Experimental Gerontology xxx (xxxx) 111420

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Effects of exercise on muscle mass, strength, and physical performance in older adults with sarcopenia: A systematic review and meta-analysis according to the EWGSOP criteria

Adrian Escriche-Escuder[a,b], Iván J. Fuentes-Abolafio[a,b,*], Cristina Roldán-Jiménez[a,b], Antonio I. Cuesta-Vargas[a,b,c]

[a] Department of Physiotherapy, University of Malaga, Malaga, Spain
[b] Instituto de Investigación Biomédica de Málaga (IBIMA), Malaga, Spain
[c] School of Clinical Sciences, Faculty of Health, Queensland University of Technology, Brisbane, Queensland, Australia

ARTICLE INFO

Section editor: Christiaan Leeuwenburgh

Keywords:
Exercise
Muscle mass
Physical performance
Sarcopenia
Strength

ABSTRACT

Background: In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP) updated the definition and the diagnosis criteria of sarcopenia. Previous systematic reviews have shown the effect of exercise on sarcopenia including people with different sarcopenia diagnostic criteria.
Objective: This systematic review and meta-analysis aims to summarise and synthesise the evidence about the effect of exercise on muscle mass, strength and physical performance in older adults with sarcopenia according to the EWGSOP criteria.
Methods: Major electronic databases were searched for articles published until September 2020. Randomised controlled trials (RCTs) and non-randomised interventional studies examining the effect of exercise on muscle mass, strength or physical performance in adults older than 60 years with sarcopenia according to the EWGSOP criteria were included.
Results: Four RCTs and three non-randomised interventional studies with a total of 235 patients with sarcopenia were included. Five of the seven included studies reported a low risk of bias. Exercise showed a large effect on physical performance ($d = 1.21$, 95%CI [0.79 to 1.62]; $P < 0.001$), a medium effect on muscle strength ($d = 0.51$, 95%CI [0.25 to 0.76]; $P < 0.001$), and no effect on muscle mass ($d = 0.27$, 95%CI [−0.05 to 0.58]; $P = 0.10$).
Conclusion: The present systematic review showed an effect of exercise on physical performance and muscle strength but an inconsistent effect on muscle mass. The grading of recommendations assessment, development and evaluation criteria showed a low level of evidence in muscle mass, a low or moderate level of evidence in muscle strength and a high level of evidence in physical performance.

1. Introduction

In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP) updated the definition of sarcopenia as a progressive and generalised disorder of skeletal muscle, associated with a higher probability of falls, fractures, physical disability and mortality (Cruz-Jentoft et al., 2019). This geriatric syndrome is considered one of the leading causes of disability in older adults (Morley et al., 2001). However, it is complex to establish incidence and prevalence value due to differences in diagnosis criteria, definitions, measurements or cut-off values (Beaudart et al., 2015; Su et al., 2019). Likewise, it is not easy to

Abbreviations: EWGSOP, European Working Group on Sarcopenia in Older People; SMI, Skeletal Muscle Mass Index; PRISMA, preferred reporting ítems for systematic reviews and meta-analyses; PROSPERO, International Prospective Register of Systematic Reviews; MeSH, medical subject headings; AMED, Allied and Complementary Medicine Database; CINAHL, Cumulative Index to Nursing and Allied Health Literature; PEDro, Physiotherapy Evidence Database; RCTs, Randomised Controlled Trials; MINORS, Methodological Index for Non-Randomised Studies; GRADE, Grading of recommendations assessment, development and evaluation; CI, confidence intervals; RevMan, review manager; SD, Standard Deviation; SPPB, Short Physical Performance Battery; m, meters; 5-STS, five times Sit To Stand Test; TUG, Timed Up and Go test

* Corresponding author at: Departamento de Fisioterapia, Universidad de Málaga, C/Arquitecto Peñalosa, 3, PC: 29071 Malaga, Spain.
E-mail address: ijfabolafio@gmail.com (I.J. Fuentes-Abolafio).

https://doi.org/10.1016/j.exger.2021.111420
Received 30 January 2021; Received in revised form 14 May 2021; Accepted 19 May 2021
0531-5565/

establish a consensus for sarcopenia diagnosis due to its multifactorial aetiology (Cruz-Jentoft et al., 2010b).

