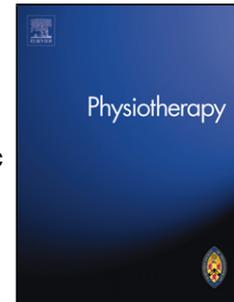


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Exercise as a treatment for sarcopenia: An umbrella review of systematic review evidence

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Abstract

Background: Sarcopenia is a progressive and generalised skeletal muscle disorder, and a powerful predictor of adverse health outcomes. Exercise is a widely recommended treatment but consensus about the best approach is lacking.

Objective: To synthesise current systematic review evidence on the effectiveness of exercise in the treatment of sarcopenia to inform clinical practice.

Data sources: Five electronic databases were searched (15 November 2018): Cochrane Database of Systematic Reviews; MEDLINE without revisions; EMBASE; Scopus; and Web of Science.

Study selection or eligibility criteria: Systematic reviews and meta-analyses of randomised controlled trials evaluating exercise to treat sarcopenia in adults including sarcopenic outcomes.

Study appraisal and synthesis methods: Review data were extracted and quality assessed (using the AMSTAR 2) by two independent assessors. Due to a lack of eligible reviews, a narrative synthesis of the evidence was performed.

Results: Two reviews were identified which included seven studies with 619 participants. Study exercise interventions included: resistance; mixed and whole body vibration training programmes.

Review findings demonstrate limited low quality evidence of positive effects of mixed and resistance training in treating sarcopenia.

Limitations: Limited eligible reviews restricted synthesis and interpretation of findings.

Conclusion and implications of key findings: There is a lack of high quality research with which to inform the treatment of sarcopenia with exercise. Further research using more precision when selecting sarcopenic populations and outcomes is required in this field. this will enable the identification of effective ways of treating sarcopenia with exercise before evidence-based clinical guidelines can be established.

Contribution of the Paper:

- x Sarcopenia is a progressive and generalised skeletal muscle disorder associated with poor health outcome. This review collated systematic review evidence on the role of exercise in the treatment of sarcopenia.
- x Findings reveal some evidence for the use of exercise to treat sarcopenia but results should be viewed with caution due to the poor quality and lack of reviews in this area.
- x Poor description of the exercise interventions included within the individual studies also limits interpretation of findings to guide clinical practice.
- x The most important finding of this review is the need for more precision in identifying individuals with sarcopenia, measuring outcome and defining interventions. The use of standardised guidelines would enable this process, expand research in this field and guide clinical practice.

Keywords: Sarcopenia, frailty, muscular diseases, exercise, ageing.

Introduction

In 2010 the European Working Group on Sarcopenia in Older People (EWGSOP) defined sarcopenia as an age-related syndrome characterised by progressive loss of both muscle mass and muscle function (muscle strength and/or physical performance) (1). These guidelines have been recently updated with a focus on low muscle strength as the key characteristic of sarcopenia, with the measurement of low muscle quantity and quality to confirm this diagnosis and identification of poor physical performance to measure severity of sarcopenia (2).

Sarcopenia is a powerful predictor of adverse health outcomes including: disability; morbidity and mortality; decreased quality of life and increased use of healthcare and institutionalisation (3-6). The

prevalence of sarcopenia is estimated to be between 1-29% in community dwelling populations, 14-33% in long-term care populations and 10% in an acute hospital-care population (7). In terms of financial burden annual health care expenditure relating to sarcopenia in the United States of America is estimated at around \$18.5 billion (8).

Exercise is arguably the intervention with the most evidence in the treatment of sarcopenia. A wealth of evidence exists demonstrating the positive effects of exercise on the individual components of sarcopenia i.e. muscle strength (10), muscle quality and quantity (11) and physical performance (12). There also exists a rapidly growing body of literature supporting the use of exercise for targeting sarcopenia as a syndrome i.e. targeting populations with both low muscle strength and reduced muscle quality and quantity (7, 13). The most appropriate type of exercise with which to target sarcopenia has yet to be established. There is however, a compelling argument to suggest that resistance exercise would be an appropriate treatment for sarcopenia as this type of exercise improves skeletal muscle strength (10) and mass (14) individually, therefore is likely to benefit a combination of both reduced muscle strength and mass.

In contrast to the evidence base for the use of exercise in the treatment of sarcopenia, evidence for nutritional and pharmaceutical interventions is sparse(13). There is a small amount of evidence indicating that a healthier diet (e.g. adequate vitamin D intake) may be beneficial in the treatment of sarcopenia, but this evidence is low quality (15). Whether a combination of exercise and nutrition could target sarcopenia also is unclear due to low quality evidence and a lack of precision defining the population included in these types of studies(16). No specific drugs are currently approved for treating sarcopenia (17).

As the recognition of sarcopenia as a syndrome and its multiple associated adverse outcomes continues to increase, it is important we find ways to target this problem in clinical practice. Although

exercise appears to be an effective method of targeting the individual components of sarcopenia. However, review evidence of the effectiveness of exercise on the treatment of sarcopenia as a syndrome has not been synthesised or used to inform the development of evidence-based clinical practice guidelines.

Aim

This review aims to synthesise current systematic review evidence on the effectiveness of exercise in the treatment of sarcopenia in adults to inform clinical practice.

Methods

Study design and eligibility criteria

We conducted an umbrella review of systematic reviews and meta-analyses of randomised controlled trials of exercise interventions used to treat sarcopenia. This type of methodology was selected as experts within the group were aware of a number of systematic reviews that may have been eligible for the review.

