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REVIEW ARTICLE

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# Nutrition interventions for body composition, physical function, cognition in hospitalized older adults: A systematic review of individuals 75 years and older

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## Abstract

**Background:** Globally, the oldest old population is expected to triple by 2050. Hospitalization and malnutrition can result in progressive functional decline in older adults. Minimizing the impact of hospitalization on functional status in older adults has the potential to maintain independence, reduce health and social care costs, and maximize years in a healthy state. This study aimed to systematically review the literature to identify nutritional interventions that target physical function, body composition, and cognition in the older population (≥ 75 years).

**Methods:** A systematic review was conducted to evaluate the efficacy of nutritional interventions on physical function, body composition, and cognition in adults aged ≥ 75 years or mean age ≥80 years. Searches of PubMed (National Institutes of Health, National Library of Medicine), Scopus (Elsevier), EMBASE (Elsevier), Cumulative Index to Nursing and Allied Health Literature (CINAHL) with Full Text (EBSCOhost), and PsycInfo (EBSCOhost) were conducted. Screening, data extraction, and quality assessment were performed in duplicate and independently (CRD42022355984; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=355984).

**Results:** Of 8311 citations identified, 2939 duplicates were excluded. From 5372 citations, 189 articles underwent full-text review leaving a total of 12 studies for inclusion. Interventions were food-based, protein-based, carbohydrate-based, personalized, or used parenteral nutrition. Ten studies monitored anthropometric or body composition changes with three showing maintenance or improvements in lean mass, body mass index, triceps skinfold, and mid-upper arm circumference compared with the control group. Six studies monitored physical function but only the largest study found a beneficial effect on activities of daily living. Two of three studies showed the beneficial effects of nutritional intervention on cognition.

**Conclusion:** There are few, high-quality, nutrition-based interventions in older adults ≥75 years. Despite heterogeneity, our findings suggest that large, longer-term (>2 weeks) nutritional interventions have the potential to maintain body composition, physical function, and cognition in adults aged 75 years and older during hospitalization.

**KEYWORDS**

body composition, cognition, hospital, nutrition, nutritional supplementation, oldest old, physical function

## INTRODUCTION

By 2050, it is estimated that one in six people worldwide will be classified as an older adult aged ≥65 years with one in four living in Europe and Northern America.[1] Globally, the population aged ≥80 years old is expected to triple by 2050.[1] These estimates are consequential as currently in the USA, adults aged ≥65 years are twice as likely (21%) to require hospital admissions than those in middle age (45–64 years; 8%).[2] This is even more pronounced in the oldest or very old population, typically defined as ≥80 years by the World Health Organization and American Geriatrics Society. Such individuals are at even higher risk of hospitalization and associated adverse health outcomes.[2–4] Reducing the impact of hospitalization on physical function is integral to maintaining independence in this growing population.[5]

Hospitalization is a major risk factor for the acceleration of functional decline, cognitive decline, and frailty in older adults.[5–10] The prevalence of older adults acquiring a new functional disability in hospital is estimated at 30%[11] with only one-third of those returning to baseline 1 year later.[12] Malnutrition can exacerbate this functional and cognitive decline.[13] Approximately 20–29% of hospitalized older adults are malnourished with higher rates in women, those aged >80 years, and those with one or more co-morbidities.[3,14,15] This combination of phenotypic (low body weight, lean mass, or body mass index) and etiological (reduced food intake, disease burden) characteristics[16] is estimated to cost $15.5 billion yearly in the US.[17] Older adults are particularly susceptible to malnutrition due to a reduced basal metabolic rate, energy requirements, and altered hormonal regulation of hunger which can compromise nutrient intake.[5] Persons at risk of malnutrition in hospital settings have a ∼ 1.43 day longer length of stay, worse functional outcomes (e.g., reduced muscle strength), body compositional changes, and an increased average cost of hospitalization.[18–20] As a result, optimizing nutritional intake in hospitals has become a target for improving functional outcomes in older adults.

**Key points**

- There is a paucity of high-quality, nutrition-based interventions in hospitalized older adults (≥ 75 years).
- Findings from this systematic review suggest that longer-term (>2 weeks) nutritional interventions have the potential to maintain body composition, physical function, and cognition in adults aged 75 years and older during hospitalization.

**Why does this paper matter?**

Identifying interventions to minimize the adverse effects of hospitalization on body composition, physical function, and cognition in the oldest old, one of the fastest-growing age groups worldwide, can maintain independence and lead to reductions in associated costs.

