></p> <ul style="list-style-type: none"> <li>▪ IG: 0.33±0.87 change since baseline; CG: -0.06±1.6 change since baseline; P-values not reported.</li> </ul> <p><u>Hospital readmission (incidence; mean±SD)</u></p> <p><i>1-month</i></p> <ul style="list-style-type: none"> <li>▪ IG: n=1/9; CG: n=5/16; P-values not reported</li> </ul> <p><i>6-months</i></p> <ul style="list-style-type: none"> <li>▪ IG: 1.5±0.58; CG: 2.0±1.5; P-values not reported</li> </ul> <p><u>Mortality (incidence at 6-months; %)</u></p>	Funded by the Danish Regions' Development and Research pool. The authors declare no COI.

				<ul style="list-style-type: none"> <li>IG: n=1/9; CG: n=3/16; P-values not reported</li> </ul>	
Sharma et al 2017 [35]	<ul style="list-style-type: none"> <li>RCT</li> <li>Australia</li> <li>N=148</li> <li>Attrition: 30%; IG: n=24; CG n=21.</li> <li>M81.8±8.7 years of age</li> <li>Female: 64%</li> <li>Mixed morbidities. All patients were malnourished PG-SGA rating B or C.</li> </ul>	<ul style="list-style-type: none"> <li>n=78</li> <li>During admission: initiated within 24hrs of admission by ward dietitian, aimed to meet EER and EPR using ONS, mid-meal snacks, food fortification, and counseling.</li> <li>Delivery: telephone counselling by dietitian at 1 and 2-months post-discharge, averaging 30 minutes per call.</li> <li>Content: weight monitoring, compliance with dietetic plan initiated in hospital, side-effects of supplements, counseling focused on adherence.</li> <li>Supplements: Provided post-discharge if &gt;50% of patients EER were met by supplements in hospital.</li> </ul>	<ul style="list-style-type: none"> <li>n=70</li> <li>During admission: Seen by ward dietitian only if referred by clinical team.</li> <li>Delivery: no contact post-discharge.</li> <li>Content: none.</li> <li>Supplements: not stated.</li> </ul>	<ul style="list-style-type: none"> <li>At 3-months post-discharge:</li> <li><u>Malnutrition</u></li> <li>PG-SGA, score (range 0 to 35, higher scores indicate more nutritional risk, mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 5.8 [4.8-6.9]; -5.9 [-7.3- -4.4] change since baseline; CG: 6.9 [5.6-8.2]; -6.2 [-8.1- -4.2] change since baseline; P=0.79 between groups.</li> </ul> </li> <li><u>Anthropometry</u></li> <li>Body weight (kg, mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 56.8 [53.3-60.3]; 0.7 [-0.5-1.9] change since baseline; CG: 59.15 [54.7-63.5]; 0.1 [-0.2-1.4] change since baseline; P=0.52 between groups.</li> </ul> </li> <li>BMI (kg/m<sup>2</sup>, mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 21.3 [20.2-22.4]; 0.4 [-0.1-0.9] change since baseline; CG: 21.8 [20.6-23.1]; -0.4 [-0.9-0.2] change since baseline; P=0.04 between groups.</li> </ul> </li> <li>Mid-upper arm circumference (cm; mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 25.6 [24.5-26.7]; 0.77 [0.2-1.3] change since baseline; CG: 25.8 [24.6-27.2]; 0.6 [0-1.3] change since baseline; P=0.75 between groups.</li> </ul> </li> <li>Triceps skinfold thickness (mm; mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 10.4 [9.1-11.7]; -0.04 [-0.99-0.90] change since baseline; CG: 10.3 [8.6-12.0]; -0.9 [-2.8-0.9] change since baseline; P=0.36 between groups.</li> </ul> </li> <li>Mid arm muscle circumference (cm, mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 22.3 [21.4-23.2]; 0.8 [0.2-1.4] change since baseline; CG: 22.6 [21.4-23.9]; 0.9 [0.1-1.8] change since baseline; P=0.77 between groups.</li> </ul> </li> <li><u>Quality of life</u></li> <li>EQ-5D 5L index (mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 0.77 [0.72-0.82]; 0.05 [-0.009 - 0.099] change since baseline; CG: 0.74 [0.675-0.805]; 0.085 [0.008 - 0.162] change since baseline; P=0.38 between groups.</li> </ul> </li> <li>EQ-5D 5L VAS (mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 61.2 [56.8-65.6]; 4.6 [-1.8-10.9] change since baseline; CG: 52.4 [45.2-59.7]; -4.7 [-11.9-2.9] change since baseline; P=0.06 between groups</li> </ul> </li> <li><u>Physical function</u></li> <li>Hand-grip strength (kg, mean [95%CI]) <ul style="list-style-type: none"> <li>IG: 18.6 [16.4-20.9]; 1.8 [0.7-2.9] change since baseline; CG: 18.2 [15.5-21.0]; 1.6 [0.15-3.0] change since baseline; P=0.77 between groups.</li> </ul> </li> <li><u>Mortality (incidence)</u> <ul style="list-style-type: none"> <li>IG: n=12/78; CG: n=14/70; groups not compared.</li> </ul> </li> </ul>	No funding sources declared. Authors declare no COI.

