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REVIEW

Nonpharmacological interventions to treat physical frailty and sarcopenia in older patients: a systematic overview – the SENATOR Project ONTOP Series

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Background: Physical frailty (PF) and sarcopenia are predictors of negative health outcomes such as falls, disability, hospitalization, and death. Some systematic reviews (SRs) have been published on different nonpharmacological treatments of frailty and sarcopenia using heterogeneous definitions of them.

Objective: To critically appraise the evidence from SRs of the primary studies on nonpharmacological interventions to treat PF (defined by Fried's frailty phenotype) and sarcopenia (defined by the EWGSOP) in older patients.

Design: Overview of SRs and meta-analysis of comparative studies.

Data sources: PubMed, Cochrane Database of Systematic Reviews, EMBASE, and CINAHL were searched in October 2015.

Eligibility criteria for selecting studies: SRs that included at least one comparative study evaluating any nonpharmacological intervention to treat PF or sarcopenia in older patients in any health care setting. Any primary study described in these SRs with experimental design was included.

Data extraction and management: Two reviewers independently screened titles, abstracts, and full-texts of articles. Quality assessment was carried out by using criteria from the Cochrane Collaboration and the GRADE working group.

Results: Ten SRs with 5 primary studies satisfied the inclusion criteria. The most frequent interventions in the included studies were physical exercise (4) and nutritional supplementation (2). Muscle strength (MS; except for one study in a frail population) and physical performance (PP; except for another study in a frail population) improved with exercise and amino acid supplementation in frail and sarcopenic old adults. Falls and activities of daily living were assessed in two studies with opposite results. The overall quality of the evidence was low.

Conclusion: This overview of SRs highlights the importance of exercise interventions with or without nutritional supplementation to improve the PP in community-dwelling patients aged >65 years with PF and sarcopenia. MS improved with multidisciplinary treatment and exercise interventions in this population.

Keywords: review, exercise, nutrition, older adults

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Introduction

Frailty can be seen as the weakening of health (defined as the resilience or capacity to cope and to maintain and restore one's integrity, equilibrium, and sense of well-being in three domains: physical, mental, and social).[1,2] Clinically, it has been defined as

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a "multidimensional syndrome characterized by decreased reserve and diminished resistance to stressors."[2] It is considered a treatable condition that may be reversible.[3] Although no definition is universally accepted, two predominant models have emerged to understand frailty:[1,4] Fried's phenotypical approach to physical frailty (PF)[5] and Rockwood's operationalization of a model of accumulation of deficits.[6] In the current scientific literature, Fried's phenotype is the most widely used method to define,[7] where PF is defined as a multifactorial syndrome characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability to develop increased dependency and/or death.[2] Rockwood's Index considers not only the physical aspects of frailty but also other domains such as psychological and social domains. A major difference is that the latter model may include any degree of disability as a vulnerability factor (ie, present disability increases frailty), whereas the former model considers frailty as a vulnerability to disability, as the previous stage to disability. These two approaches should be considered as complementary and not mutually exclusive.[8]

Sarcopenia is the presence of low muscle mass plus low muscle function (muscle strength [MS] or physical performance [PP]) associated with aging.[9] Recent research has highlighted sarcopenia as the biological substrate of PF,[10] skeletal muscle decline being one of its key components. Recent research confirms that Fried's frailty phenotype and the European Working Group on Sarcopenia in Older People (EWGSOP)-defined sarcopenia are strongly correlated.[11] Both the entities are the predictors of negative health outcomes such as falls, disability, hospitalization, and death.[12–17] Interventions are necessary to reverse the frailty status and to treat sarcopenia in order to avoid further negative health outcomes.[3]

Some systematic reviews (SRs) have been published in recent years on different nonpharmacological treatments of frailty and sarcopenia (physical exercise and nutritional supplementation being the usual components). However, the current definitions of frailty and sarcopenia that are in use are heterogeneous, and different inclusion criteria have been used. Therefore, the aims of this overview of reviews were as follows: 1) to identify all published SRs on nonpharmacological interventions of PF (defined by Fried's frailty phenotype) and sarcopenia (defined by the EWGSOP), 2) to identify and critically appraise the primary studies included in these SRs by using the Optimal evidence-based Non-drug Therapies in Older People (ONTOP) methodology,[18] and 3) to critically summarize the evidence and emphasize its limitations in order to suggest research priorities for future studies.

Methods

This paper is part of the ONTOP project, a work package of a European Union-funded FP 7 research named SENATOR (Software ENgine for the Assessment & Optimization of drug and non-drug Therapy in Older persons [www.senator-project.eu]); detailed methodology of ONTOP has been published previously.[18] Briefly, the ONTOP objective is to develop a literature overview of reviews of nonpharmacological treatments of 10 prevalent medical conditions affecting older people. The present paper reports evidence-based interventions for the treatment of sarcopenia and frailty in older people.

The ONTOP Evidence Group defined the clinical questions according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE)[19] method. A Delphi process using a group of independent international experts in Geriatric Medicine helped to establish the critical outcomes that should be considered for selecting papers and reporting results in this review (Table 1). Most critical outcomes included measures of muscle function, and some of them were compound variables. The expert group did not consider muscle mass as a critical outcome. Table 1 also lists the methods that were acceptable to assess each variable, following the EWGSOP recommendations.