Older adults have unique nutritional needs.[13,21] Older adults have a greater anabolic threshold of dietary protein/amino acid intake required to stimulate muscle protein synthesis.[22] A recent review has suggested that the oldest old require higher protein intakes (>1.0 g/kg body weight)[13] with a requirement of 0.8–1.5 g/kg body weight reported in smaller samples of healthy octogenarians.[23,24] Maintaining higher vitamin D levels between 40 and 60 nmol/L may be beneficial for cognition, strength, and musculoskeletal health.[13] Dietary patterns consisting of higher intakes of fruits, vegetables, nuts, dairy, fish, and wholegrains may delay muscle strength decline.[13] Differences in gut microbiota with age may alter nutrient availability and absorption.[25,26] Most prior work studying the unique nutritional needs of the oldest old adults have been conducted in the outpatient setting.[13]

Acute illness or procedural stressors occurring during hospitalization may trigger greater requirements for

energy and nutrients, though very little is understood. A greater understanding of the impact of existing nutritional interventions in hospitalized older adults is critical to improve functional outcomes post-hospitalization.[13] The objective of this systematic review was to identify nutritional interventions that target physical function, body composition, and cognition in older adults (≥ 75 years).

# METHODS

## Protocol registration

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed as a reference protocol standard.[27] A PRISMA flow chart is included (Figure 1). The protocol was registered with the International Prospective Register of Systematic Reviews PROSPERO, Registration Number CRD42022355984; available at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=355984.

## Eligibility criteria

The PICOS (Population, Intervention, Comparison, Outcome, Setting) framework was used to determine inclusion and exclusion criteria for this review and these criteria were developed prior to the screening phase. Older adults aged ≥75 years (or mean age ≥80 years) with or without co-morbidities were included. A lower age range of 75 years was chosen due to the expected limited research in the oldest old adults. All dietary interventions (e.g., single nutrients/nutraceuticals, supplements, whole foods, parenteral/ enteral nutrition support) were included. Interventions solely using Vitamin D were excluded as a result of previous systematic reviews in this area (e.g.,[28]). Multicomponent interventions including nutrition and exercise were also excluded. The comparator or control in the included studies was hospitalized people in the same age group without the intervention and receiving usual care. Full-text prospective intervention studies (e.g., randomized controlled trials [RCTs]) published in peer-reviewed journals were included; review papers, letters, editorials, and observational studies were excluded.

## Information sources

Searches of PubMed (National Institutes of Health, National Library of Medicine), Scopus (Elsevier), EMBASE (Elsevier), Cumulative Index to Nursing and Allied Health Literature (CINAHL) with Full Text (EBSCOhost), and PsycInfo (EBSCOhost) were

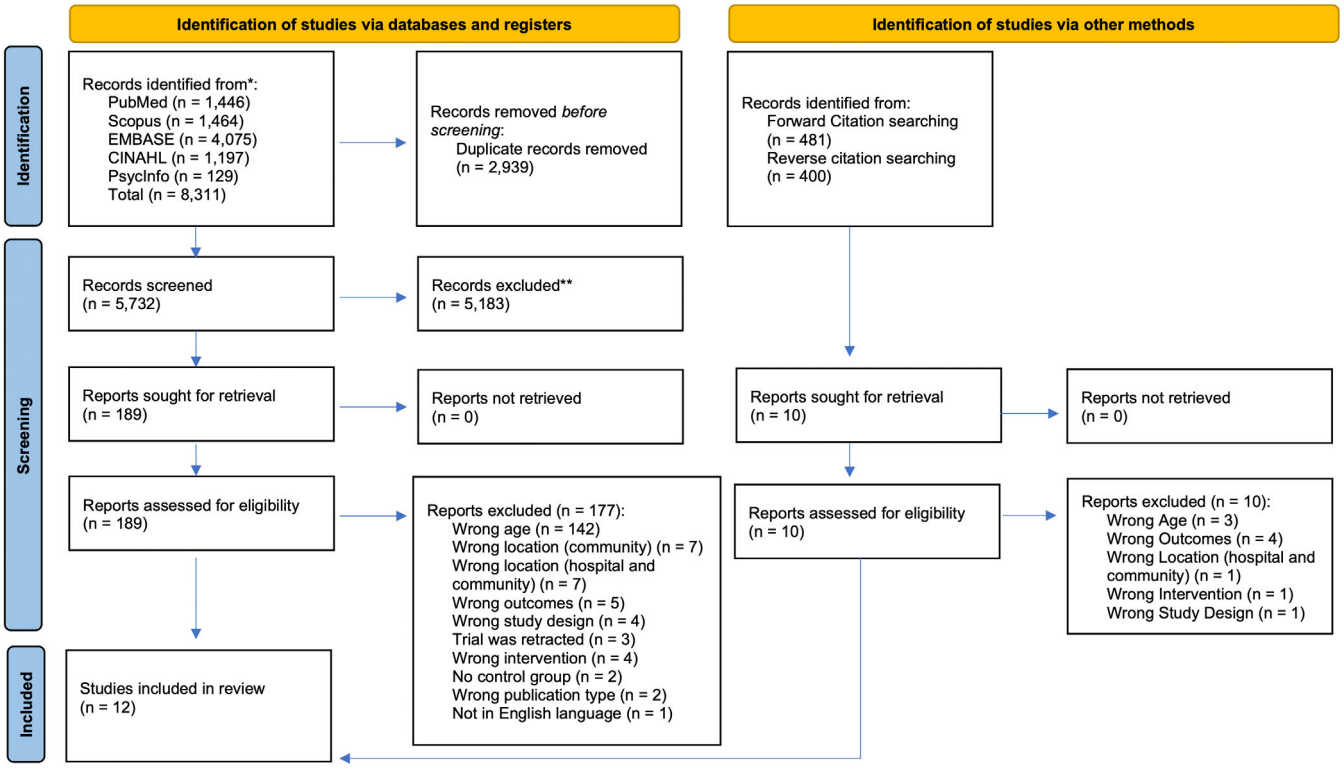


FIGURE 1 PRISMA 2020 flow diagram depicting study selection process.