<p>Neelemaat et al. 2011 [34]</p>	<ul style="list-style-type: none"> <li>▪ RCT</li> <li>▪ The Netherlands</li> <li>▪ N=210</li> <li>▪ Attrition: 28%; IG: n=30; CG n=30.</li> <li>▪ <math>\mu</math>74.5±9.5 years of age</li> <li>▪ Female: 55%</li> <li>▪ Mixed morbidities. All patients were malnourished based on BMI and unintentional weight loss criteria.</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=105</li> <li>▪ During admission: Energy and protein enriched diet (during the in-hospital period) in addition to supplement and content details below</li> <li>▪ Delivery: telephone counselling provided every other week after discharge from the hospital, n=6 in total.</li> <li>▪ Content: Telephone counseling by a dietitian to give advice and to stimulate compliance to the proposed nutritional intake.</li> <li>▪ Supplements: Two additional servings of an oral nutritional supplement, providing 2520 kJ/day and 24 g protein/day, additional supplementation of 400 UI vitamin D3 and 500 mg calcium per day</li> </ul>	<ul style="list-style-type: none"> <li>▪ n=105</li> <li>▪ During admission: not reported</li> <li>▪ Delivery: not reported</li> <li>▪ Content: usual care. Nutrition care only on prescription by their treating physician</li> <li>▪ Supplements: not reported</li> </ul>	<p>At 3 months post-baseline:</p> <p><u>Anthropometry:</u>  <i>Body weight ( kg corrected for baseline body weight tertiles, mean±SD)</i></p> <ul style="list-style-type: none"> <li>▪ n=45 Baseline &lt;53.6kg; IG: 2.2±3.4 change since baseline; CG: 3.0±4.21 change since baseline; -0.8 [95%CI: -3.2-1.5] between groups.</li> <li>▪ n=50 Baseline 53.6-63.9kg; IG: 2.7±3.8 change since baseline; CG: 0.9±5.6 change since baseline; 1.8 [95%CI: -0.9-4.4] between groups.</li> <li>▪ n=51 Baseline &gt;63.9kg; IG: 2.5±4.2 change since baseline; CG: -0.9±6.8 change since baseline; 3.4 [95%CI: 0.2-6.6] between groups.</li> </ul> <p><i>Fat free mass, bio-electrical impedance spectroscopy (kg, mean±sd)</i></p> <ul style="list-style-type: none"> <li>▪ n=48, IG: 3.3±4.3 change since baseline; n=31 CG 2.8±4.1 change since baseline; 0.5 [95%CI: -1.5-2.4] between groups</li> </ul> <p><u>Physical function</u>  <i>LASA Functional Limitation Questionnaire score (scored 0-6 where higher scores indicate worse function; mean±sd change)</i></p> <ul style="list-style-type: none"> <li>▪ n=70, IG: -0.3±1.2 change since baseline; n=74 CG: 0.2±1.5 change since baseline; -0.5 [95%CI: -1.0-0.1] between groups.</li> </ul> <p><i>LASA Physical Activity Questionnaire score (scored 0-6, higher score indicates better function; mean±sd change)</i></p> <ul style="list-style-type: none"> <li>▪ n=59, IG: 0.5±1.5 change since baseline; n=48, CG: 0.6±1.5 change since baseline; 0.8 [95%CI: -1.0-2.6] between groups.</li> </ul> <p><i>Physical performance score (scored 0-16, higher score indicates better function; mean±sd change)</i></p> <ul style="list-style-type: none"> <li>▪ n=57, IG: 3.0±4.2 change since baseline; n=53 CG: 2.1±5.4 change since baseline; -0.1 [95%CI: -0.7-0.5] between groups</li> </ul> <p><i>Handgrip strength (kg, mean±sd change)</i></p> <ul style="list-style-type: none"> <li>▪ n=65, IG: 0.2±5.6 change since baseline; n=53, CG: 1.0±6.7 change since baseline -0.8 [95%CI: -3.0-1.5] between groups</li> </ul> <p><u>Mortality (during study period; incidence)</u></p> <ul style="list-style-type: none"> <li>• IG: n=14/105; CG: n=11/105; groups not compared.</li> </ul>	<p>Funded by The Netherlands Organization for Health Research and Development.. Authors declare no COI.</p>
<p>Neelemaat, Bosmans et al. 2012 [37]; study protocol Neelemaat et al. 2010 [40]</p>	<p>Same as reported for Neelemaat et al 2011. N=185 for cost outcomes.</p>	<p>Same as reported for Neelemaat et al 2011. n=91 for cost outcomes.</p>	<p>Same as reported for Neelemaat et al 2011. n=94 for cost outcomes.</p>	<p><u>Healthcare costs</u>  <i>Total direct, non-direct and indirect costs per group (€, mean±S.E.)</i></p> <ul style="list-style-type: none"> <li>• IG: 9,129±1,227; CG: 8,684±1,361; 445 [95%CI: -2,779-3,938] between groups.</li> </ul> <p><i>Cost-effectiveness: Clinical outcome: QALY informed by EQ-5D, LASA physical activities and LASA functional limitations. Cost data: cost-diaries covering six-weeks, direct health costs (hospital admission, specialists, etc), non-direct costs (complimentary medicine, informal care) and indirect costs-absenteeism, etc).</i></p> <ul style="list-style-type: none"> <li>• 445€ [95%CI: -2779-3938]/QALY cost difference between groups</li> <li>• ICER: 26,962€/QALY<sup>a</sup></li> </ul>	<p>Same as reported for Neelemaat et al 2011</p>