Articles were deemed eligible if study populations were adults (>18 years) diagnosed with sarcopenia using the 2010 EWGSOP definition (loss of muscle mass and function (strength or physical performance)). Only ~~studies~~ ^{interventions} the specific aim of improving one or more of the components of physical fitness (cardiorespiratory fitness; muscle strength; and muscle power) through a planned structured, repetitive regime¹ (18) were eligible. Interventions delivered by healthcare and non-healthcare professionals in inpatient, outpatient and community settings were considered. Nutritional interventions were not included in the review. Interventions using combined nutrition and exercise components were included only if the components were clearly defined and analysed separately in relation to outcomes. Comparator groups within trials eligible for inclusion included: standard care; comparison of one active treatment versus another or comparisons of

different doses, intensities or timing of the same intervention. Reviews were eligible only if the outcome measures reported for the interventions included both muscle mass (e.g. bio impedance analysis (BIA), dual x-ray absorptiometry (DEXA), computed tomography (CT) or magnetic resonance imaging (MRI)) and muscle function (strength e.g. grip strength and/or physical performance e.g. gait speed). The rationale behind including papers only if they used both muscle mass and muscle function outcome measures was to determine exercise effects on sarcopenia as a syndrome defined using the 2010 EWGSOP criterion.

Protocol

Before the review was conducted a protocol was agreed on by the authors. This protocol is available on request from the corresponding author.

Search Methods

Five electronic databases were systematically searched for articles published up to, and including, 15 November 2018: Cochrane Database of Systematic Reviews (CDSR); MEDLINE without revisions; EMBASE; Scopus; and Web of Science. The search strategy was undertaken by an information specialist (LE). The range of resources selected was influenced by the research question. A decision was taken not to search CINAHL, which indexes nursing and health literature and there are no particular subject specific databases which would provide additional literature relating to sarcopenia. Grey literature sources were not searched as we were not interested in conference papers/theses/dissertations/government reports etc. The initial search was conducted in Medline (see Medline search strategy Appendix A) then translated into the other databases as closely as possible using appropriate headings and/or keywords. The search terms comprised four concept areas: (i) sarcopenia, (ii) exercise, (iii) muscle strength and (iv) systematic reviews. No language or year range limitations were applied. Searches were limited to systematic review articles. The reference lists

of selected studies were searched manually. Finally, a citation search of included studies was carried out using ISI Web of Science.

Study Selection

Titles and abstracts returned from the search were independently screened by two authors (SM, NH). Full-text articles were then independently reviewed by the same two authors using a study selection form and any disagreements were resolved via discussion or consultation with a third reviewer (MW).

Data Collection Process

A data extraction form was developed and piloted on one study (Appendix B). Two authors (SM, NH) extracted data independently from the included studies with disagreements resolved via discussion.

Data Items

For each included review, data were extracted relating to: population; methods; outcomes and results. The characteristics of the exercise interventions undertaken in the individual studies were extracted using the Template for Intervention Description and Replication checklist (TIDieR)(19) (Appendix E).

Quality Assessment

Systematic review quality was assessed using the AMSTAR 2 (A MeaSurement Tool to Assess Systematic Reviews) (20) (Appendix C). Confidence ratings were given based on the number of critical components met (20). The following criteria were applied as advised by the AMSTAR 2 working group: high confidence rating-no or one non-critical weakness; moderate confidence rating-more than one non-critical weakness; low confidence rating-one critical flaw with or without non-critical weaknesses and critically low-more than one critical flaw with or without non-critical weaknesses (20).

Methodological quality was assessed independently by two authors (SM, NH) with disagreements resolved via discussion.

Assessment of Evidence Quality

Due to heterogeneity in the quality assessment and analysis methods used within the included reviews, it was not possible to conduct an assessment using the GRADE criteria (21). Instead, the methodological quality assessment results conducted by review authors were summarised.

Evidence synthesis

Due to heterogeneity of outcome measures, a narrative synthesis of the evidence was deemed appropriate.

Re-review of excluded/included reviews using EWGSOP updated guidelines

To determine whether the updated EWGSOP operational definition of sarcopenia (2) altered the findings of this umbrella review all excluded/included reviews were re-examined (12/06/2019). The focus of the new operational definition of sarcopenia is low muscle strength defined using cut-off points for grip strength and chair stand. Whether any of the excluded/included reviews included populations using this definition was explored.

Results

Figure 1 shows the PRISMA flow diagram of the search and selection process. A total of 10,000 records were identified through the search. After removing duplicates, 7,500 records were screened. 5,000 records were excluded based on the search criteria. 2,500 records were included in the final analysis. The search was conducted in PubMed, Embase, and Cochrane Central Register of Controlled Trials (Cochrane CRD).

Review characteristics

Review characteristics are summarised in Table 1. Seven trials were identified within the two included reviews, with three of the trials included in both reviews (22-24). The total sample size was 619

participants, all of whom were aged >60. Of the 7 studies, 2 did not specify gender. Of the remaining 5 studies, 451 participants were female and 63 were male. 6 of the trials were randomised controlled trials and 1 was a quasi-experimental intervention study (25).

Confidence ratings

AMSTAR 2 quality ratings of both reviews were critically low. In Vlietstra et al. 2018 (26), issues identified were: lack of established methods prior to review conduct; study design selection; search strategy; listing of excluded studies; assessment of bias; funding sources; justification of meta-analysis; impact of risk of bias on meta-analysis and investigation of publication bias. In Yoshimura et al. 2017 (27), identified issues were: search strategy; excluded studies listing; justification and adequate investigation of risk of bias and publication bias.

Exercise Interventions

Exercise interventions used within the reviews are summarised in Table 2. Mixed training, combining resistance exercise with aerobic, balance and gait training, was the most common type of exercise used in five out of the seven trials (23, 24). The other two trials used resistance training (28) and whole body vibration (22). Only one study used a home based unsupervised exercise intervention (29), with five of the other interventions delivered in supervised groups (22-24, 28, 30) and one intervention incorporating supervised groups and unsupervised home exercise programme (25) .

