TITLE

The effectiveness of nutrition and combined nutrition plus physical activity interventions in older adults living with frailty or pre-frailty: A systematic review and meta-analysis

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DECLARATION OF AUTHOR(S) COMPETING INTERESTS

The authors declare no competing interests.

ABSTRACT

Background: Frailty is a leading contributor to functional decline and early mortality in older adults, but it is not a natural outcome of aging and can potentially be reversed. We conducted a systematic review and meta analysis to identify the effectiveness of nutrition interventions and nutrition interventions with physical activity (combined approach) in improving various outcomes related to frailty.

Methods: We searched 4 databases from inception to July 2019 for nutrition interventions involving adults ≥65 years and identified as frail using a frailty tool or assessment. Reviewers screened citations, extracted data, and assessed risk of bias and certainty of evidence. We assessed statistical and methodological heterogeneity and performed a meta-analysis of studies with similar interventions and components.

Results: 1,825 frail older participants from 15 studies were included. Seven studies were low risk of bias, 2 studies at high risk of bias, and 6 studies with an unclear risk of bias. Nutrition RCTs had small, but significant, effects on physical (SMD 0.16, 95% CI 0.02 to 0.29), mobility (SMD 0.15, 95% CI 0.00 to 0.30), and frailty (SMD -0.22, 95% CI -0.44 to -0.01) outcomes. Combined approach RCTs had small but significant effects on physical (SMD 0.19, 95% CI 0.06 to 0.32), mobility (SMD 0.25, 95% CI 0.02 to 0.48), and frailty (SMD -0.41, 95% CI -0.68 to -0.14; RR 0.72, 95% CI 0.52 to 1.00) outcomes.

Interpretation: There is moderate level evidence that nutrition, protein supplementation, and combined approach interventions are beneficial for certain components of frailty.

Protocol registration: PROSPERO-CRD42020144819

INTRODUCTION

Frailty is a leading contributor to functional decline and early mortality in older adults (1). Over 1.5 million Canadians are currently diagnosed as medically frail and this number is expected to rise to over 2 million in the next 10 years (2). Frailty is characterized by reductions in physiologic reserve and a reduced ability to respond to stress (3, 4). It is not a specific medical condition or disability, but rather frailty is a syndrome resulting from multiple factors and impairments that can reduce an individual's functional ability. Older adults with frailty are at an increased risk for adverse outcomes such as falls, mobility decline, hospitalization, and death (5, 6). However, frailty is not a natural outcome of aging, nor is it age dependent, as many adults reach advanced ages without developing frailty (7). As a syndrome, frailty is poorly understood and under recognized in a healthcare system which focuses on individual diseases, rather than the totality of the person (8). This results in a high consumption of healthcare resources (9), an increased burden on caregivers, and adverse health outcomes (10).

Research highlights that frailty progression can be slowed and is potentially reversible through nutrition interventions (1, 11). In addition, since frailty is a multi-component condition which includes physical factors such as reduced handgrip strength and gait speed, it is important to consider the enhanced impact that adequate nutrition could have on the benefits of physical activity in a frail population. Based on the mixed results from previous reviews looking at both nutrition interventions alone and physical activity interventions with nutrition supplementation (12, 13), it is still unclear the best interventions to support older adults with frailty and there is a need for a comprehensive and systematic literature search. This systematic review and meta analysis focused on nutrition interventions and nutrition interventions with physical activity to assess their effectiveness in improving various outcomes related to frailty. This review will provide the scientific evidence for the Clinical Practice Guidelines of the Canadian Frailty Network.

METHODS

This systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (14)and reports on the outcomes ranked critical from a registered protocol (PROSPERO-CRD42020144819) based on the voting of a guideline panel committee.

Key Question

What is the effectiveness of nutrition interventions and nutrition interventions that include physical activity in older adults (age 65+ years) living with frailty or pre-frailty on clinical, patient important, or health utilization outcomes?

Search Strategy

The search terms, databases, and strategy were developed in consultation with a research librarian at McMaster University and informed by previous systematic reviews (Appendix 1). We searched MEDLINE, EMBASE, Cochrane, and CINAHL databases from inception to July 2019. We manually searched reference lists of relevant reviews and included studies for citations not captured in the initial search. If PDFs could not be located, corresponding authors were contacted. Results from the search were

deduplicated, and citations were uploaded to a secure internet-based platform for screening (DistillerSR, Evidence Partners Inc., Ottawa, Canada). We used EndNote (Thompson Reuters, New York) to perform reference management.

Eligibility Criteria

We included English language studies involving adults aged 65 years and older who were selected and identified as frail using a frailty tool, assessment of frailty, or other established criteria. Studies were also included if a sub-analysis was conducted on a portion of the participants who were frail. Populations that were just described as frail by the authors (without using a measurement or tool to define) were excluded. To make this review relevant to the general frail population, studies that targeted clinical populations, such as obese or cancer patients, were excluded.

Studies must have been completed (not published protocols or in progress) and had to have a true control group defined as usual care, routine care, or minimal contact which did not include any intervention or treatment group components. Any head-to-head interventions were excluded. This review focused on 2 intervention study types: nutrition and combined approach. Nutrition intervention studies had to involve a nutritional component such as food supplementation, meal programs, education, and others. Combined approach studies had to include both nutrition and physical activity components in the same intervention that were not standardized between groups. Studies that included other intervention components, such as memory tasks, were excluded. There was no exclusion based on intervention or participant setting.

Outcomes of interest were selected by an interdisciplinary steering committee and included: health (body weight and body mass index), mortality, physical (activities of daily living (ADL), muscle strength (handgrip and non-handgrip), and appendicular lean mass), quality of life (measured by a standardized tool), health services use, frailty (measured by a valid tool), mobility (gait speed, timed up and go test, chair sit and stand test, balance test, and short physical performance battery test), diet quality (energy intake in kcal), and social/caregiver.

Study Selection, Data Extraction, and Quality Assessment

Titles and abstracts were reviewed in duplicate; articles marked for inclusion by either team member went on to full-text relevance testing. Full-text screening was completed independently by 2 team members, with consensus required for inclusion or exclusion. Multiple publications for the same primary intervention were merged. We developed, piloted, and deployed standardized forms for data extraction. One team member completed full data extraction and an assessment of study risk of bias (RoB) using the Cochrane Collaboration risk-of-bias tool (15) for randomized control trials (RCTs). If interventions had multiple treatment arms, only the interventions which met inclusion criteria were extracted. We extracted intention-to-treat data where possible. Conflicts were resolved by the lead researcher of this review (M.R.) and all data extraction was independently verified by the statistician (M.A.).

Certainty of Evidence

We evaluated the certainty of the body of evidence using the Grading of Recommendation, Assessment, Development and Evaluations (GRADE) method (16) with GRADEpro software (17). GRADE rates the certainty of a body of evidence as high, moderate, low, or very low and ratings are based on an

assessment of 5 conditions: 1. methodological quality, 2. consistency across effect estimates/statistical heterogeneity, 3. directness of the body of evidence to the populations, interventions, comparators and/or outcomes of interest, 4. precision of results, and 5. indications of reporting bias.

Data Synthesis

Data analysis, including subgroup analysis, were planned *a priori* (Appendix 2). A meta-analysis was used to combine the results across studies by outcome using the published data from included studies. For continuous outcomes, we used the change from baseline to immediate post-treatment data (means, standard deviations) for both intervention and control groups to generate the summary measures of effect in the form of standardized mean difference (SMD) (18). The SMD accounts for similar outcomes measured using different assessment tools (i.e. mobility measured as stair climb, balance test, gait speed, chair rise repetition, sit-to-stand test, gait speed, etc.). We used a random effects multi-level meta-analytic approach to account for dependency between effect sizes i.e. the correlation between effect sizes due to multiple measures or sub-measures of same outcome with-in a study or comparison of multiple interventions to a single control group. For pooling of performance measures, the direction of effect was adjusted to ensure consistency of desirable outcome responses. The SMD is interpreted based on its magnitude according to Cohen d recommended thresholds (~0.2=small effect, ~0.5=medium effect, ~0.8=large effect) (19). For dichotomous outcomes, we used the number of events at post-intervention to generate the summary measures of effect in the form of risk ratio (RR) using DerSimonian and Laird random effects models with Mantel-Haenszel method. The Cochran's Q (α=0.05) was employed to detect statistical heterogeneity and I^2 statistic to quantify the magnitude of statistical heterogeneity between studies where I^2 30% to 60% represents moderate and I^2 60% to 90% represents substantial heterogeneity across studies. Publication bias was assessed using funnel plots. All analyses were performed using R software (metaphor (20) and dmetar (21) packages).

RESULTS

From 3,163 citations, we assessed 123 full-text articles for eligibility, and included 15 studies described in 26 publications in the synthesis (Figure 1). One of the included studies consisted of both a nutrition-only treatment arm and a combined approach treatment arm (22). This study was therefore considered in the meta-analysis and qualitative description of both intervention categories. Of the remaining included citations, 7 were nutrition RCTS (11, 23-28) and 7 citations were combined approach RCT interventions (29-35). From this, all 15 studies and their outcomes were meta-analyzed based on their intervention category. The studies were published from 2000 to 2019. A total sample of 1825 frail older participants from 16 studies were included in this review with a mean age ranging from 70.0 to 83.1 years and percentage of women in the studies ranging from 51% to 100%. All the included RCTs had fewer than 250 participants.

Demographic data and characteristics of the included studies can be found in Table 1 and 2. Briefly, most interventions were conducted in Europe and Asia with community-dwelling participants and lasted between 3 and 6 months. The 2 most common tools used to measure frailty status in the participants were Fried's Frailty phenotype (36) and the Cardiovascular Health Study Criteria (36). For the nutrition studies, interventions included nutritional supplementation, fortified or enhanced foods, and nutrition or dietitian counselling. Combined approach studies also focused on the same 3 nutrition interventions

with most studies adding a resistance/strength training component. The physical activity occurred 1 to 2 times per week and between 30 minutes to over an hour in duration. Few studies reported adverse effects or harms related to the intervention. Nutrition interventions reported adverse effects as nausea, diarrhea, dyspepsia, and acute illness, and combined approach interventions reported adverse effects from back pain related to physical exercise, other pain related to exercise, and heavy study burden. For more details see Appendix 3.

Risk of Bias and Quality of Included Studies

The results of the critical appraisal of individual studies for level of bias are shown in Table 3. Overall, the Cochrane RoB showed mixed quality of study methodology: 7 studies were low risk of bias (11, 25-28, 30, 33), 2 studies at high risk of bias (29, 35), and 6 studies with an unclear risk of bias, mostly due to unclear allocation and blinding procedures (22-24, 31, 32, 34).

The certainty of evidence ranged from very low to moderate but was moderate for most outcomes due to downgrading for risk of bias or imprecision. GRADE tables for each outcome by intervention category can be found in Appendix 4.

Benefits of Treatment

The meta-analysis included an examination of the impact of all nutrition interventions together, all combined approach interventions together, and a sub-group of protein supplementation nutrition interventions. The protein supplementation subgroup had no Quality of Life (QoL) data. For all interventions, there was no data for mortality, health services use, or caregiver/social outcomes.

Nutrition Interventions

Nutrition interventions were supplementation of; protein (23-25, 27), other multi-nutrient and multi-vitamin (11, 23, 26), vitamin D (28), and fruit and dairy (22) (Table 1). One intervention also included a treatment arm that consisted of nutrition education and customized dishware (23). Overall, nutrition RCTs had small, but significant, effects on physical, mobility, and frailty outcomes with a moderate certainty of evidence. There were no significant effects on health, diet quality, or quality of life outcomes between intervention groups and control groups (Appendix 5 Figures S1-S3).

Using data from 7 RCTs (11, 23-28), which included a total of 373 intervention and 321 control participants, the pooled effect estimate for physical outcomes showed a small but significant between group difference (SMD 0.16, 95% CI 0.02 to 0.29, $p<0.03$; Figure 2). A similar effect was also observed for mobility outcomes (SMD 0.15, 95% CI 0.00 to 0.30, $p<0.05$; Figure 3). The overall certainty of the body of evidence was rated as moderate (Appendix 4 Table S1).

Frailty outcomes were reported in 3 RCTs (11, 23, 25). These studies included 155 intervention and 100 control participants. The pooled effect estimate for frailty outcomes showed a small but significant between group difference (SMD -0.22, 95% CI -0.44 to -0.01, $p=0.04$; Figure 4). The overall certainty of the body of evidence was rated as moderate (Appendix 4 Table S1).

Protein Supplementation Interventions

Five studies were identified for analysis based on the primary intervention being protein supplementation (23-27). One intervention provided protein in 2 forms as soy protein powder or milk

powder to 2 different treatment arms (23), while another used the same protein in different amounts for 2 intervention treatment arms (1.2g protein/kg bodyweight/day vs 1.5g protein/kg bodyweight/day). These protein supplementation interventions ranged from 4 weeks to 24 weeks with 195 intervention and 149 control participants. Together, the 5 interventions had small, but significant, effects on physical and mobility outcomes with a moderate certainty of evidence (Appendix 4 Table S2). The pooled effect estimates for physical and mobility outcomes between intervention and control groups were SMD 0.16, 95% CI 0.01 to 0.31, p=0.03 (Figure 5) and SMD 0.20, 95% CI 0.02 to 0.39, p=0.04 (Figure 6), respectively. There were no significant between group effects on health, frailty, or diet quality outcomes (Appendix 5 Figures S4-S6).

Combined Approach Interventions

Combined approach interventions consisted of both nutrition and physical activity components in the same treatment arm. The nutrition component of these interventions ranged from protein supplementation, provision of food, vitamin D supplementation, dietary counselling, education, and/or cooking classes. The physical activity component was mostly muscle-strengthening exercises through resistance and strength training but 3 interventions (22, 30, 34) also included aerobic exercises such as walking, coordination, and flexibility (Table 2). Together, the combined approach interventions had small, but significant, effects on physical, mobility, and frailty outcomes with a moderate certainty of evidence. There were no significant effects on health, diet quality, or quality of life outcomes between intervention groups and control groups (Appendix 5 Figures S7-S9).

The same 6 interventions had data for both physical and mobility outcomes (29-33, 35). These interventions ranged from 12 weeks to 52 weeks with 258 intervention and 256 control group participants. The pooled effect estimates for between group differences for physical and mobility outcomes were SMD 0.19, 95% CI 0.06 to 0.32, p=0.007 (Figure 7) and SMD 0.25, 95% CI 0.02 to 0.48, p=0.04 (Figure 8), respectively. The overall certainty of the body of evidence was rated as moderate (Appendix 5 Table S3).

Frailty outcomes, measured by a modified Fried's frailty phenotype, were found in 2 RCTs consisting of 100 intervention group and 113 control group participants (30, 31). The pooled effect estimate for frailty showed a significant between group difference (SMD -0.41, 95% CI -0.68 to -0.14, p<0.01; Figure 9). These interventions both included dietary counselling; 1 intervention used only muscle-strengthening exercises (31)while the other had a mixture of muscle-strengthening and walking (30). Frailty was also measured as prevalence of frailty post-intervention in 3 RCTs (30, 31, 34). These interventions ranged from 12 weeks to 52 weeks with 174 intervention and 185 control group participants. The pooled effect estimate showed a significant between group reduction in frailty post-intervention (risk ratio (RR) 0.72, 95% CI 0.52 to 1.00, p<0.05; Figure 9). The overall certainty of the body of evidence was rated as moderate (Appendix 5 Table S3).

INTERPRETATION

Main Findings

Our comprehensive search strategy and quantitative synthesis of reported data showed a small but significant benefit for nutrition, protein supplementation, and combined approach interventions when compared to control groups for physical and mobility outcomes based on moderate certainty of

evidence. Only nutrition interventions and combined interventions showed small but significant evidence of benefit for frailty outcomes, based on moderate certainty of evidence. We found no evidence of benefit from any intervention type for health, diet quality, and quality of life outcomes.

Explanation and Comparison with Other Systematic Reviews

Previous systematic reviews and meta-analyses have been conducted to evaluate various interventions and their components related to frailty prevention, progression, and reversal. Many of these syntheses have focused on specific settings, such as primary care interventions or community-dwelling adults (13, 37)or specific interventions, primarily physical activity studies (12, 38). Others have included a mixture of interventions, making their assessment more heterogeneous (5, 6, 39). While our review had specific intervention eligibility criteria to address this heterogeneity, there was still some diversity in the included studies. Other systematic reviews that have focused on nutrition interventions have often included participants that are also malnourished or sarcopenic and not necessarily frail (40-42), thus creating more heterogeneous populations compared those included in our review. Many of these reviews are also lacking meta-analyses (43, 44) or focus only on a few specific outcomes, such as body composition, leg strength, and walking speed (45). Therefore, it is not surprising that previous reviews considering nutrition intervention studies have found minimal or mixed effects of nutrition and/or protein/caloric supplementation for older adults with frailty (1).

Similarly, our review found mixed effects depending on intervention type and outcomes. Protein supplementation in older adults is a priority given that many fall below the recommended daily amounts of protein and suffer from sarcopenia, a condition that overlaps with frailty (24). Our review did not find an effect from the protein RCTs on frailty but did for physical and mobility outcomes. This aligns with previous reviews that found protein supplementation led to increases in physical performance, such as gait speed (1, 39). But similar to our work, it was from only 3 small-scale clinical trials which had issues concerning selection, performance, and attrition bias (39). It has been suggested that for nutrition interventions to work on their own, without the combination of physical activity, the population may need to be at deficiency or malnourished (1, 10) and at similar levels of baseline frailty; however, there is a lack of evidence for this second hypothesis.

Studies have also demonstrated the importance of protein supplementation in combination with resistance exercise in healthy older adults. Previous reviews show that nutrition intervention combined with physical activity is effective at improving frailty, gait speed, grip strength and physical performance (37, 39). Our review confirmed this from moderate certainty of evidence with data from 3 to 5 RCTs. In addition, the effect estimates for these interventions were slightly higher than nutrition alone; however, we did not see any additional outcomes of significance with these intervention types and overall, the effect estimates are still small. Once again though, previous reviews have found conflicting results on the benefits of protein in combination with exercise on physical function parameters in older adults with frailty (6, 39, 46). These results may be due to low number of studies and study heterogeneity (small samples or insufficient doses of nutritional supplements) (12).

Limitations

Although our search was comprehensive, we did not explicitly search the literature for combined interventions that included nutrition with physical activity components so it is possible we could have missed potentially relevant studies. In addition, while our frailty criteria for inclusion attempted to make

a more homogeneous population, it led to a large number of exclusions and the variety of tools and definitions used to describe participants still made for diverse study participants which was subject to the authors interpretation and description. The data extracted was immediate post-intervention which leaves a question regarding the long-lasting effects of these interventions. Lastly, studies of this type have been small in nature (less than 250 participants) and have risk of bias concerns, which have also been noted in other reviews (1).

Conclusion and Implications for Practice and Future Research

Our meta-analysis is unique in that it focuses explicitly on pre-frail or frail participants using validated tools/assessment criteria and combines individual measurements of outcomes (such as muscle strength and gait speed) into overall effect estimates (physical performance). With the aging population and increased prevalence of frailty, this review adds to the body of evidence to identify successful interventions that benefit components of frailty, such as physical and mobility outcomes, and frailty itself. Current research is lacking in measuring frailty as an outcome, which has been criticized as a limitation of these studies previously (1). Interventions also do not investigate the effects by frailty status since different levels of frailty may respond to different interventions. More robust, well-designed clinical trials of adequate quality for older adults living with frailty are needed to ascertain these findings. We also did not identify any studies focussing on social outcomes that are important to frail older adults and their caregivers. This warrants the need for high quality future research to address these gaps and help inform clear interventions to prevent and/or delay frailty progression.

