

Demographic and Characteristics of Included Studies

Supplemental Table S1. Demographics and 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 from standard protocol; 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

Supplemental Table S2. Demographic and 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

Appendix 4, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup.cmajca.

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
Nykänen, 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 from standard protocol; 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

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 <i>Include if modified (y/n) and how</i>	<p>Fried's Frailty Phenotype. (Y). Modifications made to the following criteria: Weight loss: unintentional weight loss of >3kg or 5% of body weight over the previous year. Self-described exhaustion: whether they had felt fatigue or exhaustion for $>$ three days in the previous week. Weak grip strength: lowest 20% group (amended for elderly people in Taiwan)</p> <p>Men:</p> <table border="1"> <thead> <tr> <th>BMI (kg/m²)</th> <th>Cut off (kg)</th> </tr> </thead> <tbody> <tr> <td>≤ 22.1</td> <td>< 25.0</td> </tr> <tr> <td>22.1–24.3</td> <td>< 26.5</td> </tr> <tr> <td>24.4–26.3</td> <td>< 26.4</td> </tr> <tr> <td>≥ 26.3</td> <td>< 27.2</td> </tr> </tbody> </table> <p>Women:</p> <table border="1"> <thead> <tr> <th>BMI (kg/m²)</th> <th>Cut off (kg)</th> </tr> </thead> <tbody> <tr> <td>≤ 22.3</td> <td>< 14.6</td> </tr> <tr> <td>22.3–24.2</td> <td>< 16.1</td> </tr> <tr> <td>24.3–26.8</td> <td>< 16.5</td> </tr> <tr> <td>≥ 26.8</td> <td>< 16.4</td> </tr> </tbody> </table> <p>Slow gait speed: 10m walk test and the slowest 20% group</p> <p>Men:</p> <table border="1"> <thead> <tr> <th>Height (cm)</th> <th>Cut off (sec)</th> </tr> </thead> <tbody> <tr> <td>≤ 163</td> <td>> 14.9</td> </tr> <tr> <td>> 163</td> <td>> 14.1</td> </tr> </tbody> </table> <p>Women:</p> <table border="1"> <thead> <tr> <th>Height (cm)</th> <th>Cut off (sec)</th> </tr> </thead> <tbody> <tr> <td>≤ 152</td> <td>> 17.5</td> </tr> <tr> <td>> 152</td> <td>> 14.9</td> </tr> </tbody> </table> <p>Low physical activity: based on the Taiwan International Physical Activity Questionnaire-Short Form and lowest 20% of caloric consumption: men < 594kcal/week, women: < 295kcal/week.</p>	BMI (kg/m ²)	Cut off (kg)	≤ 22.1	< 25.0	22.1–24.3	< 26.5	24.4–26.3	< 26.4	≥ 26.3	< 27.2	BMI (kg/m ²)	Cut off (kg)	≤ 22.3	< 14.6	22.3–24.2	< 16.1	24.3–26.8	< 16.5	≥ 26.8	< 16.4	Height (cm)	Cut off (sec)	≤ 163	> 14.9	> 163	> 14.1	Height (cm)	Cut off (sec)	≤ 152	> 17.5	> 152	> 14.9
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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 (<i>reported by income or education level ONLY</i>)	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

	<p>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.</p> <p>Intervention was three months in duration.</p>
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	<p>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.</p> <p>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.</p>
Frailty index used <i>Include if modified (y/n) and how</i>	Fried's Frailty Phenotype. (Y). The authors indicated that gait speed, grip strength and the CES-D depression scale were used for frailty assessment. However, weight loss and physical activity were not clearly indicated.
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	<p>Mean age overall (SD): 81.3 (1.0) years</p> <p>Mean age intervention (SD): 81.77 (1.68) years</p> <p>Mean age control (SD): 80.33 (1.57) years</p>
Gender: I n (%); C n (%)	<p>Female: I: 15 (68.2); C: 17 (68.0)</p> <p>Male: I: 7 (31.8); C: 8 (32.0)</p>
Race/Ethnicity	NR