conducted. See Supplemental Materials 1 and 2 for information on strategy development and the search strategies used.

## Outcome measures

Primary outcomes included measures of skeletal muscle function (e.g., sit-to-stand, hand grip strength, gait speed), body composition (e.g., lean/muscle mass, fat mass, weight, anthropometry), and cognition. Skeletal muscle function and body composition were chosen as these are components of sarcopenia, obesity, sarcopenic obesity, and frailty definitions—phenotypes associated with adverse health outcomes.[5,29,30] Cognition has an important impact on hospitalization in older adults. Individuals with cognitive impairment or dementia are at higher risk of hospital-acquired morbidity and mortality.[9] Additionally, there is mounting evidence to suggest that hospitalization leads to accelerated cognitive decline in older adults, particularly if they experience delirium during their hospital stay.[10]

If available, secondary outcomes (falls, re-hospitalization, disability, frailty, mortality) were recorded from the results of the included studies. Due to expected heterogeneity amongst the literature, an effect of the intervention on the outcome was determined by the presence of a statistically significant ($p < 0.05$) difference pre- and post-intervention or compared with the control group.

## Selection process

The final study screening process was completed in two distinct phases: title and abstract review, and then full-text article review using Covidence (Veritas Health Innovation, Melbourne, Australia). In the first phase, two reviewers independently screened title and abstracts of citations for inclusion based on the pre-defined eligibility criteria (LD, DB, CS, CMW). A second round of screening was performed by two independent reviewers assessing the full-text articles. Any conflicts in the title/abstract and full-text screening stages were resolved by a third reviewer. See Supplemental Material 1 for information on piloting the selection process and data extraction/synthesis.

## Assessment of risk of bias

Quality assessment of each article included was performed by two reviewers. Risk of bias was assessed using the Joanna Briggs Institute tools according to study type.[31] See Supplemental Material 1 for more information.

# RESULTS

## Study selection

A total of $n = 8311$ citations were identified via database searches, of which $n = 2939$ duplicates were excluded (Figure 1). The initial screen resulted in $n = 5372$ unique citations. During the title and abstract screening, $n = 5183$ citations were excluded because they did not meet the inclusion criteria. The remaining $n = 189$ full-text articles were then evaluated. Of these, $n = 177$ were excluded for not meeting inclusion criteria. The final analysis included $n = 12$ studies in this review. An additional $n = 881$ citations were identified and screened through forward/backways citations searching of the 12 included studies, but none of these met the inclusion criteria. A PRISMA flow diagram depicting the study selection process and reasons for exclusion at each stage can be found in Figure 1.

## Study characteristics

Study characteristics are outlined in Tables 1 and 2. The 12 included studies were conducted in hospitals across eight countries: Australia,[32,33] France,[34,35] Hong Kong,[36] Spain,[37,38] Sweden,[39,40] Switzerland,[41] the United Kingdom,[42] and the United States.[43] Six studies were conducted in orthopedic wards,[35,37–42] two in rehabilitation wards,[34,36] two in geriatric wards,[32,33] one in a general medical ward,[41] and one in a post-acute setting.[43] Interventions consisted of one food-based,[32] eight oral nutritional supplement-based (seven protein,[34–38,40,42] one carbohydrate-based[39]), two registered dietitian-led[33,41], and one parenteral nutrition.[43] The mean participant age ranged from 80.9 to 85.6 years with a study duration ranging from 5 to 105 days. Sample size ranged from 19 to 881 participants. Eleven studies recruited both male and female participants, while one study only recruited females.[42] Seven studies reported baseline BMI which ranged from 21.7 to 25.1 kg/m$^2$.