Comparator interventions

Four of the studies compared exercise alone to nutrition, nutrition + exercise and general health education/relaxation (23-25, 30). The nutritional supplements included tea catechins (23), amino acid supplementation (24), a combination of tea catechin and amino acid supplementation (30) and protein supplementation (25). Global sensorimotor training, vibratory mechanical-acoustic focal

therapy and no training were compared in the fifth study (28). The final two studies comparator groups were advised to maintain usual levels of physical activity (29) or received no training (22).

Outcome measures

Outcomes were recorded post-intervention but not at follow up in both reviews and selection of measurement tools varied widely. Five of the seven studies used bioelectrical impedance to measure muscle mass (23-25, 29, 30), with one study using ultrasound measurement of the cross-sectional area of the dominant vastus medialis (22) and one study not recording muscle mass (28). Muscle strength was quantified by measuring knee extension strength (handheld or isokinetic dynamometer (22, 23, 29, 30) maximal isometric strength on a leg extension machine (28)) and/or hand grip strength (23, 25, 29, 30). Walking speed (self-selected and maximal) was the most common form of physical performance measure employed in four out of the seven studies. Further measures included: gait adaptability (timed up and go (23); gait analysis (30)); physical activity (step count and energy expenditure (30)); balance (one legged stance (29) and static and dynamic balance (28)) or physical performance battery of tests (Senior Fitness Test) (25) One study did not measure physical performance (22)(Table 1).

Quality of evidence

The PEDro scale (31) and the GRADE system were used in the Vlietstra et al. (2018) review to measure individual study quality. A mean score of 5.5/10 (range 0-10) was given for the studies on the PEDro scale and the studies were rated as low quality using the GRADE system. Yoshimura et al. (2017) used the Cochrane Collaboration Risk of Bias tool (32). One study included in this review demonstrated low risk of bias for random sequence generation and incomplete outcome data, but was unclear or high risk of bias on all other measures (30). Another demonstrated low risk for random sequence generation and other bias, but unclear risk of bias for all other measures (22). The final two studies both demonstrated low risk of bias for random sequence generation, allocation concealment, blinding

of outcome assessment and incomplete outcome data and high risk of bias for blinding of participants and personnel and unclear risk of bias for selective reporting and other bias (23, 24).

Review results summary

Meta-analysis conducted by Vlietstra et al. (2018) indicated mixed exercise training can improve appendicular lean mass and leg muscle mass, knee extension strength and timed up and go (Table 1), however not all studies were included in this analysis. Only five of the six included studies measured muscle mass and measurement methods and outcomes recorded were heterogeneous making comparisons problematic (22-25, 29, 30). Muscle strength improvements were observed in five of the six studies but these were not always significant. Gait speed was measured in four of the studies (22-24, 29) but meta-analysis did not demonstrate an improvement in this variable; timed up and go speed did, however, appear to improve in the synthesis of data from two of the studies (22, 23).

Synthesis of results of three mixed exercise interventions in the Yoshimura et al. (2017) review demonstrated mixed training was effective in improving appendicular skeletal muscle mass; knee extension and walking speed but not grip strength (23, 24, 30). There was however, significant heterogeneity between the mixed training studies. The review also included a study investigating the effects of whole body vibration training on sarcopenia (22). This intervention led to no improvements in muscle mass and strength following the 12-week intervention.

Overall narrative synthesis of results of the two reviews indicates that exercise can improve appendicular skeletal muscle mass and leg muscle mass as measured by bioimpedance but does not alter cross sectional area of vastus medialis. Exercise also improves knee extension strength but not grip strength. Improvements in gait speed were noted in the first review and results were approaching significance in the second, where improvements were also observed in Timed up and go scores. These

results should be viewed with caution due to the lack of studies included in the analyses and their low quality.

Re-review of findings applying new EWGSOP sarcopenia guidelines

None of the excluded and included studies in this review used the new operational definition of sarcopenia (e.g. low muscle strength defined by chair stand and grip strength) to define study population.

Discussion

This umbrella review aimed to synthesise current systematic review evidence on the effectiveness of exercise in treating sarcopenia to inform clinical practice. Two reviews including seven individual studies and 619 participants were identified using the EWGSOP 2010 definition of sarcopenia. Both reviews demonstrated a positive effect on both muscle mass and function. Results however, should be viewed with caution due to the small sample size and the critically low methodology of both reviews. Although our search identified a number of potential systematic reviews, the majority were excluded as review populations were not diagnosed with sarcopenia and outcomes did not include both muscle mass and muscle function. A further exploration of included/excluded studies to determine whether the new EWGSOP operational definition of sarcopenia altered our results revealed that none of either the excluded or the included studies had included populations diagnosed with sarcopenia using the new definition. This finding is perhaps unsurprising as the new guidelines were recently produced, leaving little time for new research using these criteria to be undertaken. Before clinical guidelines can be established for the treatment of sarcopenia with exercise, further research using more precision regarding the inclusion of populations with sarcopenia and outcome measurement is required

Defining target population and appropriate outcomes

It was surprising to find so few eligible systematic reviews on sarcopenia and exercise within this rapidly growing field. Thirty-four out of the thirty-six full-text studies identified as potentially eligible were excluded, predominantly due to reviews not including individuals with sarcopenia and/or measures of both muscle mass and muscle function not being assessed. The papers excluded included a widely cited review supporting the use of exercise training for sarcopenia which included appropriate outcomes but not participants specifically diagnosed with sarcopenia (7).

Not one of the individual studies included in the two reviews applied the 2010 EWGSOP guidelines and cut-points for diagnosing sarcopenia. The 2010 guidelines have been recently updated with a new operational definition recognising that low muscle strength (measured by grip strength and chair stand measure) is probably indicative of sarcopenia and should be the first metric to be assessed (2). A diagnosis of sarcopenia can then be confirmed by assessment of low muscle quantity or quality (measured by DXA and BIA methods in clinical care and by DXA, MRI or CT in research). If sarcopenia is confirmed using the cut-off points for muscle strength and muscle quantity or quality, the measurement of physical performance will indicate sarcopenia severity. The cut-off points provided by the new guidelines will hopefully expand research findings in the field of exercise and sarcopenia to enable the guidance of clinical practice.