Table 1 Delphi-defined critical outcomes for studies on interventions on physical frailty and sarcopenia and assessment methods for each outcome

Critical outcomes	Assessment methods
Muscle strength	Handgrip strength
	Knee flexion/extension
	Peak expiratory flow
Physical performance	Short Physical Performance Battery
	Usual gait speed
	Timed Up and Go Test
	Stair climb power test
Muscle function: strength and performance	Handgrip strength
	Knee flexion/extension
	Peak expiratory flow
	+ physical performance assessment
Muscle mass and muscle function	Bioimpedance analysis
	Dual energy X-ray absorptiometry
	Computer tomography
	Magnetic resonance imaging
	Total or partial body potassium per fat-free soft tissue
	Anthropometric measures
	+ muscle function assessment
Activities of daily living	Barthel index
	Lawton index
Falls	Falls

Note: Data from Cruz-Jentoft.[9]

Search strategy and selection of SRs

Search strategies were launched in October 2015 in the following databases: Cochrane Database of Systematic Reviews, PubMed, EMBASE and CINAHL (Supplementary material 1). Montori's highly specific strategy was used for PubMed database.[20]

Two criteria were considered for further evaluation of any published abstract: 1) a paper defined as SR or meta-analysis and 2) the use of any nonpharmacological intervention for PF (defined by Fried's phenotype, either original or adapted)[5] or sarcopenia (defined by the EWGSOP).[9] Other records such as guidelines, conference proceedings, and program abstracts were excluded.

Later, full-texts of all relevant abstracts were obtained and screened to identify SRs of interest based on 1) the use of at least one medical literature database; 2) the inclusion of at least one primary study; 3) the use of at least one nonpharmacological intervention to treat PF or sarcopenia; and 4) the mean age of the subjects was >65 years. SRs written in English, Italian, Portuguese, or Spanish were considered.

Inclusion and exclusion criteria for primary studies

The included SRs were examined to identify any experimental comparative study, either randomized or nonrandomized, that investigated any nonpharmacological intervention to treat PF or sarcopenia in older patients.

Primary studies were excluded if they were observational studies or before–after studies with historical controls. Studies were also excluded when the mean age of subjects was <65 years, when frailty was assessed by using methods other than Fried's criteria, and when sarcopenia was not defined by the EWGSOP criteria. Trials with mixed frail and prefrail subjects were also excluded. Studies using conditions to define the population (eg, diabetes, COPD, and cancer) or using special populations (eg, athletes) were also excluded, as well as those exclusively considering patients admitted to intensive care or palliative care units. Only nutritional interventions that considered macronutrients were included; those using individual vitamins or micronutrients were excluded, as they were considered pharmacological interventions. Trials that did not assess any critical outcome (Table 1) were also excluded.

Data extraction and management

Results from primary studies were transferred onto data extraction forms. Information collected included trial and patient characteristics, intervention and comparator components as well as outcome measures. Two reviewers independently screened titles, abstracts, and full-texts of articles. Disagreement was resolved by discussion and, when needed, by a third senior reviewer.

Risk of bias assessment

Assessment of bias in the included primary studies was carried out by using criteria from the Cochrane Collaboration.[21] Domains assessed were random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential biases such as differences in baseline conditions. Overall risk of bias was graded by including each study in one of three categories: low risk, high risk, and unclear risk. Two reviewers independently assessed the risk of bias of individual studies, and any differences in quality assessment results were resolved through consensus.

Issues on the unit of analysis

Subjects were treated as the unit of analysis in all primary studies included in this review.

Data synthesis and analysis

The results were presented in a narrative way with the information provided by the included studies. Nonpharmacological interventions varied widely across studies, and therefore, meta-analysis was not feasible.

Grading the quality of evidence

The quality of evidence was assessed with GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology.[19] GRADE assessment considers the risk of bias, consistency of results across the available studies, precision of the results, directness, and likelihood of publication bias, dose–response, and strength of the association, as well as plausible confounders that may have influence on the effect of the intervention. The quality of the evidence was categorized as high, moderate, low, or very low based on the authors' judgments for the critical outcomes.

Results

SRs

This search identified 9,277 abstracts after removing duplicates (Figure 1). Among the 130 reviews identified for full-text evaluation, 10 were included (Table 2) and 120 were excluded, the main reason being that frailty and sarcopenia