SES status (<i>reported by income or education level ONLY</i>)	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	<p>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).</p> <p>Exclusion: Participants with comorbidities such as kidney or liver failure, if they were participating in another clinical trial. Unable to walk. Unable to communicate.</p> <p>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.</p>
Frailty index used <i>Include if modified (y/n) and how</i>	Fried's Frailty Phenotype. (Y). Modified Cardiovascular Health Study frailty criteria. Modifications were made to the following criteria; Unintentional weight loss: ≥ 4.5 kg during the last year. Physical activity: calculated as energy expended over the course of one week by the International Physical Activity Questionnaire. Slowness: ≤ 0.8 m/s taken from the average of three 4m walks (with 1.5m walked both before and after the walkway to allow for acceleration and deceleration). Handgrip strength: both hands were measured twice in the standing position with outstretched arms at a 30-degree angle with the use of a hand dynamometer (Takei, Niigat, Japan), and adjusted for sex and BMI.
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 (<i>reported by income or education level ONLY</i>)	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	<p>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.</p> <p>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.</p>
Frailty index used <i>Include if modified (y/n) and how</i>	<p>Cardiovascular Health Study criteria. (Y). Unintentional weight loss: BMI: <18.5 kg/m² or self-reported unintentional weight loss ≥ 10 pounds (4.5 kg) in the last six months. Slowness: assessed using 6m fast gait speed test where participants walked six meters as fast as possible, and the average of two measurements was estimated. The lowest quintile of values stratified for height and age was used to denote slowness. Weakness: muscle strength was assessed by knee extension measured isometrically in the dominant leg, with the participant seated, the angles of the hip and knee at 90 degrees using Lord's strap and strain gauge assembly component of the Physiological Profile Assessment. The average value (kg) of three trials was estimated. Knee extension was standardized based on sex and BMI quartile groups, and the lowest quintiles were used to denote weakness. Exhaustion: measured with the composite scores on three questions on vitality domain in the Medical Outcomes Study SF-12 scale: "Did you feel worn out?," "Did you feel tired?," "Did you have a lot of energy?," with appropriate reversed scorings. The total scores range from 3 to 15, with higher score indicating more energy. The lowest quintile of energy score (<10) derived in a population-based study in a previous study of frailty was used to denote exhaustion. Low activity: Physical activity was evaluated by the self-reported 31-item Longitudinal Ageing Physical Activity Questionnaire measuring the frequency and duration of six different activities in the past two weeks: walking outside, bicycling, gardening, light and heavy household activities, and sports activities. The average time (in minutes) spent per day on physical activities overall was</p>

Appendix 4, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup.cmajca.

	estimated and the lowest quintile used to classify participants with low activity.
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 (<i>reported by income or education level ONLY</i>)	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	<p>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.</p> <p>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.</p> <p>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.</p>
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	<p>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)).</p> <p>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.</p>
Frailty index used <i>Include if modified (y/n) and how</i>	Participants were considered frail if their usual gait speed was < 0.6m/s (based on the Korean Geriatric Survey 2008) and if they scored less than 24 points on the Mini Nutritional Assessment.
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

Appendix 4, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup.cmajca.

SES status (<i>reported by income or education level ONLY</i>)	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	<p>Inclusion: Age \geq 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.</p> <p>Exclusion: Individuals with diabetes mellitus type I or II (as measured by a fasted plasma glucose level \geq 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 m²).</p>
Frailty index used <i>Include if modified (y/n) and how</i>	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	<p>Mean age overall (SD): 83.1 (5.1)</p> <p>Mean age intervention (SD): 78 (1) years</p> <p>Mean age control (SD): 81 (1) years</p>
Gender: I n (%); C n (%)	<p>Female: I: 20 (59); C: 16 (52)</p> <p>Male: I: 14 (41); C: 15 (48)</p>
Race/Ethnicity	NR
SES status (<i>reported by income or education level ONLY</i>)	<p>Education, Low/Middle/High (%):</p> <p>I: 9/59/32</p> <p>C: 0/55/45</p>
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

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	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	<p>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.</p> <p>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.</p>
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	<p>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.</p> <p>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.</p>

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Frailty index used <i>Include if modified (y/n) and how</i>	Screening for frailty: Criteria and predictors of outcomes by Winograd et al. (Y). Winograd et al defined three clinical categories: Independent, Frail and Severely Impaired while Latham et al used Independent, Frail and Fully Dependent.
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 (<i>reported by income or education level ONLY</i>)	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 <i>Include if modified (y/n) and how</i>	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 (<i>reported by income or education level ONLY</i>)	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

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	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 <i>Include if modified (y/n) and how</i>	Fried's phenotype definition. (Y). Participants were considered frail if they met 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: presence of fatigue over the past week from any activity. Physical activity: $< one$ hour of outdoor activities per week.
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

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SES status (<i>reported by income or education level ONLY</i>)	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 (Nutrasomma 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 <i>Include if modified (y/n) and how</i>	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 (<i>reported by income or education level ONLY</i>)	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

Appendix 4, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup.cmajca.