Settings and exercise interventions

Due to the lack of available evidence, we were unable to establish the most appropriate dose (e.g. time, frequency, repetition) of exercise with which to treat older people with sarcopenia. Whether current guidelines for the recommended dose of exercise for older people (33, 34) would also be appropriate to treat sarcopenia has yet to be established.

Supervised group-based structured exercise was the most common mode of exercise delivery in the reviews. Group-based supervised exercise is effective in the short-term in older adults (35, 36) and this type of delivery provides social and professional support which can in turn lead to increased self-efficacy (37). However, a number of barriers exist to older adults undertaking group based sessions outside of research trials and similar barriers are likely to exist in individuals with sarcopenia. Barriers to participating in group-based exercise include: accessibility; cost; transport and lack of available or adequately trained professionals. Group based exercise also does not often lead to long-term physical activity behaviour change (38). Free-living physical activity interventions e.g. everyday physical activities including walking, have been shown to be an effective and pragmatic approach to changing long-term physical activity behaviour in older adults and reducing falls (39, 40). However, in the case of sarcopenia, although this approach may lead to improvements in functional performance outcomes (e.g. walking speed/endurance), this type of activity may not specifically target muscle strength, and mass. As muscle strength and mass are closely associated with falls (41), they are important outcomes to target in individuals with sarcopenia.

The majority of interventions were mixed exercise interventions combining aerobic, balance and strength training, with only one intervention solely delivering resistance exercise. If muscle strength is to be determined by grip strength and chair stands as recommended by EWGSOP it would seem appropriate to develop exercise programmes that target both lower limb and upper limb strength through both functional exercise (e.g. sit to stand) and resistance exercise targeting specific muscles (e.g. knee extension exercises). Whether adding aerobic and balance training to a resistance programme is valuable for targeting sarcopenia requires further investigation as although these training modes may improve overall physical performance (potentially reducing falls) they may not specifically impact on muscle strength and quantity and quality.

Whether short-term improvements can lead to long-term improvements has not been established as at present outcomes have been only assessed post-intervention and not at follow-up. As sarcopenia is likely to progress with age interventions potentially need to be long-term. Changing long-term behaviour and forming exercise habits in older people is challenging and requires further investigation (42).

Limitations

The heterogeneity of the populations; outcomes and interventions included within the two eligible reviews and the low quality of the reviews limits achievement of our original aim to guide clinicians on the use of exercise to treat sarcopenia. Even in the two reviews deemed eligible for inclusion, low quality limited interpretation of findings. For example Vlietstra et al. (2018) included a study that did not measure muscle mass and a quasi-experimental study but was deemed still appropriate for inclusion as the review only targeted trials where the population was diagnosed with sarcopenia. Yoshimura et al. (2017) included a study where the population had sarcopenic obesity and it could be argued that this population may respond very differently to an exercise intervention therefore should not have been included.

The EWGSOP 2010 definition of sarcopenia was used to identify eligible reviews as the majority of reviews were published before the new 2018 EWGSOP guidelines were available. This may limit the interpretation of the findings as the new guidelines have a focus on low muscle strength rather than muscle mass and muscle function. We did re-review the included and excluded studies in this review to determine if this altered results but as predicted none of these studies used the new operational definition of sarcopenia to define their population.

Future directions

As the evidence for the most effective method of treating those diagnosed with sarcopenia with exercise is sparse, clinicians may benefit from using current alternative guidelines on exercise in older people until the evidence base in this area expands (33). To guide clinicians on the treatment of sarcopenia with exercise, we recommend future researchers apply the new operational definition of sarcopenia using recommended cut-points to identify participants and measure outcomes. Although structured exercise programmes appear to lead to some short-term improvements in sarcopenia, research is needed on the best methods of changing long-term exercise behaviour to target this long-term condition. We also know very little about what type (e.g. resistance, mixed training) and dose (e.g. frequency, repetition, time) of exercise leads to the most benefit for people with sarcopenia, nor how best to deliver exercise programmes at scale to people with sarcopenia. Exercise is a potential low-risk, relatively low-cost treatment for sarcopenia and as sarcopenia continues to emerge as an important condition for older people, further research is required in this field to guide clinical practice.