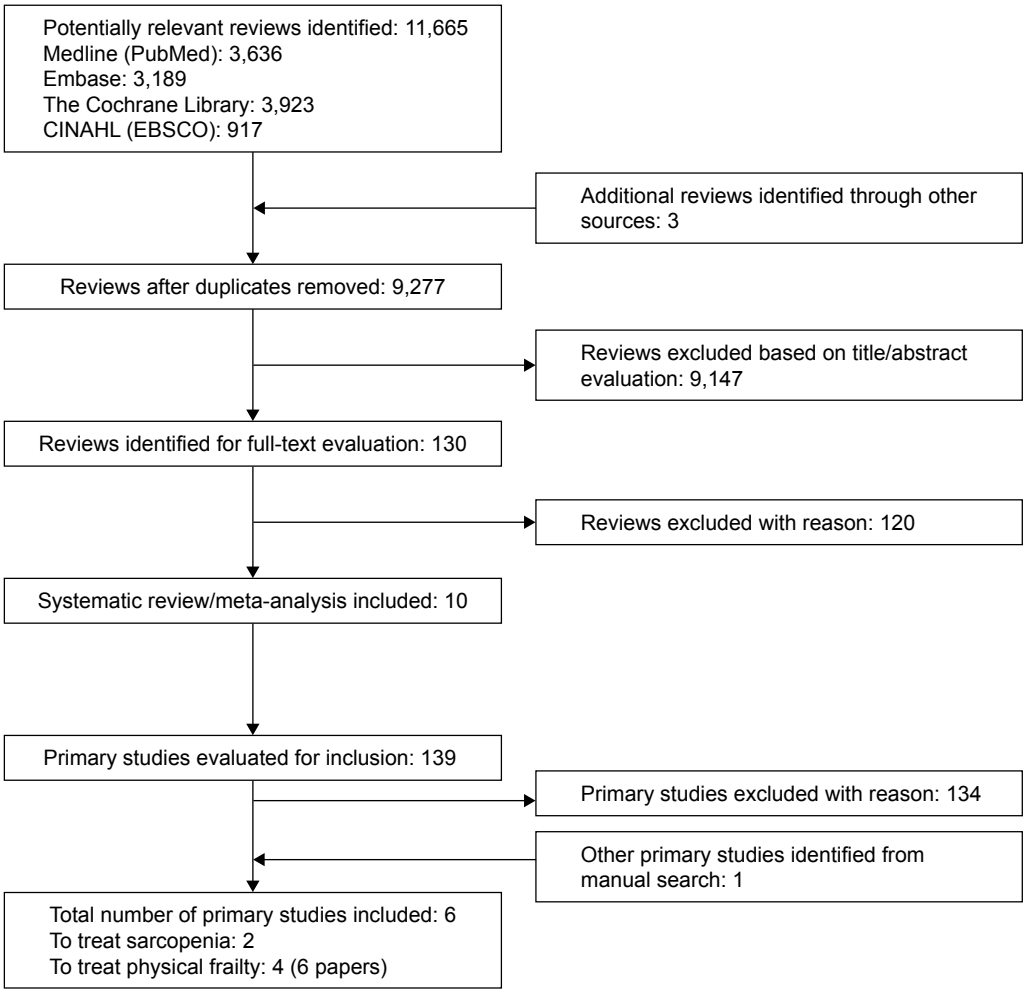

Figure 1 Screening process of the study.

were not defined using Fried's or EWGSOP criteria. The publication year of the SR included ranged from 1979 to 2015. These reviews were heterogeneous, encompassing nonpharmacological interventions such as nutritional supplementation and physical exercise for the treatment of PF and sarcopenia (Table 3).

Primary studies

Overall, the 10 SRs[22–31] yielded 140 primary studies, of which 7[32–38] satisfied the inclusion criteria, but three of these presented the results of the same study. An additional relevant study was included after manual search[39] (Table 4). The six primary studies finally included are listed in Table 5. Table 6 summarizes the risks of bias in each study, which was mostly low due to the nature of the interventions except for performance bias.

Sarcopenia

Five out of 10 SRs[22–26] included sarcopenic populations. From these SRs, only one primary study (Kim et al)[32] satisfied the inclusion criteria. In most cases, subjects were not defined by having sarcopenia, but by a range of other conditions, and in many cases, healthy subjects were included (Supplementary material 2). In addition, one relevant study was found after manual search.[39]

Evidence of exercise and amino acid supplementation (AAS) to treat sarcopenia in community-dwelling older people

One randomized controlled trial (RCT)[32] evaluated four interventions: a multicomponent exercise program (MCEP), AAS, MCEP with AAS, and health education (HE) in 155 Japanese sarcopenic community-dwelling women. PP and MS were the outcome measures. After the 3-month intervention, MS assessed by knee extension improved only with the combination of MCEP and AAS (strength increased by 7%) compared with HE (12.3% strength loss, P=0.02). PP assessed by 5-m usual gait speed improved in MCEP (+0.19 m/s) and MCEP + AAS groups (+0.16 m/s) compared with HE (+0.03 m/s, P=0.0017). The authors of this trial concluded

Table 2 Systematic reviews included

SR included	Aim	Population age (years)	Search strategy date	Intervention	Outcome	Primary studies selected
Sarcopenia						
Cadore et al[22]	To recommend training supervised exercise programs to improve muscle strength, gait ability and fall risk	>70	1990–2012	RT, ET, BT, BWRT, MCEP, TAI, FT, COOT, SUP	MS, PP, falls	1 out of 20
Cruz-Jentoft et al[23]	To review the effect of nutrition and exercise interventions on muscle function	>50	2000–2013	RT, PA, multipurpose E, Prot, EAA, HMB, fatty acids, ES	MS, PP	1 out of 19
Finger et al[24]	To summarize whether protein supplementation could optimize the effects of resistance training on muscle strength	>60	Up to January 2014	RT + Prot (or modified diet with increased protein content) vs RT vs RT + with non-Prot placebo supplementation	MS	1 out of 9
Komar et al[25]	To synthesize the literature relating to leucine supplementation on muscle strength	>65	Up to February 2014	Supplementation with Leu (at least 2 g/day)	MS	1 out of 16
Malafarina et al[26]	To analyze the effects of supplementation on muscle function	>65	1991–2012	Nutritional supplementation (AAS/ALA/EAA/HMB/Leu/Prot) ± E (≥8 weeks)	MS, PP	1 out of 17
Physical frailty						
Gine-Garriga et al[27]	To examine the effectiveness of combined diet and exercise interventions to improve physical function	≥65	April 2013	Diet interventions (based on dietary modification) ± E (RT/ST/STR/FT/BT)	MS, PP	1 out of 19
de Labra et al[28]	To investigate the benefits of exercise programs	Not stated (older adults)	2003–2015	RT, functional walking, MCEP, BWRT, BT	MS, PP, ADL, falls	3 out of 9
Orr[29]	To review the effect of whole body vibration exposure on functional mobility	≥45	Up to October 2014	WBV, WBVE	PP	1 out of 20
Plummer et al[30]	To compare any physical exercise intervention to a control group on dual-task interference during walking	≥60	Up to September 2014	Dual-task interventions	PP	1 out of 21
Zanotto et al[31]	To summarize how exercise affects dual-task performance	>59	Up to October 2013	Dual-task interventions, E, BT, TAI	PP	1 out of 17

Abbreviations: AAS, amino acid supplement; ADL, activities daily living; ALA, alpha-linoleic acid supplement; BT, balance training; BWRT, body weight resistance training; COOT, coordination training; E, exercise; EAA, essential amino acid supplementation; ES, electrical stimulation; ET, endurance training; F, falls; FT, flexibility training; HMB, beta-hydroxy-beta-methylbutyrate supplement; Leu, leucin supplement; MCEP, multicomponent exercise program; MS, muscle strength; PA, physical activity; PP, physical performance; Prot, protein supplement; PRT, progressive resistance training; RT, resistance training; SR, systematic review; ST, strength training; STR, stretching; SUP, supplementation; TAI, Tai-Chi exercise; WBV, whole body vibration; WBVE, whole body vibration plus exercise.

that exercise and nutrition may be necessary to reverse the effects of sarcopenia in community-dwelling older women, but research on larger populations and also in males is needed to confirm these results.