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Appendix 3: Characteristics of Included Studies Tables

Appendix 4: GRADE Tables for All Outcomes by Intervention Category

Appendix 5: Meta-analysis Forest Plots for Non-Significant Outcomes

Table 1. Characteristics of the Included Studies: Nutrition Studies

Study (author, year, ref)	Location	N	Age (y) mean (SD)	Gender (F/M, %)	Frailty Tool	Frailty Characteristics†	Study Design	Study Length‡	Nutrition Intervention	Control	Outcomes
Wu, 2018	Taiwan	40	O: 74; I: 73.5 (2.4), 75.0 (2.4), 72.8 (1.6); C: 75.9 (1.7)	56/44§	Fried's frailty phenotype*	I: Prefrail: 22; Frail: 4; C: Pre-frail: 8; Frail: 2	RCT	3 months	Oral nutrition supplements, Fortified/enhanced foods, Nutrition/dietitian counselling	General nutrition information	Health (and Mortality), Physical (and QoL), Mobility, Diet Quality
Niccoli, 2017	Canada	53	O: 81.3 (1.0); I: 81.77 (1.68); C: 80.33 (1.57)	68/32§	Fried's frailty phenotype*	Most participants were frail¶	RCT	Approx 3-4 weeks	Fortified/enhanced foods	Control food without supplements	Physical (and QoL), Frailty, Mobility
Park, 2018	Korea	120	I: 77.30 (3.67), 76.80 (3.70); C: 76.83 (3.86)	65/35	Cardiovascular Health Study*	I: Frail: 20; C: Frail: 5	RCT	12 weeks	Fortified/enhanced Foods	Placebo powder	Physical (and QoL), Frailty, Mobility, Diet Quality
Ng, 2015	Singapore	246	O: 70.0 (4.7); I: 69.7 (4.23); C: 70.1 (5.02)	61/39	Cardiovascular Health study	I: Pre-frail: 33; Frail: 16; C: Pre-frail: 43; Frail: 7	RCT	6 months	Oral nutrition supplements, Fortified/enhanced foods.	Placebo supplement	Health (and Mortality), Physical (and QoL), Health Services, Frailty, Mobility
Kim, 2013	South Korea	87	I: 78.9 (5.5); C: 78.4 (6.0)	79/21	Slow gait speed and MNA score	I: Frail: 43; C: Frail: 44	RCT	12 weeks	Oral nutrition supplements, Fortified/enhanced foods	No contact or care	Health (and Mortality), Physical (and QoL), Frailty, Mobility, Diet Quality
Tieland, 2012	Netherlands	65	O: 83.1 (5.1); I: 78 (1); C: 81 (1)	55/45	Fried's frailty phenotype	I: Pre-frail: 27; Frail: 7; C: Pre-frail: 20; Frail: 11	RCT	24 weeks	Fortified/enhanced foods	Placebo supplement	Health (and Mortality), Physical (and QoL), Mobility, Diet Quality
Latham, 2003	New Zealand	243	O: 79.1 (6.9); I: 79 (77-80); C: 80 (78-81)	53/47	Winograd et al	I: Frail: 121; C: Frail: 122	RCT	3 months	Oral nutrition supplements	Placebo supplement	Physical (and QoL), Mobility
de Jong, 2000††	Netherlands	217	O: 79; I: 79.6 (4.8); C: 79.3 (6.6)	70/30	Required healthcare service	I: Frail: 41; C: Frail: 37	RCT	17 weeks	Fortified/enhanced foods	Control food without supplements	Physical (and QoL), Mobility, Diet Quality

Legend: N = Number of participants randomized at start of intervention; †Total non-frail, pre-frail, and frail for entire study population by intervention and control groups (may include multiple treatment arms combined) ‡Not including follow-up, if applicable; §Values for gender are based on reported baseline which may not equal N randomized but rather the number of participants who completed the intervention; ¶Authors indicated most participants were frail however, the number of frail participants was unclear; ††Describes nutrition-only intervention arm compared to control as this study was also included in the combined approach analysis; *Authors indicated frailty tool was modified; SD = standard deviation, MNA = mini nutritional assessment; O = overall, I = intervention, C = control, QoL = quality of life, RCT = randomized controlled trial, F = female, M = male, N/A = not applicable

Table 2. Characteristics of the Included Studies: Combined Approach Studies

Study (author, year, ref)	Location	N	Age (y)	Gender (F/M, %)	Frailty Tool	Frailty Characteristics	Study Design	Study Length†	Intervention Nutrition Physical activity	Intensity Physical activity	Frequency Physical activity	Duration	Control	Delivery of Intervention	Outcomes
Kang, 2019	China	115	O: 77.3; I: 76.79 (7.11), 78.04 (6.82)	62/38	Fried's frailty phenotype	I: Frail: 71; C: Frail: 44	CCT	12 weeks	Fortified/ enhanced foods Muscle-strengthening	Resistance/ strength training	2x/day	30 minutes	Information about diet to maintain current weight and instructed to carry on daily exercise programs	Physical therapist	Health (and Mortality), Physical (and QoL), Mobility
Serra-Prat, 2017	Spain	172	O: 78.3; I: 77.9 (5.0); C: 78.8 (4.9)	56/44	Fried's frailty phenotype	I: Pre-frail: 80; C: Pre-frail: 92	RCT	12 months	Nutrition/ dietitian counselling Mixed	Light	4x/week	walking 30-45 min and exercises 20-25 min	Usual care	NR	Frailty, Health (and Mortality), Physical (and QoL), Mobility
Luger, 2016	Austria	80	O: 82.8 (8.0); I: 83.0 (8.1); C: 82.5 (8.0)	84/16	SHARE-FI	I (%): Pre-frail: 14; Frail: 24; Robust: 1; C (%): Pre-frail: 14; Frail: 27; Robust: 0	RCT	12 weeks	Nutrition/ dietitian counselling Muscle-strengthening	Resistance/ strength training	1x/week	NR	Visited 2x/week by "buddies"	Volunteer	Frailty, Physical (and QoL), Mobility
Kwon, 2015	Japan	89	O: 76.8; I: 76.5 (3.8), 77.0 (4.2); C: 76.9 (3.9)	100/0	Fried's frailty phenotype *	I: Pre-frail: 58; C: Pre-frail: 31	RCT	3 months	Nutrition/ dietitian counselling Muscle-strengthening	Resistance/ strength training	1x/week	60 minutes	General health education session once a month	Certified health fitness trainer	Frailty, Physical (and QoL), Mobility
Tieland, 2012	Netherlands	62	I: 78 (9); C: 79 (6)	66/34	Fried's frailty phenotype	I: Frail: 31; C: Frail: 31	RCT	24 weeks	Fortified/ enhanced foods Muscle-strengthening	Resistance/ strength training	2x/week	NR	Exercise training 2x/week and placebo supplement 2x/day	Self-supervised	Health (and Mortality), Physical (and QoL), Mobility, Diet Quality
Yamada, 2012	Japan	77	I: 74.4 (7.3); C: 75.6 (6)	51/49‡	Frailty status as certified by the LTC insurance service	I: Frail: 35; C: Frail: 35	Pilot trial	3 months	Oral nutrition supplements; Fortified/ enhanced foods Muscle-strengthening	Resistance/ strength training	3x/week	90 minutes	Both groups received exercise training	Physiotherapist	Physical (and QoL), Mobility
de Jong, 2000††	Netherlands	217	O: 79; I: 79.2 (6.1); C: 79.3 (6.6)	70/30	Required healthcare service (i.e. home care or meals-on-wheels).	I: Frail: 42; C: Frail: 37	RCT	17 weeks	Fortified/ enhanced foods Mixed	Moderate	2x/week	45 minutes	Control food and a social programme once every 2 weeks for 90 mins	Teacher (researcher supervised)	Physical (and QoL), Mobility, Diet Quality

Nykanen, 2012	Finland	159	O: 83.1 (5.1); I: 83.2 (5.2); C: 82.9 (5.0)	79/21	Cardiovascular Health study criteria *	I: Pre-frail: 47; Frail: 19; C: Pre-frail: 50; C: Frail: 21	CCT	1 year	Nutrition/ dietitian counselling Mixed	Resistance/ strength training	1x/week	NR	Usual care	Nutritionist and physiotherapist	Frailty, Diet Quality

Legend: N = Number of participants randomized at start of intervention; †Not including follow-up, if applicable; ‡Values for gender are based on reported baseline which may not equal N randomized but rather the number of participants who completed the intervention; ††Describes combined approach intervention arm compared to control as this study was also included in the nutrition analysis *Authors indicated frailty tool was modified; SHARE-FI = Frailty Instrument for Primary Care of the Survey of Health, Ageing, and Retirement in Europe, SD = standard deviation, MNA = mini nutritional assessment; O = overall, I = intervention, C = control, QoL = quality of life, RCT = randomized controlled trial, CCT = clinical controlled trial F = female, M = male, NR = not reported, LTC = long-term care

Table 3. Risk of Bias for the Included Studies

Author	SEQUENCE GENERATION	ALLOCATION CONCEALMENT	BLINDING OF OUTCOME ASSESSMENT	INCOMPLETE OUTCOME DATA	SELECTIVE REPORTING	OTHER BIAS
Nutrition Interventions						
Wu, 2018	L	U	U	L	H	H
Niccoli, 2017	U	L	U	L	L	H
Park, 2018	L	L	L	L	L	U
Ng, 2015	L	U	L	L	L	L
Kim, 2013	L	U	L	L	L	L
Tieland, 2012	L	L	L	H	L	L
Latham, 2003	L	L	L	L	L	L
de Jong, 2000	U	U	U	U	L	H
Combined Approach Interventions						
Serra-Prat, 2017	L	L	H	L	L	U
Luger, 2016	L	U	H	L	L	L
Kwon, 2015	L	U	U	L	L	L
Kang, 2019	H	U	U	L	H	H
Tieland, 2012	L	U	L	L	L	U
Nykanen, 2012	U	U	U	L	L	L
Yamada, 2012	H	U	L	L	L	L

H = high risk of bias (red); L = low risk of bias (green); U = unclear risk of bias (yellow)

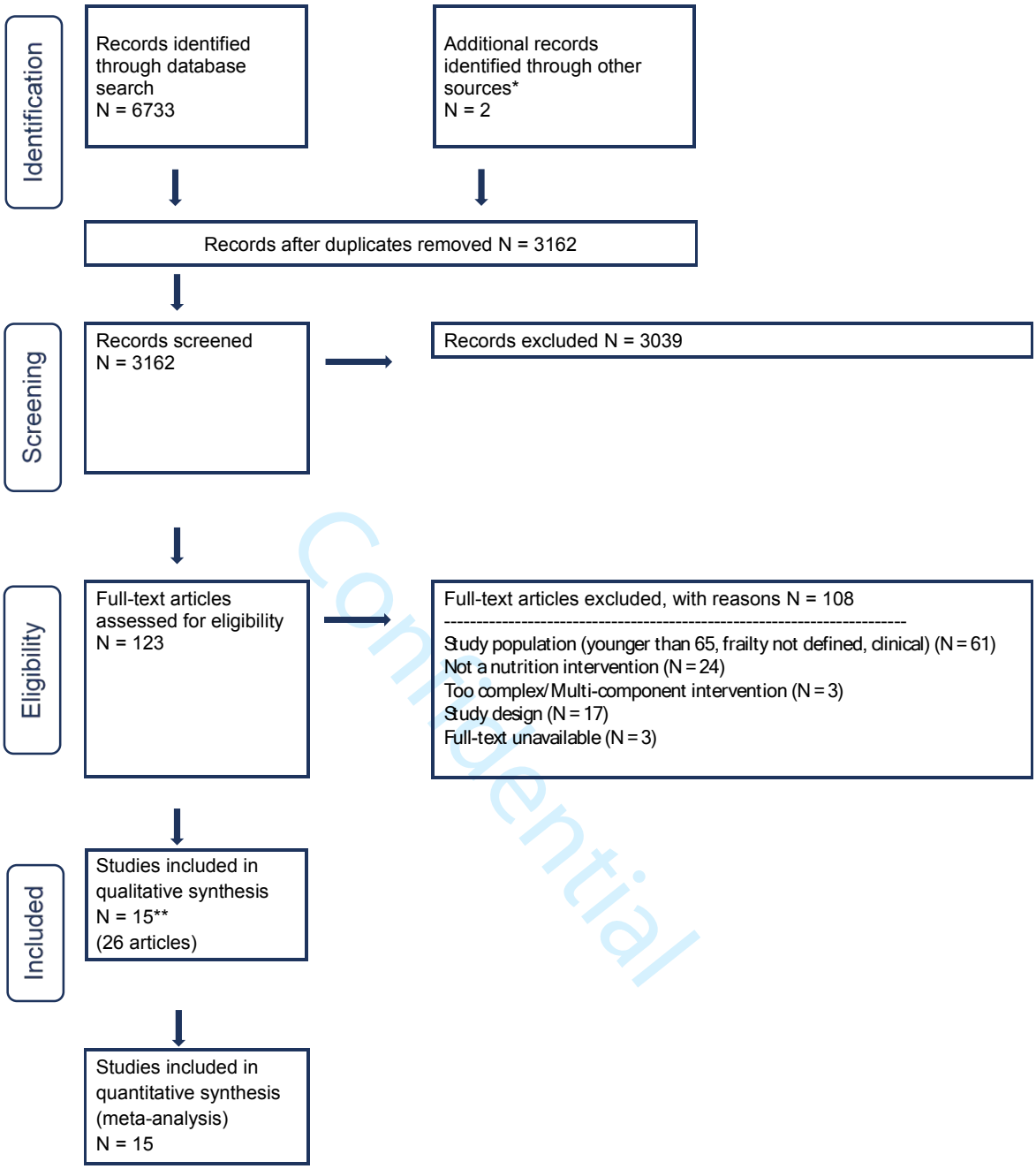


Figure 1. Study flowchart
**= identified from similar review on Physical Activity interventions in older adults with frailty*
***=1 citation with 3 articles had both a nutrition-only treatment arm and a combined approach treatment arm*

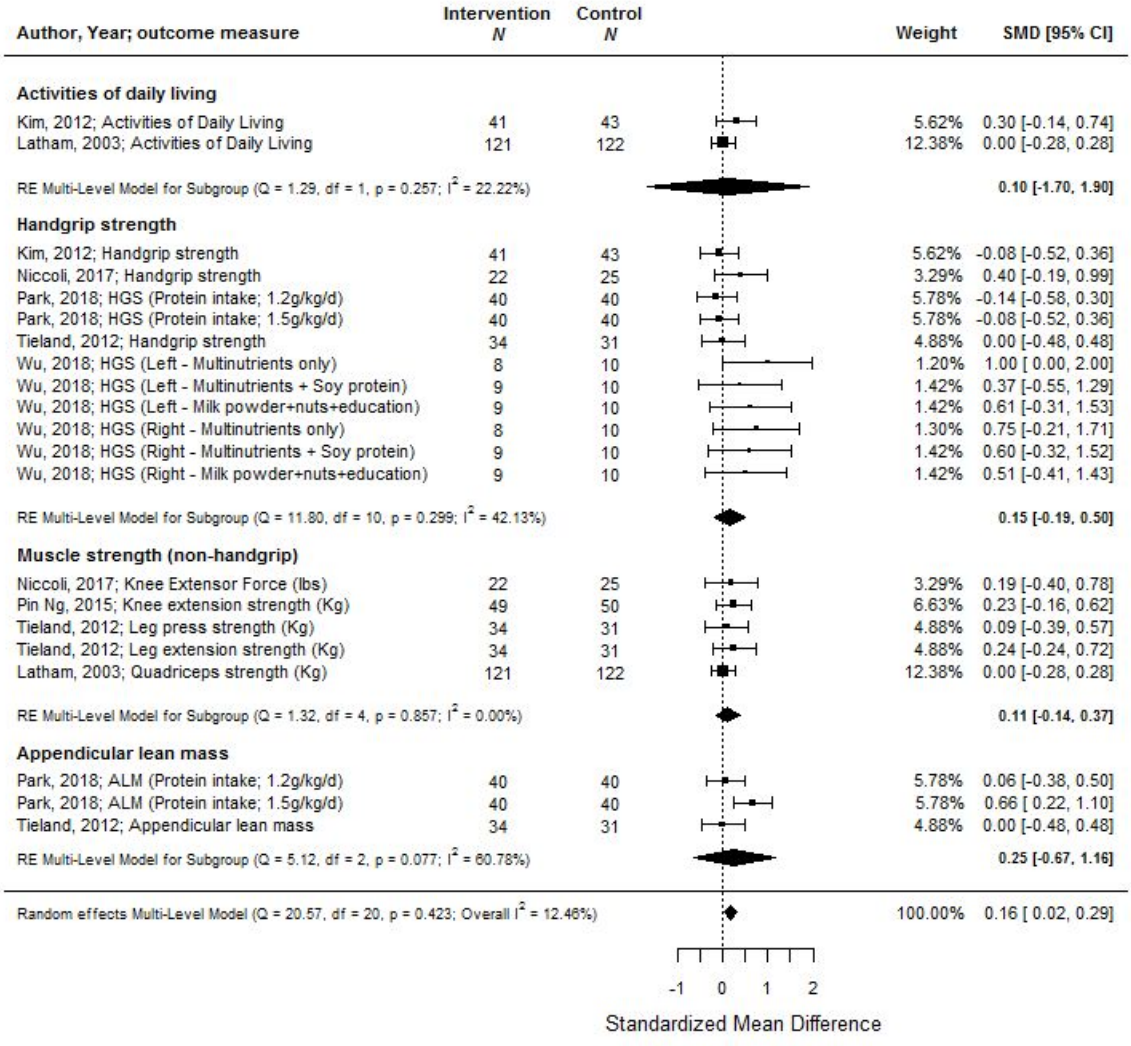


Figure 2. Effects of nutrition interventions on physical outcomes. SMD = standardized mean difference, CI = confidence interval, HGS = handgrip strength, ALM = appendicular lean mass.

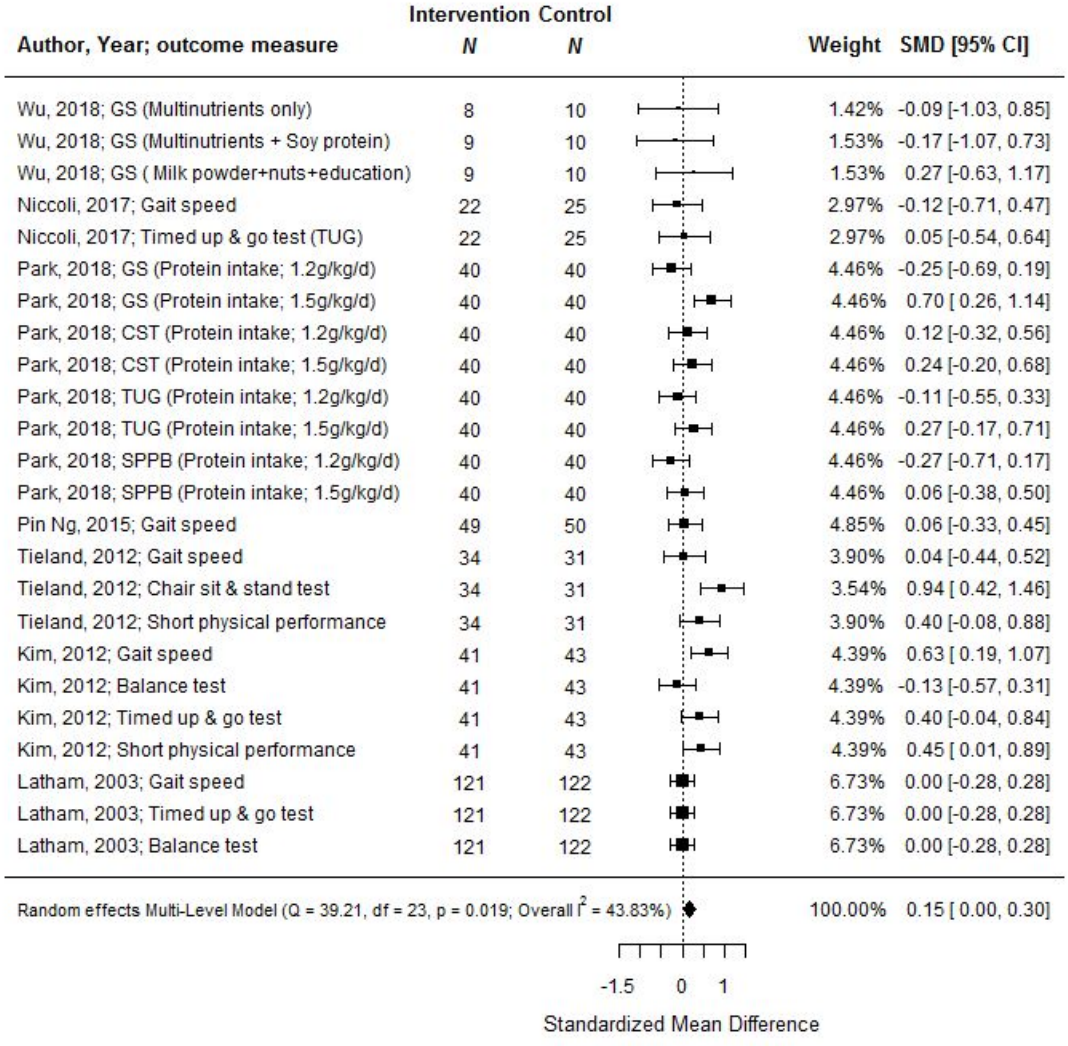


Figure 3. Effects of nutrition interventions on mobility outcomes. SMD = standardized mean difference, CI = confidence interval, GS = gait speed, CST = chair sit stand test, TUG = timed up and go test, SPPB = short physical performance battery test.

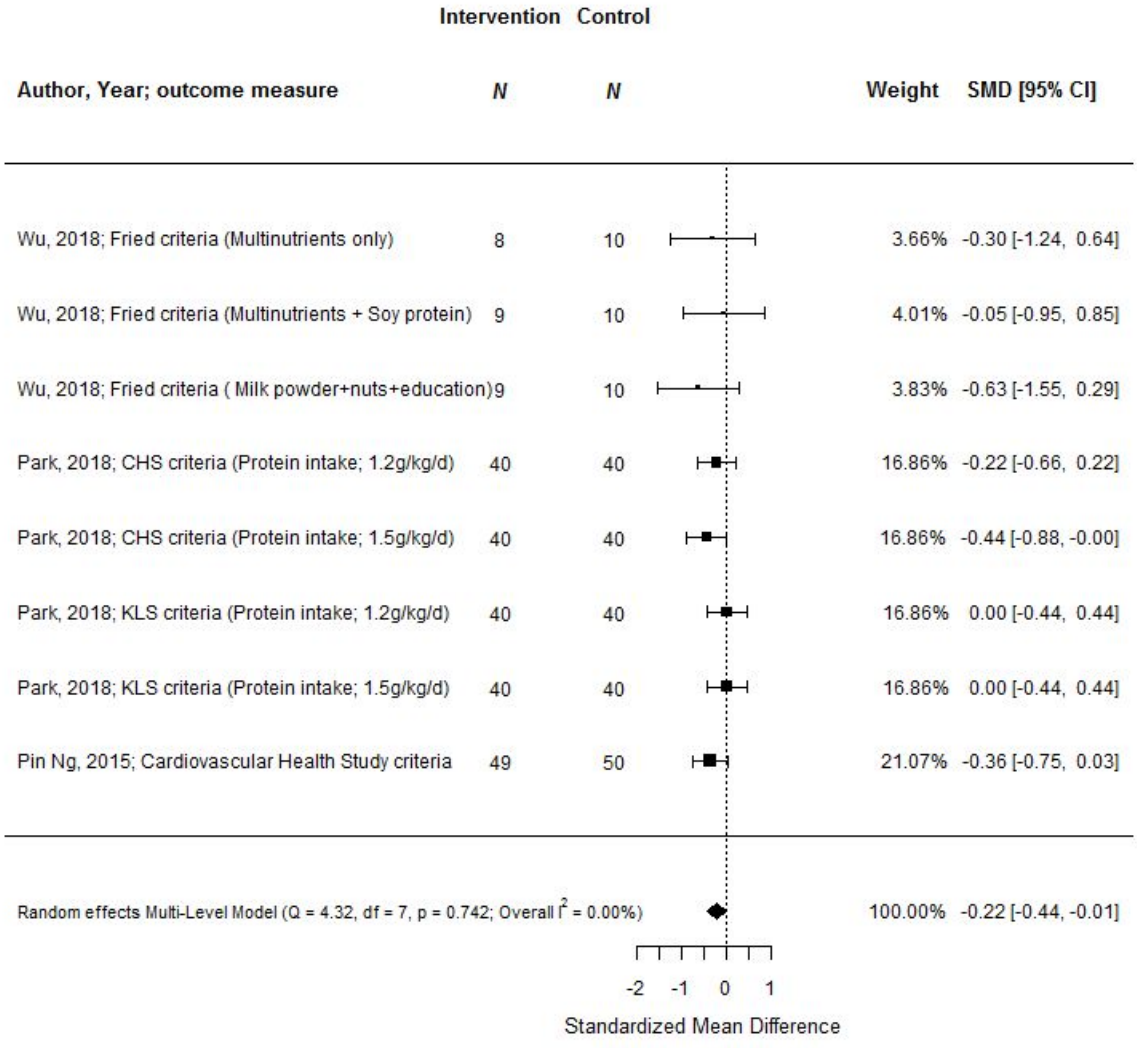


Figure 4. Effects of nutrition interventions on frailty outcomes (continuous). SMD = standardized mean difference, CI = confidence interval, CHS = cardiovascular health study, KLS = Korean longitudinal study.