				<ul style="list-style-type: none"> <li>• 445€ [95%CI: -2779-3938]/physical activity cost difference between groups</li> <li>• ICER: 4,470€/physical activity<sup>a</sup></li> <li>• 445€ [95%CI: -2779-3938]/functional limitation cost difference between groups</li> <li>• ICER: -618€/functional limitation<sup>a</sup></li> </ul>	
Neelemaat, Lips, et al. 2012 [38]	Same as reported for Neelemaat et al 2011.	Same as reported for Neelemaat et al 2011.	Same as reported for Neelemaat et al 2011.	<p>At 6-weeks post-baseline:</p> <p><u>Physical function</u></p> <p><i>Falls incidence</i></p> <ul style="list-style-type: none"> <li>• IG: n=16/73 (representing 10 fallers with one or more falls); CG: n=41/74 (representing 24 fallers with one or more falls); HR: 0.41 [95%CI: 0.19-0.86]; P=0.02.</li> </ul> <p>At 3-months post-baseline:</p> <p><u>Dietary intake</u></p> <p><i>Kcal intake/day (mean±SD)</i></p> <ul style="list-style-type: none"> <li>• n=75, IG: 2,152±752; 595±753 change since baseline; n=75, CG: 1,766±661; 315±640 change since baseline; P=0.002 between groups</li> </ul> <p><i>Protein intake/day (mean±SD)</i></p> <ul style="list-style-type: none"> <li>• n=75, IG: 78±34; 21±29 change since baseline; n=75, CG: 63±30; 10±29 change since baseline; P=0.04 between groups</li> </ul> <p><u>Anthropometry</u></p> <p><i>Body weight (representing more participants than reported in Neelemaat 2011; kg, mean±SD)</i></p> <ul style="list-style-type: none"> <li>• n=73, IG: 64±14.4; n=73, CG: 61.0±12.2; 3.7 [95%CI: 0.6-8.1] difference between groups</li> </ul> <p><i>BMI (kg/m<sup>2</sup>, mean±SD)</i></p> <ul style="list-style-type: none"> <li>• n=73, IG: 22.1±4.5; n=73, CG: 21.0±3.7; 1.1 [95%CI: 0.3-2.4] between groups</li> </ul>	Same as reported for Neelemaat et al 2011
Neelemaat et al 2017 [39]	Same as reported for Neelemaat et al 2011. N=208 for mortality.	Same as reported for Neelemaat et al 2011. n=104 for mortality.	Same as reported for Neelemaat et al 2011. n=104 for mortality.	<p><u>Mortality (incidence)</u></p> <p><i>3-months post-baseline</i></p> <ul style="list-style-type: none"> <li>• IG: n=14/104; CG: n=13/104; HR: 0.98 [95%CI: 0.71-1.35]</li> </ul> <p><i>6-months post-baseline</i></p> <ul style="list-style-type: none"> <li>• IG: n=20/104; CG: n=22/104; HR: 1.00 [95%CI: 0.73-1.39]</li> </ul> <p><i>12-months post-baseline</i></p> <ul style="list-style-type: none"> <li>• IG: n=28/104; CG: n=35/104; HR: 0.93 [95%CI: 0.68-1.29]</li> </ul> <p><i>4-years post-baseline</i></p> <ul style="list-style-type: none"> <li>• IG: n=74/104; CG: n=73/104; HR: 0.93 [95%CI: 0.67-1.28]</li> </ul>	Same as reported for Neelemaat et al 2011

CAS, Cumulated Ambulation Score; CG, control group; COI, conflict of interest; DRAQ, Disease-Related Appetite Questionnaire; EER, estimated energy requirement; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Global Quality of Life questionnaire C30; EPR, estimated energy requirement; EQ-5D, European Quality of Life Instrument; HAQ-DI, Health Assessment Questionnaire Disability Index; hr, hours; ICER, incremental cost-effectiveness ratios; IG, intervention group; LOS, length of stay; MNA, Mini Nutritional Assessment; NRS-2002, Nutrition Risk Screening tool 2002; PG-SGA, Patient Generated Subject Global Assessment; QALY, quality adjusted life year; RCT, randomized controlled trial; SCREEN-II, Seniors in the Community: Risk Evaluation for Eating and Nutrition version II; S.E., standard error; SGA, Subjective Global Assessment; VAS, Visual Analogue Scale

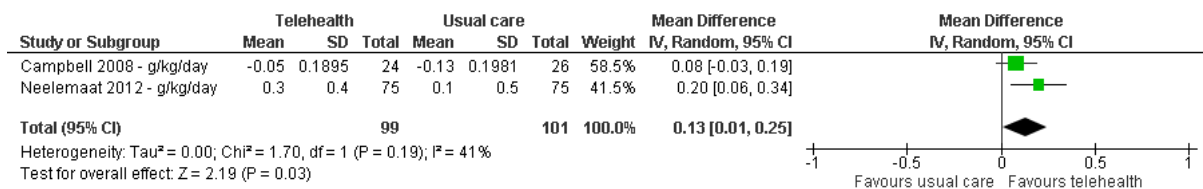
- a. Interpreted as the amount of Euros needing to be spent to gain one additional point/score in the clinical variable, e.g. to gain one additional life year.