Table 3 Nonpharmacologic interventions to treat physical frailty and sarcopenia with systematic reviews

Sarcopenia
Exercise
Amino acid supplementation
Exercise and amino acid supplementation
Health education
Physical frailty
Exercise
Nutritional supplementation
Exercise and nutritional supplementation
Multidisciplinary interventions

A second RCT[39] evaluated the effects of exercise (resistance training; RT) in combination with AAS (collagen peptides) versus exercise with placebo during 3 months in 53 older community-dwelling sarcopenic men. Knee extension strength was used as the outcome measure. MS improved significantly in both the groups after 12 weeks, the effect being higher in the collagen peptide group (+13.82%) than in the placebo group (+5.3%, $P<0.05$). Authors suggested that these results might be due to the intensive training designed to induce muscular hypertrophy and the collagen effects on increasing muscle mass.

We did not poll these studies due to differences between participants and interventions used. In both the studies, blinding of participants was not possible due to the nature of the intervention. Methodological issues are synthesized

Table 4 Distribution of primary studies in systematic reviews

Systematic reviews (10)	Primary studies (6)							
	Sarcopenia (EWGSOP)		Physical frailty (Fried's criteria)					
	Kim et al[32]	Zdzieblik et al[39]	The Frailty Intervention Trial			Cadore et al[36]	Zhang et al[37]	Kim et al[38]
			Fairhall et al[33]	Cameron et al[34]	Fairhall et al[35]			
Cadore et al[22]	X							
Malafarina et al[26]	X							
Cruz-Jentoft et al[23]	X							
Komar et al[25]	X							
Finger et al[24]	X							
Manual search		X						
Gine-Garriga et al[27]			X	X				
Zanotto et al[31]						X		
de Labra et al[28]					X	X		X
Orr[29]							X	
Plummer et al[30]						X		

in Table 6. According to GRADE assessment, the quality or certainty of the evidence has been assessed as very low (Table 7) for the critical outcomes.

PF

Five out of 10 SRs[27–31] included physically frail populations. From these SRs, 4 RCTs[33–38] (described in 6 articles) were included; three articles[33–35] described different aspects of the same study (the Frailty Intervention Trial – FIT), so that they are reported together here. Again, the main reason of exclusion was the use of varied nonstandard definitions of frailty (Supplementary material 3).

The number of patients included in these trials ranged from 32 to 241. All trials included participants over 70 years old, except one study performed in nursing homes, that included patients aged over 85 years.[36] One trial included only women.[38] The study characteristics are described in Table 5. In general, risk of bias was low, except for blinding of participants (Table 6).

Efficacy

This study considered that data of these studies could not be combined due to differences between the nonpharmacological interventions used.

Evidence on multidisciplinary interventions in physically frail community-dwelling older people

A single study, The Frail Intervention Trial (FIT)[40–42] evaluated the effects of an individualized multidisciplinary intervention versus usual care in 241 physically frail community-dwelling older people. The assessed outcomes of interest were MS, PP, falls and activities of daily living (ADL). After 12 months, there was a reduction in MS, assessed by knee extension strength, in both the groups: −16.41% in the intervention group versus −25.8% in the control group. This reduction was lower in the intervention group than the control group (between-group difference 1.84 kg, 95% confidence interval [CI] 0.17–3.51, P=0.03). PP, assessed by Short Physical Performance Battery (SPPB), just increased in the intervention group: +0.68 points versus −1.05 points in the control group (between-group difference at 12 months is 1.58 points, 95% CI 1.02–2.14, $P \leq 0.001$). There was an increment in 4-m walk test of +0.07 m/s in the intervention group compared with no changes in the control group (between-group difference at 12 months 0.06 m/s, 95% CI 0.01–0.10, P=0.02). MS, assessed by handgrip, was higher in the control group: +0.93 kg in the intervention group versus +1.88 kg control group although no significant differences were found between groups (1.18 kg, 95% CI −013 to 2.49, P=0.08). In addition, no significant differences were found in ADL, assessed by Barthel Index (BI) between groups after 12-month intervention (0.67 points, 95% CI −4.23 to 5.56, P=0.79). BI was higher in the control group than the intervention group (6.14 vs 5.56). There was no effect of the intervention on the rate of falls that was also similar in the intervention group (183 falls, 1.54 falls per person, standard deviation [SD] 2.58) and the control group (178 falls, 1.50 falls per person, SD 2.39) with an incidence rate ratio of 1.12 (95% CI 0.78–1.63, P=0.53).

The risk of bias according to methodological issues was low except for performance and detection bias (Table 6). The quality or certainty of the evidence has been assessed as low (Table 8A) for the critical outcomes.

Evidence on vibration exercise in physically frail community-dwelling older people

A pilot RCT[37] assessed the efficacy of whole-body vibration exercise (WBVE) versus usual care that included different