Ethical Approval: N/A

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References

1. Cruz-Jentoft AJ, Baeyens J, Bauer J, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis Report of the European Working Group on Sarcopenia in Older People. *Age and Ageing*. 2010;39(4):412-23.
2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age and Ageing*. 2018;afy169-afy.
3. Beaudart C, Zaaria M, Pasleau F, Reginster J-Y, Bruyère O. Health Outcomes of Sarcopenia: A Systematic Review and Meta-Analysis. *PLOS ONE*. 2017;12(1):e0169548.
4. Landi F, Cruz-Jentoft AJ, Liperoti R, Russo A, Giovannini S, Tosato M, et al. Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from the SIRENTE study. *Age and Ageing*. 2013;42(2):203-9.
5. Sousa AS, Guerra RS, Fonseca I, Pichel F, Amaral TF. Sarcopenia and length of hospital stay. *European Journal Of Clinical Nutrition*. 2015;70:595.
6. Sánchez-Rodríguez D, Marco E, Miralles R, Fayos M, Mojal S, Alvarado M, et al. Sarcopenia, physical rehabilitation and functional outcomes of patients in a subacute geriatric care unit. *Archives of Gerontology and Geriatrics*. 2014;59(1):39-43.
7. Cruz-Jentoft AJ, Landi F, Schneider SM, Zúñiga C, Arai H, Boirie Y, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age and Ageing*. 2014;43(6):748-59.
8. Janssen I, Shepard Donald S, Katzmarzyk Peter T, Roubenoff R. The Healthcare Costs of Sarcopenia in the United States. *Journal of the American Geriatrics Society*. 2003;52(1):80-5.
9. Sherrington C, Michaleff ZA, Fairhall N, Paul SS, Tiedemann A, Whitney J, et al. Exercise to prevent falls in older adults: an updated systematic review and meta-analysis. *British Journal of Sports Medicine*. 2017;51(24):1750.
10. Peterson MD, Rhea MR, Sen A, Gordon PM. Resistance Exercise for Muscular Strength in Older Adults: A Meta-Analysis. *Ageing research reviews*. 2010;9(3):226-37.
11. Tsuzuku S, Kajio T, Sakakibara H, Shimaoka K. Slow movement resistance training using body weight improves muscle mass in the elderly: A randomized controlled trial. *Scandinavian Journal of Medicine & Science in Sports*. 2017;28(4):1339-44.
12. Jadcak AD, Makwana N, Luscombe-Marsh N, Visvanathan R, Schultz TJ. Effectiveness of exercise interventions on physical function in community-dwelling frail older people: an umbrella review of systematic reviews. *JBIC Database of Systematic Reviews and Implementation Reports*. 2018;16(3):752-75.
13. Offord N, Whitham M. The emergence of sarcopenia as an important entity in older people. *Clinical Medicine*. 2017;17(4):363-6.
14. Peterson MD, Sen A, Gordon PM. Influence of resistance exercise on lean body mass in aging adults: a meta-analysis. *Medicine and science in sports and exercise*. 2011;43(2):249-58.
15. Robinson SM, Reginster JY, Rizzoli R, Shaw SC, Kanis JA, Bautmans I, et al. Does nutrition play a role in the prevention and management of sarcopenia? *Clin Nutr*. 2018;37(4):1121-32.
16. Lozano-Montoya I, Correa-Pérez A, Abraha I, Soiza RL, Cherubini A, O'Mahony D, et al. Nonpharmacological interventions to treat physical frailty and sarcopenia in older patients: a systematic overview - the SENATOR Project ONTOP Series. *Clinical interventions in aging*. 2017;12:721-40.
17. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *The Lancet*. 2019.

18. USDHHS. Physical activity advisory committee report. Atlanta: US Department of Health and Human Services Centres for Diseases Control and Prevention, National Centre for Chronic Disease and Prevention and Health Promotion.; 2008.
19. Hoffmann TC, Walker MF, Langhorne P, Eames S, Thomas E, Glasziou P. What's in a name? The challenge of describing interventions in systematic reviews: analysis of a random sample of reviews of non-pharmacological stroke interventions. *BMJ Open*. 2015;5(11):e009051.
20. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *The BMJ*. 2017;358:j4008.
21. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ : British Medical Journal*. 2008;336(7650):924-6.
22. Wei N, Pang Marco YC, Ng Shamay SM, Ng Gabriel YF. Optimal frequency/time combination of whole-body vibration training for improving muscle size and strength of people with age-related muscle loss (sarcopenia): A randomized controlled trial. *Geriatrics & Gerontology International*. 2016;17(10):1412-20.
23. Kim H, Suzuki T, Saito K, Yoshida H, Kojima N, Kim M, et al. Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: A randomized controlled trial. *Geriatrics & Gerontology International*. 2013;13(2):458-65.
24. Kim Hun K, Suzuki T, Saito K, Yoshida H, Kobayashi H, Kato H, et al. Effects of Exercise and Amino Acid Supplementation on Body Composition and Physical Function in Community-Dwelling Elderly Japanese Sarcopenic Women: A Randomized Controlled Trial. *Journal of the American Geriatrics Society*. 2012;60(1):16-23.
25. Shahar S, Kamaruddin NS, Badrasawi M, Sakian NIM, Abd Manaf Z, Yassin Z, et al. Effectiveness of exercise and protein supplementation intervention on body composition, functional fitness, and oxidative stress among elderly Malays with sarcopenia. *Clinical interventions in aging*. 2013;8:1365-75.
26. Vlietstra L, Hendrickx W, Waters DL. Exercise interventions in healthy older adults with sarcopenia: A systematic review and meta-analysis. *Australasian Journal on Ageing*. 2018;37(3):169-83.
27. Yoshimura Y, Wakabayashi H, Yamada M, Kim H, Harada A, Arai H. Interventions for treating sarcopenia: a systematic review and meta-analysis of randomized controlled studies. *Journal of the American Medical Directors Association*. 2017;18(6):553-e1.
28. Bellomo R, Iodice P, Maffulli N, Maghradze T, Coco V, Saggini R. Muscle strength and balance training in sarcopenic elderly: a pilot study with randomized controlled trial. *European Journal of Inflammation*. 2013;11(1):193-201.
29. Maruya K, Asakawa Y, Ishibashi H, Fujita H, Arai T, Yamaguchi H. Effect of a simple and adherent home exercise program on the physical function of community dwelling adults sixty years of age and older with pre-sarcopenia or sarcopenia. *Journal of Physical Therapy Science*. 2016;28(11):3183-8.
30. Kim H, Kim M, Kojima N, Fujino K, Hosoi E, Kobayashi H, et al. Exercise and Nutritional Supplementation on Community-Dwelling Elderly Japanese Women With Sarcopenic Obesity: A Randomized Controlled Trial. *Journal of the American Medical Directors Association*. 2016;17(11):1011-9.
31. Maher C, Sherrington CS, Herbert R, Moseley A, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther*. 2003;83(8):713-21.
32. Higgins J, Green S. *Cochrane handbook for systematic reviews of interventions*: John Wiley & Sons.; 2011.

