Cost-effectiveness of food, supplement and environmental interventions to address malnutrition in residential aged care: A systematic review

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**Actual title:** Cost-effectiveness of food, supplement and environmental interventions to address malnutrition in residential aged care: a systematic review

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**Journal:** Age and Ageing Journal

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**Contributors and their role in the paper**

This study was conceptualised by CH, LI, MM and SM.

CH and SM developed and ran search strategy.

CH and SM independently screened, extracted and synthesised data before meeting to compare results and resolve minor conflicts in interpretation of results.

CH and SM compiled the original manuscript. LI and MM contributed towards the manuscript revision. All authors approved the final manuscript.

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Abstract

Background: Observational studies have shown that nutritional strategies to manage malnutrition may be cost-effective in aged care; but more robust economic data is needed to support and encourage translation to practice. Therefore, the aim of this systematic review is to compare the cost-effectiveness of implementing nutrition interventions targeting malnutrition in aged care homes versus usual care.

Setting: Residential aged care homes.

Methods: Systematic literature review of studies published between January 2000 - August 2017 across 10 electronic databases. Cochrane Risk of Bias tool and GRADE were used to evaluate the quality of the studies.

Results: Eight included studies (3098 studies initially screened) reported on 11 intervention groups, evaluating the effect of modifications to dining environment (n=1), supplements (n=5) and food-based interventions (n=5). Interventions had a low cost of implementation (£2.30/resident/day) and provided clinical improvement for a range of outcomes including weight, nutritional status and dietary intake. Supplements and food-based interventions further demonstrated a low cost per quality adjusted life year or unit of physical function improvement. GRADE assessment revealed the quality of the body of evidence that introducing malnutrition interventions, whether they be environmental, supplements or food-based, are cost-effective in aged care homes was low.

Conclusion: This review suggests supplements and food-based nutrition interventions in the aged care setting are clinically effective, have a low cost of implementation and may be cost-effective at improving clinical outcomes associated with malnutrition. More studies using well-defined frameworks for economic analysis, stronger study designs with improved quality, along with validated malnutrition measures are needed to confirm and increase confidence with these findings.

Keywords – Malnutrition; Systematic Review; Cost; Aged Care; Economic

Key Points –
- Malnutrition is a significant economic burden on society.

- Nutrition offers opportunity to improve the quality of life of residents and the economic position of aged care homes.

- Quality economic studies evaluating malnutrition interventions in the aged care setting are lacking.

- More robust malnutrition economic evaluation intervention studies in aged care are needed to support research translation.
Introduction
The financial cost of residential aged care, accommodation and care support for frail and aged residents, is high and increasing [1-3]. Whilst significant resources go towards supporting the health of older residents, outcomes are often suboptimal and associated with malnutrition (undernutrition). Malnutrition is a wasting syndrome which presents most commonly in older adults, and occurs when lean body mass, with or without fat mass, is unintentionally lost due to inadequate bioavailability of energy and protein [4]. Cost-of-illness studies indicate that the annual direct cost of malnutrition in residential aged care ranges from €107 million to €1.7 billion (£98.4 million to £1.56 billion) for the Netherlands and the UK respectively [5-8].

Higher food budgets (>£4.20 per resident per day) in aged care homes decrease the risk of a resident becoming malnourished by 66% (OR: 0.66 [95%CI: 0.46-0.95] P=0.023) [9]. Recent research in developed countries demonstrate a downward trend in the amounts spent on the food budget in aged care homes [10]. There is also an increase in spending on oral nutrition supplements (“supplements”) which is believed to be in response to high malnutrition rates [10]. There is evidence that interventions such as supplements, food-first approaches (prioritising food over supplements) and environmental changes improve clinical outcomes for residents in resident aged care homes [11]. In acute care, these malnutrition interventions are ranked as one of the top strategies to produce health care cost savings by the National Institute for Health and Care Excellence (NICE) [12]. Observational studies have shown that nutritional strategies to manage malnutrition may be cost-effective in the aged care setting; but more robust economic data is needed to support and encourage translation to practice [13-16]. Therefore, the aim of this systematic review is to compare the cost-effectiveness of implementing nutrition interventions (including food fortification, supplements, menu changes and dining environment changes) targeting malnutrition in aged care homes versus no intervention or usual care for older residents.

Methods
A systematic review was planned and reported according to the PRISMA guidelines [17]. The protocol for this review was developed in consultation with topic experts and the search strategy was developed in consultation with an information specialist. The protocol was registered with PROSPERO (http://www.crd.york.ac.uk/PROSPERO) (registration number - CRD42016048175).

Search strategy
Published studies were searched for in the following electronic databases: MEDLINE (PubMed), Cochrane, CINAHL, EMBASE, EBSCO Megafile Complete, Business Source Complete, EconLit, NHS EED and Web of Science from January 2000 to 24 August 2017. Publications predating 1 January 2000 were excluded as health inflation analysis has shown that the health sector prices have grown much faster than inflation, the population, population ageing and the broader economy in the past 15 years [18]. As a result of the documented year-on-year health cost increases, comparison of data prior to the 2000 would be difficult. No language restrictions were used.

The search strategy used keywords and each database’s controlled vocabulary (Online Supplementary Material 1). The search strategy was complemented by a “snowball” search which involved pursuing article references of identified studies in addition to electronic citation tracking and brief Google Scholar searches. For this review, nutrition interventions to prevent and/or treat malnutrition in older residents (mean age of sample ≥65 years) dwelling in a residential aged care home were included. Eligibility criteria included studies that had original financial data related to the intervention and/or outcomes. Specifically, studies were included which reported data related to the direct cost, cost-effectiveness and/or cost-benefit of the interventions. Due to differences in economies, studies implemented in developing countries were excluded. Reviews, observational studies, abstracts and conference papers were also excluded from the review.

Selection of studies and data synthesis

After citations were identified from all databases, duplicates were isolated and removed. A two-step screening process was employed. In step 1, two researchers (CH and SM) scanned the titles and abstracts of studies identified by the search for their potential eligibility. At step 2, full-text articles relating to the inclusion and exclusion criteria were screened by two researchers for eligibility (CH and SM). Conflicts between the two screening authors were resolved through consensus.

A list of outcomes meaningful to the research aim was developed to identify the relevant effects of the interventions. The primary outcomes were financial and economic data relating to the interventions, including the direct cost of implementing the intervention, the cost of usual care/no intervention, the mean difference between intervention and control, the cost associated with negative patient outcomes related to malnutrition, the cost-savings relating to malnutrition outcomes, the cost per quality adjusted life years (QALYs) and disability adjusted life years.
(DALYs) associated with the intervention. Secondary outcomes included patient, health and aged care related outcomes associated with malnutrition, including nutrition status, weight change, BMI, energy and/or protein intake, plate wastage, resident satisfaction, staff satisfaction, acute and sub-acute hospital admissions, a change in the level of aged care provided, quality of life, physical function, mental health, self-efficacy, mortality, and malnutrition-related complications such as pressure ulcers, poor wound healing, oedema and falls.

Data related to the primary and secondary outcome measures, the study populations and the intervention details were extracted from the published papers into standardised tables by one researcher (CH) and checked for accuracy by a second researcher (SM).