Table 5 Description of primary studies

Author	Type of study	N (% female)	Age: years, mean ± SD	Setting	Intervention period	Intervention (N)	Outcome measures
Sarcopenia (EWGSOP definition)							
Kim et al[32]	RCT	155 (100)	MCEP: 79.0 (2.9) AAS: 79.2 (2.8) MCEP + AAS: 79.5 (2.9) HE: 78.7 (2.8)	Community dwelling (Japan)	3 months	1. MCEP (n=39). Resistance and balance training 60 min. 2 times/week (moderate intensity) 2. AAS (n=39). 3 g powdered amino acid supplements (42% leucine, 14% lysine, 10.5% valine, 10.5% isoleucine, 10.5% threonine, 7% phenyl-alanine, and 5.5% other) twice a day 3. MCEP + AAS (n=38) 4. HE (n=39). A monthly class focused on cognitive function, osteoporosis, and oral hygiene	MS: Knee extension strength PP: 5 m usual gait speed
Zdzieblik et al[39]	RCT	53 (0)	RT + AAS: 72.3 (3.7) RT + placebo: 72.1 (5.5)	Community dwelling (Germany)	12 weeks	1. RT + AAS (n=26). RT: 60 min 3 times/week (week 1–4: 15 repetitions, week 5–9: 10 repetitions, week 10–12: 8 repetitions; 4 s/repetition). AAS: 15 g of collagen peptides daily or within 1 h after RT 2. RT + placebo (n=27): silicon dioxide daily	MS: Knee extension strength
Physical frailty (Fried's criteria)							
The Frailty Intervention Trial: Fairhall et al[33] Cameron et al[34] Fairhall et al[35]	RCT	216 (68)	83.3 (5.9)	Community dwelling (Australia)	12 months	1. Multidisciplinary intervention (n=107). Tailored to each participant, based on frailty characteristics assessed at baseline interventions include nutritional, physiotherapy, physical training, and psychological support 2. Control (n=109). Usual care	MS: Handgrip strength and knee extension strength PP: 4 m usual gait speed and SPPB ADL: Barthel index Falls: Total number
Cadore et al[36]	RCT	24 (70)	MCEP: 93.4 (3.2) Control: 90.1 (1.1)	Nursing home (Spain)	12 weeks	1. MCEP (n=11). Resistance and balance training 40 min 2 times/week (moderate intensity) 2. Control (n=13). Passive stretches of individual joints 30 min 4 times/week	MS: Hand grip strength & knee extension strength PP: 5-m usual gait speed & TUGT (s) ADL: Barthel Index Falls: Incidence
Zhang et al[37]	RCT	37 (13.5)	WBVE: 88.8 (3.6) Control: 84.7 (3.7)	Community dwelling (China)	8 weeks	1. WBVE (n=19). Whole-body vertical vibration exercise (amplitude 1–3 mm; frequency 6–26 Hz; 4–5 bouts [60 s/bout]; 3–5 times/week) 2. Control (n=18). Usual care, physical therapy (phototherapy, ultrasound therapy, electrical stimulation, electromagnetic fields therapy, manipulation therapy), and routine exercises such as pedaling training	MS: Knee extension strength PP: TUGT

(*Continued*)

Table 5 (*Continued*)

Author	Type of study	N (% female)	Age: years, mean ± SD	Setting	Intervention period	Intervention (N)	Outcome measures
Kim et al[38]	RCT	131 (100)	MFGM (81.0±2.8) MCEP + placebo (81.1±2.8) MCEP + MFGM (81.0±2.6) Placebo (80.3±3.3)	Community dwelling (Japan)	3 months; 4 months follow-up	1. MFGM (n=32). Milk Fat Globule Membrane 1 g/day (21.5% protein, 44% fat, 26.5% carbohydrates, 33.3% phospholipids) 2. MCEP + placebo (n=33). Resistance and balance training 60 min 2 times/week + placebo 3. MCEP + MFGM (n=33) 4. Placebo (n=32). Whole milk powder daily (26.3% protein, 25.2% fat, 39.5% carbohydrates, 0.23% phospholipids)	MS: Knee extension strength and hand grip strength PP: 5 m usual gait speed and TUGT

Abbreviations: AAS, amino acid supplementation; ADL, activities of daily living; BT, balance training; HE, health education; MCEP, multicomponent exercise program; MFGM, milk fat globule membrane; MS, muscle strength; PP, physical performance; RCT, randomized controlled trial; RT, resistance training; s, seconds; SD, standard deviation; SPPB, Short Physical Performance Battery; TUGT, Timed Up and Go Test; WBVE, whole-body vibration exercise.

Table 6 Risk of bias of primary studies*

Author	Type of study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective outcome reporting (reporting bias)	Similar baseline characteristics between groups
Sarcopenia								
Kim et al[32]	RCT	✓	✓	X	✓	X	X	Yes
Zdzieblik et al[39]	RCT	✓	?	✓	✓	X	X	No
Physical frailty								
The frailty intervention study:								
Fairhall et al[33] Cameron et al[34] Fairhall et al[35]	RCT	✓	✓	X	X	✓	✓	Yes
Cadore et al[36]	RCT	✓	✓	X	✓	X	X	Yes
Kim et al[38]	RCT	✓	X	X	✓	✓	X	Yes
Zhang et al[37]	RCT	✓	✓	X	✓	X	X	Yes

Note: *The risk of bias was assessed according to the methodology of each primary study. ✓, low risk of bias; ?, unclear risk of bias; X, high risk of bias.
Abbreviation: RCT, randomized controlled trial.

Table 7A GRADE (sarcopenia)

Question: Exercise compared to placebo for sarcopenic older people **Setting**: Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 3 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise compared with placebo (health education) improves MS as the quality/certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 3 months; assessed with: 5-m usual gait speed [m/s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise compared with placebo (health education) improves PP as the quality/certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[32] [a]High risk of bias because of incomplete outcome data (no intention-to-treat analysis was reported) and selective outcome reporting (point estimate and confidence intervals not reported). [b]Only women were included in the study. [c]Low sample size.
Abbreviations: MS, muscle strength; PP, physical performance.

Table 7B GRADE (sarcopenia)

Question: AAS compared to placebo for sarcopenic older people **Setting**: Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 3 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether AAS improves MS compared with placebo (health education) as the quality/certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 3 months; assessed with: 5-m usual gait speed [m/s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether AAS improves PP compared with placebo (health education) as the quality/certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[32] [a]High risk of bias because of incomplete outcome data (no intention-to-treat analysis was reported) and selective outcome reporting (point estimate and confidence intervals not reported). [b]Only women were included in the study. [c]Low sample size.
Abbreviations: AAS, amino acid supplementation; MS, muscle strength; PP, physical performance.

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Table 7C GRADE (sarcopenia)

Question: Exercise and AAS compared to placebo for sarcopenic older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 3 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and AAS improves MS compared with placebo (health education) as the quality/ certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 3 months; assessed with: usual gait speed [m/s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and AAS improves PP compared with placebo (health education) as the quality/ certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[32] [a]High risk of bias because of incomplete outcome data (no intention-to-treat analysis was reported) and selective outcome reporting (point estimate and confidence intervals not reported). [b]Only women was included in the study. [c]Low sample size.
Abbreviations: AAS, amino acid supplementation; MS, muscle strength; PP, physical performance.