33. Department of Health. Start active, stay active: A report on physical activity for health
IURP WKH IRXU KRPH FRXQWULHV & KLHI DHGLFD O
http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_128210.pdf.
34. American College of Sports Medicine, Chodzko-Zajko W, Proctor D, Fiatarone Singh M, Minson C, Nigg C, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc.* 2009;41(7):1510-30.
35. Giné-Garriga M, Guerra M, Pagès E, Manini T, Jiménez R, Unnithan V. The effect of functional circuit training on physical frailty in frail older adults: a randomized controlled trial. *J Aging Phys Act.* 2010;18(4):401-24.
36. van der Bij AK, Laurant MGH, Wensing M. Effectiveness of physical activity interventions for older adults: a review. The full text of this article is available via AJPM Online at www.elsevier.com/locate/ajpmonline. *American Journal of Preventive Medicine.* 2002;22(2):120-33.
37. Beauchamp MR, Ruissen GR, Dunlop WL, Estabrooks PA, Harden SM, Wolf SA, et al. Group-based physical activity for older adults (GOAL) randomized controlled trial: Exercise adherence outcomes. *Health Psychology.* 2018;37(5):451-61.
38. Franco MR, Tong A, Howard K, Sherrington C, Ferreira PH, Pinto RZ, et al. Older peoples perspectives on participation in physical activity: a systematic review and thematic synthesis of qualitative literature. *British Journal of Sports Medicine.* 2015;49(19):1268.
39. CIHPVRQ /)LDWDURQH 6LQJK 0 %XQG \ \$ &XPPLQJ 5 *
et al. Integration of balance and strength training into daily life activity to reduce rate of falls in older people (the LiFE study): randomised parallel trial. *The BMJ.* 2012;345:e4547.
40. Harris T, Kerry SM, Limb ES, Victor CR, Iliffe S, Ussher M, et al. Effect of a Primary Care Walking Intervention with and without Nurse Support on Physical Activity Levels in 45- to 75-Year-Olds: The Pedometer And Consultation Evaluation (PACE-UP) Cluster Randomised Clinical Trial. *PLOS Medicine.* 2017;14(1):e1002210.
41. Van Ancum JM, Pijnappels M, Jonkman NH, Scheerman K, Verlaan S, Meskers CGM, et al. Muscle mass and muscle strength are associated with pre- and post-hospitalization falls in older male inpatients: a longitudinal cohort study. *BMC Geriatrics.* 2018;18:116.
42. Perracini MR, Franco MRC, Ricci NA, Blake C. Physical activity in older people ± Case studies of how to make change happen. *Best Practice & Research Clinical Rheumatology.* 2017;31(2):260-74.