### Effectiveness of telehealth

Outcomes of interest to this review are reported in Table 1; and the GRADE assessment for each pooled outcome is shown in Appendix II. No studies reported data on pressure wounds or admission to aged care facilities. Attrition rates ranged from 0 – 61% in the intervention group and 4 – 45% in the control groups. Excluding the two asynchronous telehealth devices which had the highest levels of loss-to-follow-up; attrition was lower in the intervention groups (0-31%) than control groups (4-45%) in five of the seven studies. No studies reported on participant satisfaction or burden.

All five studies with nutrition status outcomes reported improvements in the intervention group from baseline or compared to the control [27, 29, 30, 33, 35]. Three studies using the Patient Generated-Subjective Global Assessment or the Mini Nutritional Assessment scores were pooled; finding a non-significant trend toward improved nutrition status in the intervention group (SMD: -0.68 [95%CI: -1.48-0.13] P=0.10; n=3 studies; n=253 participants; I<sup>2</sup>=83%) [30, 33, 35]. Removing Silvers et al [30] during sensitivity analysis (due to including a different patient group) improved heterogeneity to I<sup>2</sup>=0%, but the effect still did not reach significance (SMD: -0.22 [95%CI: -0.49-0.06] P=0.12; GRADE level: low). The odds of being malnourished at follow-up were also not significant between groups (OR: 0.27 [95%CI: 0.01-5.24] P=0.39; n=2 studies; n=70 participants; I<sup>2</sup>=62%).

The two studies which measured energy and protein intake reported significant improvements compared with control [29, 38]. Pooled data showing a trend in improved energy intake at follow-up did not reach significance (SMD: 0.85 [95%CI: -0.11-1.81] P=0.08; n=2 studies; n=200 participants; I<sup>2</sup>87%; GRADE level: very low) [29, 38]. However, telehealth interventions significantly improved protein intake by 0.13g/kg/day ([95%CI: 0.01-0.25]; P=0.03; GRADE level: low) [29, 38] compared to the control group (Figure 3), representing 10g of protein per day difference in an 80kg individual.

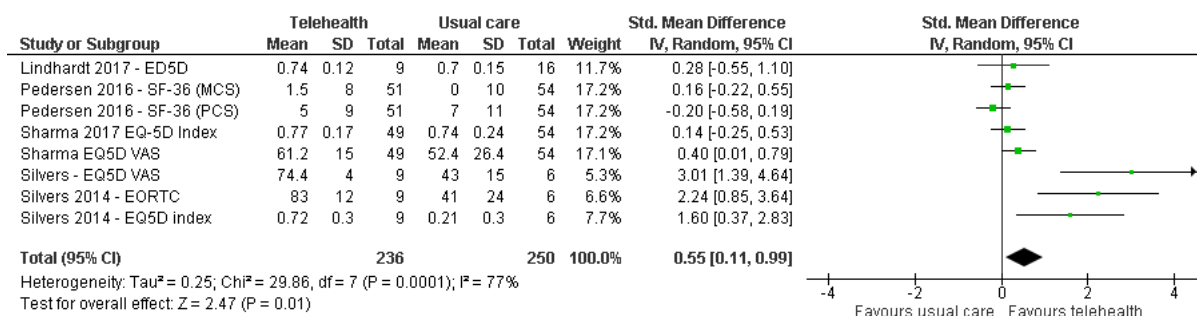


**Figure 3:** Malnutrition-focused telehealth interventions were found to improve protein intake in older adults by 0.13g/kg body weight per day ([95%CI: 0.01-0.25]; P=0.03; n=2 studies; n=200 participants; I<sup>2</sup>=41%).

Six of the eight studies which reported body weight showed improvements compared with baseline or control [27, 28, 30-32, 34, 35, 38]; however, when pooled, there was no difference between groups (MD: 0.59 [95%CI: -5.64-6.83] P=0.85; n=5 studies; n=303 participants; I<sup>2</sup>=62%; GRADE level: very low) [28, 30, 32, 35, 38]. Similar findings were found for other measures of body composition, where most studies reported modest improvements in the intervention group for BMI [28, 32, 35], mid-arm circumference [27, 35], fat-free mass [34], mid-arm muscle circumference [27, 35] and triceps skinfold thickness [27, 35].