Sarcopenia was defined in 1989 as the progressive loss of muscle mass with advancing age (Rosenberg, 1989, 2011), which has been shown to be an inadequate description of the syndrome. Since then, several definitions and diagnostic criteria of sarcopenia have been proposed (Bhasin et al., 2020; Cruz-Jentoft et al., 2019, 2010a; Fielding et al., 2011; Newman et al., 2003; Studenski et al., 2014). However, the lack of consensus on clear diagnostic criteria and the consequent disparity of criteria used in clinical and research settings have been a problem not only for its correct management but also for the characterisation and the study of the effects of different treatments in their different phases (Lee et al., 2013). In this regard, when sarcopenia studies that have used disparate diagnostic criteria are compared and analysed, the results should be interpreted with some caution, also in systematic reviews.

In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) developed a clinical definition and a consensus diagnostic criteria for age-related sarcopenia (Cruz-Jentoft et al., 2010a). These diagnostic criteria included a decrease of muscle mass together with low muscle strength and/or low physical performance (Cruz-Jentoft et al., 2010a). The combined use of at least two different criteria responded to the characteristics of the syndrome presentation: muscle strength does not depend solely on muscle mass (Goodpaster et al., 2006; Janssen et al., 2004).

In 2018, the EWGSOP2 updated the definition and the diagnostic criteria for sarcopenia, requiring a decrease of muscle strength and low muscle quantity or quality to confirm the diagnosis, assessing the severity of the syndrome with the physical performance level (Cruz-Jentoft et al., 2019). Due to the recentness of these new criteria, published in 2019, there is still a lack of studies with selection criteria based on these parameters to carry out an exhaustive analysis. By all of the above, according to the most current criteria, people previously diagnosed with sarcopenia could now be considered only as a population at risk or in a phase of presarcopenia.

Sedentary lifestyles have been described as contributors to loss of muscle mass, strength, and function. Thus, several studies have hypothesised about the slowing down of the decline of lean mass and the reversibility of the symptoms related to ageing and sarcopenia through specific exercise programmes (Akune et al., 2014; Hassan et al., 2016; Liao et al., 2017). Although the results seem to be related to the type and intensity of the training, there is a lack of consensus for specific exercise modality parameters, intensity, frequency, or duration of programmes (Landi et al., 2014). In this sense, sarcopenia could be being undertreated, possibly due to the lack of consensus on the practical application of the existing theoretical concepts.

Previous systematic reviews and meta-analyses have found that exercise programmes produce significant positive effects overall on muscle strength and physical performance, but not on muscle mass in sarcopenic older adults (Bao et al., 2020; Šarabon et al., 2020; Wu et al., 2020). However, most of these reviews included all those studies that declared to include subjects with sarcopenia, whatever the diagnostic criteria were chosen (De Mello et al., 2019; Gonzalez et al., 2021; Liao et al., 2019; Montoro et al., 2015; Šarabon et al., 2020; Talar et al., 2021; Wu et al., 2020). This fact is relevant because an analysis applying strict study selection criteria for the current definition of sarcopenia could show differences in the previous findings. The lack of reviews and meta-analyses adjusted to the EWGSOP criteria (from 2010 or 2018) could be hiding larger effect sizes, as well as effects on other variables such as the quantity and quality of muscle mass.

We hypothesise that isolated exercise is an effective treatment to reverse the main signs of sarcopenia (low quantity or quality muscle mass, low muscle strength, and low physical performance). Furthermore, we propose that selecting those studies that applied an inclusion criterion based on the most recent diagnostic criteria (EWGSOP and EWGSOP2) will allow the extraction of more precise results, eliminating the bias produced by the inclusion of subjects at risk of sarcopenia or with presarcopenia. Thus, this systematic review and meta-analysis aimed to summarise and synthesise the evidence about the effect of therapeutic exercise on muscle mass, strength and physical performance in older adults with sarcopenia according to the EWGSOP and EWGSOP2 criteria.

2. Methods

The present study was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009) (Appendix A). The systematic review protocol was prospectively registered at the International Prospective Register of Systematic Reviews (PROSPERO: CRD42020142688).