**Review of study strength and quality**

Risk of bias of individual studies was assessed using the Cochrane Risk of Bias tool [19] covering six domains of bias: selection, performance, detection, attrition, reporting, and other bias (e.g. funding sources, conflicts of interest). The quality of the body of evidence for each type of intervention and outcome was determined using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system rated from very low to high quality based on study design, reporting risk of bias, consistency, directness, effect size, and precision [20]. The GRADE system is a formal process to rate the quality of scientific evidence in systematic reviews [20].
Results

The search identified 3,098 records (Figure 1). Of these, 87 were considered suitable for full text review following removal of duplicates and initial screening of title/abstracts. From these papers, eight intervention studies met eligibility criteria. Due to inconsistent intervention approaches and methods of reporting cost-related outcomes, data could not be pooled. Interventions ranged in duration from 6-weeks to 6-months with follow-up ranging from 10 to 29 weeks (Table 1). The seven intervention studies were from USA (n=3), Taiwan (n=1), Sweden (n=2), Netherlands (n=1) and United Kingdom (n=1) with a total of 774 enrolled older adults.

Study Quality (Risk of Bias)
Of the studies reviewed, four were RCTs [21-24], three were non-randomised controlled trials [25-27] and one was a 2-armed non-controlled intervention trial [28]. There was a high risk of bias across studies, particularly with lack of, and poor description of, randomisation and blinded allocation, intervention and assessment of outcomes (Figure 2; justifications in Online Supplementary Material 2). There was also a high risk of bias regarding outcomes (detection bias), as several studies did not use systematic or validated methods to measure and report financial data. Other bias considered included funding sources and conflicts of interest.

**Figure 2**: Risk of bias of included studies

**Types of interventions**
The eight studies included 11 intervention groups – supplements (n=5), food-based interventions (n=5) and dining environment changes (n=1).

The study incorporating dining environment changes involved the addition of fish aquariums into the dining area of three dementia units, with no other intervention factors.

There were five studies which used ONS, one combined with a high protein-high energy diet and post-hospital discharge telehealth (Table 1). This study was primarily implemented in the hospital setting with post-discharge ONS and fortnightly telehealth consultations from a dietitian to participants, but it is unclear if the telehealth was provided to aged care home-dwelling residents or only those in their own homes [22]. The supplements used had 9.5g to 12g of protein and 250-330kcal; however, two studies did not specify the nutritional content of the ONS used. Timing and dosage of ONS interventions varied from one to two a day, and from weekends only to daily.

Food-based interventions were simple, and included offering additional appetisers and snacks, providing advice to eat high protein-high energy foods, and fortifying usual meals with cream and butter. However, one food-based study implemented three 2-hour education sessions to staff promoting nourishing snacks for residents [27] to support the provision of additional foods; and the high protein-high energy intervention received the advice from a dietitian at two time-points over 3-months [28]. The group which received food fortification received an additional 2100kcal/day; however, no other study reported the additional protein or energy provided.

Financial outcomes by intervention type
Cost data was largely heterogeneous in terms of costs measured, analysis method and style of reporting which prevented synthesis or identification of a consistent finding across studies (Table 1).

The one environmental study reported a cost saving of $11.44 (assumed USD; £8.93) in decreased ONS use; however, this was measured in one third of the group only [25]. The quality of the evidence that the true financial effect of environmental interventions to improve nutrition was assessed as very low, downgraded due to uncertainty across most domains assessed by GRADE (Table 2).

Three of the studies which used an ONS intervention reported direct cost of the intervention, with a difference of USD$0.40 (£0.10) to USD$2.54 (£1.99) per resident per day between
intervention and control groups [24, 29, 30]. Elia et al [28] reported a direct cost of £162.30 per resident across 12-weeks (estimated as £1.93 per resident per day); but did not compare this with a control. Four ONS intervention studies also included cost-effectiveness analyses. The study by Neelemaat et al [22] reveals that the study may be cost-effective in improving functional limitations (€618/functional limitation improvement) but not for improving QALYs (£24,798/QALY); but the cost is not reflective of savings only to aged care homes but rather to the health and aged care sector combined. The other two studies reported by Simmons et al [24, 30] compare ONS with food-based interventions, with conflicting results; both interventions may be considered to have good probability of cost-efficacy (Table 1). The study by Elia et al [28] reported £9857/QALY; however, this reflects the cost of ONS minus cost of the high protein-high energy group; and actual cost/QALY was not reported for either intervention. Certainty in the body of evidence that ONS is cost-effective to improve malnutrition in aged care homes was assessed as very low; primarily due to high risk of bias and heterogeneity across studies (Table 2).

Three of the five studies which used food-based interventions reported the direct cost of food-related interventions had a difference of £0.10 to USD$3.85 (£3.01) per resident per day [24, 26, 30]. Lorefalt et al [31] also reported a difference between groups of direct cost of £77.26 per year; however, this included staff training as well as additional food items [27]. There was low confidence in the body of evidence that food-based interventions are cost-effective in aged care homes; due to a risk of bias and heterogeneity across studies (Table 2).

Clinical outcomes
Regarding clinical outcomes, two of the studies [21, 27] used the Mini Nutritional Assessment (MNA) in addition to other measures; however, most did not use validated malnutrition assessments [22-26] (Table 1). Body weight was reported in all of the studies [21-27, 32], and BMI in six. The next most reported outcomes were energy intake (n=4 studies) and physical function (n=3 studies). Some of the studies reported gender differences between malnutrition, however this was not listed in most of the studies.

All studies showed significant clinical improvement in the intervention groups; excepting the high protein-high energy advice group which was reported by Elia et. al. 2017 [28] and also included in Parsons et. al. 2017 [32] (results reported across two papers). Seven of the eight
studies showed increases in weight and six interventions (reported in n=4 studies) reported improvements in energy intake compared with control and/or baseline.
### Table 1: Study design, characteristics and outcomes of intervention studies with financial outcome data which aim to improve malnutrition in residential aged care