Table 7D GRADE (sarcopenia)

Question: Exercise and AAS compared to exercise and placebo for sarcopenic older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 3 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and AAS improves MS compared with exercise and placebo as the quality/ certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical

Notes: Data from Zdzieblik et al.[39] [a]High risk of bias because of attrition bias (no intention-to-treat analysis was reported). [b]Only men were included in the study. [c]Low sample size.
Abbreviations: AAS, amino acid supplementation; MS, muscle strength.

Table 8A GRADE (physical frailty)

Question: Multidisciplinary interventions compared to usual care for physical frailty (Fried's criteria) older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 12 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Serious[a]	Not serious	Not serious	Serious[b]	None	Multidisciplinary interventions may increase MS (knee extension strength) compared with usual care (low quality/ certainty evidence)	⊕⊕◯◯ LOW	Critical
Muscle strength (follow-up: 12 months; assessed with: grip strength [Nm/kg])									
1	Randomized trials	Serious[a]	Not serious	Not serious	Serious[b]	None	Multidisciplinary intervention may increase MS (grip strength) compared with usual care (low certainty evidence) however the 95% confidence interval includes the possibility of both increased and reduced MS	⊕⊕◯◯ LOW	Critical
Physical performance (follow-up: 12 months; assessed with: SPPB)									
1	Randomized trials	Serious[a]	Not serious	Not serious	Serious[b]	None	Multidisciplinary interventions may increase PP (SPPB) compared with usual care (low quality/certainty evidence)	⊕⊕◯◯ LOW	Critical
Physical performance (follow-up: 12 months; assessed with: 4-m walk test [m/s])									
1	Randomized trials	Serious[a]	Not serious	Not serious	Serious[b]	None	Multidisciplinary interventions may increase PP (4-m walk) compared with usual care (low quality/certainty evidence)	⊕⊕◯◯ LOW	Critical
Activities of daily living (follow-up: 12 months; assessed with: Barthel Index)									
1	Randomized trials	Serious[a]	Not serious	Not serious	Serious[b]	None	Multidisciplinary intervention may increase ADL improvement (Barthel Index) compared with usual care (low certainty evidence) however the 95% confidence interval includes the possibility of both increased and reduced ADL improvement	⊕⊕◯◯ LOW	Critical
Fall rate (follow-up: 12 months)									
1	Randomized trials	Serious[a]	Not serious	Not serious	Serious[b]	None	Multidisciplinary intervention may increase fall rate compared with usual care (low certainty evidence) however the 95% confidence interval includes the possibility of both increased and reduced fall rate	⊕⊕◯◯ LOW	Critical

Notes: Data from Fairhall et al[33,35] and Cameron et al.[34] [a]High risk of detection bias (unblinding outcome assessor in 51% of participants). [b]Low sample size. Large CI.
Abbreviations: ADL, activities of daily living; CI, confidence interval; MS, muscle strength; PP, physical performance; SPPB, Short Physical Performance Battery.

Table 8B GRADE (physical frailty)

Question: WBVE compared to usual care for physical frail (Fried's criteria) older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 8 weeks; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether WBVE compared to usual care improves MS (knee extension strength) as the quality/ certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 8 weeks; assessed with: Time Up and Go Test [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether WBVE compared to usual care improves PP (TUGT) as the quality/certainty of the evidence has been assessed as very low	⊕OOO VERY LOW	Critical

Notes: Data from Zhang et al.[37] [a]High risk of bias because of incomplete outcome data (although intention-to-treat analysis was reported, no reasons of losses were provided) and selective outcome reporting (point estimate and confidence intervals not reported). [b]Ratio male/female 6/1. [c]Low sample size.
Abbreviations: MS, muscle strength; PP, physical performance; TUGT, Timed Up and Go Test; WBVE, whole-body vibration exercise.

Table 8C GRADE (physical frailty)

Question: Exercise + placebo compared to placebo for physical frail (Fried's criteria) older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 7 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and placebo improves MS (knee extension strength) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Muscle strength (follow-up: 7 months; assessed with: grip strength [kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and placebo improves MS (grip strength) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: 5-m usual: gait speed [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and placebo Improves PP (5-m walking) compared with placebo (as the certainty of the evidence has been assessed as very ow)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: TUGT [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and placebo Improves PP (TUGT) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[38] [a]High risk of bias because of inadequate allocation concealment and sclective outcome reporting (point estimate and confidence intervals not reported). [b]Only women were included in the study. [c]Low sample size.
Abbreviations: MS, muscle strength; PP, physical performance; TUGT, Timed Up and Go Test.

Table 8D GRADE (physical frailty)

Question: Phospholipid supplementation compared to placebo for physical frail (Fried's criteria) older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 7 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether phospholipid supplementation improves MS (knee extension strength) compared with placebo (as the certainty of the evidence has been assessed as very low)"	⊕OOO VERY LOW	Critical
Muscle strength (follow-up: 7 months; assessed with: grip strength [kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether phospholipid supplementation improves MS (grip strength) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: 5-m usual gait speed [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether phospholipid supplementation Improves PP (5-m walking) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: TUGT [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether phospholipid supplementation improves PP (TUGT) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[38] [a]High risk of bias because of inadequate allocation concealment and selective outcome reporting (point estimate and confidence intervals not reported). [b]Only women were included in the study. [c]Low sample size.

Abbreviations: MS, muscle strength; PP, physical performance; TUGT, Timed Up and Go Test.

Table 8E GRADE (physical frailty)

Question: Exercise + phospholipid supplemention compared to placebo for physical frail (Fried's criteria) older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 7 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves MS (knee extension strength) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Muscle strength (follow-up: 7 months; assessed with: grip strength [kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves MS (grip strength) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: 5-m usual gait speed [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves PP (5-m walking) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: TUGT [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves PP (TUGT) compared with placebo (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[38] [a]High risk of bias because of inadequate allocation concealment and selective outcome reporting (point estimate and confidence intervals not reported). [b]Only women were included in the study. [c]Low sample size.