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	<p>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.</p> <p>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.</p>
Frailty index used <i>Include if modified (y/n) and how</i>	Frailty Instrument for Primary Care of the Survey of Health, Ageing, and Retirement in Europe (SHARE-FI). (Y). Weakness: Luger et al performed three hand grip strength measurements on each side and the highest one was selected. The SHARE-fi protocol consists of only two consecutive measurements on each side. SHARE-fi consisted of three frailty categories: non-frail, pre-frail and frail whereas Luger et al used robust, pre-frail and frail.
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	<p>Mean age overall (SD): 82.8 (8.0)</p> <p>Mean age intervention (SD): 83.0 (8.1)</p> <p>Mean age control (SD): 82.5 (8.0)</p>

Gender: I %; C %	Female: I: 85; C: 83 Male: I: 15; C: 17
Race/Ethnicity	NR
SES status (<i>reported by income or education level ONLY</i>)	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	<p>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.</p> <p>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</p>

	<p>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.</p> <p>In addition to the physical training and nutritional intervention, the older persons gained social contacts.</p>
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	<p>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).</p> <p>Exclusion: participants with serum albumin 4.5 mg/dL, serious musculoskeletal conditions, and taking calcium or vitamin D supplements</p>
Frailty index used <i>Include if modified (y/n) and how</i>	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). Kwon et al measured hand grip strength by using the Smedley’s Hand Dynamometer where the higher of two measurements on the dominant hand (instead of three measurements according to Fried et al) was used in the analysis. For walking speed, the participants were instructed to walk at their usual pace on a straight walkway 11m in length on a flat floor. The time taken to walk a marked 5m distance (between 3 and 8m from the start of the walkway) was measured.
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 (<i>reported by income or education level ONLY</i>)	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	<p>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.</p> <p>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</p>

	<p>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.</p>
Type of intervention	<p>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,</p>
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	<p>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.</p>
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 <i>Include if modified (y/n) and how</i>	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 (<i>reported by income or education level ONLY</i>)	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

Appendix 4, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup.cmajca.

	<p>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.</p> <p>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.</p>
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 <i>Include if modified (y/n) and how</i>	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 (<i>reported by income or education level ONLY</i>)	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	<p>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.</p> <p>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.</p>
Type of intervention	<p>Type of Intervention (Nutrition): Oral nutrition supplements; fortified/enhanced foods</p> <p>Physical Activity Intervention Category: Muscle-strengthening</p> <p>Type of Intervention (Physical Activity): Resistance/strength training</p>
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 $< 25 \text{ kg/m}^2$ (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 <i>Include if modified (y/n) and how</i>	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 (<i>reported by income or education level ONLY</i>)	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): $24.4 (2.5) \text{ kg/m}^2$; $25.0 (2.5) \text{ kg/m}^2$ Control Mean (SD): $24.1 (3.2) \text{ kg/m}^2$

<p>Description of Intervention *combined approach treatment arm</p>	<p>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.</p>
<p>Type of intervention</p>	<p>Type of Intervention (Nutrition): Fortified/enhanced foods Physical Activity Intervention Category: Mixed Type of Intervention (Physical Activity): Resistance/strength training, walking/marching, jogging, running</p>
<p>Physical Activity Intervention Intensity</p>	<p>Moderate intensity.</p>
<p>Frequency and Duration of Physical Activity Intervention</p>	<p>2x/week, 45 minutes.</p>
<p>Who Delivered the Intervention (Nutrition and/or Physical Activity), (i.e. doctor,</p>	<p>Teacher (researcher supervised).</p>

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 <i>Include if modified (y/n) and how</i>	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. (Y). Shrinking/Sarcopenia: defined as a weight loss of $\geq 5\%$ of body weight in the prior year, however Nykanen et al did not specify if the weight loss was unintentional. Weakness: Grip strength was measured on both sides instead of measuring the dominant side exclusively. Participants who were unable to perform the grip strength test received the value of zero. Poor endurance and energy: based on the answer to the following item of the self-report Geriatric Depression Scale (GDS): "Do you feel full of energy? Yes/No". Participants who answered "No" were positively identified for this criterion. Slowness: Participants were instructed to walk 10-m adjusted for gender, and as the participants that were unable to perform this test. A 2-m run-in distance was applied. Low physical activity level: defined using a modified version of the six-grade Grimby scale for classification of physical activity. Participants who reported to be in the lowest grade ("I do not move any more than necessary to cope with activities of daily life") or who were bedridden were defined as having a 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)

Appendix 4, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup.cmajca.

Race/Ethnicity	NR
SES status (<i>reported by income or education level ONLY</i>)	Education \geq 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.