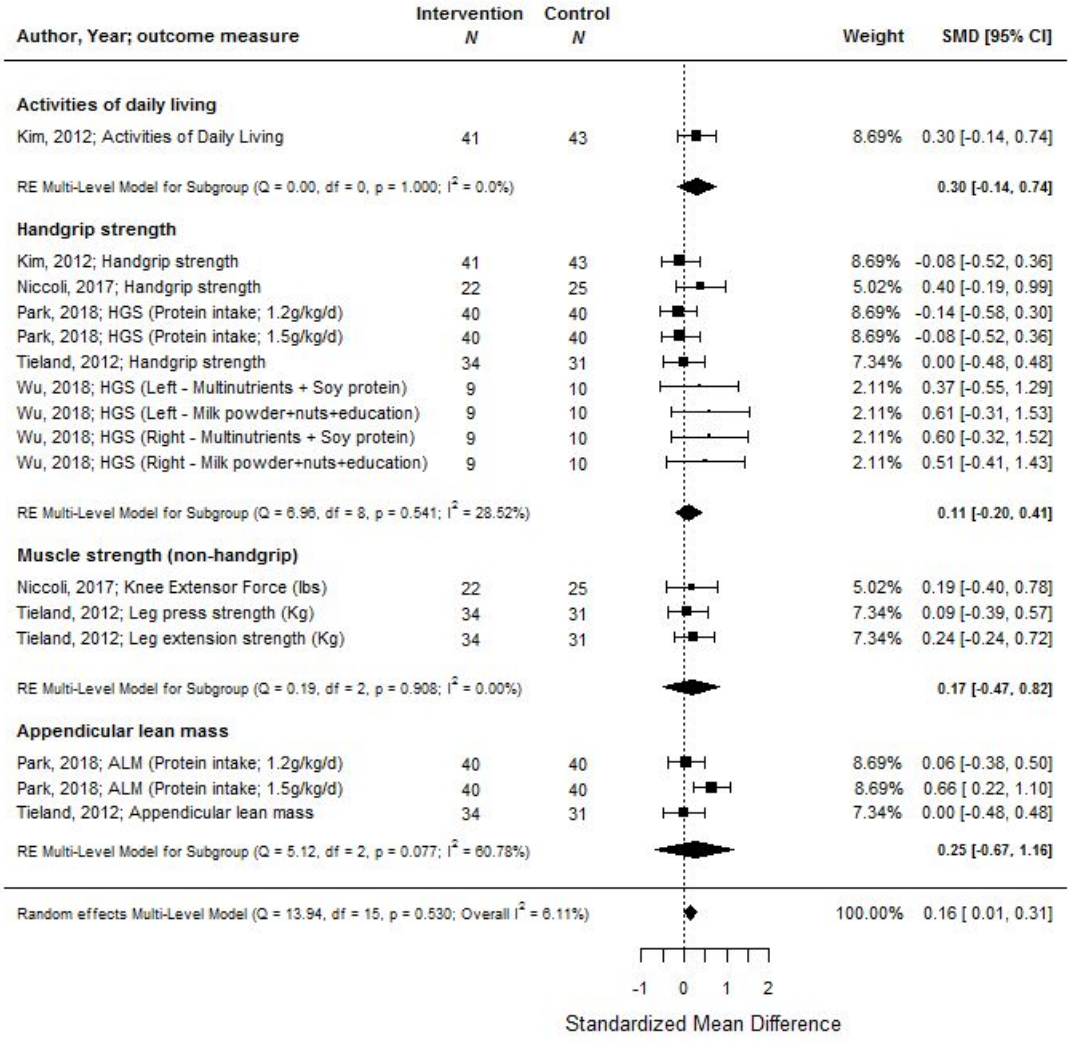


Figure 5. Effects of protein supplementation interventions on physical outcomes. SMD = standardized mean difference, CI = confidence interval, HGS = handgrip strength, ALM = appendicular lean mass.

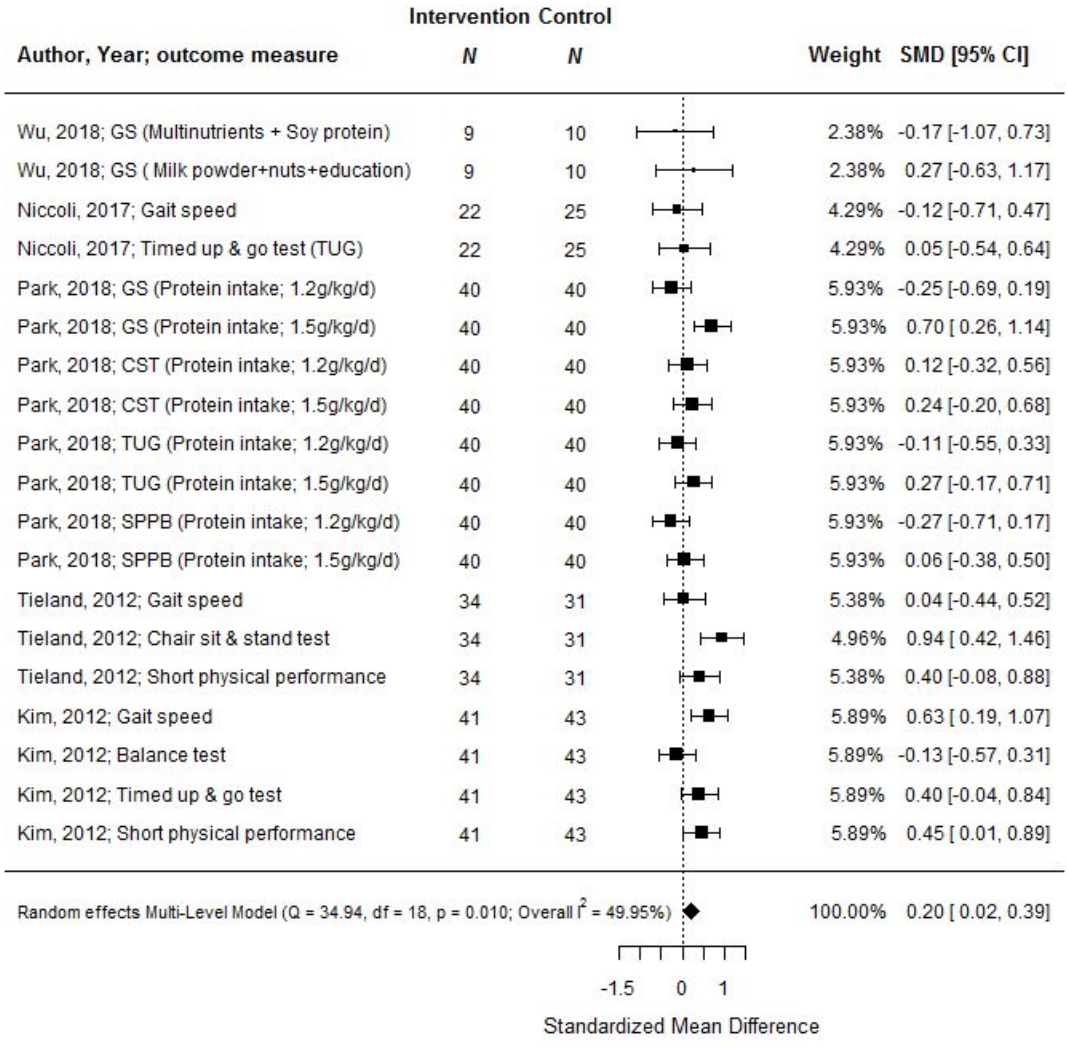


Figure 6. Effects of protein supplementation interventions on mobility outcomes. SMD = standardized mean difference, CI = confidence interval, GS = gait speed, CST = chair sit stand test, TUG = timed up and go test, SPPB = short physical performance battery test.

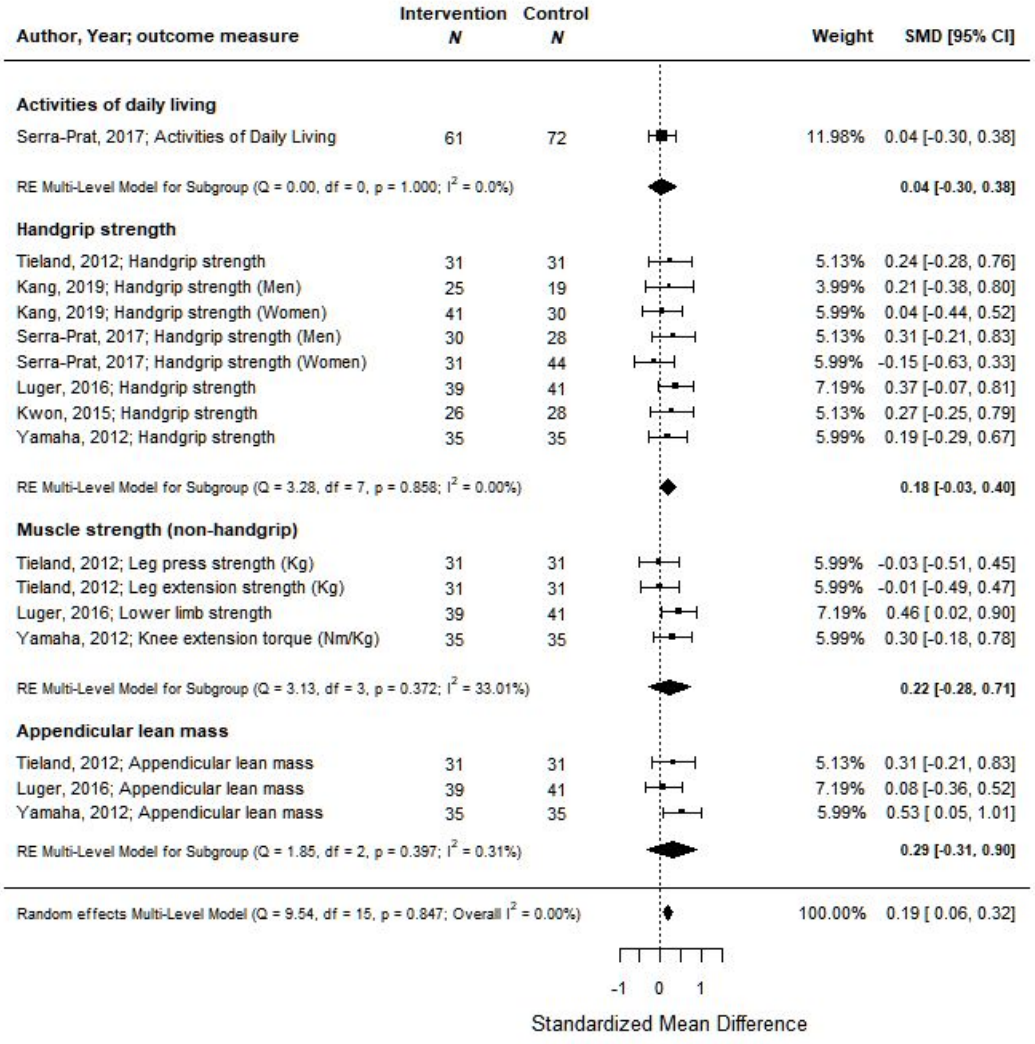


Figure 7. Effects of combined approach interventions on physical outcomes. SMD = standardized mean difference, CI = confidence interval.

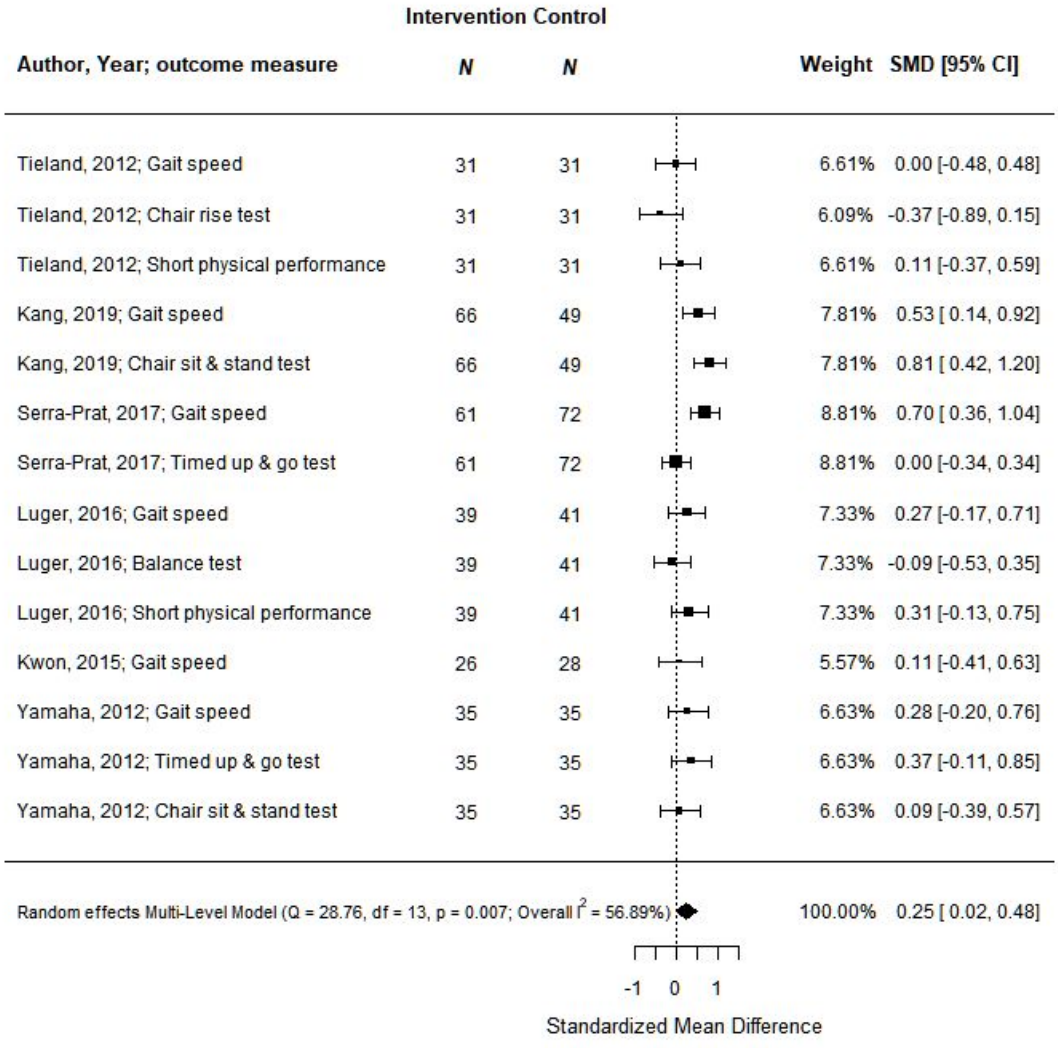


Figure 8. Effects of combined approach interventions on mobility outcomes. SMD = standardized mean difference, CI = confidence interval.

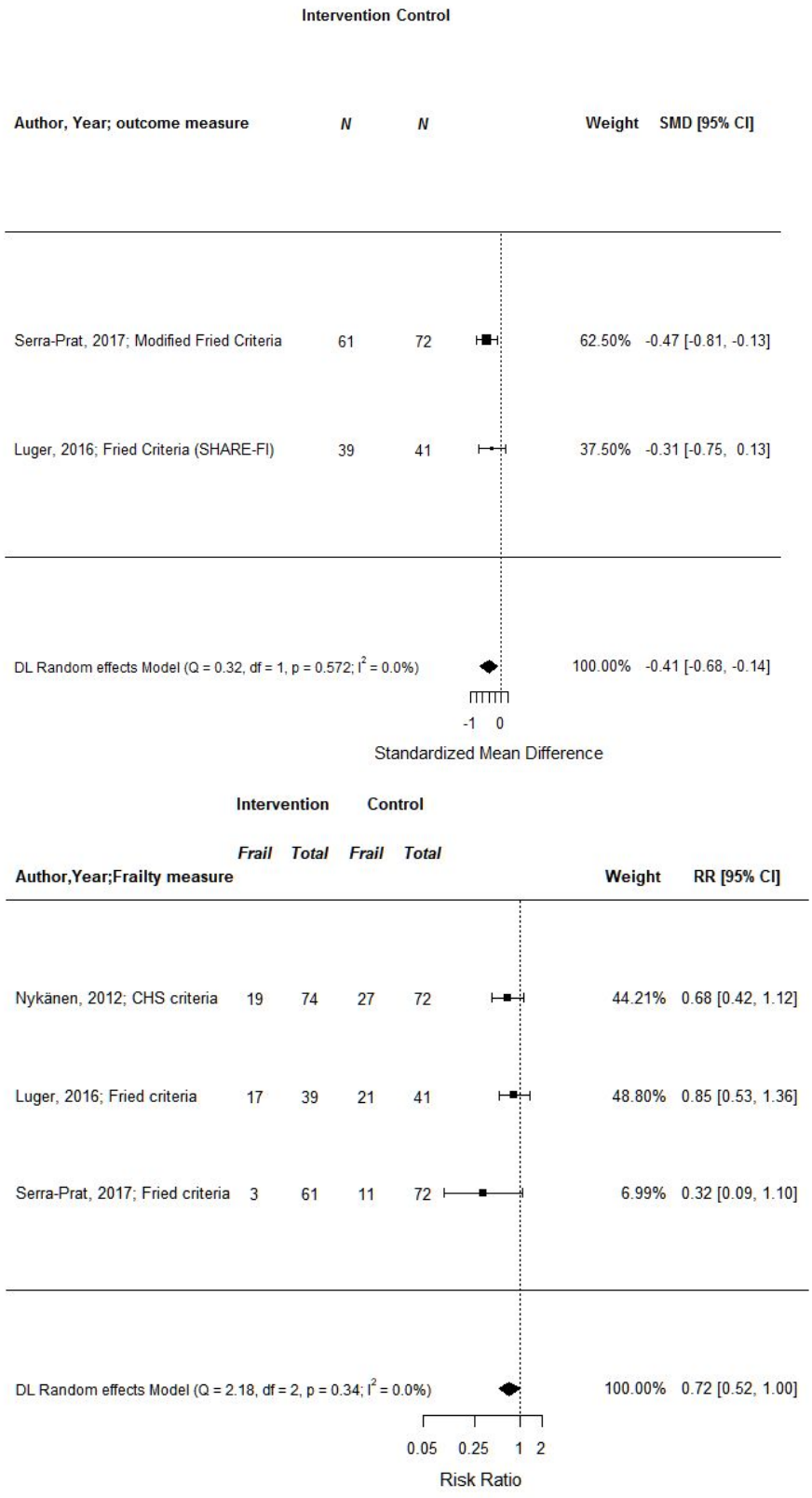


Figure 9. Effects of combined approach interventions on frailty outcomes (continuous and binary). SMD = standardized mean difference, RR = risk ratio, CI = confidence interval, CHS = cardiovascular health study.

Appendix 1: Search Strategy

FRAILTY AND NUTRITION SEARCH STRATEGIES
JUNE 2019

MEDLINE
1951 refs

1	Frail Elderly/ or Frailty/
2	frailty.tw.
3	(frail adj3 (person? or people or elderly or patient? or individual? or adult? or outpatient?)).tw.
4	or/1-3
5	exp nutrition therapy/
6	nutrition$.tw.
7	exp diet/
8	(eat or eating).tw.
9	(diet? or dietary).tw.
10	(meals or mealtime or meal time).tw.
11	or/5-10
12	4 and 11
13	animals/ not (animals/ and human/)
14	12 not 13

EMBASE
3351 refs

Database: Embase <1974 to 2019 June 10>
Search Strategy:
---
1 frail elderly/ (9392)
2 frailty/ (6812)
3 (frail adj3 (person? or people or elderly or patient? or individual? or adult? or outpatient?)).tw. (10767)
4 frailty.tw. (16350)
5 or/1-4 (28736)
6 nutrition/ or exp diet/ or exp dietary intake/ or geriatric nutrition/ or nutrition education/ or nutritional assessment/ or nutritional counseling/ or nutritional health/ (808869)
7 nutrition$.tw. (328534)
8 (eat or eating).tw. (108746)
9 (diet? or dietary).tw. (582389)
10 or/6-9 (1255505)
11 5 and 10 (3514)
12 limit 11 to human (3351)

COCHRANE
81 reviews
444 trials

ID	Search	Hits
#1	MeSH descriptor: [Nutrition Therapy] explode all trees	8720

#2 MeSH descriptor: [Diet] explode all trees 17123
#3 nutrition or eat or eating or diet* or meal* 121080
#4 #1 or #2 or #3 122560
#5 MeSH descriptor: [Frailty] explode all trees 29
#6 MeSH descriptor: [Frail Elderly] explode all trees 659
#7 frail NEAR/3 (person? or people or elderly or patient? or individual? or adult? or outpatient?) 1907
#8 frail* 3135
#9 #5 or #6 or #7 or #8 3135
#10 #4 and #9 537

CINAHL
882 refs

S12 S4 AND S11
S11 S5 OR S6 OR S7 OR S8 OR S9 OR S10
S10 TI (meals or mealtime or meal time) OR AB (meals or mealtime or meal time)
S9 TI nutrition* OR AB nutrition*
S8 TI (diet# or dietary) OR AB (diet# or dietary)
S7 TI (eat or eating) OR AB (eat or eating)
S6 (MH "Diet Therapy+") Search modes - Boolean/Phrase
S5 (MH "Nutrition") OR (MH "Diet+") OR (MH "Geriatric Nutrition")
S4 S1 OR S2 OR S3
S3 TI (frail N3 (person# or people or elderly or patient# or individual# or adult# or outpatient#)) OR AB (frail N3 (person# or people or elderly or patient# or individual# or adult# or outpatient#))
S2 (MH "Frail Elderly")
S1 (MH "Frailty Syndrome")

Appendix 2: Data Analysis Plan

Nutrition and Combined Approach Meta Analysis

Data will be analysed for each intervention category by outcome category. Intervention categories and outcomes are outlined in the lists below. Figure 1 contains the intervention category and the corresponding data found within each intervention category. Not every outcome was found within each intervention category.

Nutrition Intervention Category

1. Overall Nutrition interventions
2. Protein Supplementation interventions
3. Combined Approach interventions

Outcomes (by broad category)

1. Health (and mortality)
2. Physical
3. Quality of Life
4. Health Service Use
5. Frailty
6. Mobility
7. Diet Quality
8. Social/Caregiver

CFN NUTRITION AND COMBINED APPROACH PREDICTED DATA ANALYSIS
**meta analysis forest plots and GRADE tables for each of the following*

Intervention Type	Data Extracted for Outcome
Nutrition Interventions (overall)	Health
	Physical
	Quality of Life
	Frailty
	Mobility
	Diet Quality
Protein Supplementation Nutrition Interventions	Health
	Physical
	Frailty
	Mobility
	Diet Quality
Combined Approach (overall)	Health
	Physical
	Quality of Life
	Frailty
	Mobility
	Diet Quality

*Predicted total of 17 Forest Plots and GRADE Tables.