## Assessment of risk of bias

Of the 12 studies included, nine were assessed using the JBI for RCTs and three were assessed using the JBI tool for pseudo-randomized control trials

**TABLE 1** Baseline characteristics of the included studies-food-based and protein oral supplementation interventions.

| Author | Country location duration | Intervention arms | *n* | % Female | Age (years) | BMI (kg/m$^2$) |
|---|---|---|---|---|---|---|
| Food-based intervention | | | | | | |
| Collins et al.[32] | Australia Geriatric Ward 14 days | Control: Standard hospital diet | 61 | 52% | Median 80 (range 75–85) | N/A |
| | | Case: Modified menu with more calorie-rich options + low calorie options removed | 61 | 48% | Median 84 (range 75–88) | N/A |
| Protein oral supplementation | | | | | | |
| Olofsson et al.[40] | Sweden Orthopedic Department 27.4 ± 15.9 days | Control: Regular post-operative care | 74 | 77% | 82.2 ± 5.6 | 23.3 ± 4.0 |
| | | Case: Protein enriched meals (30 kcal/kg), protein drinks twice daily (2 × 200 mL) | 83 | 75% | 82.1 ± 6.8 | 25.1 ± 4.1 |
| Botella-Carretero et al.[38] | Spain Hip Fracture Orthopedic Ward 2 weeks | Control: Standard hospital menu | 30 | 77% | 83.7 ± 7.9 | 23.6 ± 2.4 |
| | | Case 1: Protein powder (9 g protein and 38 kcal) × 4/day | 30 | 90% | 83.1 ± 6 | 24.2 ± 3.0 |
| | | Case 2: Supplement drinks (200 mL, 18.8 g protein, 250 kcal) × 2/day | 30 | 70% | 84.6 ± 5.7 | 23.7 ± 3.5 |
| Bouillanne et al.[34] | France Geriatric Rehabilitation Ward 6 weeks | Control: Dietary protein was spread over the meals | 34 | 67% | 85.6 | 20.9 |
| | | Case: 78% protein intake delivered at 12:00 pm. | 29 | 79% | 84.1 | 20.7 |
| Abalan et al.[35] | France Orthopedic surgery ward 105 days | Control: Standard hospital menu (1386 ± 440 kcal, 64 ± 23 g protein) | 14 | 100% | 85.36 ± 6.28 | N/A |
| | | Case: Oral liquid supplements (400 kcal; 22.5 g protein per 2 cartons) in addition to normal hospital menu. | 15 | 93% | 85.13 ± 7.78 | N/A |
| Botella-Carretero et al.[37] | N/A Orthopedic Ward N/A | Control: Standard or texture-adapted diet to meet calculated metabolic rate | 30 | 66.70% | 82.1 ± 7.3 | 24.3 +/− 3.0 |
| | | Case: Oral nutritional supplements (20 g protein and 200 kcal each; × 2/day) | 30 | 80% | 85.1 ± 4.4 | 24.6 +/− 3.2 |
| Myint et al.[36] | Hong Kong Department of Rehabilitation Maximum 29.9 days | Control: Standard hospital diet | 60 | 63% | 81.7 ± 6.4 | N/A |
| | | Case: Oral nutritional supplement × 2/day (total 18–24 g protein and 500 kcal per day) on top of standard hospital diet | 61 | 69% | 80.9 ± 6.5 | N/A |
| Williams et al.[42] | UK Orthopedic ward 20.2 ± 5.9 days | Control: Standard hospital menu | 19 | 100% | 81.9 ± 7.7 | N/A |
| | | Case: Two to three oral nutritional supplements/day in addition to normal food (mean 8.8 g protein; 240 Kcal /can) | 19 | 100% | 81.4 ± 6.6 | N/A |

*Note*: *All values are mean ± SD unless otherwise specified.
Abbreviations: BMI = Body Mass Index.

(Supplemental Tables 1 and 2). One study did not conceal the allocation to the treatment group,[41] two studies had outcome assessors who were not blind to treatment assignment,[40,41] two studies had intervention team members who were not blind to treatment assignment,[33,41] and one study had participants who were not blind to treatment assignment.[41] In another study, it was unclear whether allocation to treatment groups was concealed and whether participants, those delivering treatment, or outcome assesors were blind to treatment assignment.[35] Two studies lacked sufficient information to allow for an overall appraisal.[40,43] One of these studies was evaluated as needing more information because the study lacked a thorough description of the control group and chose not to blind the outcome assessors to treatment assignment.[40] The second study was evaluated as needing more information due to a lack of clarity regarding both concealment of treatment group allocation and whether participants were blind to their respective group assignment.[43]

## Primary outcome measures

Below, we present a narrative synthesis of the results grouped by intervention type and further sub-grouped by primary outcome type; outcomes are outlined in Table 3.

**TABLE 2** Baseline characteristics of the included studies-carbohydrate oral supplementation, personalized interventions, parenteral nutrition.