Abbreviations: MS, muscle strength; PP, physical performance; TUGT, Timed Up and Go Test.

Table 8F GRADE (physical frailty)

Question: Active exercise compared to passive exercise for physical frailty (Fried's criteria) older people **Setting:** Nursing home									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 3 months; assessed with: handgrip strength [N])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether active exercise improves MS (handgrip strength) compared with passive exercise (as the quality/certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Muscle strength (follow-up: 3 months; assessed with: knee extension strength [N])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether active exercise improves MS (knee extension strength) compared with passive exercise (as the quality/certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 3 months; assessed with: 5-m usual: gait speed [m/s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether active exercise improves PP (gait speed) compared with passive exercise (as the quality/certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 3 months; assessed with: TUGT [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether active exercise improves PP (TUGT) compared with passive exercise (as the quality/certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Activities of daily living (follow-up: 3 months; assessed with: Barthel index)									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether active exercise improves ADL (Barthel index) compared with passive exercise (as the quality/certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Falls (follow-up: 3 months)									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether active exercise reduces the incidence of falls compared with passive exercise (as the quality/certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical

Notes: Data from Cadore et al.[36] [a]High risk of bias because of incomplete outcome data (no intention-to-treat analysis was reported) and selective outcome reporting (point estimate and confidence intervals not reported). [b]Excluded: dementia, Barthel index <60, inability to walk without help of other person. [c]Low sample size.
Abbreviations: ADL, activities of daily living; MS, muscle strength; PP, physical performance; TUGT, Timed Up and Go Test.

Table 8G GRADE (physical frailty)

Question: Exercise + phospholipid supplementation compared to phospholipid supplementation for physical frail (Fried's criteria) older people **Setting:** Community dwelling									
Quality assessment							**Impact**	**Quality**	**Importance**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Muscle strength (follow-up: 7 months; assessed with: knee extension strength [Nm/kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves MS (knee extension strength) compared with phospholipid supplementation (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Muscle strength (follow-up: 7 months; assessed with: grip strength [kg])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves MS (grip strength) compared with phospholipid supplementation (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: 5-m usual gait speed [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves PP (5-m walking) compared with phospholipid supplementation (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical
Physical performance (follow-up: 7 months; assessed with: TUGT [s])									
1	Randomized trials	Very serious[a]	Not serious	Serious[b]	Serious[c]	None	We are uncertain whether exercise and phospholipid supplementation improves PP (TUGT) compared with phospholipid supplementation (as the certainty of the evidence has been assessed as very low)	⊕OOO VERY LOW	Critical

Notes: Data from Kim et al.[38] [a]High risk of bias because of inadequate allocation concealment and selective outcome reporting (point estimate and confidence intervals not reported). [b]Only women were included in the study. [c]Low sample size.

Abbreviations: ADL, activities of daily living; MS, muscle strength; PP, physical performance; TUGT, Timed Up and Go Test.

physical therapies and routine exercises, in 44 frail older Chinese subjects (mean age ± SD =85.3±3.6 years) during 8 weeks. Both the groups showed an improvement in MS (bilateral knee extension strength) by 52.31% versus 35.18% on the right leg and 61.78% versus 25.62% on the left leg in the intervention group versus control group, respectively. Moreover, PP (Timed Up and Go Test [TUGT]) also improved in both the groups: −19.13 s in the intervention group versus −7.37 s in the control group. These differences were statistically significant between groups ($P<0.05$). However, further studies with larger sample sizes, longer study period, and follow-up period are needed to confirm these results.

The risk of bias according to methodological issues was low except for performance, attrition, and reporting bias (Table 6). In general, the quality or certainty of the evidence has been assessed as very low (Table 8B) for the critical outcomes.

Evidence on exercise plus nutritional supplementation in physically frail community-dwelling older people

One RCT[38] evaluated the combined and separate effects of a MCEP and supplementation with milk fat globule membrane (MFGM) in 131 Japanese women aged >75 years during 3 months of intervention and 4 months of additional follow-up. The outcomes assessed were MS (handgrip strength and knee extension strength) and PP (5-m usual gait speed and TUGT). After 3-month intervention, there were no significant differences between groups in MS improvement. PP assessed by 5-m usual gait speed improved in the MCEP + MFGM group (0.1 s) compared with the MFGM group (0.02 s, $P=0.005$). TUGT also improved with the MCEP + MFGM group (1.65 s) and the MCEP + placebo group (2.02 s) compared to MFGM (0.24 s) and placebo group (0.44 s, $P<0.001$). However, an analysis of the effects of the intervention revealed that these effects were not maintained at 4 months of follow-up.

The risk of bias according to methodological issues was low except for selection, performance and reporting bias (Table 6). In general, the quality or certainty of the evidence has been assessed as very low (Table 8C–F) for the critical outcomes.

Evidence on exercise in physically frail older people living in nursing homes

Finally, a single RCT[36] evaluated the efficacy of a MCEP (resistance, balance, and gait training) versus passive stretches in 24 nonagenarian institutionalized Spanish subjects during 12 weeks. The outcomes evaluated were MS (handgrip strength, knee extension strength), PP (5-m usual gait speed and TUGT), incidence of falls, and ADL status (BI). After the training period, there were significant differences between groups in MS ($P<0.01$): handgrip strength and knee extension strength improved by 11% and 20%, respectively, in the intervention group versus a reduction of 17% and 14%, respectively, in the control group. Moreover, the exercise group had a lower incidence of falls (from 0.77 to 0) and less ADL (BI score) deterioration than the control group with significant difference between them ($P<0.001$). There were no significant differences in PP between groups.

The risk of bias according to methodological issues was low except for performance, attrition, and reporting bias (Table 6). In general, the quality or certainty of the evidence has been assessed as very low (Table 8G) for the critical outcomes.