<table>
<thead>
<tr>
<th>Citation</th>
<th>Setting and population</th>
<th>Study design and economic methods</th>
<th>Intervention and comparator conditions</th>
<th>Summary of findings</th>
</tr>
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<tbody>
<tr>
<td><strong>Interventions modifying the dining environment</strong></td>
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</table>
Mean age 80.1yrs  
N=62 participants with Alzheimer’s Disease  
Females=61%  
N=3 clusters (aged care homes) | Cluster non-randomised controlled cross-over trial.  
Intervention: 8 weeks.  
Follow-up: 10 weeks.  
Economic method: Basic economic figures. No analysis.  
Economic cost vs. benefit/effect measured: Cost =none reported; Benefit/effect = Financial benefit (cost saving) reported for one aged care home related to supplement use. | IG: 8 weeks with fish aquarium in the dining room. IG did not cross-over to CG.  
CG: 2 weeks with scenic ocean picture introduced to dining room followed by a 2-week washout period (no picture and no aquarium) followed then by 8 weeks with aquarium. | IG: Food intake increased significantly (27.1% increased compared with baseline; p<0.000). Mean weight increase (1.65lbs; p<0.000) compared with baseline.  
CG: No significant changes observed in food intake or body weight observed.  
Between groups: not compared.  
Economic Findings: $11.44 decreased daily cost of ONS in n=1/3 facilities. Currency unclear; assumed to be USD. |
| **Interventions providing oral nutritional supplementation** | | | | |
| Lee et. al. (2013)[21] | Taiwan  
Mean age 79-80±8yrs  
N=92.  
Females=58%.  
N=1 aged care homes | Double-blind RCT.  
Intervention: minimum of 12-24 weeks depending on needs of participant.  
Follow-up: 24 weeks + 12months for mortality  
Economic method: Cost of Intervention/supplement reported. No analysis.  
Economic cost versus benefit/effect measured: cost = direct cost of supplement. Benefit/Effect = none included in economic analysis. | IG: If BMI <24 km/m2 and MNA score <24 were provided a 50g/day soy protein-based supplement (9.5g protein, 250kcal, all essential micronutrients) as a warm drink at AT until MNA or BMI improved to >24 and >24kg/m2 respectively + encouragement to consume by staff.  
CG: Including non-eligible persons for supplement in IG received normal meals including warm soup at AT. | Between groups: Accounting for group allocation and time, at 24 weeks follow-up, IG participants increased body weight (β[1.62][95%CI: 0.21-3.03], P<0.05), BMI (β[0.57][95%CI: 0.05-1.09], P<0.05), MAC (β[0.91][95%CI: 0.40-141], P<0.001) and CC (β[1.00][95%CI: 0.43-1.80], P<0.001). No improvement in albumin, cholesterol. Mortality not reported.  
Economic Findings: $0.40 (£0.24 per resident per day. Analysis by review authors estimates approximately $2,024 for the cost of supplementation for the entire study period. Assumed dollar is USD. |
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Mean age (yrs.)</th>
<th>Female (%)</th>
<th>Sample size</th>
<th>Study Design</th>
<th>Intervention</th>
<th>Follow-up</th>
<th>Economic Method</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neelemaat et al.</td>
<td>Netherlands</td>
<td>74.6±9.5</td>
<td>55%</td>
<td>N=210</td>
<td>RCT</td>
<td>In hospital nutrition support: HPHE diet + 2 ONS (330kcal; 12g protein per supplement) + 1 vitamin/mineral supplement (400IE Vit D3 + 500mg Ca/day); post-hospital nutrition support: 2 ONS continued, 1 vitamin/mineral supplement continued + 6 weeks of fortnightly telehealth (6 sessions total) by dietitian until 3/12 post hospital discharge.</td>
<td>3-months after hospital discharge</td>
<td>CEA and CUA</td>
<td>Functional limitation change μ -0.24±S.E.0.15; hospital LOS μ13±16.8; QALYs μ0.15±0.01; physical activities μ0.52±0.17. Significance of change not reported.</td>
</tr>
<tr>
<td>Simmons et al.</td>
<td>USA</td>
<td>86.9±11.3</td>
<td>62%</td>
<td>N=86</td>
<td>Three-armed RCT.</td>
<td>ONS [not further described] offered twice daily at 10am and 2pm. Second intervention arm reported below. Second IG was food based (see below).</td>
<td>6 weeks</td>
<td>CEA</td>
<td>Functional limitation change μ -0.47±S.E.0.15; hospital LOS μ14±12.5; QALYs μ0.13±S.E.0.01; physical activities μ0.42±0.26. Significance of change not reported.</td>
</tr>
</tbody>
</table>

**Economic Findings:**
- Overall results (not aged care home specific) £24,798/QALY.
- £4.111/physical activity scale improvement. £618/functional limitation improvement. Probability that intervention is cost-effective for improvement in QALYs and physical activity are low (0.5 and 0.6 respectively). £5978 (below £18395 maximum) investment from Netherlands society, 0.95 probability the intervention is cost effective for improvement in functional limitations.

**Summary:**
- Mean difference of direct costs of hospital support: IG £24,798/QALY. £4.111/physical activity scale improvement. £618/functional limitation improvement. Probability that intervention is cost-effective for improvement in QALYs and physical activity are low (0.5 and 0.6 respectively). £5978 (below £18395 maximum) investment from Netherlands society, 0.95 probability the intervention is cost effective for improvement in functional limitations.
- Mean difference of indirect costs was absenteeism paid, unpaid labour. Costs were Dutch standard costs. Effect/Benefit; CEA = nutritional status and physical function. CUA: QALY generated by the EQ-D instrument.
- Mean difference of total calories relative to the snack intervention (see below). CEA acceptability curves show snack intervention consistently exceeds supplement intervention for net benefit (e.g. USD$0.04 value of one-unit caloric gain, probability of net benefit is 65% for supplement group and 80% for snack group).
| Simmons et al. (2015) [24] | USA | Mean age 83.1±11.9yrs. | N=175. | Female = 81%. | N=5 aged care homes | Three-armed RCT | Intervention: 6-months | Follow-up: 6-months | Economic method: CEA. | Economic cost vs. benefit/effect measured: cost = additional daily food, fluid or supplement spending and salary for staff time for nutritional care delivery. Benefits/effects = between meal and total daily energy intake. | IG ONS [not further described] offered twice daily in the morning and afternoon for five days per week. Second IG was food based (see below). | CG: no foods or ONS offered, only usual provided food and beverages (not further described). | IG: Average of 1.8kg weight gain, the mean difference of total energy intake was 253kcal (95%CI: 109-397). Mid-meal energy intake increased (151kcal; P<0.05) but this caused an overall decrease in total energy intake. | CG: Average loss of 0.5kg body weight in control group. | Between groups: not compared. | Economic Findings: Mean difference of direct costs of intervention at 6-months compared with the control group was USD$2.54 per resident per day. Incremental cost-effectiveness ratios 103kcal/USD$. CEA acceptability curves show supplement intervention consistently exceeds snack intervention (see below) for net benefit (e.g. USD$0.01 value of one-unit caloric gain, probability of net benefit is 57%). |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Elia et al 2017. [28] | UK | Mean age 88.8±8yrs. | N=104 (incl 57 aged care home residents) | Female=86%. | N=53 aged care homes | Two-armed, non-controlled, intervention trial. | Intervention: 12 weeks | Follow-up: 12 weeks | Economic method: CEA | Economic cost vs. benefit/effect measured: cost = direct costs of intervention, unit costs of health care utilisation. Benefits/effects = QALYs adjusted for malnutrition and other factors. | IG: ONS (1.5-2.4kCal/ml) aiming to increase intake by at least 600kCal/day and 16g protein a day. Saw dietitian at baseline and 6 weeks to receive advice relating to ONS. | CG: none. Compared to 12-week baseline observation period. | IG: Quality of life (EQ-5D-TTO) decreased (μ change: -0.02) (not tested statistically). Body weight improved (μ change: 1.22±0.45kg; P=0.010). Energy increased (μ change: 286kcal) (not tested statistically). QALY gained μ 0.130±0.0084. | CG: N/A. | Economic Findings: Direct cost of intervention: £162.30 per resident. Direct unit cost of health care utilisation: £376±34. Significantly higher than HPHE group (see below). Cost/QALY: £9857 (ONS group minus HPHE group; actual cost/QALY not reported for each group). |