Appendix 3: Characteristics of Included Studies Tables

Dietary education with customised dishware and food supplements can reduce frailty and improve mental well-being in elderly people: A single-blind randomized controlled study. Wu et al.	
Study (Year Published)	2018
Country	Taiwan
Objective/purpose	Compared the effects of supplementation with multiple micronutrients and/or protein powders, and those of a diet followed the recommendations in Taiwan's Daily Food Guide on frailty and mental health in prefrail and frail elderly people.
Study Design	Single-blind, randomised controlled trial.
Recruitment setting and/or recruitment methods	From November 2014 to April 2015, participants aged ≥ 65 years were recruited at Miaoli General Hospital, Miaoli City, Taiwan, through poster advertisements or physician referral.
Inclusion Criteria/Exclusion Criteria	Candidates without severe disease (e.g. cancers under treatment, immobilization, or severe arthritis), diagnosed dementia, mental illness, or an inability to communicate were subjected to a simplified geriatric assessment conducted using a modified version of the L. Fried criteria for identifying individuals at the prefrail to frail stage.
Frailty index used *Include if modified (y/n) and how*	Fried's Frailty Phenotype. (Y). Modifications made to the following criteria: Weight loss, self-described exhaustion, weak grip strength, slow gait speed, low physical activity.
Total sample n (number invited)	40
Intervention n (number invited)	30
Control n (number invited)	10
Loss to follow-up: I n (%); C n (%)	I: 4 (13.3), C: 0 (0)
Age	Mean age overall (SD): 74 years (NR) Mean age intervention (SD): 73.5 (2.4) years, 75.0 (2.4) years, 72.8 (1.6) years Mean age control (SD): 75.9 (1.7) years
Gender: I n (%); C n (%)	Female: I: 16 (61.5), C: 4 (40.0) Male: I: 10 (38.5), C: 6 (60.0)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	Education level at junior school and above, n (%): I: 3 (37.5), 4 (44.4), 2 (22.2) C: 3 (30)
Co-morbidities/chronic conditions	Clinical Profile, n (%): Hypertension: I: 6 (75), 5 (55.6), 6 (66.7); C: 6 (60) Diabetes: I: 3 (37.5), 2 (22.2), 3 (33.3); C: 2 (20)
Smoking Status	n (%):

	I: 1 (12.5), 1 (11.1), 0 (0); C: 1 (10)
BMI	Overall Mean (SD): 26 (NR) kg/m^2 Intervention Mean (SD): 25.5 (0.9) kg/m^2, 25.5 (1.1) kg/m^2, 28.4 (1.2) kg/m^2 Control Mean (SD): 24.6 (1.1) kg/m^2
Description of Intervention	Multinutrient: Daily Food Guide education leaflet and 1.3 g/d multivitamin & mineral powder. Multinutrient and soy protein: Daily Food Guide education leaflet, 1.3 g/d of multivitamin & mineral powder, and 16 g/d of isolated soy protein powder. Nutrition education, customised dishware, and food supplement: Participants received two sessions of individualised nutrition education from a licensed dietitian (at baseline and one month follow-up). The objective of the provided education was to help the participants consume a nutritious diet with the appropriate distribution of the six food groups and achieve the recommended dietary allowance level of nutrients. 10 g/d of mixed nuts (cashews, pumpkin seeds, walnuts, macadamia, pine nuts, and almonds) and 25 g/d of milk powder (skimmed with calcium added). The measuring dishware set comprised a four-compartment divided plate, a bowl, a mug, and a spoon. The objective was for the participant to fill the designated space on the plate with protein-rich foods and vegetables to consume the appropriate amounts of each. The bowl, mug, and spoon similarly assisted the participants with gauging the correct amounts of rice and fruits, dairy, and nuts and seeds. Food supplements were provided because the Daily Food Guide recommends consuming one to two serving(s) of low-fat dairy products (one serving is 240 cc. of milk or 25 g of milk powder) and one serving (approximately 10 g) of nut and seeds per day, the intake of which was low among elderly people in Taiwan. Intervention was three months in duration.
Type of intervention	Oral nutrition supplements, Fortified/enhanced foods, Nutrition/dietitian counselling.
Description of Control	Participants received the Daily Food Guide leaflet.
Length of Follow-Up	Post intervention (three months).
Serious adverse events	NR
Funding Source	Sustainability Project Grant, Academia Sinica, Taipei, Taiwan.

Whey Protein Supplementation Improves Rehabilitation Outcomes in Hospitalized Geriatric Patients: A Double Blinded, Randomized Controlled Trial. Niccoli et al.	
Study (Year Published)	2017
Country	Canada
Objective/purpose	Tested the efficacy of a leucine-rich protein supplementation from a whey source in promoting higher protein intake in hospitalized patients enrolled in daily geriatric rehabilitative care.
Study Design	Double-blinded randomized controlled trial.
Recruitment setting and/or recruitment methods	Participants aged greater than 60 years were recruited from the Geriatric Assessment and Rehabilitative Care (GARC) Program at St. Joseph's Care Group (SJCG), Thunder Bay, Ontario, Canada.
Inclusion Criteria/Exclusion Criteria	Inclusion: Men and women aged > 60 years. Ability to perform the functional tests (with or without the use of an assistive device). Willing to give informed consent to be randomized to either the protein supplement or standard of care group and willing to follow the study protocol. Exclusion: New York Heart Association Class III or IV congestive heart failure, clinically significant aortic stenosis, history of cardiac arrest, use of a cardiac defibrillator, or uncontrolled angina. Lung disease requiring either oral or injected steroids, or the use of supplemental oxygen. Modified Mini-Mental State (3MS) < 70. Severe arthritis (either osteoarthritis or rheumatoid arthritis). Cancer requiring treatment in the past three years. Parkinson's disease or other serious neurological disorders; renal disease requiring dialysis; other illness of such severity that life expectancy is considered to be less than 12 months. Current diagnosis of schizophrenia, other psychotic disorders, or bipolar disorder. Current consumption of more than 14 alcoholic drinks per week. Clinical judgment concerning participant safety or noncompliance.
Frailty index used *Include if modified (y/n) and how*	Fried's Frailty Phenotype.
Total sample n (number invited)	53
Intervention n (number invited)	27
Control n (number invited)	26
Loss to follow-up: I n (%); C n (%)	I: 3 (11); C: 1 (4)
Age	Mean age overall (SD): 81.3 (1.0) years Mean age intervention (SD): 81.77 (1.68) years Mean age control (SD): 80.33 (1.57) years
Gender: I n (%); C n (%)	Female: I: 15 (68.2); C: 17 (68.0) Male: I: 7 (31.8); C: 8 (32.0)
Race/Ethnicity	NR

SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	NR
Smoking Status	NR
BMI	Intervention Mean (SD): 24.2 (5.2) kg/m^2 Control Mean (SD): 26.4 (6.6) kg/m^2
Description of Intervention	All subjects in the whey protein supplementation group received an oral dietary product containing 24 g of whey protein per day in addition to their usual diet. The whey protein supplement was mixed into the participant's hot cereal (9 g at breakfast) and milk products (7.5 g/drink at lunch and dinner) throughout each day. Throughout the study, all participants took part in their prescribed rehabilitation program.
Type of intervention	Fortified/enhanced foods
Description of Control	The control group participants received the hot cereal and milk products without the whey protein supplement.
Length of Follow-Up	Post intervention (length of hospital stay was approximately 3-4 weeks; I: 26.51 (3.65) days; C: 20.93 (3.02) days).
Serious adverse events	NR
Funding Source	Northern Ontario Academic Medical Association.

Protein supplementation improves muscle mass and physical performance in undernourished prefrail and frail elderly subjects: a randomized, double-blind, placebo-controlled trial. Park et al.	
Study (Year Published)	2018
Country	Korea
Objective/purpose	Investigated a dose-dependent effect of protein supplementation on muscle mass and frailty in prefrail or frail malnourished elderly people. To investigate the hypothesis that protein intake of 1.2 g protein/kg/d and 1.5 g protein/kg/d increases muscle mass and physical performance dose dependently in prefrail or frail community-dwelling elderly people at risk of malnutrition.
Study Design	Randomized, double-blind, placebo-controlled, three-parallel-group trial.
Recruitment setting and/or recruitment methods	Recruited consecutively at four welfare centers in Soel, Korea between May 2016 and August 2017.
Inclusion Criteria/Exclusion Criteria	Inclusion: Participants aged 70–85 years. Prefrail or frail (Prefrailty and frailty were defined as meeting ≥1 and ≥3 of modified Cardiovascular Health Study frailty criteria, respectively). At risk of malnutrition (defined as Mini Nutritional Assessment score ≤23.5). Exclusion: Participants with comorbidities such as kidney or liver failure, if they were participating in another clinical trial. Unable to walk. Unable to communicate. During the screening visit, Cardiovascular Health Study frailty criteria, the Mini Nutritional Assessment, demographic and medical information, BMI, and three day dietary intake were measured.
Frailty index used *Include if modified (y/n) and how*	Fried's Frailty Phenotype. (Y). Modified Cardiovascular Health Study frailty criteria included unintentional weight loss ≥4.5 kg during the last year, exhaustion, low physical activity, slowness, and low handgrip strength.
Total sample n (number invited)	120
Intervention n (number invited)	40; 40
Control n (number invited)	40
Loss to follow-up: I n (%); C n (%)	I: 7 (17.5), 8 (20); C: 6 (15)
Age	Mean age intervention (SD): 77.30 (3.67) years, 76.80 (3.70) years Mean age control (SD): 76.83 (3.86) years
Gender: I n (%); C n (%)	Female: I: 26 (65.0), 28 (70.0); C: 24 (60.0) Male: I: 14 (35.0), 12 (30.0); C: 16 (40.0)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	Medical history, Intervention groups (1.2 g protein/kg/d and 1.5 g protein/kg/d) n (%); Control n (%):

	Hypertension: 28 (70), 23 (58); 22 (55) Hyperlipidemia: 10 (25), 8 (20); 7 (18) Diabetes: 18 (45), 9 (23); 11 (28) Osteoporosis: 2 (5), 7 (18); 7 (18) Arthritis: 5 (13), 5 (13); 2 (5)
Smoking Status	NR
BMI	Intervention Mean (SD): 24.16 (3.04), 23.65 (2.53) kg/m^2 Control Mean (SD): 24.16 (33.82*) kg/m^2
Description of Intervention	Eligible participants were randomly assigned to one of three groups: 0.8, 1.2, or 1.5 g protein/kg/d in the ratio of 1:1:1 for the 12-week trial. Participants were asked to maintain their usual diet and physical activity during the 12-week intervention. All participants were provided a total of 5 × 10-g packs containing placebo or protein powders. Protein powder contained 0.5 g fat, 0.2 g cocoa powder, and 9.3 g whey protein/10-g pack, whereas placebo powder contained 0.5 g fat, 0.2 g cocoa powder, and 9.3 g maltodextrin/10-g pack. Both protein and placebo powders contained 200 kcal/d and were provided with 340 mL of corn silk tea. The 0.8 g protein/kg/d group consumed only placebo powder, and the 1.2 and 1.5 g protein/kg/d protein groups consumed a combination of protein and placebo powder based on their usual intake of protein estimated by three days of 24-hour recall during screening. Participants in both the 1.2 and 1.5 g protein/kg/d groups received an individually adjusted amount of protein powder to fulfill 1.2 or 1.5 g protein/kg/d. Placebo and protein supplements were provided at weeks 0, 6, and 12.
Type of intervention	Fortified/Enhanced Foods
Description of Control	Participants were asked to maintain their usual diet and physical activity during the 12-week intervention. All participants were provided a total of 5 × 10-g packs containing placebo powders. Placebo powder contained 0.5 g fat, 0.2 g cocoa powder, and 9.3 g maltodextrin/10-g pack. Powder contained 200 kcal/d and were provided with 340 mL of corn silk tea. The 0.8-g protein/kg/d group consumed only placebo powder.
Length of Follow-Up	Post intervention (12 weeks)
Serious adverse events	No harmful adverse effects were observed.
Funding Source	Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), Ministry of Health & Welfare, Republic of Korea.

*Suspected data error in publication

Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal Among Older Adults: A Randomized Controlled Trial. Ng et al.	
Study (Year Published)	2015
Country	Singapore
Objective/purpose	Compared the effects of six-month interventions with physical exercise, nutritional supplementation, cognitive training, and a combination of these interventions with usual care control in reducing frailty among community-dwelling older persons.
Study Design	Randomized controlled trial.
Recruitment setting and/or recruitment methods	Potential participants were identified from among community residents in the southwest region of Singapore through door-to-door open invitation from October 2009 to August 2012.
Inclusion Criteria/Exclusion Criteria	Inclusion: Prefrail and frail older adults were identified based on five Cardiovascular Health Study criteria defining physical frailty. Prefrail or frail older adults were eligible for the trial if they were aged 65 years and above, able to ambulate without personal assistance, and living at home. Exclusion: Significant cognitive impairment (Mini Mental State Examination score 23); major depression; severe audiovisual impairment; any progressive, degenerative neurologic disease; terminal illness with life expectancy <12 months; were participating in other interventional studies; or were unavailable to participate for the full duration of the study.
Frailty index used *Include if modified (y/n) and how*	Cardiovascular Health Study criteria.
Total sample n (number invited)	246
Intervention n (number invited)	49
Control n (number invited)	50
Loss to follow-up: I n (%); C n (%)	10 (8); 6 (8)
Age	Mean age overall (SD): 70.0 (4.7) Mean age intervention (SD): 69.7 (4.23) Mean age control (SD): 70.1 (5.02)
Gender: I n (%); C n (%)	Female: I: 32 (65.0); C: 28 (56.0) Male: I: 17 (35.0); C: 22 (44.0)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	Education level, n (%): No formal schooling: I: 13 (26.5); C: 10 (20.0) Primary school: I: 20 (40.8); C: 29 (58.0) Secondary or higher: I: 16 (32.7); C: 11 (22.0)
Co-morbidities/chronic conditions	≥ Five medical comorbidities, n (%): I: 0 (0); C: 2 (4)
Smoking Status	NR
BMI	Intervention Mean (SD): 24.0 (4.31) kg/m^2

	Control Mean (SD): 23.6 (3.35) kg/m^2
Description of Intervention	Eligible participants were allocated randomly into one of five interventions of 24 weeks duration each: nutritional supplementation, cognitive training, physical training, combination treatment, and usual care control. Nutritional Intervention. Each participant was provided a commercial formula (Fortisip Multi Fibre), iron and folate supplement, vitamin B6 and vitamin B12 supplement, and calcium and vitamin D supplement taken daily for 24 weeks, which was designed to augment caloric intake by about 20% and provide about one third of the recommended daily allowances of vitamins and minerals. Given the variability in individual energy requirements, participants were encouraged to attain the maximal tolerable energy intake to gain 0.5 kg per week. Both the active supplement and the control were administered by interventional nurses who had no knowledge of the participant's assignment status. Fortisip Multi Fibre is a 200-mL liquid formula, supplying 300 kcal in the form of carbohydrate (49%), fat (35%), protein (35%), and dietary fiber (4.6 g per 200 mL). One capsule of Sangobion contains 1 mg folate and 29 mg iron; one tablet of Neuroforte contains 200 mg of vitamin B12 and 200 mg of vitamin B6; and one tablet of Caltrate with vitamin D contains 200 IU vitamin D and 600 mg of calcium.
Type of intervention	Oral nutrition supplements. Fortified/enhanced foods.
Description of Control	Control Group. Participants had access to one standard care from health and aged care services that were normally available to older people, including primary and secondary level care from government or private clinics and hospitals, and community-based social, recreational, and daycare rehabilitation services. They were given an equal volume of artificially sweetened, vanilla-flavored liquid (ingredients: non-dairy creamer, liquid caramel, sugar, and water), two capsules and one tablet (ingredients: cornstarch, lactose, magnesium stearate) that were identical in appearance to the active nutritional supplements, with instructions not to replace their meals with the supplements. Both the active supplement and the control were administered by interventional nurses who had no knowledge of the participant's assignment status.
Length of Follow-Up	Six months
Serious adverse events	Two subjects who participated in exercise training had joint pain (hip and knee) initially that was relieved after adjusting training regimen. No other adverse events occurred during the study.
Funding Source	National Medical Research Council.

Preventive Effect of Protein-Energy Supplementation on the Functional Decline of Frail Older Adults with Low Socioeconomic Status: A Community-Based Randomized Controlled Study. Kim et al.	
Study (Year Published)	2013
Country	South Korea
Objective/purpose	Evaluate whether protein-energy supplementation can prevent functional decline in frail older adults of low socioeconomic status (SES).
Study Design	Randomized controlled trial.
Recruitment setting and/or recruitment methods	Study participants were recruited from the National Home Healthcare Services (NHHS) registration database in Gangbuk-gu, Seoul, South Korea from April to June 2011. Registration for NHHS is limited by family income level, so only those below 120% of the national absolute poverty line qualify for the service (ie, $572/month for a one-person household, $974/month for a two-person household, and $1260/month for a three-person household).
Inclusion Criteria/Exclusion Criteria	Inclusion: Older adults aged 65 years and older who could not walk a 3-m course within 5 seconds at their usual pace were identified. A trained physiotherapist re-examined the test and a research dietitian performed a nutritional assessment for each eligible subject using a standardized procedure. Using this process, the researchers selected the study participants who met the frailty criteria (Participants were considered frail if their UGS was less than 0.6 m/second and if they scored less than 24 points on the Mini Nutritional Assessment (MNA)). Exclusion: Study subjects who were participating in any kind of exercise program or clinical nutrition program were excluded. Participants who were ordered to restrict a high-protein diet by an internist (ie, for liver failure or severe renal failure) were also excluded. Participants who are unable to walk or are too functionally deteriorated to receive home health care services are automatically transferred to the National Long-Term Care Service; thus, all eligible subjects were able to walk inside a room, at a minimum
Frailty index used *Include if modified (y/n) and how*	Slow gait speed and MNA score
Total sample n (number invited)	87
Intervention n (number invited)	43
Control n (number invited)	44
Loss to follow-up: I n (%); C n (%)	6 (14); 1 (2)
Age	Mean age intervention (SD): 78.9 (5.5) Mean age control (SD): 78.4 (6.0)
Gender: I n (%); C n (%)	Female: I: 34 (79.1); C: 35 (79.6) Male: I: 9 (20.9); C: 9 (20.4)
Race/Ethnicity	NR

SES status *(reported by income or education level ONLY)*	Education level, n (%): ≤6 years (elementary school): I: 30 (69.8); C: 35 (79.6)
Co-morbidities/chronic conditions	Number of chronic diseases, median (inter-quartile range): I: 5 (3, 6); C: 3 (2, 5)
Smoking Status: I n (%); C n (%)	3 (7.0); 7 (15.9)
BMI	NR
Description of Intervention	Each participant in the intervention group was provided with two 200-mL cans of commercial liquid formula per day for 12 weeks. Using this nutritional supplement, the researchers were able to offer an additional 400 kcal of energy, 25g of protein, 9.4g of essential amino acids (60.2% leucine), 56g of carbohydrate, 9g of lipid, 400mL of water, and micronutrients (vitamin A, 0.3mg; thiamin, 0.42mg; riboflavin B2, 0.6mg; pyridoxine, B6 0.6mg; vitamin B12, 0.96 µg; vitamin C, 40mg; vitamin D3, 2 µg; vitamin E, 4mg; vitamin K1, 30 µg; folate, 0.16mg; niacin, 6.4mg; biotin 12 µg; pantothenic acid, 2mg; choline, 146mg; L-carnitine, 40mg; taurine, 40mg; calcium, 280mg; phosphorus, 280mg; magnesium, 88mg; zinc, 4mg; iron, 4mg; iodine, 60 µg; and copper, 0.32mg) per day. Compliance was measured every 2 weeks during a home visit by the research dietitian. At that time, the participants were clearly instructed not to replace their usual meal with the liquid supplement; rather, they were encouraged to use the supplement to increase overall food intake.
Type of intervention	Oral nutrition supplements. Fortified/enhanced foods.
Description of Control	Participants in the control group did not receive any treatment or counseling during the study period. To control for any effect of greater attention to one group, the same research dietitian visited the participants in the control group and gave a small gift every month. During the study period, home healthcare services provided by NHHS workers were suspended.
Length of Follow-Up	Post intervention (12 weeks)
Serious adverse events	Among the participants in the intervention group, three (7%) complained of dyspepsia and three (7%) experienced acute illness, so they withdrew prematurely. The serum level of blood nitrogen urea in the intervention group was increased significantly by 2.0±4.8mg/dL (minimum, −10.8mg/dL; maximum, 17.1mg/dL; paired t test, p = 0.011). However, estimated creatinine clearance increased significantly by 2.5±6.5mL/min (minimum, −9.1mL/min; maximum, 19.5mL/min; paired t test, p = 0.018).
Funding Source	Health Promotion Fund, Ministry of Health & Welfare, Republic of Korea

Protein supplementation improves physical performance in frail elderly people: a randomized, double-blind, placebo-controlled trial. Tieland et al.	
Study (Year Published)	2012
Country	Netherlands
Objective/purpose	Assessed the impact of 24 weeks of dietary protein supplementation on muscle mass, strength, and physical performance in frail elderly people.
Study Design	Randomized, double-blind, placebo-controlled trial.
Recruitment setting and/or recruitment methods	Subjects 65 years or older were recruited from an existing database of subjects, through distribution of information flyers, and by local information meetings organized between December 2009 and October 2010.
Inclusion Criteria/Exclusion Criteria	Inclusion: Age ≥ 65 years old and being pre-frail or frail according to the criteria from Fried et al. The five criteria to define frailty were as follows: unintentional weight loss, weakness (low handgrip strength), self-reported exhaustion, slow walking speed, and low physical activity. Pre-frailty was classified when one or two of these criteria were present, and frailty was classified when three or more criteria were present. Exclusion: Individuals with diabetes mellitus type I or II (as measured by a fasted plasma glucose level ≥ 7.0 mmol/L), cancer, chronic obstructive pulmonary disease, participation in any structured exercise training program in the past two years, and/or renal insufficiency (estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2).
Frailty index used *Include if modified (y/n) and how*	Fried Frailty Phenotype.
Total sample n (number invited)	65
Intervention n (number invited)	34
Control n (number invited)	31
Loss to follow-up: I n (%); C n (%)	I: 4 (6.2); C: 4 (6.2)
Age	Mean age overall (SD): 83.1 (5.1) Mean age intervention (SD): 78 (1) years Mean age control (SD): 81 (1) years
Gender: I n (%); C n (%)	Female: I: 20 (59); C: 16 (52) Male: I: 14 (41); C: 15 (48)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	Education, Low/Middle/High (%): I: 9/59/32 C: 0/55/45
Co-morbidities/chronic conditions	NR
Smoking Status	Protein, n (%) = 5 (15), Placebo, n (%) = 1 (3)
BMI	Overall Mean (SD): 26.2 (5.1) kg/m^2

	Intervention Mean (SD): 27.0 (0.6) kg/m^2 Control Mean (SD): 26.2 (0.6) kg/m^2
Description of Intervention	24-week duration. 250-mL protein-supplemented beverage that contained 15 g protein (milk protein concentrate [MPC80], 7.1 g lactose, 0.5 g fat, and 0.4 g calcium). The subjects consumed one beverage after breakfast and one beverage after lunch. All beverages were provided in non-transparent packages and were vanilla flavored to mask the contents of the drinks.
Type of intervention	Fortified/enhanced foods.
Description of Control	Matching 250-mL placebo beverage that contained no protein, 7.1 g lactose, and 0.4 g calcium. The subjects consumed one beverage after breakfast and one beverage after lunch.
Length of Follow-Up	Post intervention (24 weeks).
Serious adverse events	Side effects of the drink (diarrhea, nausea; n = 3).
Funding Source	Top Institute Food and Nutrition and Dutch Dairy Organization (NZO).