Summary of main results

This overview was aimed to identify SRs of nonpharmacological interventions used to treat PF and sarcopenia in older patients from different care settings. From 10 SRs[22–31] meeting the inclusion criteria, data from 5 RCTs (7 articles)[3–38] and one additional identified RCT,[39] all published in the last 4 years were examined. In order to provide a summary for decision makers and guideline developers, the risk of bias (RoB) and the GRADE quality of evidence were assessed across outcomes for each individual study. The overall GRADE quality of evidence was judged to be low (Tables 7 and 8). In summary, this evidence points to some efficacy of physical exercise programs (that include resistance and balance training) in improving relevant outcomes. An additional relevant finding is the small number of articles that use standard definitions of frailty and sarcopenia.

Discussion

Agreements and disagreements with other studies or reviews

Some guidelines issued by official organizations have included recommendations on frailty. The Agency for Healthcare Research and Quality guideline[43] recommends physical activity and monitoring diet and body weight as the main strategies to stabilize and control frailty. The British Geriatrics Society (BGS)[44] recommends a holistic medical review based on the comprehensive geriatric assessment as gold standard to create an individualized care and support plan to manage frail people. The results of the FIT trial[33–35]

seem to support this recommendation, as it showed significant improvement on MS and PP (SPPB, gait speed) with a multidisciplinary intervention based on the assessment of deficiencies versus usual care. In addition, the BGS[44] recognizes that exercise, in particular strength and balance training, improves both mobility and functional ability. However, the optimal exercise regimen to minimize frailty and sarcopenia remains uncertain. Moreover, the BGS indicates that nutritional interventions also need to be considered, although evidence to support this remains limited. Nutrition recommendations currently include optimizing protein intake and correcting vitamin D insufficiency. The European Society for Clinical Nutrition and Metabolism (ESPEN)[40] recommends that the diet should provide at least 1.0–1.2 g protein/kg body weight/day and up to 1.2–1.5 g protein/kg body weight/day for malnourished/at risk of malnutrition older people, but this recommendation is based on data coming from longitudinal epidemiological studies, not on intervention trials. Higher intake of proteins is recommended for individuals with severe illness or injury. Daily physical activity or exercise (RT and aerobic exercise) should be undertaken by all older people, for as long as possible. These recommendations are in line with the results of the study by Kim et al in 2012[32] included in this overview: an improvement in MS and PP (measured by GS) was achieved with the combination of exercise and AAS. However, in the study by Kim et al in 2015,[38] based on nutritional supplementation with phospholipids, an improvement only on PP was shown.

Although MS and PP are relevant intermediate outcomes,[41] the studies included in this overview did not show improvements on hard outcomes, such as reduction in the incidence of falls or improved basic ADLs, with the exception of the only study performed in a very old population living in a nursing home.[36] In this study, exercise significantly reduced the incidence of falls and attenuated ADL functional loss. Current guidelines of frailty do not consider these outcomes.

The majority of the populations included in the studies selected in this overview are Asian (from China and Japan), except for the FIT[33–35] study (Australian) and the study in nursing homes[36] (Spanish). This is important because the results and conclusion from these trials may not be fully extrapolated to other populations and in other health care settings.

Strengths and weaknesses of the study

This study has several strengths compared with previously published studies, namely: 1) The authors conducted comprehensive searches in four electronic databases to ensure all published trials were identified. The search terms for this overview of SRs were intentionally broad to capture all studies, and this led to >9,000 abstracts. They used a multidisciplinary review group of authors with experience in conducting SRs to independently examine and select studies. 2) This is the first overview of SRs fully designed to gather the evidence of nonpharmacological interventions on specific populations defined by validated definitions of PF and sarcopenia; hence, the populations considered in this review are relatively homogeneous. An issue raised in previous SRs was the heterogeneous populations defined by very different and nonstandardized criteria, both for sarcopenia and frailty. 3) The interventions considered are deliverable in clinical practice. 4) The outcome measures considered in this study were pre-specified by a panel of experts and use validated and reproducible measures. Variability in outcome measures is limiting research in this area.[42] 5) The strength of evidence is evaluated according to the GRADE system.

On the other hand, this review has several limitations. First, the potential nondetection/nondiscovery of primary studies that were not found in any of the SRs. However, the methodology that is used has been previously used to gather evidence on other nonpharmacological approaches to common geriatric syndromes[45–52] and is well described in medical research.[18] Second, the arbitrary cut-off age of 65 years may limit the applicability of the evidence from the present overview of SRs in patients aged <65 years. Moreover, institutionalized patients are not well represented, and there are no data on hospitalized patients. Third, the studies included were heterogeneous in terms of interventions, with short intervention periods of 3 months in the majority of trials and scanty data on longer follow-up outcomes. The number of studies included and sample sizes were small, and as a result, meta-analysis was not possible.

Conclusion

General conclusion

This overview of SR highlights the importance of exercise interventions with or without nutritional supplementation to improve PP (TUGT, GS) in community-dwelling patients aged >65 years with PF and sarcopenia. MS was improved with multidisciplinary and exercise interventions in this population. However, more trials with precise definitions of sarcopenia and PF with standardized outcome measures are clearly needed, especially in nutrition intervention studies.

Implications for practice

Sarcopenia and frailty are associated with multiple adverse events in older patients; hence, they warrant intervention.

This overview suggests that resistance and balance exercise may be the first treatment step, with a possible effect of nutritional supplementation added to exercise to improve outcomes. Exercise and nutritional interventions seem to be safe and are recommended from a public health point of view in older populations, both healthy or with a wide range of co-morbid problems. Therefore, there seem to be no clear reasons to avoid these interventions in frail or sarcopenic patients. However, expected impact on outcomes needs to be interpreted with caution due to methodological limitations in the small number of trials available and the risk of bias in several domains.

Implications of the research

This overview of SRs emphasizes the need for well-designed, large-scale RCTs with validated definitions of PF and sarcopenia, and standardized outcomes before conclusions can be drawn on its effectiveness.

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