| Author | Country location duration | Intervention arms | *n* | % Female | Age (years) | BMI (kg/m$^2$) |
|---|---|---|---|---|---|---|
| Carbohydrate oral supplementation | | | | | | |
| Gunnarsson et al.[39] | Sweden<br>Orthopedic Ward<br>Carbohydrate drink = 5 days post-operatively | Control: Standard hospital food and intravenous fluids | 50 | 76% | 80.9 ± 8.4 | N/A |
| | | Case: Carbohydrate supplement drink three times a day (900 kcal total) and glucose infusion (1000 mL/12 h) | 50 | 66% | 81.5 ± 9 | N/A |
| Personalized interventions | | | | | | |
| Holyday et al.[33] | Australia<br>Geriatric Medicine Wards<br>12.5 ± 1.2 days | Control: Standard nutritional care | 72 | 54% | 83.4 ± 0.9 | 23.3 ± 0.7 |
| | | Case: Texture modified meals, oral nutritional supplements, nutrient dense snack options, extra assistance from staff | 71 | 61% | 83.7 ± 0.8 | 23.8 ± 0.7 |
| Baumgartner et al.[41] | Switzerland<br>General medical ward<br>Mean 10 days | Control: Standard hospital menu | 442 | 51% | 82.5 ± 8.8 | 24.0 ± 4.4 |
| | | Case: individualized nutritional support (daily protein intake of 1.2 to 1.5 g/kg, with lower targets for those with acute renal failure (0.8 g/kg of body weight) | 439 | 53% | 82.2 ± 9.0 | 24.4 ± 4.9 |
| Parenteral nutrition | | | | | | |
| Thomas et al.[43] | USA<br>Post-acute setting<br>15.8 ± 6.7 days (range 8–23) for PPN group. | Control: nutritionally balanced diet without parenteral supplementation | 10 | 70% | 82.5 ± 9.8 | 21.8 ± 4.6 |
| | | Case: 1.5 g/kg protein and 30 kcal/kg as peripheral parenteral nutrition + oral nutrition (PPN; 3% amino acid, 3% glycerin, electrolyte solution) in addition to a standard diet. | 9 | 44.40% | 84.2 ± 9.2 | 21.7 ± 4.8 |

*Note*: *All values are mean ± SD unless otherwise specified.
Abbreviations: BMI, body mass index; PPN, peripheral parenteral nutrition.

## Food-based interventions

Collins et al. provided a modified hospital menu with more calorie-rich options compared to a standard menu with low-calorie options.[32] Despite a greater intake of protein and energy, the intervention had no effect on handgrip strength or change in body weight after 14 days (Table 3).

## Protein-based interventions

### *Physical function*

Seven nutrition interventions were protein-based, three of which measured physical function as an outcome[34,38,42] (Table 3). Botella-Carretero et al. conducted a three-arm trial for 2 weeks—a standard hospital menu (control), supplemental protein powder, or oral nutritional supplement drinks.[38] There was no benefit of either intervention on post-surgical duration of immobilization. Bouillanne et al. provided the majority of daily protein as a bolus for 6 weeks and found no improvement in handgrip strength and activity of daily living score (ADLS).[34] Williams et al. provided oral nutritional supplement drinks for 3 weeks and found similar handgrip strength and time taken to achieve mobility using a walking frame compared to the control group.[42] The protein-based nutrition interventions did not have a significant impact on physical function.

### *Body composition and anthropometry*

Six protein-based interventions measured body composition and anthropometry as outcomes[34,36–38,40,42]

**TABLE 3** Effects of nutritional intervention on physical function, body composition and cognition in hospitalized oldest-old adults.

| Author | Physical function | Body composition | Cognitive function |
|---|---|---|---|
| Food-based intervention | | | |
| Collins et al.[32]<br>Mann Whitney *U* test (mean ± SD) | Handgrip strength (kg): 1.4 ± 5.8 versus 1.7 ± 5.1; NS[#] | Δ Body weight (%): 0.26 ± 3.33 versus −0.55 ± 3.43; NS | N/A |
| Protein-based interventions | | | |
| Olofsson et al.[40]<br>Student's *t*-test (mean ± SD) | N/A | Δ BMI (kg/m$^2$): 23.0 ± 3.8 versus 24.7 ± 4.2; NS<br>Δ Body weight (kg): 61.7 ± 13.0 versus 66.2 ± 14.1; NS | Post-operative Delirium (%): 73 versus 55 ($p = 0.02$)<br>Days with Delirium: 7.9 ± 13.4 versus 2.3 ± 4.1 ($p < 0.001$) |
| Botella-Carretero et al.[38]<br>Student's *t*-test or Mann–Whitney *U* test | Post-surgical mobility: NS | Δ BMI (kg/m$^2$): NS<br>Tricipital Fold (mm): NS<br>Mid-brachial Circumference (cm): NS | N/A |
| Bouillanne et al.[34]<br>Mann Whitney *U* test (medians presented) | Handgrip strength (N): 0.00 versus +3.5; NS[#]<br>Activities of daily living score: 0.00 versus 0.00 score; NS[#] | Lean mass index (kg/m$^2$): −0.21 versus +0.38 ($p = 0.011$)[#]<br>Lean mass (kg): −0.41 versus + 0.91, ($p = 0.012$)[#]<br>Appendicular muscle mass index (kg/m$^2$): −0.11 versus 0.21 ($p = 0.047$)[#]<br>Appendicular muscle mass (kg): −0.11 versus 0.21; NS[#] | N/A |
| Abalan et al.[35]<br>Student's *t*-test or Mann Whitney *U* test (mean ± SD) | N/A | N/A | ΔMini mental state score: −2.71 ± 4.29 versus 3.47 ± 2.10 ($p < 0.001$)[#] |
| Botella-Carretero et al.[37]<br>ANOVA with Tukey's post hoc | N/A | Δ BMI (kg/m$^2$): NS<br>Δ Tricipital fold: NS<br>Δ Mid upper arm circumference (MUAC) (cm): NS | N/A |
| Myint et al.[36]<br>Mann Whitney *U* test (mean ± SD) | N/A | Δ Discharge BMI: −0.72 ± 0.91 versus −0.25 ± 0.83 kg/m$^2$ ($p = 0.012$)[#]<br>4-weeks Δ post-discharge BMI: −0.49 ± 1.01 versus 0.03 ± 1.21 kg/m$^2$ ($p = 0.012$)[#]<br>Δ MUAC (cm): −0.09 ± 0.83 versus −0.01 ± 0.99; NS[#]<br>Triceps Skinfold Δ: −0.66 ± 1.78 versus −0.13 ± 1.16; NS[#] | N/A |
| Williams et al.[42]<br>Paired Student's *t*-test (difference in means) | Δ Handgrip strength (mmHg)<br>Control: −0.3 (NS)<br>Intervention: +0.5 (NS) | Δ Triceps Skinfold (mm):<br>Control: −1.2 ($p < 0.01$)<br>Intervention: +0.1 (NS)<br>Δ MUAC (cm): | N/A |