**Interventions providing food-based modifications**

<p>| Simmons et al. (2010) [23] | As per above. | As per above. | IG: Variety of snacks (yoghurt, pudding, fruit, juices) offered twice daily at 10am and 2pm. | CG: As per above. | IG: Compared with baseline, the mean difference of energy intake was 163kcal (P&lt;0.001) for the snack group. No change in body weight. | CG: as per above. | Between groups: not compared. | Economic Findings: Mean difference of direct costs of intervention from baseline to 6-weeks were USD$2.06 per resident per day for the snack group, and USD$-0.03 for the control group per resident per day. |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Participants</th>
<th>Intervention</th>
<th>Main Findings</th>
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<tbody>
<tr>
<td>Simmons et al. (2015)</td>
<td>Sweden</td>
<td>Mean age 83-86 yrs, N=109, females 50%</td>
<td>Variety of snacks (yoghurt, pudding, juices, liquid supplements) offered twice daily in the morning and afternoon.</td>
<td>IG: Compared with the control group, the mean difference of total energy intake was 288 kcal (95% CI 144-432). No change in body weight.</td>
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</tbody>
</table>

Elia et al. (2017) | UK, aged care homes | N=6 aged care homes | Dietary advice for HPHE snacks and drinks with aid of a diet sheet. Saw dietitian at baseline and 6 weeks to receive advice about HPHE diet. | IG: MNA >24 (well nourished) offered snack (e.g. fruit, yoghurt) at mid meals. MNA <24 (risk of malnutrition/malnourished) had modified food choices within existing food availability and costs, e.g., soups, egg, horseradish, additional snacks (e.g., smoothies, bread and butter, milk and yoghurt) distributed throughout the day. |

Lorefalt et al. (2011) | Sweden | Mean age 83-86 yrs, N=109, females 50% | Non-randomised controlled trial | IG: Direct advice for HPHE snacks and drinks was provided by project leader, a nurse with nutrition background. IG, MN prevalence 26% at baseline and 12% at follow-up; body weight change at 3/12 follow-up 2.7±3.9 kg; BMI at 3/12 follow-up 25.6±4.9 kg/m². IG: MNA >24 (well nourished) offered snack (e.g. fruit, yoghurt) at mid meals. MNA <24 (risk of malnutrition/malnourished) had modified food choices within existing food availability and costs, e.g., soups, egg, horseradish, additional snacks (e.g., smoothies, bread and butter, milk and yoghurt) distributed throughout the day. |

Odlund Olin et al. (2003) [26]

- Sweden
- Median age 80-83yrs (IQR 71-89)
- N=40.
- Female: 52%.
- N=1 aged care home recruited (N=2 clusters [wards]).

- Non-randomised clustered controlled intervention trial.

- Intervention: 15 weeks
- Follow-up: 29 weeks post-baseline/27 weeks post intervention commencement.
- Economic method: Cost of Intervention. No analysis.
- Economic cost vs. benefit/effect measured: cost = Cost of additional butter and cream; Benefit/Effect = none included in economic analysis.

- IG: Served regular hospital diet fortified with butter and cream (2100kCal/day).
- CG: Served regular hospital diet (1600kCal/day).

- IG: Compared with baseline, IG increased protein intake (median 48.3 [IQR: 41.8-54.3g] vs median 57.9 [IQR: 46.2-61.2g], P<0.001). ADL remained unchanged.
- CG: worsened in ADL during the intervention (median score 15.5 [IQR: 10.0-17.0] increased to 16.0 [IQR: 15.0-18.0], P<0.001). Between groups: No difference for number of infections. IG increased energy intake (median 1437 [IQR: 1252-1617kcal] vs median 1840 [IQR: 1497-2012kcal], P<0.01).
- Economic Findings: £0.10 per resident per day

Table 2: GRADE assessment of the cost-effectiveness environmental, oral nutrition support or food-based malnutrition interventions

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>Number of patients</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention group</th>
<th>Control group (no intervention)</th>
<th>Quality</th>
<th>Importance</th>
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<td>No. of studies</td>
<td>No. of patients</td>
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<td>OUTCOME: Cost-effectiveness (assessed with: direct cost, cost utility analysis or cost effectiveness analysis)</td>
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<td>Question: Environmental changes compared to any other method of nutrition intervention or provision for cost-effectively preventing and/or managing malnutrition in residential aged care</td>
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<td>1</td>
<td>45</td>
<td>Randomised trials</td>
<td>Very serious</td>
<td>Very serious</td>
<td>Very serious</td>
<td>Very serious</td>
<td>None</td>
<td>Intervention group</td>
<td>Control group (no intervention)</td>
<td>☄️abcd</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Question: Supplements compared to usual are for cost-effectively preventing and/or managing malnutrition in residential aged care</td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td>275</td>
<td>Randomised trials</td>
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<td>Not serious</td>
<td>None</td>
<td>Intervention group</td>
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<td>☄️abcd</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Question: Food modifications compared to any other method of nutrition intervention or provision for cost-effectively preventing and/or managing malnutrition in residential aged care</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5</td>
<td>292</td>
<td>Randomised and non-randomised controlled trials</td>
<td>Serious</td>
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<td>Not serious</td>
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<td>None</td>
<td>Intervention group</td>
<td>Control group (no intervention)</td>
<td>☄️abcd</td>
<td>LOW</td>
</tr>
</tbody>
</table>

- a. Cluster non-randomised controlled trial
- b. Risk of bias assessed by the Cochrane risk of bias tool (Figure 2)
c. Data relating to cost outcomes were reported for only one of the groups. No data provided for consistency within study groups (three groups received intervention in cross-over design). Could not be compared to any other studies.
d. Cost-saving data was reported for the decreased spend of supplements; which is not a direct measure of the environmental intervention. There is no confidence that the cost-related outcome is due to the intervention.
e. No measure of variability reported.
f. Some inconsistency between the two most clinically homogenous studies (Simmons 2010 and 2015). Combined studies all show cost of ONS is low and results in clinical benefit.
g. Three studies were non-randomised controlled trials; two were RCTs.
h. Interventions included significant clinical heterogeneity; however, cost-related results were reported differently between studies making comparison of consistency difficult.
Discussion
There is good evidence that malnutrition places a significant financial burden on our healthcare system [33-35] as well as good evidence that supplements and other nutrition interventions improve intake and nutritional status [36, 37]. This review, however, revealed there is a lack of confidence in the body of economic evidence that introducing malnutrition interventions, whether they be environmental, supplements or food-based, are cost-effective in residential aged care. This lack of confidence is due to the small number and poor-quality of studies economically evaluating nutritional interventions in aged care; particularly for environmental interventions. Despite this, the review showed that included interventions had a low direct cost of implementation (less than £2.30 per resident per day) and provided clinical improvement in patients. Supplements and food-based interventions further demonstrated a low cost per QALY or unit of physical function improvement.

There is great variation in the scope of economic reviews on the topic of malnutrition. One large nutrition and health economics review looked at malnutrition across all ages and settings and concluded nutrition to be a powerful force improving both the health and economic status of society [16]. However, in agreement with the current review, the study found large variations in the approach to economic modelling of malnutrition interventions, and highlighted the need for a well-defined framework for economic analysis on nutrition interventions [16].