2.1. Data sources and search strategy

Two independent reviewers (IJF-A and AE-E) conducted a systematic search using relevant search terms like Medical Subject Headings (MeSH) terms or keywords from other similar studies. Therefore, were identified articles published until September, 21st 2020, using optimised search strategies in the following electronic databases: PubMed, AMED, SCOPUS, EMBASE, PEDro, Web of Science (Appendix B). A manual search of relevant eligible studies to select any studies missed during the electronic search was also conducted using cross-references identified in the reference lists within both original and review articles. The grey literature databases, such as the New York Academy of Medicine Grey Literature Report, Open Grey and Google Scholar (Haddaway et al., 2015), were explored to detect any relevant unpublished data. Mendeley desktop V.1.19.2 was used for the studies selection, references exportation and duplicates removal.

2.2. Eligibility criteria

The PICOs framework (Population, Intervention, Control, Outcome, Study) was followed to determine which studies were included in the present systematic review. Each study had to meet the following inclusion criteria:

1. Randomised Controlled Trials (RCTs) or non-randomised interventional studies (S, studies) examining whether exercise (I, intervention) could improve sarcopenia (O, outcome) compared or not compared to any other treatment (C, control) in older adults (older than 60 years old) with sarcopenia (P, population).
2. Studies in which sarcopenia was diagnosed according to the EWGSOP definition and diagnosis of sarcopenia, either its first version (Cruz-Jentoft et al., 2010a) or its recent update (Cruz-Jentoft et al., 2019).
3. RCTs and non-randomised interventional studies that included any exercise programmes (include isometric, isokinetic, plyometric, concentric, eccentric or any other type of exercises with or without additional equipment).
4. No restriction was applied to the language.
5. Studies recruiting participants from any setting (general population, primary or secondary care).

The exclusion criteria were as follows:

1. All studies that did not include an experimental design (e.g. longitudinal observational studies, systematic reviews).
2. Studies in which the intervention was mainly based on nutritional or pharmacological management.
3. Studies in which exercise was not applied as monotherapy in any of the study groups.

4. Studies including patients with sarcopenia younger than 60 years old.

2.3. Study selection

During the selection process, two independent reviewers (IJF-A and AE-E) followed a short checklist to select the relevant studies (Appendix C). In the first step, potential articles were screened by title and abstract, and those documents that were not original papers were excluded. In the second step, those articles that met all inclusion criteria were screened. In case of disagreements, a decision was made by consensus or, when necessary, a third reviewer (AIC-V) solved the disagreements.

2.4. Data extraction

Using an extraction form, two reviewers (IJF-A and AE-E) retrieved and analysed the full texts of the remaining studies. The extraction form included data from: study details (first author and year of publication), region, setting, sample size, participants data (mean age, %females, BMI), EWGSOP criteria that articles meet (muscle strength, muscle mass and physical performance with their measurement tools, selection criteria and baseline means), intervention and control groups if any, follow-up, outcome, main results and effect size (Cohen's d). Regarding the outcomes, the EWGSOP2 consider the body composition, strength and physical performance as essential criteria for preparing a differential diagnosis of sarcopenia and determining its severity. It may be of great relevance in determining the effect of the different interventions (Cohen, 1988). Thus, outcomes related to these three dimensions were explicitly highlighted.

2.5. Quality assessment

The same two reviewers (IJF-A and AE-E) assessed the risk of bias of the included RCTs using the Cochrane Collaboration's Tool (Higgins et al., 2011). The Cochrane Collaboration's Tool has been described as a reliable and valid tool for assessing the quality of RCTs (Higgins et al., 2011; Ma et al., 2020; Zeng et al., 2015). In order to assess the risk of bias of non-randomised interventional studies, the Methodological Index for Non-Randomised Studies (MINORS) was used (Slim et al., 2003). The MINORS has also been described as a reliable and valid tool for assessing the quality of non-randomised interventional studies (Ma et al., 2020; Slim et al., 2003; Zeng et al., 2015).