A randomized, controlled trial of quadriceps resistance exercise and vitamin D in frail older people: the Frailty Interventions Trial in Elderly Subjects (FITNESS). Latham et al.	
Study (Year Published)	2003
Country	New Zealand
Objective/purpose	Determined (in a two by two factorial design) whether a simple home-based program of resistance exercise to the quadriceps muscles or a single high dose of vitamin D (calciferol) could improve self-reported physical health and reduce the risk of falls in frail older people who had recently been discharged from hospital. FITNESS was a multicenter, randomized, controlled trial with a factorial design to compare the effects of a 10-week program of resistance exercise to the quadriceps muscles with frequency-matched social home visits and a single high dose of vitamin D (calciferol) with placebo on self-reported physical health and falls in frail older people after hospitalization.
Study Design	Multicenter, randomized, controlled trial.
Recruitment setting and/or recruitment methods	Recruitment took place in three large public metropolitan acute care and rehabilitation teaching hospitals in Auckland, New Zealand, and two such hospitals in Sydney, Australia, from February 1999 to December 2000.
Inclusion Criteria/Exclusion Criteria	Inclusion: Aged 65 and older, considered frail according to simple clinical measures of frailty as described by Winograd et al., and no clear indication or contraindication to either of the study treatments (i.e., the clinician had substantial uncertainty about the benefits of the treatments for a specific patient). The research officers prospectively screened the medical records of all patients admitted to the hospital wards and, using simple clinical criteria, classified the patients into one of three groups: independent, frail, or fully dependent. Frail patients were those who had one or more health problems or functional limitations from a list of indicators that included dependency in an activity of daily living (ADL), prolonged bed rest, impaired mobility, or a recent fall. Exclusion: Not frail (i.e., fit and independent or fully dependent in ADL) or if, in the opinion of the responsible clinician, that treatment was considered to be potentially hazardous or definitely indicated for a patient. Because this was a pragmatic trial that screened a large number of patients admitted to hospital wards, no specific test or cut-off score was used to exclude participants, with the exception of the frailty assessment. Patients were excluded if they had a poor prognosis and were unlikely to survive six months, severe cognitive impairment that would compromise adherence to the exercise program (generally people with scores 20 on a 30-point Mini Mental State Examination (MMSE)), physical limitations that could limit adherence to the exercise program (e.g., poor upper limb function that limited application of the weights), unstable cardiac status, or large ulcers about the ankles that would preclude safe application of the ankle weights. In addition, because of difficulties that would arise with their follow-up assessments, people who lived outside the hospitals' normal geographical zones and patients who were not fluent in English were excluded.

Frailty index used *Include if modified (y/n) and how*	Screening for frailty: Criteria and predictors of outcomes by Winograd et al.
Total sample n (number invited)	243
Intervention n (number invited)	121
Control n (number invited)	122
Loss to follow-up: I n (%); C n (%)	I: 13 (10.7); C: 8 (6.6)
Age	Mean age overall (SD): 79.1 (6.9) Mean age intervention (95% CI): 79 (77-80) Mean age control (95% CI): 80 (78-81)
Gender: I n (%); C n (%)	Female: I: 64 (53); C: 65 (53) Male: I: 57 (47); C: 57 (47)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	n, %: Ischemic heart disease: I: 30 (25); C: 26 (21) Stroke: I: 59 (49); C: 50 (41)
Smoking Status	NR
BMI	Intervention (Mean and 95% CI): 24 (23-25) kg/m^2 Control (Mean and 95% CI): 25 (24-26) kg/m^2
Description of Intervention	The vitamin D intervention was given in a single oral dose. Patients received either six 1.25-mg calciferol (300,000 IU) or matching placebo tablets.
Type of intervention	Oral nutrition supplements.
Description of Control	Patients received matching placebo tablets.
Length of Follow-Up	Post-intervention (three months), six months.
Serious adverse events	None related to study.
Funding Source	Health Research Council of New Zealand, Auckland University of Technology Research Fund, and Lenore Wilson Estate.

Effect of dietary supplements and physical exercise on sensory perception, appetite, dietary intake and body weight in frail elderly subjects. de Jong et al.	
Study (Year Published)	2000
Country	Netherlands
Objective/purpose	This study was part of a large-scale intervention trial in frail elderly and was designed to investigate the effect of the consumption of micronutrient-dense products, a physical exercise programme or a combination of both on the variables mentioned.
Study Design	Randomized controlled trial.
Recruitment setting and/or recruitment methods	A total of 7080 letters were sent to elderly people living in the neighbourhood of Wageningen, The Netherlands, resulting in a study population of 217 free-living frail elderly, who were interested in the study and met the selection criteria. Enrolment took place between January (first starting group) and June 1997 (sixth starting group), depending on the area of residence.
Inclusion Criteria/Exclusion Criteria	To fulfill the criteria "frail", subjects must have required some kind of health care, such as home care or meals-on-wheels. The other main selection criteria that were applied were: age (70 years or older); inactivity (no regular participation in physical activities of moderate to high intensity); BMI < 25 kg/m^2 (based on self-reported weight and height) or recent involuntary weight loss; no use of multivitamin supplements; ability to understand the study procedures.
Frailty index used *Include if modified (y/n) and how*	Required healthcare service (i.e. home care or meals-on-wheels).
Total sample n (number invited)	217
Intervention n (number invited)	58
Control n (number invited)	44
Loss to follow-up: I n (%); C n (%)	16; 6
Age	Mean age overall (SD): 79 Mean age intervention (SD): 79.6 (4.8) Mean age control (SD): 79.3 (6.6)
Gender: I (%); C (%)	Female: I: 73; C: 68 Male: I: 27; C: 32
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	Number of self-reported diseases, Mean (SD): I: 1.9 (1.2); C: 1.9 (1.4) Cardiovascular (%): I: 51; C: 35 Musculoskeletal (%): I: 33; C: 30 Pulmonary (%): I: 10; C: 5
Smoking Status (%)	I: 13; C: 16
BMI	Overall: 24.5 kg/m^2

	Intervention Mean (SD): 24.4 (2.5) kg/m^2 Control Mean (SD): 24.1 (3.2) kg/m^2
Description of Intervention *nutrition-only intervention treatment arm	The micronutrient-dense products as well as the regular products were comprised of two categories: a fruit-based category and a dairy category. All subjects were asked to consume one product daily out of each category (one dairy product and one fruit-based product per day). Within the two categories several products were developed. Availability of a variety of products was intended to help to prevent boredom and to increase acceptability of the enriched products. Since these foods had a limited shelf-life each participant was given a cooled container with fresh stock each week, containing the following: fruit-based category, four portions of apple/berry/grape juice (portion size 100 g), four portions of orange/peach juice (portion size 100 g), two portions of apple compote (portion size 100 g), two portions of apple/peach compote (portion size 100 g); dairy category, four portions of vanilla custard (portion size 100 g), four portions of strawberry yoghurt (portion size 100 g), four portions of vanilla/apple yoghurt (portion size 100 g), four portions of vanilla/mixed fruit quark (portion size 75 g due to the "satiating" effect of quark). Due to daily consumption of two nutrient-dense products, subjects in the nutrition group and combination group got about 100 % of the Dutch recommended dietary allowance of vitamins D, E, B1, B2, B6, folic acid, B12, C and about 25±100 % of the Dutch recommended dietary allowance of the following minerals: Ca (25 %), Mg (25 %), Zn (50 %), Fe (50 %), I (100 %) in addition to their normal intake. Consumption of two products per day delivered a mean energy intake of 0×48 MJ/day.
Type of intervention	Fortified/enhanced foods
Description of Control	Subjects in the control group got the natural amount of the regular products in addition to their normal intake (the amount of vitamins and minerals in the regular products was negligible compared with the nutrient-dense products). The energy content of the nutrient-dense products was the same as the regular products. A social programme was organized as a control for the exercise programme, in order to check for possible effects of attention. Sessions of 90 minutes were organized once every two weeks by a skilled creative therapist. This programme focused on creative activities, social activities and lectures about topics of interest for elderly people. Transport to and from all the sessions was arranged.
Length of Follow-Up	Post-intervention (18 weeks).
Serious adverse events	Two subjects, both with rheumatoid arthritis, quit because of pain while exercising. No adverse events occurred during the sessions.
Funding Source	Dutch Dairy Foundation on Nutrition and Health and Health Research Council.

Effects of whey protein nutritional supplement on muscle function among community-dwelling frail older people: A multicenter study in China. Kang et al.	
Study (Year Published)	2019
Country	China
Objective/purpose	To evaluate whether whey protein supplements can improve muscle function of frail older people in addition to resistance exercise. To provide a targeted nutritional supplement containing whey protein in a timely bolus amount, to investigate the potential benefits of whey protein on muscle function and mobility among pre-frail and frail older adults.
Study Design	Multicenter, interventional, two parallel-group case–control.
Recruitment setting and/or recruitment methods	Four general hospitals in Beijing which are Peking Union Medical College Hospital, Tongren Hospital, Chaoyang Hospital and Aerospace Central Hospital investigated from August 30, 2017 to November 30, 2017.
Inclusion Criteria/Exclusion Criteria	Inclusion: Age ≥60 years. Meeting at least two of the five components of physical frailty: weakness (handgrip strength < 26 kg in men and < 18 kg in women); slowness (6-m usual gait speed < 1.0 m/s); unintentional weight loss (> 3 kg or 5% during half a year); fatigue over the past week from any activity; and < 1 hour of outdoor activities per week; able to communicate with the research team; and able to understand and sign the informed consent. Exclusion: Unable to stand from the chair independently; unable to perform home exercise programs due to underlying diseases; unable to perform usual daily activities due to cardiopulmonary distress; presence of renal insufficiency (estimated glomerular filtration rate < 60 mL/min/1.73 m^2); active liver disease (serum levels of transaminase higher than two folds of normal reference value); malignancy; and milk allergy.
Frailty index used *Include if modified (y/n) and how*	Fried's phenotype definition.
Total sample n (number invited)	115
Intervention n (number invited)	66
Control n (number invited)	49
Loss to follow-up: I n (%); C n (%)	0
Age	Mean age overall (SD): 77.3 years (NR) Mean age intervention (SD): 76.79 (7.11) years Mean age control (SD): 78.04 (6.82) years
Gender: I n (%); C n (%)	Female: I: 41 (62.1), C: 30 (61.2) Male: I: 25 (37.9), C: 19 (38.8)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR

Co-morbidities/chronic conditions	Charlson's Index, mean (interquartile ranges (IQR)): Active = 2.00 (1.00–3.50) Control = 1.00 (0.00–2.00)
Smoking Status	NR
BMI	I: 21.02 (3.45) kg/m^2 C: 22.73 (4.40) kg/m^2
Description of Intervention	All participants received home-based resistance exercise programs, and participants of the active group received daily whey protein supplementation. The 30-minute home-based resistance exercise programs were taught by a professional physical therapist at the beginning and the participants also received an educational video to exercise twice a day. Participants in both groups were given information regarding a diet that aimed to maintain their current weight and carry on daily resistance exercise programs. For participants in the active group, they were provided whey protein (Nutrasumma brand), which contained 32.4 g of whey protein and was administered with 100–150 mL warm water. Daily Whey protein supplementation (32.4 g) was provided and participants consumed them before breakfast and lunch or 30 minutes after resistance exercises in addition to their meals. Intervention duration was 12 weeks.
Type of intervention	Type of Intervention (Nutrition): Fortified/Enhanced foods Physical Activity Intervention Category: Muscle-strengthening Type of Intervention (Physical Activity): Resistance/strength training
Physical Activity Intervention Intensity	Resistance/strength training.
Frequency and Duration of Physical Activity Intervention	2x/day, 30 minutes.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	Physical therapist.
Description of Control	All participants received home-based resistance exercise programs. Participants in both groups were given information regarding a diet that aimed to maintain their current weight and carry on daily resistance exercise programs.
Length of Follow-Up	Four, eight, and twelve weeks.
Serious adverse events	NR
Funding Source	National Key R&D Program of China and CAMS Innovation Fund for Medical Sciences.

Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial. Serra-Prat et al.	
Study (Year Published)	2017
Country	Spain
Objective/purpose	Assessed the effect of a nutritional and physical activity programme on preventing frailty progression in pre-frail older people consulting in primary care centres for any reason.
Study Design	Randomised, open label, controlled trial with two parallel arms.
Recruitment setting and/or recruitment methods	All non-institutionalised patients aged ≥70 years consulting for any reason at any of three participating primary care centres in Mataró (Barcelona, Spain) were screened.
Inclusion Criteria/Exclusion Criteria	Inclusion: screened for frailty according to Fried criteria. Prefrail status, as defined by the presence of one or two of the Fried criteria. Exclusion: unable to stand without assistance; completely blind; with previous diagnosis of dementia recorded in clinical notes; and receiving palliative care or with life expectancy below six months.
Frailty index used *Include if modified (y/n) and how*	Fried's Frailty Phenotype.
Total sample n (number invited)	172
Intervention n (number invited)	80
Control n (number invited)	92
Loss to follow-up: I n (%); C n (%)	I: 19 (23.7); C: 20 (21.7)
Age	Mean age overall (SD): 78.3 Mean age intervention (SD): 77.9 (5.0) Mean age control (SD): 78.8 (4.9)
Gender: I n (%); C n (%)	Female: I: 41 (51.3); C: 56 (60.9) Male: I: 39 (48.7); C: 36 (39.1)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	Mean number of co-morbidities (SD): I: 3.92 (1.7); C: 3.5 (1.7) Chronic diseases n (%) Arthritis: I: 36 (58.1); C: 32 (43.8) Heart diseases: I: 8 (12.9); C: 16 (21.9) Peripheral vasculopathy: I: 10 (16.1); C: 12 (16.4) Stroke: I: 6 (9.7); C: 6 (8.2) Parkinson disease: I: 1 (1.6); C: 0 (0) Depression: I: 12 (19.4); C: 9 (12.3) Cancer: I: 5 (8.1); C: 4 (5.5) Chronic lung diseases: I: 3 (4.9); C: 15 (20.5) Diabetes: I: 21 (33.9); C: 26 (35.6) Chronic renal failure: I: 4 (6.5); C: 7 (9.6)
Smoking Status	NR

BMI	Intervention Mean (SD): men 28.0 (4.2) kg/m^2; women 30.5 (4.6) kg/m^2 Control Mean (SD): men 27.6 (3.7) kg/m^2; women 29.0 (4.2) kg/m^2
Description of Intervention	The study intervention included nutritional and physical activity components. Individuals in the intervention group were screened for malnutrition using the Short-Form Mini Nutritional Assessment questionnaire (MNA-sf) and those at risk were referred to the Nutritional Unit for further assessment, follow-up and the establishment of the usual dietary recommendations and corrective measures. The physical activity programme included two main components: aerobic exercise consisting of walking outdoors for 30–45 min/day at least four days/week and a set of 15 mixed exercises (three for strengthening arms, seven for strengthening legs and five for balance and coordination) to be done at home for 20–25 min at least four days/week. Each exercise had to be repeated 10 times a minute (progressively increasing up to 15 times after two–three months), with a rest of half a minute between each set of exercises. An initial training session was held in each primary care centre and participants all received an illustrated leaflet summarising the exercises to be done at home.
Type of intervention	Type of Intervention (Nutrition): Nutrition/dietitian counselling Physical Activity Intervention Category: Mixed Type of Intervention (Physical Activity): Resistance/strength training, Walking/marching, jogging, running
Physical Activity Intervention Intensity	Light
Frequency and Duration of Physical Activity Intervention	Walking 4x/week, 30-45 minutes/day; 15 exercises 4x/week, 20-25 minutes/day.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	NR
Description of Control	There was no special intervention for the control group patients who received their usual care and recommendations.
Length of Follow-Up	Post intervention (12 months)
Serious adverse events	No adverse events of note were reported.
Funding Source	Spanish Ministry of Health (Instituto de Salud Carlos III, Fondo de Investigación Sanitaria [FIS] programme).

Effects of a Home-Based and Volunteer-Administered Physical Training, Nutritional, and Social Support Program on Malnutrition and Frailty in Older Persons: A Randomized Controlled Trial. Luger et al.	
Study (Year Published)	2016
Country	Austria
Objective/purpose	Explored the effects of a home-based and volunteer-administered physical training and nutritional program compared with social support intervention alone on nutritional and frailty status in prefrail and frail older persons living at home.
Study Design	Randomized controlled trial.
Recruitment setting and/or recruitment methods	Older persons were recruited in three Viennese hospital wards between January 2014 and April 2014. In addition, following articles about the study in local newspapers and a report on television, other potential participants indicated their interest and were screened for eligibility between April 2014 and October 2014.
Inclusion Criteria/Exclusion Criteria	Inclusion: at risk of malnutrition or malnourished persons, according to the Mini Nutritional Assessment short form (MNA-SF); prefrail or frail, according to the Frailty Instrument for Primary Care of the Survey of Health, Ageing, and Retirement in Europe (SHARE-FI); older than 65 years; living in Vienna; ability to walk; and signed informed consent. Exclusion: impaired cognitive function, according to the Mini Mental State Examination (MMSE 17 points); planned admission to a nursing home; undergoing chemo- or radiotherapy; comorbidities (eg, insulin-treated diabetes mellitus); chronic obstructive pulmonary disease stage three or four; chronic kidney insufficiency; and persons classified as nursing level six or seven. In Austria, nursing levels six and seven are intended for people whose disability requires 180 hours per month of care or more.
Frailty index used *Include if modified (y/n) and how*	Frailty Instrument for Primary Care of the Survey of Health, Ageing, and Retirement in Europe (SHARE-FI).
Total sample n (number invited)	80
Intervention n (number invited)	39
Control n (number invited)	41
Loss to follow-up: I n (%); C n (%)	I: 5 (13); C: 9 (22)
Age	Mean age overall (SD): 82.8 (8.0) Mean age intervention (SD): 83.0 (8.1) Mean age control (SD): 82.5 (8.0)
Gender: I %; C %	Female: I: 85; C: 83 Male: I: 15; C: 17
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	Educational level, % (total, intervention, control) Primary: 54, 62, 46

	Secondary: 34, 28, 39 Tertiary: 13, 10, 15 (Primary: elementary school or no degree; Secondary: secondary school; Tertiary: university entrance diploma or higher degree)
Co-morbidities/chronic conditions	Comorbidities, % (total, intervention, control) Heart failure: 23, 21, 24 Diabetes mellitus: 9, 8, 10 Hypertension: 74, 74, 73 Dyslipidemia: 34, 33, 34 History of stroke: 9, 15, 2 Osteoporosis: 43, 44, 41 Rheumatoid arthritis: 25, 33, 17 Morbus Parkinson: 8, 8, 7 Depression: 10, 8, 12
Smoking Status	NR
BMI	Overall Mean (SD): 27.2 (4.3) kg/m^2 Intervention Mean (SD): 26.9 (4.5) kg/m^2 Control Mean (SD): 27.4 (4.3) kg/m^2
Description of Intervention	The aim of the nutritional intervention was to ensure adequate fluid, protein, and energy intake, preferably by regular foods and beverages, without the use of nutritional supplements. Therefore, buddies discussed nutritional-related messages with the older persons, with the aid of a guidebook. This booklet, which was designed by nutritional scientists, included three main nutritional aspects: fluid intake, animal and plant protein intake, and energy intake. In total, eight nutritional-related messages could be discussed, including a section for individual goal setting and tools to reinforce the self-efficacy. Moreover, the older persons were provided with ideas of how to enrich food with protein, and they were provided with recipes of dishes that are protein and energy rich. To show the variance between recommended and actual food intake, buddies were equipped with the “Healthy-for-Life Plate” guide, which is a modification of the Healthy Eating Plate guide created by Harvard University. The physical training intervention aimed to improve muscle strength. A warm-up with mobilization exercises was followed by six strength exercises designed by sports scientists. Participants performed the strength exercises in circuit form with two sets. The strength training was focused on the main muscle groups: femoral, pectoral, abdominal, ischiocrural, upper back muscles, and muscles of the arms and shoulders. The exercises were conducted with 15 repetitions until muscular exhaustion. Further on, during the physical training intervention, the buddies and the older persons set individual goals concerning physical activity. The buddies also advised the older persons to practice these strength exercises once a week on their own. To perform the strength exercises, the participants were provided with a Dyna-Band and a guidebook showing all the strength exercises as pictures. The buddies had the

	opportunity to call health professionals, including the nutritionist and the physiotherapist of the study team, as deemed necessary, who provided practical advice. In addition to the physical training and nutritional intervention, the older persons gained social contacts.
Type of intervention	Type of Intervention (Nutrition): Nutrition/dietitian counselling Physical Activity Intervention Category: Muscle-strengthening Type of Intervention (Physical Activity): Resistance/strength training
Physical Activity Intervention Intensity	Resistance/strength training
Frequency and Duration of Physical Activity Intervention	1x/week
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	Volunteer
Description of Control	A social support intervention served as an active control group. We used this design to examine whether the additional physical training and nutritional intervention was more effective than social support alone on nutritional and frailty status. Participants in the SoSu group were also visited twice a week by buddies over 12 weeks, but without discussing nutrition-related aspects or performing strength training. The buddies supported the older persons, for example, to get out, have a chat, or sharing interests. Additionally, besides this social contact, the buddies had also the opportunity to perform cognitive training with the older persons.
Length of Follow-Up	Post-intervention (12 weeks).
Serious adverse events	One participant in the intervention group reported an adverse event (back pain) that may have been associated with the exercise program.
Funding Source	Vienna Science and Technology Fund (a non-commercial fund, which had no role in the design and conduct of the study; the collection, analysis, and interpretation of data; in the preparation of the manuscript; or in the review or approval of the manuscript).