Although this current review found insufficient evidence supporting the cost-effectiveness of malnutrition interventions in aged care homes, evidence in the acute setting is stronger as evaluated by three recent systematic reviews [13, 37, 38]. Mitchell et al [13] in a systematic review concluded that malnutrition interventions in the hospital setting showed positive cost-effectiveness for improving outcomes, informed by intervention studies from 2003 to 2013. Although Mitchell et al. only identified three studies for inclusion, they were comprehensive and of a high quality. In 2017, the systematic review by Muscaratoli et al [38] found that there was insufficient evidence as to whether supplements significantly reduced hospital readmissions when given to malnourished hospitalised patients and outpatients. However, Muscaratoli [38] found supplements resulted in cost savings with a return of investment of $52.63 in net savings for every dollar spend on supplements in terms of reduced episode cost amongst young patients. The systematic review by Elia et al [37] also examined the cost-effectiveness of using supplements in hospitals, and subgroup analysis found supplements to be cost-effective with a mean net cost saving of £746 per patient. In this same review, the mean
cost saving across 12 of the 14 cost analysis studies comparing supplements with routine care found 12.2% mean cost saving with supplements use [37]. Further hospital-based economic modelling by Banks et al [39] showed cost-effective reduction in risk of developing pressure ulcers with the use of nutritional intervention (including costs of additional food, supplements and additional nutrition/nursing support staff time). This strong and consistent evidence in support of nutrition interventions to cost-effectively improve malnutrition in the acute care setting suggests that similar conclusions may be found in the aged care setting once further well-conducted studies including economic data are undertaken.

Limitations and implications for future research
This systematic literature review focussed on interventional studies only, as these studies provide a higher quality of evidence to evaluate the research question. However, it is acknowledged that excluding observational studies may limit potential learnings [40], particularly regarding external validity. All but two included studies did not sufficiently evaluate the impact of interventions on malnutrition, and none used malnutrition in the cost-utility analysis. Instead, the outcomes of weight, BMI, energy intake and physical function were most frequently used. Although these are important components of malnutrition assessment, they do not reflect malnutrition risk or status alone.

Future research on cost-effectiveness of nutrition-related interventions in the aged care setting need to accurately measure malnutrition, clearly describe interventions and economic methods and provide a detailed description of research design. Rigorous intervention and economic study designs, such as RCTs and cost-utility analyses in future malnutrition studies in the aged care setting may further strengthen and increase confidence in the cost-effective treatment of malnutrition. Although research has demonstrated nutrition interventions are low risk and effective in improving clinical outcomes, stronger evidence regarding cost-effectiveness will support aged care funders and governance to select the most cost-effective treatment options.

Conclusion interventions
Malnutrition places significant economic burden upon the aged care sector and nutrition may be a powerful force for improving both the health and economic status of aged care homes. While there is good evidence that nutrition improves clinical outcomes, the limited and poor-quality studies including economic data in this review indicate evidence of cost-effectiveness in the aged care setting is still limited. This systematic review suggests that supplements and food-based nutrition interventions in the aged care setting have a low cost of implementation, low risk of harm, and may be cost-effective. More studies using well-defined frameworks for
economic analysis, stronger study designs such as double-blinded RCTs, improved quality (reduced risk of bias), along with validated malnutrition measures are needed.

References -


## Online Supplementary Material 1 – Search Strategy

This table has been provided by the authors to give readers additional information about this work.

<table>
<thead>
<tr>
<th>Database</th>
<th>Search terms</th>
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</thead>
<tbody>
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<td>(1 OR 2) AND (3 OR 4) AND 6</td>
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<tr>
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<tr>
<td>6. (1 OR 2) AND (3 OR 4) AND 5</td>
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</table>

**Embase using Emtree terms**


4. Nutrition [exp] [Emtree term] OR malnutrition [exp] [Emtree term] OR protein calorie malnutrition [exp] [Emtree term] OR nutritional status [exp] [Emtree term]


6. cost benefit analysis [exp] [Emtree term] OR economic evaluation [exp] [Emtree term] OR cost effectiveness analysis [exp] [Emtree term]]

7. (1 OR 2) AND (3 OR 4) AND 6

**Econlit**


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<tr>
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<td></td>
</tr>
<tr>
<td>4. 1 AND 2 AND 3</td>
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</tr>
<tr>
<td>2. Nursing Homes [exp] [CINAHL heading] OR Gerontologic Nursing [exp] [CINAHL heading] OR Gerontologic Care [exp] [CINAHL heading] OR Housing for the Elderly [exp] [CINAHL heading] OR Nursing Home Patients [exp] [CINAHL heading] OR Residential Care [exp] [CINAHL heading]</td>
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<td>NHS Economic Evaluation Database</td>
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<td></td>
</tr>
</tbody>
</table>

**Table 1:** Keywords used for searching in the NHS Economic Evaluation Database.

**Keywords:**
- Savings
- Cost Effectiveness
- healthcare cost
- health care cost
- Economic
- Financial
- Cost Savings
- Cost and Cost Analysis
- Health Care Costs
- Cost Benefit Analysis

**Medical Subject Headings (MeSH):**
- "nursing home*
- "aged care"
- "residential care"
- "care home*"
- "residential facilit*"
- "assisted living"
- residential facilities
- assisted living facility
- group homes
- homes for the aged
- nursing homes
- health services for the aged
- malnutrition*
- nutrition*
- undernutrition
- under nutrition
- emaciation
- undernourish*
- under nourish*
- malnourish*
- Diet, Food and Nutrition
- protein energy malnutrition
- malnutrition
- nutritional status
- undernutrition
- nutritional deficiency
- protein calorie malnutrition
- emaciation
- nutrition status
- protein deficiency
Online Supplementary Material 2

Supplementary Table 1: Study design, characteristics and outcomes of intervention studies with financial outcome data which aim to improve malnutrition in residential aged care