Figure 1. PRISMA flow -chart

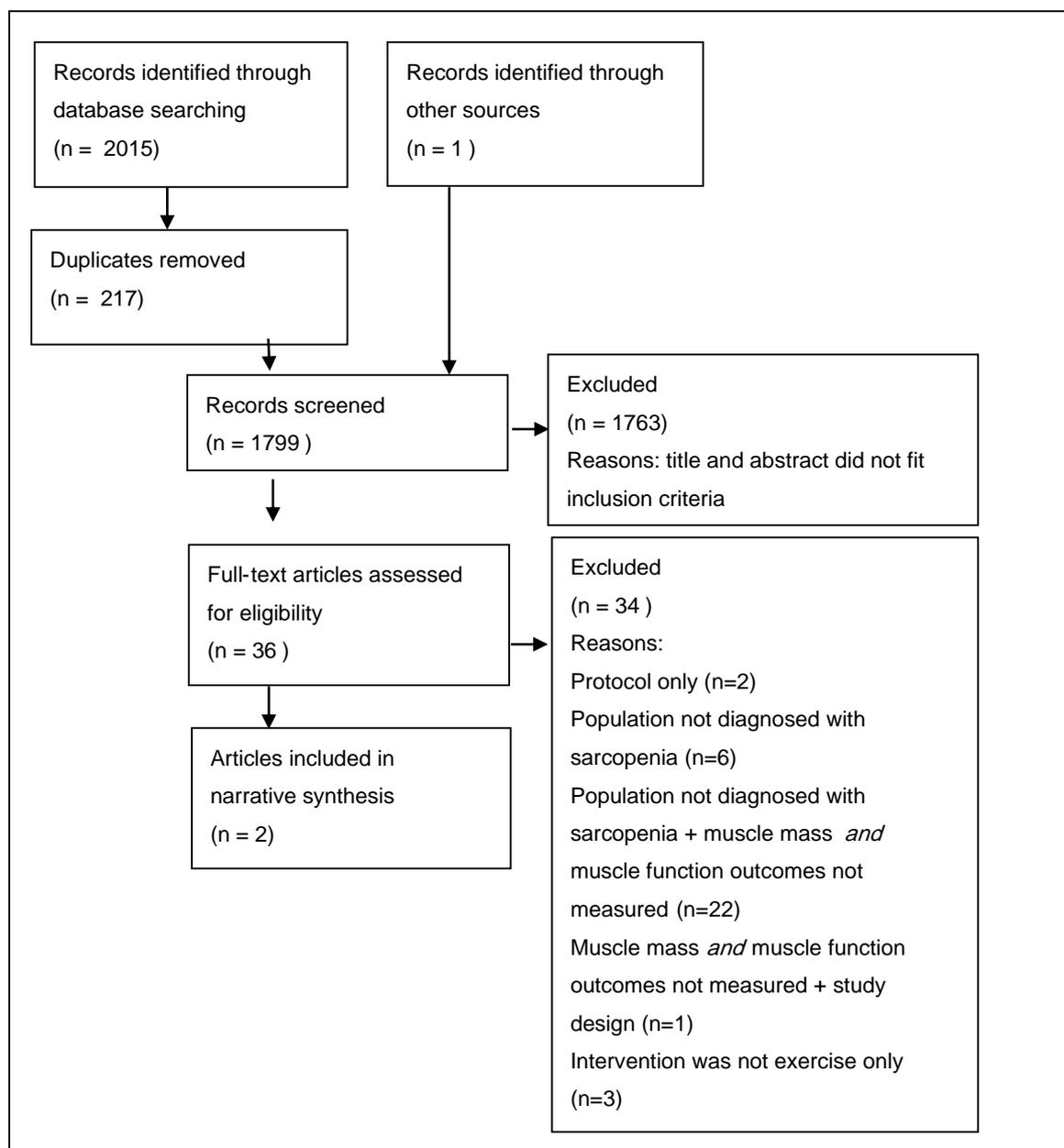


Table 1. Characteristics of included reviews

Review details	Aim	Participant information	Exercise and comparator interventions	Outcome measures	Summary of findings of review
<p>Author and date: Vlietstra et al. 2018 (26)</p> <p>No. of included studies: 6</p> <p>AMSTAR 2 rating: Critically low</p>	<p>To systematically assess the effects of exercise interventions on body composition, muscle strength and functional outcomes in older adults with sarcopenia</p>	<p>Sample size: n=480</p> <p>Age (mean (SD)): Ranged between 67 (5) and 81 (4) years</p> <p>Gender: 4 trials (n=115)</p> <p>F: 90</p>	<p>Exercise interventions</p> <p>Resistance exercise training (n=1)</p> <p>Mixed training (n=4) (strengthening, balance and gait (n=2); aerobic, balance and resistance exercise (n=1); home exercise programme (lower limb resistance and balance), (n=1))</p> <p>Vibration exercise (n=1)</p>	<p>Muscle mass: Ultrasound cross-sectional area vastus medialis of dominant leg; bioelectrical impedance analysis (muscle mass; appendicular skeleton muscle mass; leg muscle mass) and anthropometry.</p> <p>Muscle strength: Grip strength (hand held dynamometer) and knee extension strength (leg press; isokinetic dynamometer and hand held dynamometer)</p>	<p>Muscle mass</p> <p>No significant effect on whole body muscle mass [Z=1.49, CI -0.19 to 1.37, P= 0.14] (23-25).</p> <p>nAppendicular skeletal muscle mass [Z= 2.11, CI 0.03 to 0.87, p=0.04] (23, 24)</p> <p>nleg muscle mass [Z=2.08, CI 0.02 to 0.68, p=0.04] (20,21)</p> <p>Muscle strength</p> <p>Muscle strength improved with exercise in five of the six studies and</p>

		<p>M: 25</p> <p>2 trials not described in full</p>	<p>Mode: Supervised group training (n=5); home exercise programme (n=1).</p> <p>Duration: 3 to 6 months</p> <p>Comparator interventions</p> <p>Nutrition, exercise + nutrition, health education/relaxation (n=3): no training (n=2); global sensorimotor training, vibratory therapy and information and advice (n=1);</p>	<p>Physical performance: Gait analysis usual and maximal walking speed (5 metre walk test); timed up and go; balance ability (single leg standing time); Senior fitness test.</p>	<p>was maintained in contrast to a decline in controls in one study</p> <p>n Knee extension strength (adjusted and not adjusted for weight) [Z=2.52, CI 0.03 to 0.26, p=0.01; Z=2.81, (24, 29) CI 3.74 to 21.03, p=0.005, (22, 23, 28) respectively]</p> <p>No significant difference in grip strength [Z=0.17, CI -2.36 to 2.80, p=0.87] (23, 25, 29)</p> <p>Physical performance</p> <p>No significant difference in gait speed [Z=1.84, CI -0.01 to 0.24, p=0.07] (22, 23, 29)</p> <p>n Timed up and go [Z=4.33, CI -2.43 to -0.91, p<0.001] (22, 23)</p>
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Author and date: Yoshimura et al. 2017(27) No. included studies: 4 AMSTAR 2 rating: Critically low	To determine the effectiveness of exercise, nutritional, drug, and combination interventions for treating sarcopenia in older people	Sample size: 448 Age: \leq 60 years Gender: F: 422 M: 0 1 trial not described in full	Exercise interventions Procedures: Mixed training program (n=3) Whole body vibration training (n=1) Mode: Supervised group training (n=4) Duration: 12 weeks \pm 3 months Comparator interventions Nutrition, exercise + nutrition, health education (n=3) and no training (n=1)	Muscle mass: Bioelectrical impedance analysis (muscle mass, appendicular skeleton muscle, leg muscle mass); ultrasound cross-sectional area vastus medialis of dominant leg Muscle strength: Grip strength (hand held dynamometry) and knee extension (isokinetic dynamometer/hand held dynamometer) Physical performance: Usual and maximal walking speed (5 metre walk test); gait analysis; timed up and go; balance ability (one leg standing time with eyes	Mixed training vs. control (n=3) (23, 24, 30) Muscle mass n Appendicular skeletal muscle mass [0.38 kg; 95% CI 0.01-0.74; p=0.04] Muscle strength n Knee extension strength [0.11Nm/kg; 95% CI 0.03-0.20; p=0.01] No significant effect on grip strength [0.42kg; 95% CI -2.46-3.30; p=0.78] Physical performance n Usual walking speed [0.11 m/s; 95%CI 0.04-0.19; p=0.004] n Maximum walking speed 0.26m/s; 95% CI 0.03-0.20; p<0.001]
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				open); and step count and energy expenditure (accelerometer)	<p>Significant heterogeneity between studies</p> <p>Whole body vibration training vs. control (n=1)(22):</p> <p>Muscle mass</p> <p>No improvement in the cross-sectional area of the vastus medialis [0.04 cm²; 95% CI -0.59 to 0.67; p=0.89]</p> <p>Muscle strength</p> <p>No improvement isometric knee extension [7.23 Nm; 95% CI-5.34-19.81; p=0.26]</p>
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CI, confidence interval; M, male; AMSTAR, A MeaSurement Tool to Assess Systematic Reviews; F, female; Kg, kilogram; M, Male; Nm, Newton metre; No., number; vs., versus.