Four of the six studies which reported quality of life using the EQ-5D, SF-36 or EORTC found improvements in the intervention group [27, 28, 30, 31, 33, 35]. Four of the studies could be pooled [28, 30, 33, 35], finding a significant improvement in quality of life with a moderate but imprecise effect size, and substantial heterogeneity, which was not improved with sensitivity analysis (SMD: 0.55 [95%CI: 0.11-0.99]; I<sup>2</sup>: 77%; GRADE level: very low) (Figure 4). When converted into the EQ-5D Visual Analogue Scale using the baseline standard deviations from Silver et al. [30], this represents an effect of 11/100 [95%CI: 2.2 – 19.8] between groups.





**Figure 4:** Malnutrition-focused telehealth interventions were found to improve quality of life in older adults (SMD: 0.55 [95%CI: 0.11-0.99]; P=0.01; n=4 studies with n=9 quality of life tools; n=248 participants; I<sup>2</sup>=84%).

Regarding physical function, only one of the three studies which measured physical function via an assessment tool reported significant improvements [27, 33, 34]. Two of these studies could be pooled using four assessment tools. Although a clear trend showed the intervention improved physical function, this did not reach statistical significance (SMD: 0.19 [95%CI: -0.01-0.39]; P=0.07; n=2 studies; n=4 physical function tools; n=169 participants; I<sup>2</sup>=0%; GRADE level: very low) [28, 34]. Although two of the four studies which measured handgrip strength reported improvements [27, 33-35]; pooling of all four studies found no effect (MD: 0.09 [95%CI: -0.83-1.01]; P=0.85; n=4 studies; n=351 participants; I<sup>2</sup>=0%; GRADE level: low). Only one study measured and found improvements in the rate of falls between the intervention and control group [38].

Both Lindegaard Pedersen et al. [36] and Lindhard et al. [28] reported significantly decreased hospital readmission in the intervention groups. When pooled, there was a non-significant 48% decreased odds of hospital readmission in the intervention groups (OR: 0.52 [95%CI: 0.24-1.16] P=0.11; n=2 studies; n=160 participants; I<sup>2</sup>=0%; GRADE level: very low).

Although most studies did not compare the groups statistically, four of the eight studies reporting all-cause mortality (range of 1.5-months to 4-years post-baseline) found a higher incidence in the control groups [28-33, 35, 39]. When pooled using data from 1.5-6 months

post-baseline, there was a non-significant trend showing 23% decreased risk of all-cause mortality in the intervention group (OR: 0.77 [95%CI: 0.41-1.48] P=0.44; n=8 studies; n=734 participants; I<sup>2</sup>=21%; GRADE level: low). The study by Neelemaat et al. [37], which used oral nutritional supplements combined with telehealth consultations, found the intervention was cost-effective at improving physical function but not quality adjusted life years. Additionally, the intervention group and control groups had no significant difference between direct, non-direct and indirect costs [37].

## **Discussion**

This systematic review and meta analysis found that telephone consultations are feasible and cost-effective methods to deliver interventions to older adults at risk of malnutrition. Compared with usual care, this review found evidence that malnutrition-related interventions delivered via telehealth are effective in improving quality of life and protein-intake, although confidence in the estimated effect sizes for these outcomes is low to very low. While pooled data did not find statistical significance, many studies also reported statistically and clinically significant improvements in nutrition status, physical function, energy intake, falls, hospital readmissions and all-cause mortality. For many of these outcomes, pooled data showed clear trends towards improvement; suggesting the small sample sizes in many studies may have led the outcomes to be underpowered, particularly where effect sizes are small. For all outcomes, the small number of studies and their small sample sizes of these studies decreased confidence in the body of evidence for the estimated effect sizes, leading to GRADE assessments of “very low” to “low” (Appendix II).

Seven of the nine intervention studies used telephone consultations, which overall had much lower attrition rates (0-31%) than those which used telemonitoring devices (50-61%). As no study reported on participant satisfaction, the reasonably low attrition rates in the telephone consultation groups imply that telehealth is a feasible and acceptable option in this patient

group; however, asynchronistic approaches which rely on computerised devices may be less desirable as at least half of all participants were lost-to-follow-up.

Malnutrition-focused interventions delivered via non-telehealth methods such as group education and home visits have shown improvements in health-related outcomes in this patient group [41, 42]. The studies in this review compared telehealth to no or minimal intervention, and therefore, this review provides no insight as to whether telehealth is non-inferior to face-to-face methods. In the study reported by Lim et al. [27], hospital patients in the control group were given appointments with the outpatient dietitian following discharge. Despite reminder calls, attendance at the outpatient follow-up was so poor that outcome data could not be used. This aligns with other research showing poor attendance by malnourished older adults at dietitian outpatient clinics [6]; suggesting this option may not be feasible or desirable for this patient group. Barriers to attending outpatient clinics have been explored in older rural patients, which suggests issues around transport and finance limit access to outpatient health care [43]. In the study by Pedersen et al. [33], there was a second intervention group which received home visits compared with telehealth and control (no intervention). Attrition rates were similar between all groups, but the home visit group had substantial improvements in physical function compared with telehealth and control; although no difference was found for quality of life or anthropometry [33]. Although the clinical- and cost-efficacy of telehealth interventions compared with home visits are not established, compared with no intervention, telehealth interventions are cost-effective [37] and have increased feasibility from a health care point of view making it more likely patients will receive the intervention [8].