<table>
<thead>
<tr>
<th>Citation</th>
<th>Setting and population</th>
<th>Study design and economic methods</th>
<th>Study purpose</th>
<th>Intervention and comparator conditions</th>
<th>Summary of clinical findings</th>
<th>Summary of economic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interventions modifying the dining environment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Edwards and Beck. (2002) [26] | • USA  
• Mean age 80.1yrs  
• N=62 participants with Alzheimer’s Disease  
• Females=61%  
• N=3 clusters (aged care homes) | • Cluster non-randomised controlled cross-over trial.  
• Intervention: 8 weeks.  
• Follow-up: 10 weeks.  
• Economic method: Basic economic figures. No analysis.  
• Economic cost vs. benefit/effect measured: Cost =none reported; Benefit/effect = Financial benefit (cost saving) reported for one aged care home related to supplement use. | Examining the influence of animal assisted therapy, specifically fish aquariums, on nutritional intake in individuals with Alzheimer’s Disease. | • IG: 8 weeks with fish aquarium in the dining room. IG did not cross-over to CG.  
• CG: 2 weeks with scenic ocean picture introduced to dining room followed by a 2-week washout period (no picture and no aquarium) followed then by 8 weeks with aquarium. | • IG: Food intake increased significantly (27.1% increase compared with baseline; p<0.000). Mean weight increase (1.65lbs; p<0.000) compared with baseline.  
• CG: No significant changes observed in food intake or body weight observed.  
• Between groups: not compared. | $11.44 decreased daily cost of ONS in n=1/3 facilities. Currency unclear; assumed to be USD. |
| **Interventions providing oral nutritional supplementation** |
| Lee et. al. (2013) [22] | • Taiwan  
• Mean age 79-80±8yrs  
• N=92.  
• Females=58%.  
• N=1 aged care homes | • Double-blind RCT.  
• Intervention: minimum of 12-24 weeks depending on needs of participant.  
• Follow-up: 24 weeks + 12months for mortality  
• Economic method: Cost of Intervention/supplement reported. No analysis.  
• Economic cost versus benefit/effect measured: cost = direct cost of | Examining the effectiveness of routine screening and nutrition supplementation in improving the nutritional status of persons living in NH’s. | • IG: If BMI <24 km/m2 and MNA score <24 were provided a 50g/day soy protein-based supplement (9.5g protein, 250kcal, all essential micronutrients) as a warm drink at AT until MNA or BMI improved to >24 and >24kg/m2 respectively + encouragement to  
• Between groups: Accounting for group allocation and time, at 24 weeks follow-up, IG participants increased body weight (8.162[95%CI: 0.21-3.03], P<0.05), BMI (8.05[95%CI: 0.05-1.09], P<0.05), MAC (8.91[95%CI: 0.40-141], P<0.001) and CC $0.40 (£0.24 per resident per day. Analysis by review authors estimates approximately $2,024 for the cost of supplementation for the entire study period. Assumed dollar is USD. |
| Neelemaat et al. (2012) [23] | • Netherlands | Mean age 74.6±9.5yrs.  |  |  |  | Overall results (not aged care home specific) | £24,798/QALY.  |
| |  | N=210. |  |  |  | £4.111/physical activity scale improvement.  |
| |  | Female: 55%.  |  |  |  | £618/functional limitation improvement. Probability that intervention is cost-effective for improvement in QALYs and physical activity are low (0.5 and 0.6 respectively). £5978 (below £18395 maximum) investment from Netherlands society, 0.95 probability the intervention is cost effective for improvement in functional limitations.  |
| |  | N=0 aged care homes sampled. Sample is a hospitalised population; approx. 10% of which were dwelling in an Aged care home |  |  |  |  |  |
| | • RCT. |  |  |  |  |  |  |
| | • Intervention: hospital admission period + 3-months post discharge follow-up.  |  |  |  |  |  |  |
| | • Follow-up: 3-months after hospital discharge  |  |  |  |  |  |  |
| | • Economic method: CEA and CUA.  |  |  |  |  |  |  |
| | • Economic cost vs. benefit/effect measured: Cost = Direct costs were supplement costs, telehealth cost, hospital admission costs, specialist visits. Non-direct health costs were included using a diary e.g complementary medicine, informal care, and other indirect costs were absenteeism paid, unpaid labour. Costs were Dutch standard costs. Effect/Benefit: CEA = nutritional status and physical function. CUA: QALY generated by the EQ-D instrument.  |  |  |  |  |  |  |
| | • IG: In hospital nutrition support: HPHE diet + 2 ONS (330kcal; 12g protein per supplement) + 1 vitamin/mineral supplement (400IE Vit D3 + 500mg Ca/day); post-hospital nutrition support: 2 ONS continued, 1 vitamin/mineral supplement continued + 6 weeks of fortnightly telehealth (6 sessions total) by dietitian until 3/12 post hospital discharge.  |  |  |  |  |  |  |
| | • CG: Usual care with ONS/other supplements only if physician prescribed. No post-hospital support.  |  |  |  |  |  |  |
| | • IG: Functional limitation change μ -0.24±S.E.0.15; hospital LOS - μ13±16.8; QALYs μ0.15±0.01; physical activities μ0.52±0.17. Significance of change not reported.  |  |  |  |  |  |  |
| | • CG: Functional limitation change μ-0.47±0.15; hospital LOS μ14±12.5; QALYs μ0.13±S.E.0.01; physical activities μ0.42±0.26. Significance of change not reported.  |  |  |  |  |  |  |
| | • Between groups: No significant difference in hospital LOS, QALYs at 3-months follow-up or physical function. IG improved in functional limitations (CG change: μ-0.24±S.E.0.15 vs IG change μ-0.47±0.15; difference -0.72 [95%CI: -1.15 to -0.28; P-value not reported]).  |  |  |  |  |  |  |
**Simmons et al. (2010) [24]**

- **USA**
- Mean age: 86.9±11.3 yrs.
- N=86.
- Female=62%.
- N=3 aged care homes

**Three-armed RCT.**

- Intervention: 6 weeks
- Follow-up: 6 weeks
- Economic method: CEA.
- Economic cost vs. benefit/effort measured: cost = additional daily food, fluid or supplement spending and salary for staff time for nutritional care delivery. Benefit/Effect = between meal and total daily energy intake.

**Aim was to determine the cost-effectiveness of supplements or snacks foods between meals to increase caloric intake compared to usual care.**

**IG:** ONS [not further described] offered twice daily at 10am and 2pm. Second intervention arm reported below. Second IG was food based (see below).

**CG:** no foods or ONS offered, only usual provided food and beverages (not further described).

**IG:** Compared with baseline, the mean difference of energy intake was -125kCal (P<0.05), Increased energy intake in mid-meals (151kcal; P<0.05) but this caused an overall ↓ in total energy intake. No significant change in body weight.

**CG:** Compared with baseline, the mean difference of energy intake was 5kcal. No significant change in body weight.

**Between groups:** not compared.

Mean difference of direct costs of intervention from baseline to 6-weeks were USD$2.10 per resident per day for the supplement group and USD$-0.03 for the control group per resident per day. CEA analysis shows supplement group more likely to result in a decrease in total calories relative to the snack intervention (see below). CEA acceptability curves show snack intervention consistently exceeds supplement intervention for net benefit (e.g. USD$0.04 value of one-unit caloric gain, probability of net benefit is 65% for supplement group and 80% for snack group).
### Simmons et al. (2015) [25]
- **USA**
- Mean age 83.1±11.9yrs.
- N=175.
- Female = 81%.
- N=5 aged care homes
- Three-armed RCT
- Intervention: 6-months
- Follow-up: 6-months
- Economic method: CEA
- Economic cost vs. benefit/effect measured: cost = additional daily food, fluid or supplement spending and salary for staff time for nutritional care delivery. Benefits/effects = between meal and total daily energy intake.
- Aim was to determine the cost-effectiveness of supplements or snacks foods between meals to increase caloric intake compared to usual care.
- IG ONS [not further described] offered twice daily in the morning and afternoon for five days per week. Second IG was food based (see below).
- CG: no foods or ONS offered, only usual provided food and beverages (not further described).
- IG: Average of 1.8kg weight gain, the mean difference of total energy intake was 253kcal (95%CI: 109-397). Mid-meal energy intake increased (151kcal; P<0.05) but this caused an overall decrease in total energy intake.
- CG: Average loss of 0.5kg body weight in control group.
- Between groups: not compared.
- Mean difference of direct costs of intervention at 6-months compared with the control group was USD$2.54 per resident per day. Incremental cost-effectiveness ratios 103kcal/USD$. CEA acceptability curves show supplement intervention consistently exceeds snack intervention (see below) for net benefit (e.g. USD$0.01 value of one-unit caloric gain, probability of net benefit is 57%).