Table 2 Individual study intervention details described by Template for Intervention Description and Replication* (TIDieR)

Individual studies taken from the reviews	Item 1 Item 1 and 2 TIDieR	Item 2 Intervention procedures Item 3 TIDieR	Item 3 Intervention materials Item 4 TIDieR	Item 4 the intervention, Item 5 Item 5-7 TIDieR	Item 5 Intervention dose) Item 8 TIDieR	Item 6 intervention Item 9 TIDieR	Item 7 of Item 11-12 TIDieR
Review 1							
Bellomo et al. 2013 (28) Study population: 40 community dwelling older men with sarcopenia	Brief name: Resistance exercise training (RET) Why: Resistance training has been shown to reduce the effects of sarcopenia. Comparison of	Procedures: Warm up on stationary bike followed by RET for lower limbs performed on a leg press and leg extension machine	Materials: Stationary bike; leg press and leg extension machine	Who: Not reported How: Group training Where: Italy Setting: not reported	How much: 12 weeks 2 x week	Tailoring: Resistance calculated as a percentage of the maximum theoretical force (FMT). Weeks 1-4, 3 x 12 reps at 60-70% FMT; weeks 5-	How well: Not reported

(diagnosis based on Centres for disease control and prevention criterion) aged 70 (5.2) years	resistance training to two other forms of exercise stimuli					8, 3 x 10 reps at 75-80% of FMT and weeks 9-12, 3 x 6-8 reps at 80-85% of FMT	
Kim et al. 2012 (24) Study population: 155 community dwelling women >75 diagnosed with sarcopenia (defined by set	Brief name: Mixed training Why: Few studies on effects of exercise and amino acid supplementation on body composition	Procedures: Strengthening, balance and gait training	Materials: Resistance bands; ankle weights; Borg Scale and chairs	Who: Principal investigator, exercise instructor and assistant trainer How: Supervised group training Where: Tokyo	How much: 3 months 2 x week 60 mins	Tailoring: Intensity increased through resistance and weights measured by Borg scale, chairs used for stability	How well: Not reported

cut points for muscle mass and function)	and functional capacity in elderly			Community			
Kim et al. 2013 (23) Study population: 125 community dwelling women >75 diagnosed with sarcopenia (defined by set cut points for muscle mass and function)	Brief name: Mixed training Why: Few studies on effects of exercise and tea catechins on basic function in the elderly	Procedures: Strengthening, balance and gait training	Materials: Resistance bands; ankle weights; Borg Scale and chairs	Who: Principal investigator, exercise instructor and assistant trainer How: Supervised group training Where: Tokyo Community	How much: 3 months 2 x week 60 mins	Tailoring: Intensity increased through resistance and weights measured by Borg scale, chairs used for stability	How well: Not reported

	Brief name:	Procedures:	Materials:	Who:	How much:	Tailoring:	How well:
Maruya et al. (2016) (29) Study population: 52 older people with pre sarcopenia or sarcopenia (diagnosis based on Asia Working Group for Sarcopenia criterion) aged ≥80 years	Mixed training Why: Previous studies demonstrate improvement in strength with daily exercise in elderly and similar improvements may be observed with sarcopenia	Lower limb resistance and balance exercises (squats x 6/session; single-leg standing x 1 minute and heel raises x 20/session) and 20-30 minutes walking per day.	Guidebook on exercises	Physiotherapists provided a guidebook but exercise was unsupervised How: Unsupervised home exercise programme Where: Japan	6 months	Not tailored to individual	Not reported

Shahar et al.	Brief name:	Procedures:	Materials:	Who:	How much:	Tailoring:	How well:
(2013) (25)	Mixed training	General warm up and aerobic exercises; balance work; resistance exercise using an elastic band and cool down.. Exercise at home with the aid of a pictorial guidebook and CD	Pictorial exercise guide and CD; Thera band elastic exercise bands	Trained exercise instructors supervised by study researchers How: Supervised group sessions and home exercise programme Where: Malaysia Local community centre	12 weeks 2 x week 60 mins	Intensity of resistance exercise adjusted to individual performance by changing tension of elastic band	Not reported
Study population: 65 sarcopenic subjects (assessed using bio impedance analysis and cut- off points suggested by Janssen et al (2004)). Aged 67 (5) years	Why: Previous studies demonstrate improvement in strength in elderly with daily home exercise same may be observed in sarcopenia						

Wei et al.	Brief name:	Procedures:	Materials:	Who:	How much:	Tailoring:	How well:
2017 (22)	Whole-body vibration (WBV) training	14,400 vertical vibrations divided into four cycles peak amplitude 4mm.	WBV machine	Researcher	12 weeks 3 x week	None	Not reported
Study population: 80 community dwelling older adults (>65 years) diagnosed sarcopenia (skeletal mass index)	Why: No consensus on optimal frequency and time for WBV training targeting muscle performance in older adults with sarcopenia	Participants stood barefoot with knee flexed 60 degrees on platform with hands holding support rail		How: Supervised group training Where: Hong Kong			

Review 2 (also includes Kim et al. (2012), Kim et al (2013) and Wei et al (2016) see review 1 for exercise intervention details)

Kim et al.	Brief name:	Procedures:	Materials:	Who:	How much:	Tailoring:	How well:
2016 (30)	Mixed training	Resistance and weight bearing exercises;	Chair resistance band; hydraulic exercise machine and stationary bike	One instructor and three assistant trainers	3 months 2 x week 60 mins	Intensity increased based on repetitions and resistance	Not reported
Study population: 139 community dwelling women >75 diagnosed with sarcopenic obesity	Why: No research examining effects of exercise and nutritional supplementation on women with sarcopenic obesity	resistance band exercises; hydraulic exercise machines and aerobic training (stationary bike)		How: Supervised group training Where: Tokyo			

CD, compact disc; FMT, maximum theoretical force; HEP, home exercise programme; kg, kilograms; m/s, metres per second; Mins, minutes; 1 RM, one repetition maximum; RET, resistance training; TIDieR, Template for Intervention Description and Replication; WBV, whole body vibration.