Effects of a combined physical training and nutrition intervention on physical performance and health-related quality of life in prefrail older women living in the community: a randomized controlled trial. Kwon et al.	
Study (Year Published)	2015
Country	Japan
Objective/purpose	Examined the effects of a combined physical training and nutritional program administered through a cooking class on physical performance and health-related quality of life (HRQOL) in prefrail older women living in the community.
Study Design	Three-arm randomized controlled trial.
Recruitment setting and/or recruitment methods	The participants were recruited from a "mass health checkup" of older residents in Itabashi Ward, Tokyo, Japan. The mass health checkup is a public comprehensive health examination program for community-dwelling older adults with the aim of preventing geriatric syndromes. The health checkup was conducted from November 5 to 12, 2006 by the Tokyo Metropolitan Institute of Gerontology. The checkup items included an interview, anthropometric measurements, blood analysis, and physical performance testing.
Inclusion Criteria/Exclusion Criteria	Inclusion: Prefrail elderly women aged 70 years or older living in the community. Frailty was defined as the lowest 20th percentile on handgrip strength and walking ability among the total participants (n = 666). Muscle weakness (handgrip strength in the lowest quartile at baseline, 23 kg) and slow gait speed (lowest quartile of timed usual walking speed at baseline, 1.52 m/seconds). Exclusion: participants with serum albumin 4.5 mg/dL, serious musculoskeletal conditions, and taking calcium or vitamin D supplements
Frailty index used *Include if modified (y/n) and how*	Fried's Frailty Phenotype. (Y). Prefrail participants were selected based on muscle weakness (handgrip strength in the lowest quartile at baseline, 23 kg) and slow gait speed (lowest quartile of timed usual walking speed at baseline, 1.52 m/seconds).
Total sample n (number invited)	89
Intervention n (number invited)	30; 28
Control n (number invited)	31
Loss to follow-up: I n (%); C n (%)	I: 5, 3; C: 4
Age	Mean age overall (Range): 76.8 (70 - 84 yrs) Mean age intervention (SD): 76.5 (3.8), 77.0 (4.2) Mean age control (SD): 76.9 (3.9)
Gender: %	Female: 100
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR

Co-morbidities/chronic conditions	Chronic disease condition, % Hypertension: I: 46.2, 44.0; C: 42.9 Stroke: I: 3.8, 4.0; C: 10.7 Diabetes mellitus: I: 3.8, 8.0; C: 7.1 Heart disease: I: 19.2, 16.0; C: 17.9 Hyperlipidemia: I: 38.5, 52.0; C: 57.1
Smoking Status	NR
BMI	NR
Description of Intervention	The physical training was conducted once a week for a duration of one hour per session. The program consisted of warm-up and stretching exercise (10-15 minutes), special exercise aiming to increase muscle strength and balance capability (20-45 minutes), and cool-down (5-10 minutes), in that order. Four classes were held, with 15 persons in each class. The program was conducted by a certified health fitness trainer, with the participation of one physician and two assistants. The program consisted of strength-training bodyweight exercises as well as exercises using Thera bands, dumbbells, and balls. Strength-training bodyweight exercise started with one set of five-time repetition of the same motion, progressing to one set of 10-time repetition. The exercises involved: holding the edge of a Thera band with open arms standing with feet shoulder-width apart; raising dumbbells above the head, alternating between each hand, standing with feet shoulder-width apart. To enhance enjoyment, participants were engaged in game-like activities using different sized balls. Other activities were also performed, such as walking, kneeling, and chair stands. Each exercise was performed in three or four variations to provide individually tailored, different levels of complexity. The main objective of the nutritional intervention program was to acquire an eating habit that helps to strengthen muscles, through cooking practice using food ingredients rich in protein and vitamin D. This program included preparation of cooking ingredients, nutrition guidance, cooking instructions, cooking practice, eating together, washing dishes, and tidying up, in that order. The cooking class was held once a week, with each session taking two to three hours. Nutritional education on food and eating habits that help to strengthen muscles was given as a 10- to 15-minute lecture before cooking instructions. At the end of each cooking class, participants were given advice to cook at home using the main cooking ingredients used in the class. To ensure that the participants consumed diverse food items, a dietary variety checklist was distributed and participants were instructed to circle the food items they ate every day. The main ingredients used in the cooking class were foods rich in protein and vitamin D, including meats such as beef, pork, chicken, and lamb; fishes such as mackerel, salmon, and eel; canned tuna; eggs; and mushrooms. Excluding rice or bread as staple food, a typical meal with side dishes contained 350-400 Kcal, 20-22 g protein, and 5-10 mg Vitamin D. Considering the weakened

	digestion and absorption functions of older people, cooking methods such as boiling and steaming were used.
Type of intervention	Type of Intervention (Nutrition): Nutrition/dietitian counselling Physical Activity Intervention Category: Muscle-strengthening Type of Intervention (Physical Activity): Resistance/strength training, walking/marching, jogging, running,
Physical Activity Intervention Intensity	Resistance/strength training
Frequency and Duration of Physical Activity Intervention	1x/week, 60 minutes.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	Certified health fitness trainer.
Description of Control	Participants participated in a general health education session conducted once a month for a total of three sessions during the 12-week intervention period. The project physician, certified health fitness trainer, and dietician provided the participants with information on physical training for preventing falls and urinary incontinence as well as a dietary guideline for healthy aging. After the trial was completed, this group was offered a 12-week exercise and nutritional program as in the same manner for the exercise and nutrition (EN) and exercise only (E) groups.
Length of Follow-Up	Three-month intervention; Six-month follow up (nine months from baseline).
Serious adverse events	NR
Funding Source	Ministry of Education, Science and Culture of Japan, and the Basic Science Research Program through the National Research Foundation of Korea (NRF).

Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. Tieland et al.	
Study (Year Published)	2012
Country	Netherlands
Objective/purpose	Assessed the impact of protein supplementation on muscle mass, strength, and physical performance during prolonged resistance-type exercise training in frail elderly men and women.
Study Design	Randomized, double-blind, placebo-controlled trial.
Recruitment setting and/or recruitment methods	Elderly subjects (≥65 years old) were recruited from an existing database, through distribution of flyers, and by local information meetings between December 2009 and September 2010.
Inclusion Criteria/Exclusion Criteria	Inclusion: unintentional weight loss; weakness; self-reported exhaustion; slow walking speed; and low physical activity. Prefrailty was classified when one or two criteria were present, and frailty was defined when three or more criteria were present. Exclusion: diagnosed with cancer, chronic obstructive pulmonary disease, or muscle disease; unable to perform the exercise regimen; type II diabetes (≥7 mmol/L); renal insufficiency (eGFR <60 mL/min/1.73 m^2); silent ischemia.
Frailty index used *Include if modified (y/n) and how*	Fried Frailty Phenotype.
Total sample n (number invited)	62
Intervention n (number invited)	31
Control n (number invited)	31
Loss to follow-up: I n (%); C n (%)	I: 5 (16); C: 6 (19)
Age	Mean age intervention (SD): 78 (9) Mean age control (SD): 79 (6)
Gender: I n (%); C n (%)	Female: I: 20 (65); C: 21 (68) Male: I: 11 (35); C: 10 (32)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	NR
Smoking Status	NR
BMI	Intervention Mean (SD): 28.7 (4.5) kg/m^2 Control Mean (SD): 28.2 (4.6) kg/m^2
Description of Intervention	Both groups were included in a 24-week resistance-type exercise training program. The resistance-type exercise training was performed two times per week under personal supervision for a 24-week period. The sessions

	were performed in the morning and afternoon with at least 72 hours between sessions. The training consisted of a five-minute warm-up on a cycle ergometer, followed by four sets on the leg-press and leg-extension machines and three sets on chest press, lat pulldown, pecdec, and vertical row machines (Technogym, Rotterdam, the Netherlands). The workload started at 50% of one repetition-maximum (10-15 repetitions per set) and was increased to 75% of one repetition-maximum (8-10 repetitions) to stimulate muscle hypertrophy. Resting periods of one minute were allowed between sets and two minutes between exercises. To evaluate changes in muscle strength, one repetition-maximum was repeated after 4, 8, 12, 16, and 20 weeks of training. Workload intensity was adjusted based on the one repetition-maximum outcomes. Twice daily, the subjects received either a 250-mL protein supplemented beverage containing 15 g protein (MPC80; milk protein concentrate), 7.1 g lactose, 0.5 g fat, and 0.4 g calcium. All beverages were vanilla flavored to mask the contents of the drinks and packages were non-transparent. The subjects consumed one beverage directly after breakfast and one beverage directly after lunch.
Type of intervention	Type of Intervention (Nutrition): Fortified/enhanced foods Physical Activity Intervention Category: Muscle-strengthening Type of Intervention (Physical Activity): Resistance/strength training
Physical Activity Intervention Intensity	Resistance/strength training.
Frequency and Duration of Physical Activity Intervention	2x/week.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	The resistance program was “under personal supervision”.
Description of Control	Exercise (Described above). Matching placebo supplement containing no protein, 7.1 g lactose and 0.4 g calcium. All beverages were vanilla flavored to mask the contents of the drinks and packages were non-transparent. The subjects consumed one beverage directly after breakfast and one beverage directly after lunch.
Length of Follow-Up	Post-intervention (24 weeks).
Serious adverse events	One subject gave heavy burden of the study as reason for withdrawal.
Funding Source	NR

Nutritional supplementation during resistance training improved skeletal muscle mass in community-dwelling frail older adults. Yamada et al.	
Study (Year Published)	2012
Country	Japan
Objective/purpose	Investigated the effects of the combination of resistance training and multi-nutrient supplementation (including vitamin D and protein) on muscle mass and physical performance in frail older adults.
Study Design	Pilot trial.
Recruitment setting and/or recruitment methods	Participants were recruited by an advertisement in the local press and public ads. There were 96 community-dwelling older adults recruited from two communities with similar environment in Kyoto city.
Inclusion Criteria/Exclusion Criteria	Inclusion: frailty status as certified by the long-term care insurance service; presence of low muscle mass (defined as appendicular muscle mass divided by height squared, <6.87 kg/m^2 in men, and <5.46 kg/m^2 in women); age of 65 years and older; living in the community; no severe cognitive impairment (defined as a Rapid Dementia Screening Test score higher than four); ability to independently walk (even with a cane); no regular supplementation of vitamin D and protein during the previous 12 months. Exclusion: severe cardiac, pulmonary, or musculoskeletal disorders; presence of comorbidities associated with an increased risk of falls, such as Parkinson's disease or stroke; use of psychotropic drugs.
Frailty index used *Include if modified (y/n) and how*	Frailty status as certified by the long-term care insurance service.
Total sample n (number invited)	77
Intervention n (number invited)	38
Control n (number invited)	39
Loss to follow-up: I n (%); C n (%)	I: 3 (7.9), 4 (10.3)
Age	Mean age intervention (SD): 74.4 (7.3), 75.6 (6)
Gender: I n (%); C n (%)	Female: I: 17 (48.6), 19 (54.3) Male: I: 18 (51.4), 16 (45.7)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	Medication, Mean (SD): 5.2 (2.9), 5.7 (3.7) Walking aid user, n (%): 24 (68.6), 25 (71.4) Falls in past year, n (%): 12 (34.3), 14 (40.0)
Smoking Status	NR
BMI	Intervention Mean (SD): 22.6 (3.1) kg/m^2, 22.5 (3.3) kg/m^2

Description of Intervention	A multi-nutrient supplement was provided three times per week for three months to participants in the nutrition intervention and resistance training (S/Ex) group to increase vitamin D and protein intakes. The supplement (Resource PemPal Active®) consisted of 12.5 µg of vitamin D and 10.0 g of protein with branched chain amino acids; 200kcal, 41% carbohydrate, 37% fat, 20% protein, 2% oligosaccharide. Participants performed 90 minutes of group training sessions three times per week for three months. Each exercise class used a standardized format that included 10 minutes of warm-up exercises, 60 minutes of progressive strength training, 10 minutes of flexibility and balance exercises, and 10 minutes of cool-down activities. The warm-up exercise consisted of movement of legs, trunk, and arms to include all joints and major muscle groups in activities such as mild dancing. Strength training consisted of progressive resistive exercises using an elastic band and exercise machines. Participants performed biceps curls, double arm pull downs, seated row, leg press, leg curl, and leg extension exercises on the resistance training machines. Training loads were chosen using the 10-repetition maximum (10-RM, the maximal weight that could be lifted 10 times). Participants used the 10-RM for three sets of 10 repetitions for each machine exercise. Participants were required to adjust the training weight to ensure failure at the 10-RM. A sequence of progressively more difficult exercises was also performed to improve static and dynamic balance. Although exercises could be performed in a sitting position, the importance of performing in a standing position to improve balance was encouraged. Physiotherapists evaluated each participant twice during the study period to ensure adherence to the exercise protocols during classes. The duration of the intervention was three months.
Type of intervention	Type of Intervention (Nutrition): Oral nutrition supplements; fortified/enhanced foods Physical Activity Intervention Category: Muscle-strengthening Type of Intervention (Physical Activity): Resistance/strength training
Physical Activity Intervention Intensity	Resistance/strength training.
Frequency and Duration of Physical Activity Intervention	3x/week, 90 minutes.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	Physiotherapist
Description of Control	N/A
Length of Follow-Up	Post-intervention (three months).
Serious adverse events	NR
Funding Source	No financial disclosures.

Effect of dietary supplements and physical exercise on sensory perception, appetite, dietary intake and body weight in frail elderly subjects. de Jong et al.	
Study (Year Published)	2000
Country	Netherlands
Objective/purpose	This study was part of a large-scale intervention trial in frail elderly and was designed to investigate the effect of the consumption of micronutrient-dense products, a physical exercise programme or a combination of both on the variables mentioned.
Study Design	Randomized controlled trial.
Recruitment setting and/or recruitment methods	A total of 7080 letters were sent to elderly people living in the neighbourhood of Wageningen, The Netherlands, resulting in a study population of 217 free-living frail elderly, who were interested in the study and met the selection criteria. Enrolment took place between January (first starting group) and June 1997 (sixth starting group), depending on the area of residence.
Inclusion Criteria/Exclusion Criteria	Inclusion: required some kind of health care, such as home care or meals-on-wheels; aged ≥70 years); inactivity (no regular participation in physical activities of moderate to high intensity); BMI < 25 kg/m^2 (based on self-reported weight and height) or recent involuntary weight loss; no use of multivitamin supplements; ability to understand the study procedures.
Frailty index used *Include if modified (y/n) and how*	Required healthcare service (i.e. home care or meals-on-wheels).
Total sample n (number invited)	217
Intervention n (number invited)	58; 60
Control n (number invited)	44
Loss to follow-up: I n (%); C n (%)	16; 15; 6
Age	Mean age overall (SD): 79 Mean age intervention (SD): 79.6 (4.8); 79.2 (6.1) Mean age control (SD): 79.3 (6.6)
Gender: I %; C %	Female: I: 73, 72; C: 68 Male: I: 27, 28; C: 32
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	NR
Co-morbidities/chronic conditions	Number of self-reported diseases, Mean (SD): I: 1.9 (1.2), 1.9 (1.2); C: 1.9 (1.4) Cardiovascular (%): I: 51, 36; C: 35 Musculoskeletal (%): I: 33, 38; C: 30 Pulmonary (%): I: 10, 19; C: 5
Smoking Status: I %; C %	I: 12, 7; C: 16
BMI	Overall: 24.5 kg/m^2 Intervention Mean (SD): 24.4 (2.5) kg/m^2; 25.0 (2.5) kg/m^2 Control Mean (SD): 24.1 (3.2) kg/m^2

Description of Intervention *combined approach treatment arm	The micronutrient-dense products as well as the regular products were comprised of two categories: a fruit-based category and a dairy category. All subjects were asked to consume one product daily out of each category (one dairy product and one fruit-based product per day). Within the two categories several products were developed. Availability of a variety of products was intended to help to prevent boredom and to increase acceptability of the enriched products. Since these foods had a limited shelf-life each participant was given a cooled container with fresh stock each week, containing the following: fruit-based category, four portions of apple/berry/grape juice (portion size 100 g), four portions of orange/peach juice (portion size 100 g), two portions of apple compote (portion size 100 g), two portions of apple/peach compote (portion size 100 g); dairy category, four portions of vanilla custard (portion size 100 g), four portions of strawberry yoghurt (portion size 100 g), four portions of vanilla/apple yoghurt (portion size 100 g), four portions of vanilla/mixed fruit quark (portion size 75 g due to the "satiating" effect of quark). Due to daily consumption of two nutrient-dense products, subjects in the nutrition group and combination group got about 100 % of the Dutch recommended dietary allowance of vitamins D, E, B1, B2, B6, folic acid, B12, C and about 25±100 % of the Dutch recommended dietary allowance of the following minerals: Ca (25 %), Mg (25 %), Zn (50 %), Fe (50 %), I (100 %) in addition to their normal intake. Consumption of two products per day delivered a mean energy intake of 0×48 MJ/day. Emphasis was placed on skill training; muscle strength, coordination, flexibility, speed and endurance were trained by exercises such as walking, stooping and chair stands, thereby improving performance of daily activities. Different equipment was used, for example, balls, ropes, weights and dynabands. Group sessions were organized twice per week for 45 minutes and were of moderate, gradually increasing intensity. The sessions were coordinated by skilled teachers and supervised by one of the project leaders (M.CAP). In order to guarantee uniformity all sessions were extensively rehearsed with all teachers together, and an instruction video and manual was made in advance.
Type of intervention	Type of Intervention (Nutrition): Fortified/enhanced foods Physical Activity Intervention Category: Mixed Type of Intervention (Physical Activity): Resistance/strength training, walking/marching, jogging, running
Physical Activity Intervention Intensity	Moderate intensity.
Frequency and Duration of Physical Activity Intervention	2x/week, 45 minutes.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor,	Teacher (researcher supervised).

volunteer, researcher, physiotherapist)	
Description of Control	Subjects in the control group and the exercise group got the natural amount of the regular products in addition to their normal intake (the amount of vitamins and minerals in the regular products was negligible compared with the nutrient-dense products). The energy content of the nutrient-dense products was the same as the regular products. A social programme was organized as a control for the exercise programme, in order to check for possible effects of attention. Sessions of 90 minutes were organized once every two weeks by a skilled creative therapist. This programme focused on creative activities, social activities and lectures about topics of interest for elderly people. Transport to and from all the sessions was arranged.
Length of Follow-Up	Post-intervention (18 weeks).
Serious adverse events	Two subjects, both with rheumatoid arthritis, quit because of pain while exercising. No adverse events occurred during the sessions.
Funding Source	Dutch Dairy Foundation on Nutrition and Health and Health Research Council.

Effects of individual dietary counseling as part of a comprehensive geriatric assessment (CGA) on frailty status: A population-based intervention study. Nykanen et al.	
Study (Year Published)	2012
Country	Finland
Objective/purpose	Evaluated the effects of individual dietary counseling as part of a comprehensive geriatric assessment (CGA) on frailty status among community-dwelling people aged 75 years or older.
Study Design	Clinical controlled trial.
Recruitment setting and/or recruitment methods	This study is based on a subpopulation of participants in the population-based Geriatric Multidisciplinary Strategy for the Good Care of the Elderly (GeMS) intervention aimed at preventing disability and maintaining autonomy in older people.
Inclusion Criteria/Exclusion Criteria	Inclusion: at risk of malnutrition (Mini Nutritional Assessment scores 23.5-17.0).
Frailty index used *Include if modified (y/n) and how*	Frailty was defined according to the five frailty criteria used in the Cardiovascular Health Study: shrinking/sarcopenia, weakness, poor endurance and energy, slowness and low physical activity level.
Total sample n (number invited)	159
Intervention n (number invited)	77
Control n (number invited)	82
Loss to follow-up: total n (%)	14 (8.8)
Age	Mean age overall (SD): 83.1 (5.1) years Mean age intervention (SD): 83.2 (5.2) years Mean age control (SD): 82.9 (5.0) years
Gender: I n (%); C n (%)	Female: I: 61 (79.2); C: 65 (79.3) Male: I: 16 (20.8); C: 17 (20.7)
Race/Ethnicity	NR
SES status *(reported by income or education level ONLY)*	Education ≥ seven years, n (%): I: 28 (37.8); C: 41 (50.0)
Co-morbidities/chronic conditions	NR
Smoking Status	NR
BMI	Intervention Mean (SD): 26.7 (5.1) kg/m^2 Control Mean (SD): 26.3(5.1) kg/m^2
Description of Intervention	In the physical activity component, the participants were offered an opportunity to participate the individually tailored physical activity counseling by a physiotherapist and in strength and balance training once a week where one of the main objectives was to prevent mobility disability, the emphasis of strength training was the lower extremities. Nutritional intervention included an individually tailored comprehensive geriatric intervention in which the other components were medical, oral

	health and physical intervention. The tailored nutritional treatment consisted of individual dietary counseling based on the baseline Mini Nutritional Assessment. Each participant had two nutritional treatment meetings with the nutritionist, the first in 2005, and the second in 2006. During the first visit, the authorized nutritionist collected important information, such as the client's history of health problems, current dietary intake and specific nutritional problems, food preferences and appetite status. Based on this evaluation, the nutritionist helped the participants draw up their own meal plan with enough energy and proteins. Special leaflets covering, for example, snacking, were handed out. Telephone calls between the visits, as deemed necessary by the nutritionist, provided opportunities to reinforce the dietary advice and give additional support. All participants received telephone counseling every two months during the intervention. Participants' family members were encouraged to attend dietary counseling sessions. Participants with cognitive impairments had a caregiver present during the sessions; participants and caregivers provided written informed consent. During the second visit, the nutritionist evaluated the dietary intake of the participants and made changes according to the treatment protocol, if necessary. At the same time, participants as well as family members and caregivers received instructions on how to follow the recommended diet.
Type of intervention	Type of Intervention (Nutrition): Nutrition/dietitian Counselling Physical Activity Intervention Category: Mixed Type of Intervention (Physical Activity): Resistance/strength training, counselling with physiotherapist
Physical Activity Intervention Intensity	Resistance/strength training.
Frequency and Duration of Physical Activity Intervention	1x/week.
Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor, volunteer, researcher, physiotherapist)	Nutritionist and physiotherapist.
Description of Control	The participants of the control group did not receive any interventions but took part in the annual interviews and measurements and used normal health care services.
Length of Follow-Up	Post intervention (one year)
Serious adverse events	NR
Funding Source	The Social Insurance of Institute of Finland and the City of Kuopio.