### Limitations

This review found the body of research supporting malnutrition-related interventions delivered to older adults living at home is limited by studies using small sample sizes and a lack of diverse patient groups, where most patients were those discharged from hospital. Although a

systematic approach was used, this review may have missed relevant studies, such as mobile applications, which were not explicitly included in the search strategy, and did not include grey literature. Excepting all-cause mortality, there may be undetected publication bias for some outcomes as the few number of studies prevented evaluation via funnel plots. Further well conducted randomised controlled trials with economic analyses and measures of participant satisfaction, compared with both control or other methods of intervention such as outpatient clinics and home visits, will strengthen the body of evidence for supporting telehealth to deliver malnutrition-related interventions to older adults.

## **Conclusion**

Malnutrition-related telehealth interventions to older adults living at home are likely to result in improvements to quality of life and dietary intake, and appear feasible and cost-effective. Evidence suggests telehealth may also improve nutrition status, physical function, hospital readmission and mortality; however, further research is required to strengthen the body of evidence.

## Appendix I: Search strategy implemented across six electronic databases and results of total records retrieved

Set	Search Terms
	<p><b><i>MEDLINE (via PubMed) - searched 2 November using keywords (title and abstract) and MeSH Terms. Result = 631 records</i></b></p>
	<p>((("Protein-Energy Malnutrition"[Mesh] OR Malnutrition[Mesh] OR "Nutritional Status"[Mesh] OR "Wasting Syndrome"[Mesh] OR Starvation[Mesh] OR Emaciation[Mesh] OR "Protein Deficiency"[Mesh]) OR (malnutrition[tiab] OR "nutrition status"[tiab] OR undernutrition[tiab] OR undernourish*[tiab] OR malnourish*[tiab] OR "nutritional status"[tiab] OR wasting[tiab] OR protein[tiab]))</p> <p>AND</p> <p>((Computers[Mesh] OR Telecommunications[Mesh] OR Internet[Mesh] OR "Remote Consultation"[Mesh] OR Telemedicine[Mesh] OR Videoconferencing[Mesh] OR "Wireless Technology"[Mesh] OR Telephone[Mesh]) OR (computer*[tiab] OR telecommunication*[tiab] OR teleconference*[tiab] OR internet[tiab] OR telehealth[tiab] OR eHealth[tiab] OR mHealth[tiab] OR remote*[tiab] OR mobile[tiab] OR telemedicine[tiab] OR videoconference*[tiab] OR teleconsultat*[tiab] OR telephone[tiab] OR ecare[tiab] OR e-care[tiab] OR web-based[tiab] OR online*[tiab]))</p> <p>AND</p> <p>("Aged, 80 and over"[Mesh] OR Aged[Mesh] OR "Frail Elderly"[Mesh] OR geriatrics[Mesh] OR older[tiab] OR elder*[tiab] OR geriatric[tiab] OR veteran[tiab] OR old[tiab])</p> <p>AND</p> <p>("clinical study"[pt] OR "clinical trial"[pt] OR randomized[tiab] OR randomised[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "single blind"[tiab] OR "double blind"[tiab] OR intervention[tiab])</p>
	<p><b><i>CINAHL (via Ebscohost) was searched on 2 November 2017 using keywords and CINAHL Headings. Results 123 records</i></b></p>
	<p>((((MH "Protein-Energy Malnutrition+") OR (MH "Malnutrition+") OR (MH "Nutritional Status+") OR (MH "Nutrition Status+") OR (MH "Wasting Syndrome+") OR (MH "Starvation+") OR (MH "Undernutrition+") OR (MH "Nutritional Deficiency+") OR (MH "Protein-calorie Malnutrition+") OR (MH "Marasmus+") OR (MH "Emaciation+") OR (MH "Protein Deficiency+") OR (MH "Malnourishment+") OR TI malnutrition OR AB malnutrition OR TI "nutrition status" OR AB "nutrition status" OR TI undernutrition OR AB undernutrition OR TI undernourish* OR AB undernourish* OR TI malnourish* OR AB malnourish* OR TI "nutritional status" OR AB "nutritional status" OR TI wasting OR AB wasting OR TI protein OR AB protein))</p> <p>AND</p> <p>(((((MH "Computers+") OR (MH "Telecommunications+") OR (MH "Teleconference+") OR (MH "Internet+") OR (MH "Telehealth+") OR (MH "eHealth+") OR (MH "mHealth+") OR (MH "Remote Consultation+") OR (MH "Mobile Health+") OR (MH "Telemedicine+") OR (MH "Videoconferencing+") OR (MH "Teleconsultation+") OR (MH "Wireless Technology+") OR (MH "Telephone+") OR TI computer* OR AB computer* OR TI telecommunication* OR AB telecommunication* OR TI teleconference* OR AB teleconference* OR TI internet OR AB internet OR TI telehealth OR AB telehealth OR TI eHealth OR AB eHealth OR TI mHealth OR AB mHealth OR TI remote* OR AB remote* OR TI mobile OR AB mobile OR TI telemedicine OR AB telemedicine OR TI videoconference* OR AB videoconference* OR TI teleconsultat* OR AB teleconsultat* OR TI telephone OR AB telephone OR TI ecare OR AB ecare OR TI e-care OR AB e-care OR TI web-based OR AB web-based OR TI online* OR AB online*))</p> <p>AND</p> <p>((((MH "Aged, 80 and over+") OR (MH "Aged+") OR (MH "Frail Elderly+") OR (MH "geriatrics+") OR TI older OR AB older OR TI elder* OR AB elder* OR TI geriatric OR AB</p>

geriatric OR TI veteran OR AB veteran OR TI old OR AB old))