(Continues)

**TABLE 3** (Continued)

| Author | Physical function | Body composition | Cognitive function |
|---|---|---|---|
| | Time to frame mobility (days): mean ± SD; 5.8 ± 5.0 versus 4.3 ± 2.2; NS[#] (difference in means) | Control: −1.5 ($p < 0.01$)<br>Intervention: +0.2 (NS) | |
| Carbohydrate-based intervention | | | |
| Gunnarsson et al.[39]<br>Mann Whitney *U* test (mean ± SD) | Walking assistance score: 3.6 ± 0.9 versus 3.5 ± 0.8; NS[#]<br>Functional Ability Score: 12.8 ± 3.7 versus 11.9 ± 4.1; NS[#] | Δ Body weight (kg): 62.6 versus 68; NS | Short portable mental status questionnaire (SPMSQ): 6.0 ± 3.7 versus 6.6 ± 3.5; NS[#] |
| Personalized interventions | | | |
| Holyday et al.[33]<br>Student's *t*-test<br>(difference in means) | N/A | Δ Body weight (kg): −0.9 ± 0.4 versus −0.9 ± 0.6; NS | N/A |
| Baumgartner et al.[41]<br>Student's *t*-test and linear regression models (odds ratios) | DFS: *N* (%):<br>80 (18.1%) versus 47 (10.7%); odds ratio 0.54 (0.37, 0.8)<br>($p = 0.002^{\#}$)<br>LFS: *N* (%)<br>80 (33%) versus 87 (26%); odds ratio 6.42 (2.48, 10.37)<br>($p = 0.001^{\#}$) | N/A | N/A |
| Parenteral nutrition interventions | | | |
| Thomas et al.[43]<br>Student's *t*-test (mean ± SD) | Δ Functional inventory measure score: 8.9 ± 12.3 versus 6.2 ± 3.3; NS[#]<br>Δ 6-metre walk time (s): −27.8 ± 16.1 versus −16.7 ± 11.55 NS[#] | Δ Body weight (kg): 1.12 ± 1.73 versus −2.42 ± 3.31; NS[#] | N/A |

*Note*: Throughout, results presented as control versus case. #- indicating comparison between both groups over time. Figures were not provided for two studies.[37,38]

Abbreviations: DFS, decline in functional status (Barthel's index) of >10% at 30 days; FIM, functional inventory measure; LFS, low functional status at 30 days (Barthel's index ≤30); MUAC, mid-upper arm muscle circumference (cm).

(Table 3). Four of these studies measured BMI[36–38,40]—three of which showed no significant differences.[37,38,40] Both studies by Botella-Carretero et al. provided protein-enriched oral nutritional supplements and had short durations of approximately 2 weeks.[37,38] Olofsson et al. used a similar intervention that was longer in duration (27.4 ± 15.9 days) but still found no effect on BMI between groups.[40] Dietary intake of the controls was not documented and it is unclear whether both groups consumed similar amounts. Only Myint et al. found that the nutritional intervention maintained BMI both at discharge and 4 weeks later, compared to the control group whose BMI reduced.[36] Oral nutritional supplements were provided twice daily for approximately 1 month; BMI was then measured at discharge and after 4 weeks. Results showed that, unlike the control group, the intervention group maintained their BMI.[36] Three interventions measured tricipital fold thickness as a body composition parameter.[37,38,42] Williams et al. showed a significant reduction in the control group ($p < 0.01$) but maintenance in the intervention group.[42] The two studies conducted by Botella-Carreterro et al. did not show any effect of the intervention on tricipital fold thickness.[37,38] Two interventions measured mid-upper arm muscle circumference (MUAC).[36,42] Only Williams et al. found a significant reduction in MUAC in the control group ($p < 0.01$) but maintenance in the intervention group.[42] Bouillanne et al. showed significant improvements in lean mass, lean mass index, and appendicular skeletal muscle mass index in the intervention group.[34]