### Elia et al. 2017. [29]
Data also reported in Parsons et al. [32]
- **UK**
- Mean age 88.8±8yrs.
- N=104 (incl 57 aged care home residents)
- Female=86%.
- N=53 aged care homes
- Two-armed, non-controlled, intervention trial.
- Intervention: 12 weeks
- Follow-up: 12 weeks
- Economic method: CEA
- Economic cost vs. benefit/effect measured: cost = direct costs of intervention, unit costs of health care utilisation. Benefits/effects = QALYs adjusted for malnutrition and other factors.
- Aim was to complete a cost-utility analysis to specifically examine whether the use of ONS in care home residents, with a wide variety of diseases and clinical conditions is cost effective relative to dietary advice.
- IG: ONS (1.5-2.4kCal/ml) aiming to increase intake by at least 600kCal/day and 16g protein a day. Saw dietitian at baseline and 6 weeks to receive advice relating to ONS.
- CG: none. Compared to 12-week baseline observation period.
- IG: Quality of life (EQ-5D-TTO) decreased (μ change: -0.02) (not tested statistically).
- Body weight improved (μ change: 1.22±0.45kg; P=0.010). Energy increased (μ change: 286kcal) (not tested statistically). QALY gained μ 0.1302±0.0084.
- CG: N/A.
- Direct cost of intervention: £162.30 per resident. Direct unit cost of health care utilisation: £376±34. Significantly higher than HPHE group (see below). Cost/QALY: £9857 (ONS group minus HPHE group; actual cost/QALY not reported for each group).

### Interventions providing food-based modifications

<table>
<thead>
<tr>
<th>Simmons et. al. (2010) [24]</th>
<th>As per above.</th>
<th>As per above.</th>
<th>As per above.</th>
<th>IG: Variety of snacks (yoghurt, pudding, fruit, juices) offered twice daily</th>
<th>IG: Compared with baseline, the mean difference of energy</th>
<th>Mean difference of direct costs of intervention at 6-months compared with the control group was USD$2.54 per resident per day. Incremental cost-effectiveness ratios 103kcal/USD$. CEA acceptability curves show supplement intervention consistently exceeds snack intervention (see below) for net benefit (e.g. USD$0.01 value of one-unit caloric gain, probability of net benefit is 57%).</th>
</tr>
</thead>
</table>

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*CEA: Cost-Effectiveness Analysis, ONS: Oral Nutritional Supplements, CG: Control Group, IG: Intervention Group.*
<table>
<thead>
<tr>
<th>Study</th>
<th>Group Description</th>
<th>Results</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simmons et al. (2015) [25]</td>
<td>IG: Variety of snacks (yoghurt, pudding, juices, liquid supplements) offered twice daily in the morning and afternoon.</td>
<td>Intake was 163 kcal (P&lt;0.001) for the snack group. No change in body weight. CG: as per above.</td>
<td>USD$2.06 per resident per day for the snack group, and USD$-0.03 for the control group per resident per day.</td>
</tr>
<tr>
<td></td>
<td>IG: Compared with the control group, the mean difference of total energy intake was 288 kcal (95% CI: 144-432). No change in body weight. CG: as per above.</td>
<td><strong>Between groups: not compared.</strong></td>
<td></td>
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<tr>
<td></td>
<td>IG: Quality of life (EQ-5D-TTO) decreased (μ change: -0.159) (not tested statistically). No change in body weight. KCal decreased (μ change: -93 kcal) (not tested statistically). QALY gained μ 0.1128±0.0086. CG: N/A.</td>
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<tr>
<td>Sweden</td>
<td>IG: MN prevalence 26% at baseline and 12% at follow-up; body weight. PG: N/A.</td>
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<tr>
<td>Direct health care cost in IG: median £924, CG: £847 per year. Not</td>
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</table>
To determine if a food-first approach will improve energy intake and activities of daily living (ADL) and infection rates.

**IG**: Served regular hospital diet fortified with butter and cream (2100kCal/day).
**CG**: Served regular hospital diet (1600kCal/day).

Compared with baseline, IG increased protein intake (median 48.3 [IQR: 41.8-54.3g] vs median 57.9 [IQR: 46.2-61.2g], P<0.001). ADL remained unchanged.

Between groups: No change to routine meals.

£0.10 per resident per day change at 3/12 follow-up.

**CG**: No change to routine meals.

**Between groups**

<table>
<thead>
<tr>
<th>Difference (p-value)</th>
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<tbody>
<tr>
<td>10.0 (p=0.001)</td>
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</tbody>
</table>

**CG**: worsened in ADL during the intervention (median score 15.5 [IQR: 10.0-17.0] increased to 16.0 [IQR: 15.0-18.0], p=0.005). BMI at baseline 27.3 kg/m²; change at 3/12 follow-up 27.3 kg/m² (p=0.10). Grade of malnutrition/ malnourished had no impact on caregiver outcomes.

**IG**: Compared with baseline, IG increased body weight change up to 0.6 kg (p=0.045). BMI at baseline 23.7 kg/m²; change after 3/12 follow-up 23.7 kg/m² (p=0.001).

**Between groups**

<table>
<thead>
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<td>0.010 (p=0.0001)</td>
</tr>
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</table>
analysis.

energy intake (median 1437 [IQR: 1252-1617 kcal] vs median 1840 [IQR: 1497-2012 kcal], P<0.01).

**Supplementary Table 2 – Cochrane Risk of Bias Table**

Cochrane Risk of Bias: Quality assessment for interventional studies which report cost data related to nutrition in residential aged care

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
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<tbody>
<tr>
<td><strong>Rating</strong></td>
<td>High risk of bias</td>
<td>High risk of bias</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Low risk of bias</td>
<td>Unclear</td>
</tr>
<tr>
<td><strong>Evidence</strong></td>
<td>No randomisation was used (page 701-702). Due to the cross-over design, the CG received the intervention; however, the IG did not cross-over to the control group.</td>
<td>Allocations were not concealed from participants and not described for investigators (page 702-703).</td>
<td>Participants were not blinded from the intervention allocation; however, due to the study population (Alzheimer’s Disease), the study participants could be considered to have been blinded. There was no description of blinding for the investigators (page 702-703).</td>
<td>Blinding of investigators not described, but as reported using objective clinical measures, risk of bias is low (page 702-703). However, risk of bias for economic outcome reported is high as there is no method described.</td>
<td>No attrition is reported; there was likely some attrition present due to the high risk sample (705-706).</td>
<td>None detected</td>
<td>No bias from funding organisation likely; however conflicts of interest were not declared.</td>
</tr>
<tr>
<td><strong>Rating</strong></td>
<td>Low risk of bias</td>
<td>Unclear</td>
<td>Low risk of bias</td>
<td>Low risk of bias</td>
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<td><strong>Lee et. al. 2013</strong></td>
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</tbody>
</table>
**Evidence**

- Stratified by gender then allocated to group based on drawing pieces of folded paper from a bag (page 1581).
- It is not clear what was written on the pieces of paper and how they were then used by investigators to allocate group.
- The study was double blind. Although participants could have observed they had a different afternoon tea, no discussion of the study allocation or intervention was made with the participant (pages 1581 and 1582).
- Double blinded study, with anthropometry measured by non-staff research assistants (page 1583).
- All participants accounted for, and <20% attrition (page 1582).
- None detected