AND

((PT "clinical study" OR PT "clinical trial" OR TI randomized OR AB randomized OR TI randomised OR AB randomised OR TI randomly OR AB randomly OR TI trial OR AB trial OR TI groups OR AB groups OR TI "single blind" OR AB "single blind" OR TI "double blind" OR AB "double blind" OR TI intervention OR AB intervention))

***The Cochrane Library was searched on 2 November 2017 using keywords and MeSH Headings. Results = 97 records***

((([mh "Protein Energy Malnutrition"] OR [mh Malnutrition] OR [mh "Nutritional Status"] OR [mh "Wasting Syndrome"] OR [mh Starvation] OR [mh Emaciation] OR [mh "Protein Deficiency"]) OR (malnutrition:ti,ab OR "nutrition status":ti,ab OR undernutrition:ti,ab OR undernourish:ti,ab OR undernourished:ti,ab OR malnourished:ti,ab OR "nutritional status":ti,ab OR wasting:ti,ab OR protein:ti,ab OR malnourishment:ti,ab))

AND

((([mh Computers] OR [mh Telecommunications] OR [mh Internet] OR [mh "Remote Consultation"] OR [mh Telemedicine] OR [mh Videoconferencing] OR [mh "Wireless Technology"] OR [mh Telephone] OR [mh "Cell Phones"]) OR (computer\*:ti,ab OR telecommunication\*:ti,ab OR teleconference\*:ti,ab OR internet:ti,ab OR telehealth:ti,ab OR eHealth:ti,ab OR mHealth:ti,ab OR remote\*:ti,ab OR mobile:ti,ab OR telemedicine:ti,ab OR videoconference\*:ti,ab OR teleconsultat\*:ti,ab OR telephone:ti,ab OR ecare:ti,ab OR e-care:ti,ab OR web-based:ti,ab OR online\*:ti,ab))

AND

((([mh "Aged, 80 and over"] OR [mh Aged] OR [mh "Frail Elderly"] OR [mh geriatrics] OR older:ti,ab OR elder\*:ti,ab OR geriatric:ti,ab OR veteran:ti,ab OR old:ti,ab))

***EMBASE was searched 2 November 2017 for citations from both Embase and MEDLINE using keywords (abstract and title) and Emtree terms Results = 790 records***

((('Protein-Energy Malnutrition'/exp OR 'Malnutrition'/exp OR 'Nutritional Status'/exp OR 'Nutrition Status'/exp OR 'Wasting Syndrome'/exp OR 'Starvation'/exp OR 'Undernutrition'/exp OR 'Nutritional Deficiency'/exp OR 'Protein-calorie Malnutrition'/exp OR 'Marasmus'/exp OR 'Emaciation'/exp OR 'Protein Deficiency'/exp OR 'Malnourishment'/exp) OR (malnutrition:ti,ab OR "nutrition status":ti,ab OR undernutrition:ti,ab OR undernourish\*:ti,ab OR malnourish\*:ti,ab OR "nutritional status":ti,ab OR wasting:ti,ab OR protein:ti,ab))

AND

((('Computers'/exp OR 'Telecommunications'/exp OR 'Teleconference'/exp OR 'Internet'/exp OR 'Telehealth'/exp OR 'eHealth'/exp OR 'mHealth'/exp OR 'Remote Consultation'/exp OR 'Mobile Health'/exp OR 'Telemedicine'/exp OR 'Videoconferencing'/exp OR 'Teleconsultation'/exp OR 'Wireless Technology'/exp OR 'Telephone'/exp) OR (computer\*:ti,ab OR telecommunication\*:ti,ab OR teleconference\*:ti,ab OR internet:ti,ab OR telehealth:ti,ab OR eHealth:ti,ab OR mHealth:ti,ab OR remote\*:ti,ab OR mobile:ti,ab OR telemedicine:ti,ab OR videoconference\*:ti,ab OR teleconsultat\*:ti,ab OR telephone:ti,ab OR ecare:ti,ab OR e-care:ti,ab OR web-based:ti,ab OR online\*:ti,ab))

AND

('Aged, 80 and over'/exp OR 'Aged'/exp OR 'Frail Elderly'/exp OR 'geriatrics'/exp OR older:ti,ab OR elder\*:ti,ab OR geriatric:ti,ab OR veteran:ti,ab OR old:ti,ab)

AND  
("clinical study":it OR "clinical trial":it OR randomized:ti,ab OR randomised:ti,ab OR randomly:ti,ab OR trial:ti,ab OR groups:ti,ab OR "single blind":ti,ab OR "double blind":ti,ab OR intervention:ti,ab)

***Web of Science was searched 2 November 2017 for the following keywords in topic or title (limits: article, editorial material). Results = 1,351 records***