*Cognitive function*

Two protein-based interventions measured cognitive function[35,40] (Table 3). Olofsson et al. found the intervention group had improved post-operative delirium ($p = 0.02$) and a reduced number of days with delirium ($p < 0.001$). Abalan et al. provided oral nutritional supplements for 105 days on average and found the intervention group had an improvement in their mini-mental state score ($p < 0.001$).[35]

*Carbohydrate based intervention*

There was only one short (5-day) carbohydrate-based intervention[39] (Table 3). The intervention group consumed four carbohydrate supplements (1000 kcals) and received a glucose infusion (600 kcals), while the control group received intravenous fluid (200 kcals) only on the morning of orthopedic surgery. The intervention did not have any significant impact on walking assistance, functional ability, body weight, or short portable mental status at post-operative day five.

*Other*

Holyday et al. implemented an intervention (control 13.4 ± 1.3 days vs. intervention 12.5 ± 1.2 days) that included modified hospital meals, oral nutritional supplements, assistance with meals, and nutritional education[33] (Table 3). The intervention did not have any significant effect on body weight. An intervention of individualized nutritional support (approximately 10 days) by Baumgartner et al. found improvements in functional status in the intervention group compared to the control group (10.7% vs. 18.1% experienced >10% decline in Barthel's index at 30 days).[41]

*Parenteral nutrition*

Only one study used parenteral nutrition (Table 2) and found no effect of the 15.8 (±6.7) day intervention on the functional inventory measure, change in timed 6-meter walk, and change in body weight.[43]

## Secondary outcome measures

There was no effect of any nutritional intervention on falls,[37] re-hospitalization,[33,37] or fractures.[37] Three studies reported the effect of nutritional interventions on mortality—two reported no effect[33,36] whereas Botella-Carreterro et al. provided oral energy and protein supplements twice daily and found a lower risk of all-cause mortality in the intervention group up to 180 days post-discharge.[37]

# DISCUSSION

In this systematic review of the literature, we identified 12 nutritional intervention trials for older adults (≥ 75 years) in hospital-based settings. Our key findings from these heterogeneous studies were that only longer duration, protein-based interventions maintained or improved body compositional measures ($n = 3/10$), physical function ($n = 1/6$) or cognition ($n = 2/3$) in hospitalized older adults. No effects tended to be found in smaller studies of shorter durations. Thus, our findings suggest that hospital-based nutritional interventions have the potential to maintain body composition, physical function, and cognition in adults aged 75 years and older but further research is required.

Aging is associated with a yearly loss of muscle mass (~1%)[44] and hospitalization results in even greater losses of total, lean, and fat mass.[20] The quantity and quality of dietary protein is important for maintaining and improving muscle mass, especially in older adults who have greater dietary protein requirements due to the anabolic

resistance of aging.[22,45] In a systematic review of hospitalized and community-dwelling older adults (>60 y), protein-rich foods and supplements had a small effect size on fat-free mass although there was no association with duration or quantity.[46] Body composition was the most commonly measured outcome category reported in this review. Seven studies identified no beneficial effect of the intervention on either BMI or body weight.[32,33,37–40,43] However, these studies were primarily of either short one or two-week durations,[32,33,37–40] or had low enrollment.[43] The studies that did show an effect were of a longer duration and either found a small improvement in lean or muscle mass[34] or maintenance of post-discharge BMI in contrast with the control group ($-0.49 \pm 1.01$ vs. $0.03 \pm 1.21$ kg/m$^2$, $p = 0.012$).[36] Maintaining muscle mass is integral to maintaining physical function[29] and, particularly relevant to our aim, we found that the study by Bouillanne et al. led to improvements in lean mass.[34] It is possible that this may relate to the anabolic threshold of dietary protein/amino acid intake in older adults[22] whereby only the intervention group exceeded this threshold in one meal (> 40 g).[34] Therefore, future research should consider the quantity and timing of protein intake in relation to body composition of hospitalized older adults.

In older adults, muscle strength reduces at a rate of ~3% per year[44] which is exacerbated by hospitalization.[20] While a recent umbrella review found an unclear effect of nutritional interventions alone on muscle strength in older adults, the review found that protein enhanced the effects of resistance exercise on strength.[47] In this present review, the majority of studies found no effect of nutritional interventions on different measures of physical function.[32,34,38,39,42] However, most studies were small ($n = 38$–$122$) and of varying duration (approx. 14 days to 6 weeks),[32,34,38,39,42] making it unclear whether these studies were sufficiently powered to identify minimal detectable changes.[48]

Findings in older adults (> 60 y) suggest that oral nutritional supplements are associated with improvements in physical function.[46] Indeed, we identified a large study providing individualized high-protein nutritional support which showed improved Barthel's index (a composite self-reported measure of physical function) scores.[41] The favorable effect of nutrition in this study may relate to the large sample size. These findings contrast with a similar study by Bouillanne et al. which found no difference in the effect of a pulsed protein diet on ADLS over a six-week period.[34] Although both interventions aimed for levels of protein intake greater than the recommended daily allowance, the duration and mode of administration were different. Another potential reason for the discordant findings of these two studies may relate to differences in the outcome tools: ADL score[34] versus the Barthel's Index.[41] The Barthel's Index includes additional measures of mobility and stair climbing that are not included in the ADL score.