Appendix 4: GRADE Tables for All Outcomes by Intervention Category

Table S1: GRADE evidence rating: Nutritional interventions compared to usual care for older adults living with frailty or pre-frailty

GRADE evidence rating: Nutritional interventions compared to usual care for older adults living with frailty or pre-frailty

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition	usual care	Absolute (95% CI)		
1. Physical ***(follow up: range 4 weeks to 24 weeks; assessed with: Activities of daily living (ADL), Muscle strength (handgrip & non-handgrip), Appendicular Lean mass (ALM))***											
7 [a]	randomised trials	serious [b]	not serious [c]	not serious	not serious [d]	none	373	321	SMD **0.16 SD higher** (0.02 higher to 0.29 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
2. Mobility ***(follow up: range 4 weeks to 24 weeks; assessed with: Performance measures (Gait speed, Timed up & go, chair sit & stand, balance, short physical performance battery))***											
7 [a]	randomised trials	serious [b]	not serious [e]	not serious	not serious	none	373	321	SMD **0.15 SD higher** (0.001 higher to 0.3 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
3. Health ***(follow up: range 12 weeks to 24 weeks; assessed with: Body weight & Body mass index)***											
4 [f]	randomised trials	serious [g]	not serious [c]	not serious	serious [h]	none	150	134	SMD **0.18 SD lower** (0.51 lower to 0.16 higher)	⊕⊕◯◯ LOW	CRITICAL
4. Frailty ***(follow up: range 12 weeks to 24 weeks; assessed with: Frailty criteria (Cardiovascular Health Study, Korean Longitudinal Study, Modified Fried))***											
3 [i]	randomised trials	serious [j]	not serious [c]	not serious	not serious [k]	none	155	100	SMD **0.22 SD lower** (0.44 lower to 0.01 lower)	⊕⊕⊕◯ MODERATE	CRITICAL

GRADE – Nutrition-only Studies

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition	usual care	Absolute (95% CI)		
5. Diet quality ***(follow up: range 12 weeks to 24 weeks; assessed with: Kcal / day, MJ / day)***											
5 [l]	randomised trials	serious [m]	serious [n]	not serious	serious [o]	none	222	161	SMD **0.1 SD higher** (0.47 lower to 0.67 higher)	⊕◯◯◯ VERY LOW	CRITICAL
6. Quality of life ***(follow up: mean 24 weeks; assessed with: SF-36 Physical and Mental component score)***											
1 [p]	randomised trials	not serious	not serious	not serious	serious [o]	none	121	122	SMD **0.12 SD lower** (1.39 lower to 1.15 higher)	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference

Note: There was no data in the included studies for the following outcomes; Mortality, Health Service Use, and Social/Caregiver

Explanations

a. Latham, 2003; Kim, 2012; Tieland, 2012; Pin Ng, 2015; Niccoli, 2017; Park, 2018; Wu, 2018

b. 2 out of 7 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

c. The confidence intervals overlap with low statistical heterogeneity observed across studies.

d. The sample size is adequate (=>300) in both intervention and control arms and effect estimate is precise (Confidence intervals do not include the no effect value "0").

e. The confidence intervals overlap with moderate level of statistical heterogeneity observed across studies.

f. Kim, 2012; Tieland, 2012; Pin Ng, 2015; Wu, 2018

g. 1 out of 4 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

h. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0".

i. Pin Ng, 2015; Park, 2018; Wu, 2018

j. 1 out of 3 studies rated as unclear risk with concerns regarding selective outcome reporting and other risk of bias (such as baseline imbalance across groups).

k. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "0".

l. Jong, 2000; Kim, 2012; Tieland, 2012; Park, 2018; Wu, 2018

m. 2 out of 5 studies rated as unclear risk with concerns regarding allocation concealment, blinding, incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

n. The confidence intervals do not overlap with substantial level of statistical heterogeneity observed across studies.

o. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0".

p. Latham, 2003

Table S2: GRADE evidence rating: Protein supplementation interventions compared to usual care for older adults living with frailty or pre-frailty

GRADE evidence rating: Protein supplementation compared to usual care for older adults living with frailty or pre-frailty

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Protein suppl.	usual care	Absolute (95% CI)		
1. Physical ***(follow up: range 4 weeks to 24 weeks; assessed with: Activities of daily living (ADL), Muscle strength (handgrip & non-handgrip), Appendicular Lean mass (ALM))***											
5 [a]	randomised trials	serious [b]	not serious [c]	not serious	not serious [d]	none	195	149	SMD **0.16 SD higher** (0.01 higher to 0.31 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
2. Mobility ***(follow up: range 4 weeks to 24 weeks; assessed with: Performance measures (Gait speed, Timed up & go, chair sit & stand, balance, short physical performance battery))***											
5 [a]	randomised trials	serious [b]	not serious [e]	not serious	not serious [d]	none	195	149	SMD **0.2 SD higher** (0.02 higher to 0.39 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
3. Health ***(follow up: range 12 weeks to 24 weeks; assessed with: Body weight & Body mass index)***											
3 [f]	randomised trials	serious [g]	not serious [c]	not serious	serious [h]	none	93	84	SMD **0.12 SD lower** (0.58 lower to 0.34 higher)	⊕⊕◯◯ LOW	CRITICAL
4. Frailty ***(follow up: mean 12 weeks; assessed with: Frailty criteria (Cardiovascular Health Study, Korean Longitudinal Study, Modified Fried))***											
2 [i]	randomised trials	serious [j]	not serious [c]	not serious	serious [h]	none	98	50	SMD **0.18 SD lower** (0.45 lower to 0.09 higher)	⊕⊕◯◯ LOW	CRITICAL

GRADE – Nutrition Protein Supplementation Studies

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Protein suppl.	usual care	Absolute (95% CI)		
5. Diet quality ***(follow up: range 12 weeks to 24 weeks; assessed with: Kcal / day, MJ / day)***											
4 [k]	randomised trials	serious [l]	serious [m]	not serious	serious [h]	none	173	124	SMD **0.01 SD lower** (0.69 lower to 0.67 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference

Note: There was no data in the included studies for the following outcomes; Mortality, Quality of Life, Health Service Use, and Social/Caregiver

Explanations

a. Kim, 2012; Tieland, 2012; Niccoli, 2017; Park, 2018; Wu, 2018

b. 2 out of 5 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

c. The confidence intervals overlap with low statistical heterogeneity observed across studies.

d. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "0".

e. The confidence intervals overlap with moderate level of statistical heterogeneity observed across studies.

f. Kim, 2012; Tieland, 2012; Wu, 2018

g. 1 out of 3 studies rated as unclear risk with concerns regarding selective outcome reporting and other risk of bias (such as baseline imbalance across groups).

h. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0".

i. Park, 2018; Wu, 2018

j. 1 out of 2 studies rated as unclear risk with concerns regarding selective outcome reporting and other risk of bias (such as baseline imbalance across groups).

k. Kim, 2012; Tieland, 2012; Park, 2018; Wu, 2018

l. 1 out of 4 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

m. The confidence intervals do not overlap with substantial level of statistical heterogeneity observed across studies.

Table S3: GRADE evidence rating: Combined Approach interventions compared to usual care for older adults living with frailty or pre-frailty

GRADE evidence rating: Nutrition plus physical activity interventions compared to usual care for older adults living with frailty or pre-frailty

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition & physical activity	Usual care	Relative / Absolute (95% CI)		
1. Physical ***(follow up: range 12 weeks to 52 weeks; assessed with: Activities of daily living (ADL), Muscle strength (handgrip & non-handgrip), Appendicular Lean mass (ALM))***											
6 [a]	randomised trials	serious [b]	not serious [c]	not serious	not serious [d]	none	258	256	SMD **0.19 SD higher** (0.06 higher to 0.32 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
2. Mobility ***(follow up: range 12 weeks to 52 weeks; assessed with: Performance measures (Gait speed, Timed up & go, chair sit & stand, balance, short physical performance battery))***											
6 [a]	randomised trials	serious [b]	not serious [e]	not serious	not serious [d]	none	258	256	SMD **0.25 SD higher** (0.02 higher to 0.48 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
3. Health ***(follow up: range 12 weeks to 52 weeks; assessed with: Body weight & Body mass index)***											
3 [f]	randomised trials	serious [g]	not serious [c]	not serious	serious [h]	none	158	152	SMD **0.05 SD lower** (0.42 lower to 0.33 higher)	⊕⊕◯◯ LOW	CRITICAL
4. Frailty ***(follow up: range 12 weeks to 52 weeks; assessed with: Modified Fried criteria)***											
2 [i]	randomised trials	serious [j]	not serious [c]	not serious	not serious [d]	none	100	113	SMD **0.41 SD lower** (0.68 lower to 0.14 lower)	⊕⊕⊕◯ MODERATE	CRITICAL

GRADE – Combined Approach Studies

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition & physical activity	Usual care	Relative / Absolute (95% CI)			
5. Frailty *(follow up: range 12 weeks to 52 weeks; assessed with: Prevalence of frailty at post-intervention)*												
3 [k]	randomised trials	serious [l]	not serious [c]	not serious	not serious [m]	none	39 / 174 (22.4%)	59 / 185 (31.9 %)	**RR 0.720** (0.520 to 0.999)	**89 fewer per 1,000** (from 153 fewer to 0 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
6. Diet quality (follow up: range 18 weeks to 24 weeks; assessed with: MJ / day)												
2 [n]	randomised trials	serious [o]	serious [p]	not serious	serious [h]	none	73	68	SMD **0.53 SD higher** (0.98 lower to 2.04 higher)		⨁◯◯◯ VERY LOW	CRITICAL
7. Quality of life (follow up: range 12 weeks to 52 weeks; assessed with: SF-36 Physical & Mental component, EQ5D-VAS, WHOQOL-BREF score)												
3 [q]	randomised trials	serious [l]	not serious [c]	not serious	serious [h]	none	126	141	SMD **0.31 SD higher** (0.05 lower to 0.67 higher)		⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference; **RR:** Risk ratio

Note: There was no data in the included studies for the following outcomes; Mortality, Health Service Use, and Social/Caregiver

GRADE – Combined Approach Studies

Explanations

a. Tieland, 2012; Yamaha, 2012; Kwon, 2015; Luger, 2016; Serra-Prat, 2017; Kang, 2019

b. 4 out of 7 studies rated as unclear risk (2 studies) and high risk (2 studies) with concerns regarding randomization, allocation concealment, blinding, incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

c. The confidence intervals overlap with low statistical heterogeneity observed across studies.

d. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "0".

e. The confidence intervals overlap with moderate level of statistical heterogeneity observed across studies.

f. Tieland, 2012; Serra-Prat, 2017; Kang, 2019

g. 1 out of 3 studies rated as high risk with concerns regarding randomization, allocation concealment, blinding, incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

h. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0".

i. Luger, 2016; Serra-Prat, 2017

j. 1 out of 2 studies rated as unclear risk with concerns regarding blinding and other risk of bias (such as baseline imbalance across groups).

k. Nykänen, 2012, Luger, 2016; Serra-Prat, 2017

l. 2 out of 3 studies rated as unclear risk with concerns regarding blinding and other risk of bias (such as baseline imbalance across groups).

m. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "1".

n. Jong, 2000; Tieland, 2012

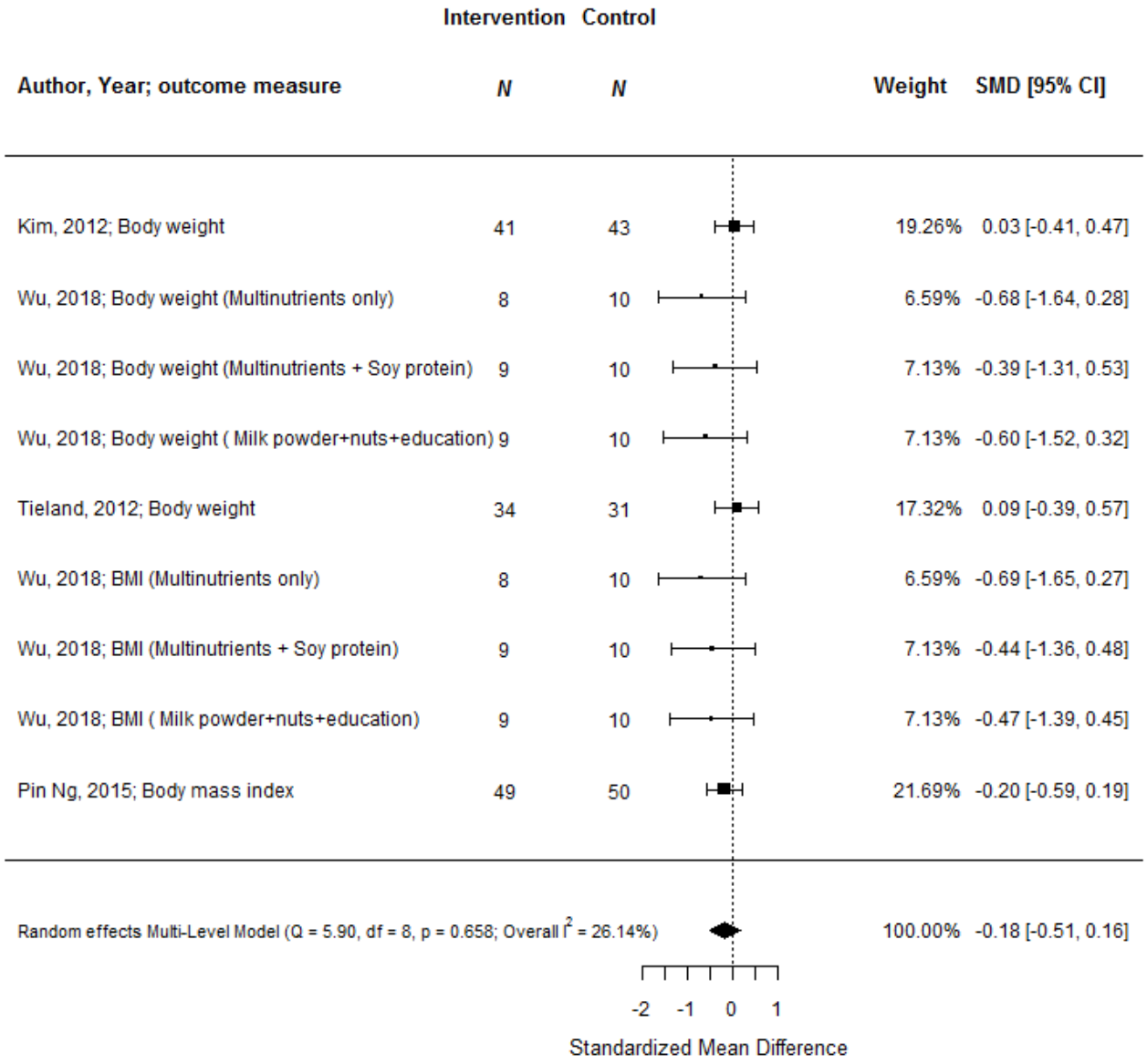
o. 1 out of 2 studies rated as unclear risk with concerns regarding blinding and other risk of bias (such as baseline imbalance across groups).

p. The confidence intervals do not overlap with substantial level of statistical heterogeneity observed across studies.

q. Kwon, 2015; Luger, 2016; Serra-Prat, 2017

Appendix 5: Meta-analysis Forest Plots for Non-Significant Outcomes

Figure S1. Effect on Health outcomes (nutrition interventions)

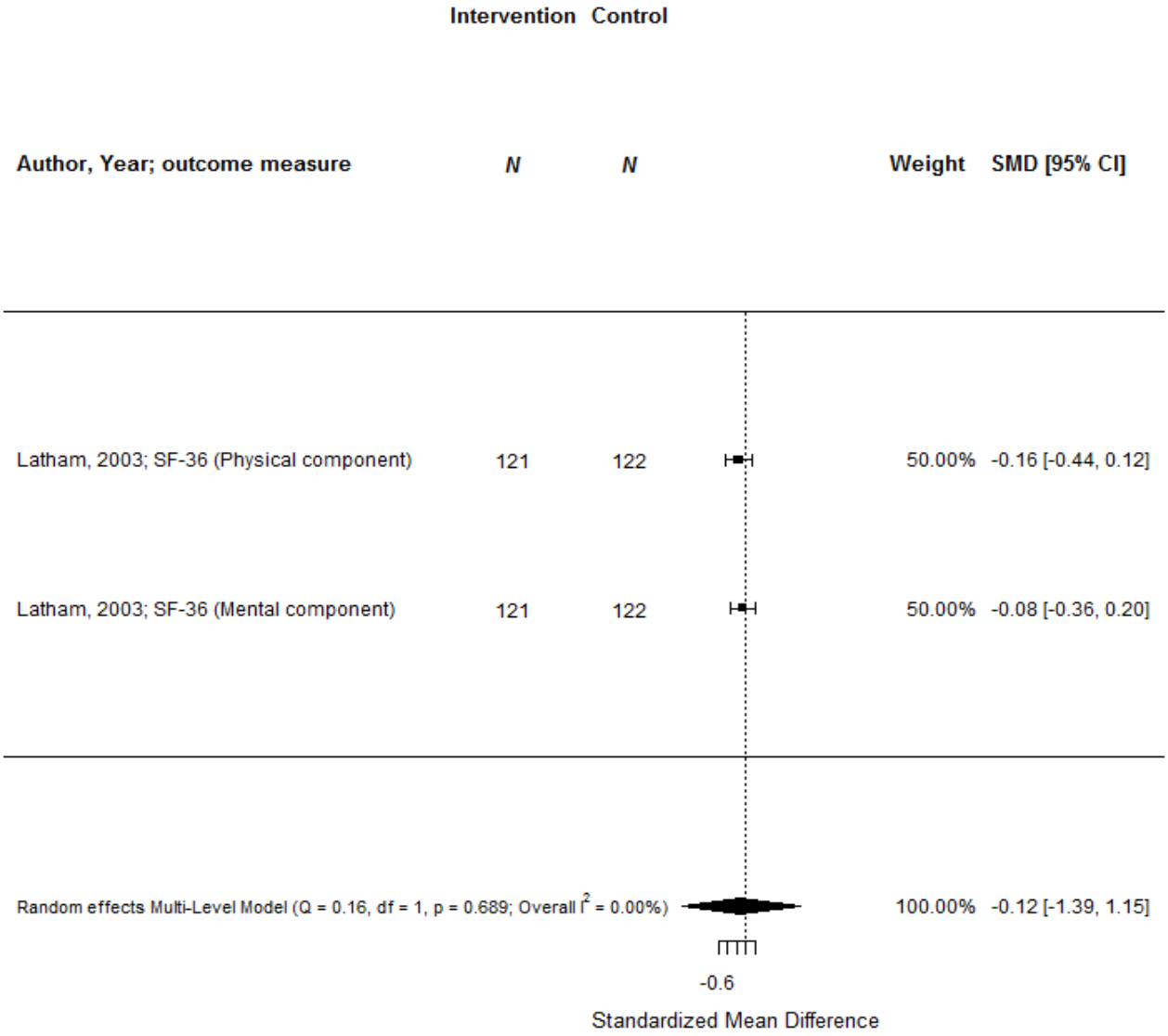



```
Model Results:

estimate      se     tval    pval    ci.lb   ci.ub
 -0.1772  0.1461  -1.2133  0.2596  -0.5140  0.1596

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S2. Effect on Quality of life outcomes (nutrition interventions)

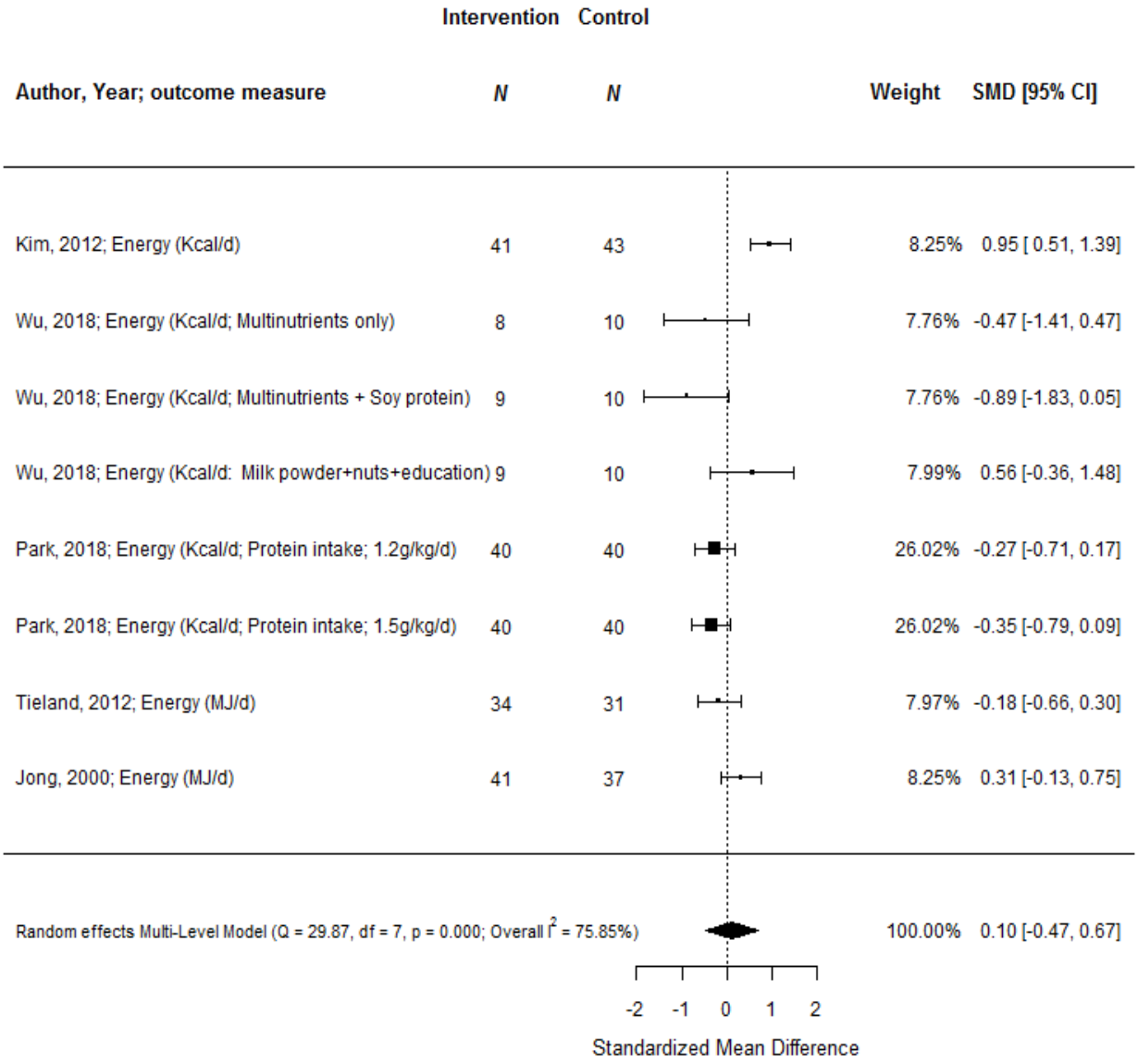



```
Model Results:

estimate      se     tval    pval    ci.lb   ci.ub
 -0.1200  0.1000  -1.2000  0.4423  -1.3906  1.1506

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S3. Effect on Diet Quality outcome (nutrition interventions)