**Rating**

<table>
<thead>
<tr>
<th>Lorefalt et. al. 2011</th>
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<tbody>
<tr>
<td>High risk of bias</td>
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<tr>
<td>Unclear</td>
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<tr>
<td>Unclear</td>
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<tr>
<td>High risk of bias for clinical outcomes; low risk of bias for health care outcomes</td>
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<tr>
<td>Low risk of bias</td>
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<td>Low risk of bias</td>
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<td>Unclear</td>
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</table>

**Evidence**

<table>
<thead>
<tr>
<th>No allocation method described in paper. Does not appear to be randomised.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocations and concealments of participants and investigators were not described at all. It is assumed the nurses implementing the intervention were aware that they formed an intervention group but it is not clear. It is not clear if participants were told they were in an intervention or control group.</td>
</tr>
<tr>
<td>Allocations and concealments of participants and investigators were not described at all. It is assumed the nurses implementing the intervention were aware that they formed an intervention group but it is not clear. It is not clear if participants were told they were in an intervention or control group.</td>
</tr>
<tr>
<td>Although it is not clear, it appears that the MNA and anthropometry outcomes were performed by the nurses who attended training and implemented the interventions. No blinding discussed for investigators or participants. Health care data does appear to be objective.</td>
</tr>
<tr>
<td>All 109 participants accounted for at 3 month follow-up (page 95). Assumed all accounted for in 1 year economic follow-up although not described.</td>
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<tr>
<td>None detected</td>
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</table>

**Rating**

| None detected |
| Unclear |

**Evidence**

- No bias from funding organisation likely; however conflicts of interest were not declared.
<table>
<thead>
<tr>
<th>Rating</th>
<th>Neelemaat et. al. 2012</th>
<th>Odlund Olin, et. al.</th>
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</thead>
<tbody>
<tr>
<td>Evidence</td>
<td>Computerised random number generator used to assign participants (page 184). Allocation concealed in consecutiely numbered opaque envelopes (page 184). Participants, research assistant and researcher were no longer blinded from the intervention after the allocation was made (page 184). Researchers were not blinded. Although cost data is mostly objective, results are related to subjectively completed tools of quality of life and physical function, which can be influenced by participant and researcher bias due to knowledge of intervention purpose.</td>
<td>Low risk of bias</td>
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<tr>
<td>High rate of attrition (32%); however was equally distributed between groups and unlikely to be related to intervention (12% due to death). Data presented with complete cases and per protocol.</td>
<td>None detected</td>
<td>Appears to be no conflicts of interest or likely conflicts due to financial interests of funders/investigators.</td>
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<tr>
<td>Evidence</td>
<td>No description of how wards were allocated to intervention and control. Seems to be conveniently selected (page 125).</td>
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<tr>
<td>Study 1</td>
<td>It is not clear if participants in each ward were informed that the ward food was different (i.e. an intervention provided in one), or if any allocation concealment attempt was made.</td>
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<tr>
<td>Study 2</td>
<td>Participants in the intervention group and RAC staff were told that a change to the meal composition will be made, but not further description. It is not clear if they were told this was part of a study. Nursing staff completed measurement of food consumption. It is not therefore clear if they understood the difference between meals being studied, and if this would affect performance and outcome assessment bias.</td>
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<tr>
<td>Study 3</td>
<td>Participants in the intervention group and RAC staff were told that a change to the meal composition will be made, but not further description. It is not clear if they were told this was part of a study. Nursing staff completed measurement of outcomes. It is not therefore clear if they understood the difference between meals being studied, and if this would affect performance and outcome assessment bias.</td>
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<tr>
<td>Rating</td>
<td>Unclear</td>
<td>Unclear</td>
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<tr>
<td>Evidence</td>
<td>Study describes that participants are randomised, but gives not detail as to how the sequence was generated (page 368)</td>
<td>Study describes that participants are randomised, but gives not detail as to how the participants were allocated (page 368)</td>
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Simmons et al. 2010
<table>
<thead>
<tr>
<th>Rating</th>
<th>Evidence</th>
<th>Low risk of bias</th>
<th>Unclear</th>
<th>Unclear</th>
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<th>Low risk of bias</th>
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<tr>
<td>Simmons et. al. 2015</td>
<td>Participants were randomised using a computer-generated random numbers table (page 2309)</td>
<td>Method of allocating the participants to groups was not described in the study.</td>
<td>There was no description of blinding of participants or personnel.</td>
<td>There was no description of blinding outcome assessors. As nurses timed themselves in the delivery of the intervention, this outcome does have some bias. Research staff completed other outcome measures, but it is not described if they were blinded (page 2309).</td>
<td>Attrition was substantial (36%); however, it was mostly even across groups and it was mostly for reasons common in RAC populations including death, transfer to hospice. There were low rates of consent withdrawal and nutritional order changes.</td>
<td>None detected</td>
<td>Appears to be no conflicts of interest or likely conflicts due to financial interests of funders/investigators.</td>
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<td>Elia et. al. 2017</td>
<td>Low risk of bias</td>
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<td>Evidence &amp; Parsons et. al. 2017</td>
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<td>&quot;Randomisation, stratified according to malnutrition risk (medium or high risk of malnutrition) and type of care (residential or nursing care) was undertaken independently of the researchers using random number tables produced by Microsoft Excel for Windows 2003. The randomisation codes were generated by the chief investigator prior to commencement of the trial.&quot; (Parsons et al. page 135)</td>
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<td>&quot;The research dietitian enrolled and assigned participants to the interventions using opaque, sealed envelopes labeled with the random numbers containing the designated interventions. At the point of randomisation both the residents and the researchers were blinded to the designated intervention.&quot; (Parsons et al. page 135)</td>
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<td>&quot;...a prospective, randomised, parallel, open-label trial, which took place between August 2007 and March 2010&quot; (Parsons et al. page 135). Acknowledged that both groups biased equally; however, likely to impact upon change from baseline variables.</td>
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<td>&quot;Due to the nature of the two different interventions researchers and participants were not blinded to the interventions after randomisation&quot; (Parsons et al. page 141). Although cost data is mostly objective, results are related to subjectively completed tools of quality of life and physical function, which can be influenced by participant and researcher bias due to knowledge of intervention purpose.</td>
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<td>Attrition was substantial (33%); however, it was mostly even across groups and it was mostly for reasons common in RAC populations including death and decline in health. A well-described intention-to-treat analysis was conducted and reported.</td>
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<td>Data was reported in relation to ONS versus dietary advice; however, change from baseline was not tested for statistical significance for most outcomes. Therefore, it is not clear if dietary advice may have also been beneficial. Results are reported in such a way as to favour one intervention over the other. Cost/QALY was not reported for each intervention, but only in regards to ONS minus the dietary advice.</td>
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</table>
| The study was funded by an unrestricted grant from a company which made the supplement; which results and conclusion favoured (see comment on selective reporting). In addition, there is significant concern about the possibility of poorly implementing the second comparator group (dietary advice group). Such an intervention is highly dependent on the skills of the particular dietitian. In addition, one of dietary advice followed by a 6-week follow-up for a malnourished patient would be seen as inadequate intervention, monitoring and follow-up by a treating clinical dietitian. A poor outcome in the dietary advice group would only serve to make the ONS (a standardised intervention which does not necessarily need follow-up or regular modification)
appear superior. This considered in how results are analysed and the study funder is of concern.