Cognition was the least reported outcome measure in the studies identified; however, two of three studies identified favorable effects. Using similar protein-based interventions of oral nutritional supplements but with differing durations (1 month[40] to 105 days[35]), improvements in delirium-related outcomes or mini mental state scores were found. In contrast, a much shorter carbohydrate-based study by Gunnarsson et al. found no effect on cognition.[39] These discordant findings may relate to differences in the actual intervention itself or the cognition outcome used: short portable mental status questionnaire versus the mini mental state score.[35] The exact mechanism of the positive associations found between nutrition and cognition in this review is unclear. Others have hypothesized that the Mediterranean diet[49] and omega three fatty acids[50] may lead to improved neurovascular health, reduced oxidative stress, or reductions in chronic inflammation and thus improve or maintain cognition in older adults. However, the studies so far have been heterogeneous or failed to find an effect.[49,50] Similar to physical function, there are inherent challenges when measuring baseline cognition in hospital whereby it may be speculated that a patient's improvement in cognition relates to their medical recovery rather than a nutritional intervention. However, given the favorable results identified in randomized controlled trials, further research is warranted.

## LIMITATIONS OF EXISTING EVIDENCE AND FUTURE DIRECTIONS FOR RESEARCH

The findings of this systematic review are limited by the few, heterogenous interventions, mostly of short durations, and outcomes identified. The primary outcomes chosen are inherently affected by the effects of recovering from an acute illness and as such it is difficult to extricate the specific impact of the nutritional intervention which should be considered when interpreting the findings presented. Moreover, it is unclear whether statistically significant changes in the outcomes are clinically significant in this particular context. We chose not to include nutrition interventions that were paired with exercise despite the well-acknowledged beneficial effects of exercise on the outcomes included in this review. The rationale for this was due to (i) a similar systematic review in this area which was recently published[51] and, (ii) patients often receive individualized physiotherapy in the hospital

setting. Lastly, we restricted our search to studies published in English and, although recent evidence suggests such filters do not affect estimates or conclusions,[52] we may have omitted relevant studies. There are strengths to this study whereby a thorough, peer-reviewed search strategy was utilized. Screening, data extraction, and risk of bias assessment were independently assessed by two reviewers and a tabular and narrative synthesis of findings is presented.

Further research is required in the adults aged 75 years and older; however, care should be taken regarding the choice of outcomes used, study duration, and having a sufficiently powered sample size to detect a difference. Interventions that are protein-based and of sufficient quality and quantity which consider the anabolic threshold of aging may be most effective. Future studies should consider including a broad array of objective and subjective physical function measures, detailed body composition metrics, and comprehensive cognitive assessments that include delirium. None of the studies we reviewed included biomeasures (e.g., blood or stool markers) which may be earlier, more sensitive markers of diet change.

## CONCLUSION

There are few, high-quality, nutrition-based interventions in the oldest-old hospitalized adults. Despite heterogeneity in the interventions identified in this study, we found that smaller, shorter-duration studies failed to find favorable effects. However, one large individualized, high-protein nutritional intervention was beneficial for physical function (activities of daily living), the protein content of meals was identified as important for muscle mass by another, and oral nutritional supplementation was beneficial for cognition. Future work should include larger samples and be conducted over longer periods of time to move the field forward.

### AUTHOR CONTRIBUTIONS

Lisa Dowling, David H. Lynch, and John A. Batsis designed research. John A. Batsis, Micah Prochaska, and Megan Huisingh-Sheetz provided study oversight. Dakota Batchek, Chang Sun, Charlotte Mark-Wagstaff, Emily Jones conducted research. Lisa Dowling, Dakota Batchek, Chang Sun, analyzed data and wrote the paper. Lisa Dowling had primary responsibility for final content. All authors have read and approved the final manuscript.

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### CONFLICT OF INTEREST STATEMENT

LD, DL, DB, CS, CMW, EJ, MP, MHS-none to declare. JAB-Equity in SynchroHealth LLC.

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Sponsors had no role in the design, analysis or interpretation of this work.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**Data S1.** Supplemental Material 1: Supplementary methods.

**Supplemental Material 2.** Search strategies used for the systematic review.

**Supplemental Table 1.** Risk of bias using Joanna Briggs Institute tool for Randomized Control Trials.

**Supplemental Table 2.** Risk of bias using Joanna Briggs Institute tool for Pseudo-Randomized Control Trials.

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