("Protein-Energy Malnutrition" OR Malnutrition OR "Nutritional Status" OR "Nutrition Status" OR "Wasting Syndrome" OR Starvation OR Undernutrition OR "Nutritional Deficiency" OR "Protein-calorie Malnutrition" OR Marasmus OR Emaciation OR "Protein Deficiency" OR Malnourishment OR malnutrition OR "nutrition status" OR undernutrition OR undernourish\* OR malnourish\* OR "nutritional status" OR wasting OR protein)  
AND

(Computers OR Telecommunications OR Teleconference OR Internet OR Telehealth OR eHealth OR mHealth OR "Remote Consultation" OR "Mobile Health" OR Telemedicine OR Videoconferencing OR Teleconsultation OR "Wireless Technology" OR Telephone OR computer\* OR telecommunication\* OR teleconference\* OR internet OR telehealth OR eHealth OR mHealth OR remote\* OR mobile OR telemedicine OR videoconference\* OR teleconsultat\* OR telephone OR ecare OR e-care OR web-based OR online\*)  
AND

("Aged, 80 and over" OR Aged OR "Frail Elderly" OR geriatrics OR older OR elder\* OR geriatric OR veteran OR old)  
AND

("clinical study" OR "clinical trial" OR randomized OR randomised OR randomly OR trial OR groups OR "single blind" OR "double blind" OR intervention)

<b>Total</b>	<b><i>2992 records</i></b>
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## Appendix II: GRADE assessment

**Question:** Telehealth compared to usual care for managing malnutrition in community older adults

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	telehealth	usual care	Relative (95% CI)	Absolute (95% CI)	
Nutritional status (assessed with: nutrition assessment tool)											
3	randomised trials	not serious	not serious	not serious	very serious <sup>a</sup>	none	105	103	-	SMD <b>0.22</b> SD lower (0.49 lower to 0.06 higher)	⊕⊕○○ LOW
Quality of life (assessed with: various assessment tools)											
4	randomised trials	not serious	serious <sup>b</sup>	not serious	very serious <sup>d</sup>	none	118	130	-	SMD <b>0.55</b> SD lower (0.11 lower to 0.99 higher)	⊕○○○ VERY LOW
Physical function (assessed with: various assessment tools)											
2	randomised trials	very serious <sub>f</sub>	not serious	not serious	very serious <sup>a</sup>	none	79	90	-	SMD <b>0.19</b> SD lower (-0.01 lower to 0.39 higher)	⊕○○○ VERY LOW
Protein intake (assessed with: g/kg/day)											



Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	telehealth	usual care	Relative (95% CI)	Absolute (95% CI)	
2	randomised trials	not serious	not serious	not serious	very serious <sup>a</sup>	none	99	101	-	MD <b>0.13 g higher</b> (0.01 higher to 0.25 higher)	⊕⊕○○ LOW
Energy intake (assessed with: Kj or Kcal/day or per Kg/day)											
2	randomised trials	not serious	serious <sup>b</sup>	not serious	very serious <sup>a</sup>	none	99	101	-	SMD <b>0.85 SD higher</b> (0.11 lower to 1.81 higher)	⊕○○○ VERY LOW
All-cause mortality (follow up: range 1.5 months to 6 months; assessed with: incidence of death)											
8	randomised trials	serious <sup>c</sup>	not serious	not serious	serious <sup>d</sup>	none	35/369 (9.5%)	41/365 (11.2%)	<b>OR 0.77</b> (0.41 to 1.48)	<b>24 fewer per 1,000</b> (from 45 more to 63 fewer)	⊕⊕○○ LOW
Hospital readmission (follow up: mean 1 months; assessed with: Incidence)											
2	randomised trials	serious <sup>c</sup>	not serious	not serious	very serious <sup>a</sup>	none	12/77 (15.6%)	22/83 (26.5%)	<b>OR 0.52</b> (0.24 to 1.16)	<b>107 fewer per 1,000</b> (from 30 more to 185 fewer)	⊕○○○ VERY LOW
Handgrip strength (assessed with: kg)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	telehealth	usual care	Relative (95% CI)	Absolute (95% CI)	
4	randomised trials	serious <sup>c</sup>	not serious	serious <sup>c</sup>	not serious	none	179	172	-	MD <b>0.09 kg higher</b> (0.83 lower to 1.01 higher)	⊕⊕○○ LOW
Body weight (assessed with: kg or change in kg)											
5	randomised trials	serious <sup>c</sup>	serious <sup>b</sup>	not serious	very serious <sup>a</sup>		150	153	-	MD <b>0.59 kg higher</b> (5.64 lower to 6.83 higher)	⊕○○○ VERY LOW

**CI:** Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference; **OR:** Odds ratio

*Explanations*

- a. The large confidence interval and small combined sample size decreases the precision of the estimate effect
- b. There is substantial heterogeneity as per the I2 statistic
- c. Some studies show significant risk of bias; however, the majority had low risk across most domains.
- d. Confidence intervals show substantial variance
- e. Handgrip strength is an indicator of physical function but not a direct measure
- f. Both studies included in this analysis had substantial risk of bias across both domains

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