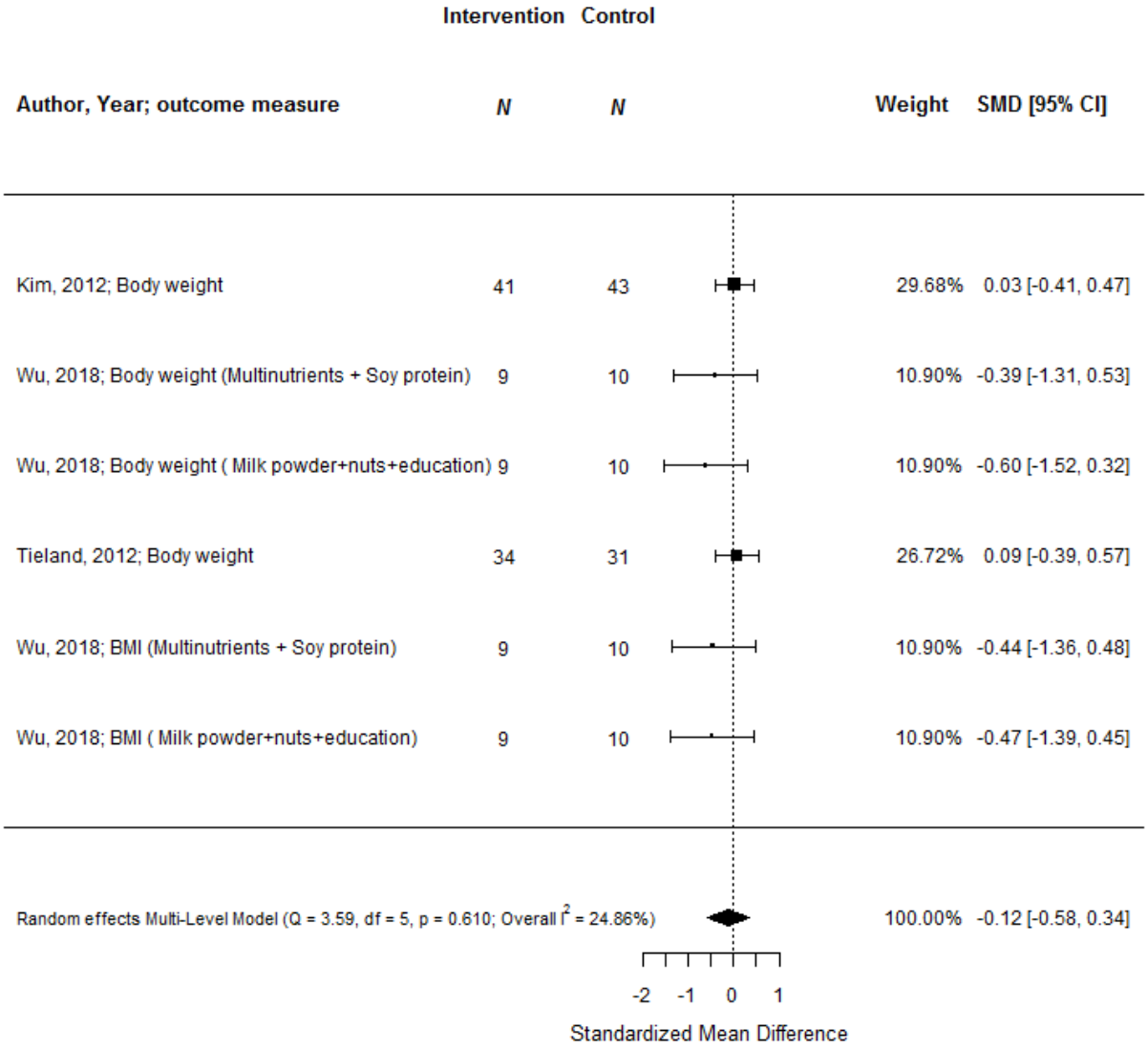



```
Model Results:

estimate      se    tval    pval    ci.lb   ci.ub
  0.1030  0.2406  0.4282  0.6814  -0.4659  0.6719

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S4. Effect on Health outcomes (protein supplementation interventions)

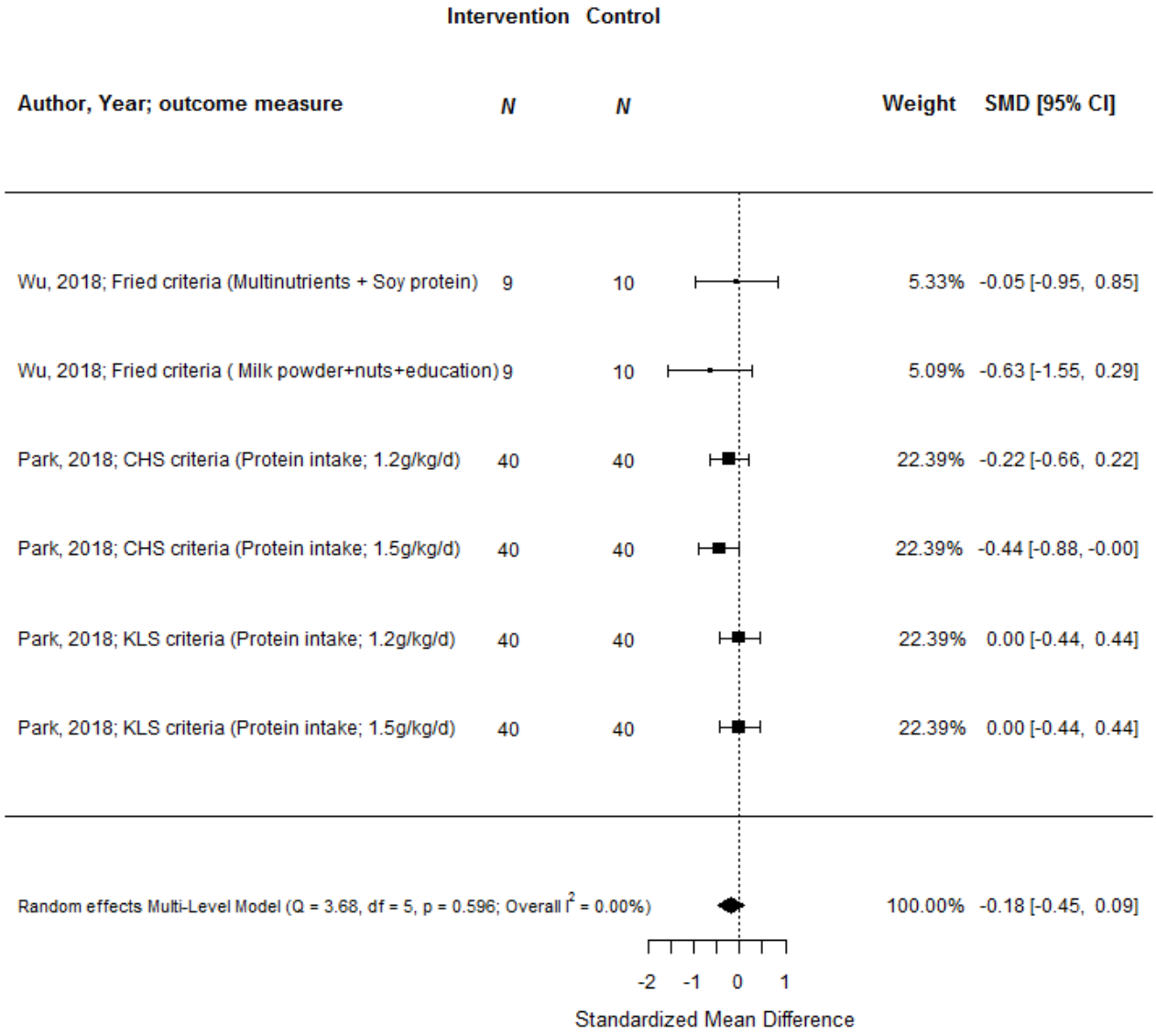



```
Model Results:

estimate      se     tval    pval    ci.lb   ci.ub
 -0.1191  0.1781  -0.6684  0.5335  -0.5769  0.3388

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S5. Effect on Frailty outcome (protein supplementation interventions)

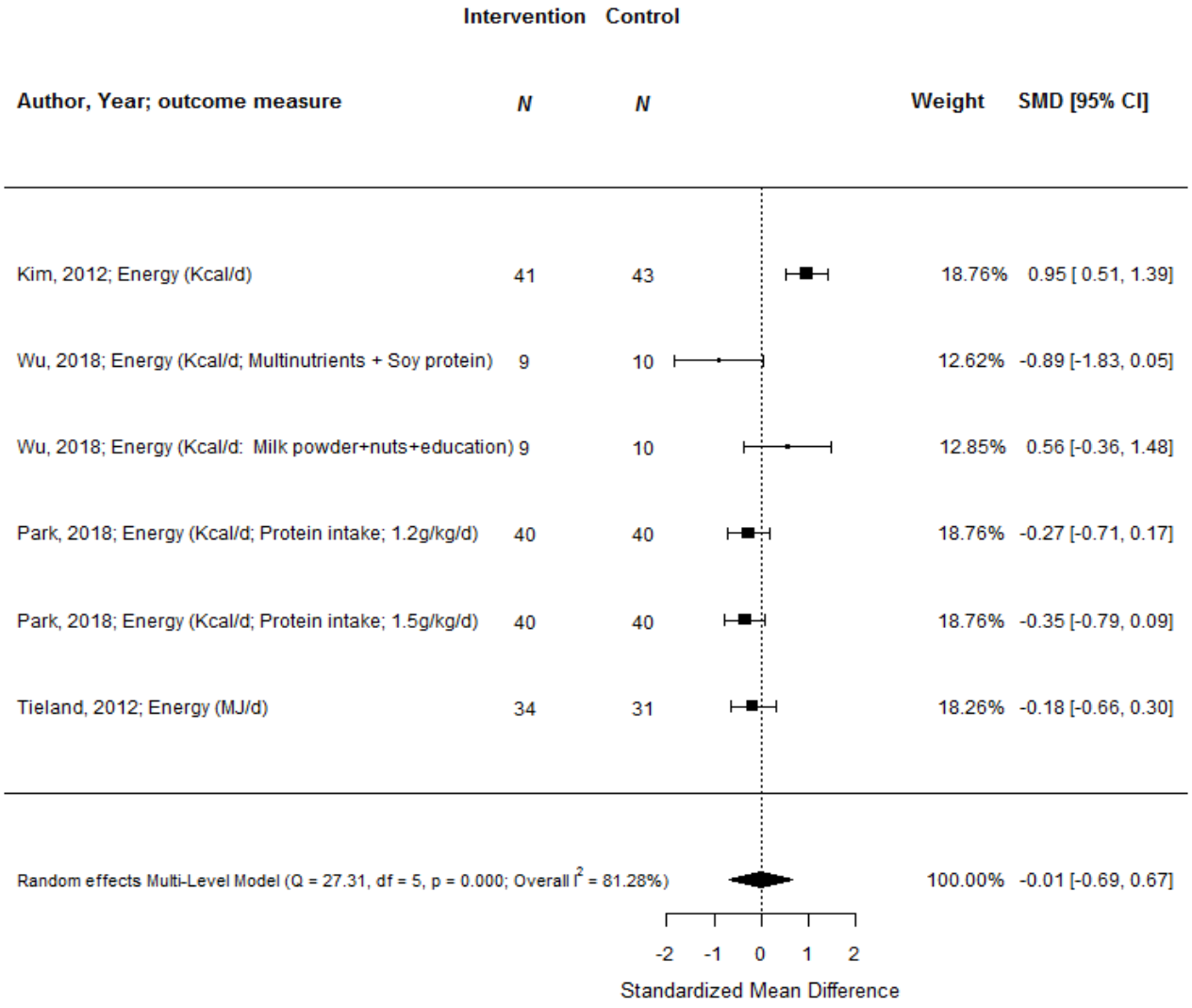



```
Model Results:

estimate      se     tval    pval    ci.lb   ci.ub
 -0.1825  0.1058  -1.7250  0.1451  -0.4545  0.0895

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S6. Effect on Diet Quality outcome (protein supplementation interventions)

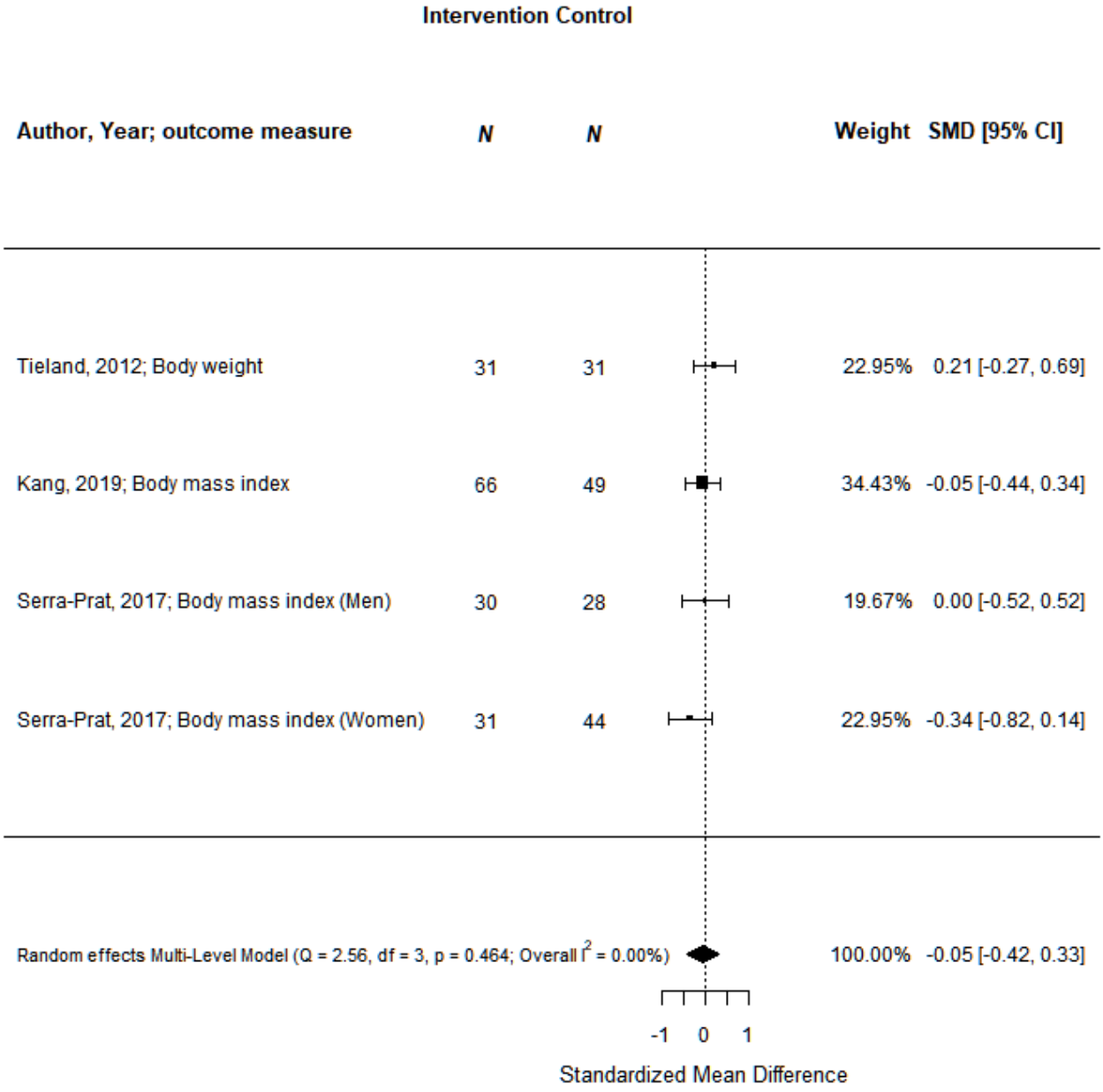



```
Model Results:

estimate      se     tval    pval    ci.lb   ci.ub
 -0.0113  0.2635  -0.0429  0.9674  -0.6886  0.6660

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S7. Effect on Health outcomes (combined approach interventions)

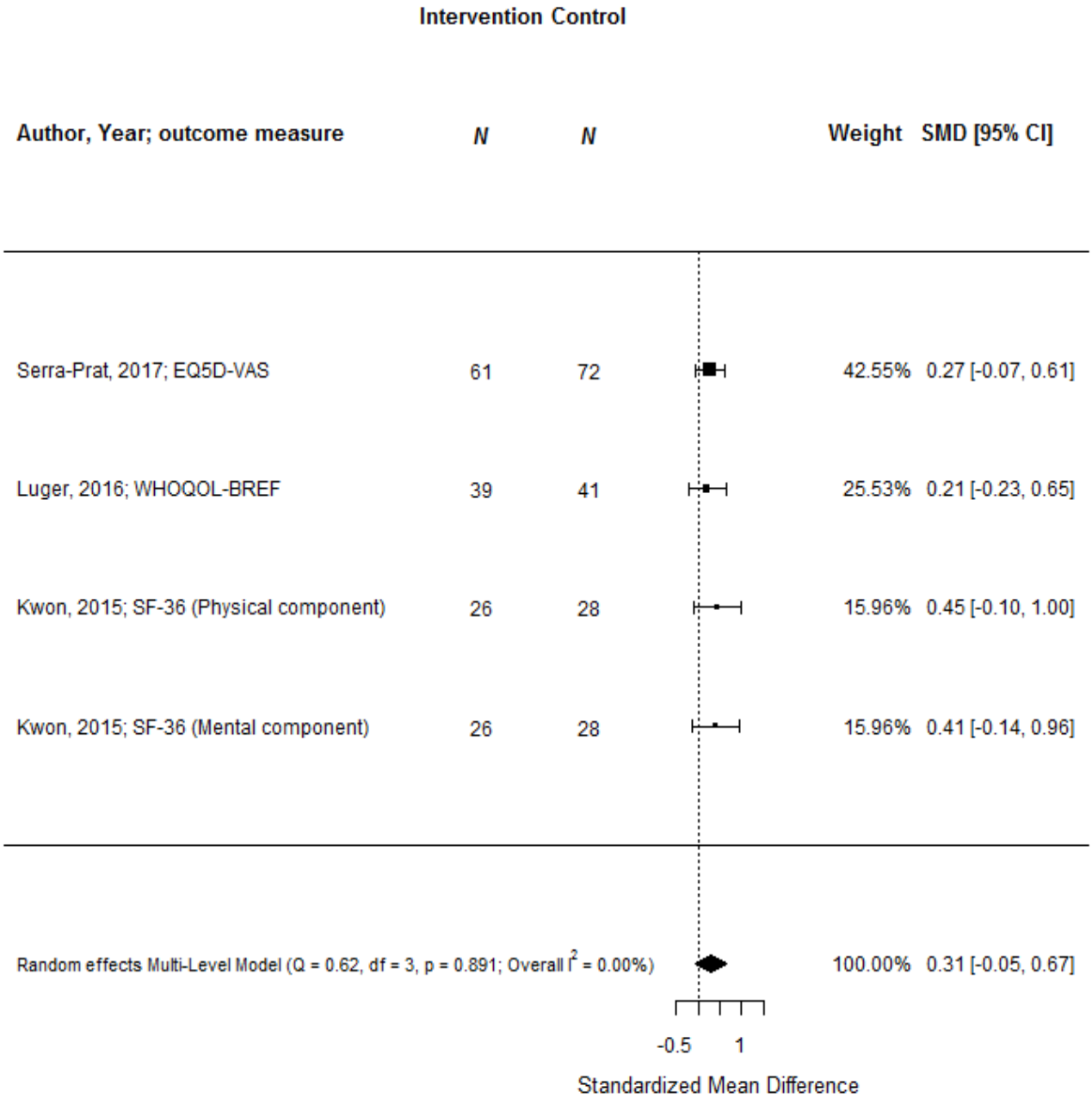



```
Model Results:

estimate      se     tval    pval    ci.lb   ci.ub
 -0.0470  0.1173  -0.4009  0.7153  -0.4205  0.3264

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S8. Effect on Quality of life outcomes (combined approach interventions)

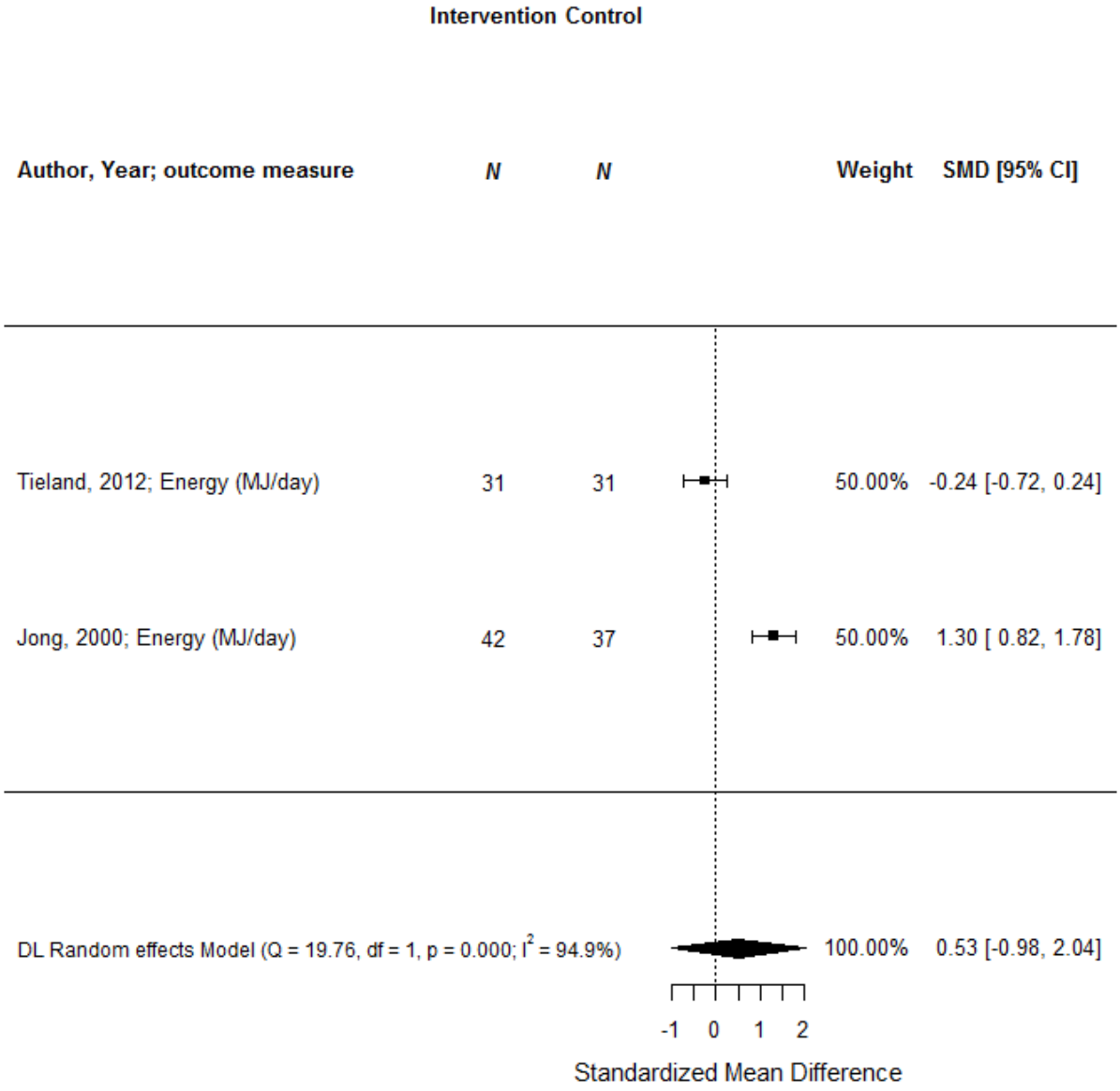



```
Model Results:

estimate      se    tval    pval    ci.lb   ci.ub
  0.3057  0.1130  2.7060  0.0734  -0.0538  0.6653  .

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure S9. Effect on Diet Quality outcome (combined approach interventions)




```
Model Results:

estimate      se    zval    pval    ci.lb    ci.ub
    0.53    0.77    0.69    0.49    -0.98     2.04

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```