2.6. Data synthesis and analysis

Two researchers (IJF-A and AE-E) assessed the overall quality and the strength of the evidence per outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Atkins et al., 2004; Guyatt et al., 2008). These researchers judged whether these factors were present for each outcome reported at least in two studies. Included studies in which the control group involved a supplemented modality of the exercise performed in the intervention group were considered for the study as quasi-experimental pre-post, because they did not allow adequate comparative analysis of the effects of exercise, but rather only a within-group analysis. Meta-analysis was conducted for each outcome reported in two or more studies, as long as studies assessed the same outcome with the same measurement unit. In each meta-analysis, it was decided to use the inverse variance as the statistical method for continuous outcomes, random effects as the analysis model and the standardised mean difference as the effect measures. Although sarcopenia outcomes included in the meta-analyses were assessed with the same measurement unit, the standardised mean difference and random effects were chosen to avoid heterogeneity. Furthermore, in this way, the results shown in the meta-analyses could be underestimated, being the effect of exercise on sarcopenia even more significant than reported. The outcome of each meta-analysis was the overall effect size (Cohens' d), representing the standardised mean difference. Heterogeneity was assessed using I^2 statistic (Higgins et al., 2003; Higgins and Thompson, 2002). Values of > 25% were considered as low heterogeneity, >50% moderate heterogeneity, and >75% high heterogeneity (Higgins et al., 2003; Higgins and Thompson, 2002). When meta-analyses included RCTs and non-randomised interventional studies to assess the effect of exercise on sarcopenia outcomes studying within-group changes, sensitivity analysis was carried out analysing the RCTs and the non-randomised interventional studies independently, which could also avoid heterogeneity. The mean effect sizes, 95% confidence intervals (95%CI), and I^2 were calculated for each outcome and used to create forest plots for visualization of each meta-analysis using the Review Manager (RevMan) version 5.3 (Review Manager (RevMan 5.3), 2014). Outcomes not included in the meta-analyses were reported using descriptive quantitative analysis to analyse the effect of exercise on sarcopenia. Thus, the most relevant summary measure with the 95%CI for each study was provided. Moreover, the changes within and between group, as well as the Cohen's d of the main outcome also were analysed to quantify the effectiveness of the interventions (Cohen, 1988). The changes and the Cohen's d between group could only be calculated in the RCTs because they included a control group. The within-group changes were considered as the mean difference between the assessment after exercise and the baseline assessment. The within-group Cohen's d was calculated as $\frac{\text{PostExercise} - \text{Baseline}}{\text{SD}}$. In order to calculate the Cohen's d between groups, the difference between the intervention group mean after the exercise programme and the control group mean after the control intervention was calculated because all included studies reported the mean and the standard deviation (SD) of each group at baseline and after the intervention. This analysis was used because no study showed the within-group mean difference with its SD, its standard error or its CI, so it was not possible to assign the SD of the within-group differences to calculate Cohen's d between groups. Thus, the Cohen's d between group was calculated as $\frac{\text{PostExerciseA} - \text{PostExercise B}}{\text{SD}}$. The effect size was classified into four levels: trivial ($d < 0.2$); small ($d \geq 0.2$); medium ($d \geq 0.5$); or large ($d \geq 0.8$) (Cohen, 1988). The level of significance was established at 0.05.

2.7. Interrater reliability

Interrater reliability for screening, data extraction, risk of bias assessment, and quality of the evidence rating was assessed using percentage agreement and Cohen's kappa coefficient (McHugh, 2012; Cohen, 1968). There was strong agreement between reviewers for the screening records and full texts (98.8% agreement rate and k = 0.87), the data extraction process (94% agreement rate and k = 0.84), the risk of bias assessment (92.8% agreement rate and k = 0.88) and the quality and strength of the evidence assessment (91% rate and k = 0.82) (McHugh, 2012; Cohen, 1968).

3. Results

3.1. Characteristics of included studies

A total of 8181 citations were identified through electronic databases, with 262 additional studies identified through Grey Literature Sources and 11 studies identified through manual search. After duplicates removal, 3673 titles and abstracts were screened, and 173 original papers were assessed. Appendix D reports the number of studies retrieved from each database and the number of studies excluded in each screening phase. The complete reference of excluded studies in the second stage (n = 166) is reported in Appendix E. The conflict of interest of included studies is shown in Appendix F. Of these, four RCTs and three non-randomised interventional with a total of 235 patients with sarcopenia were included. All included studies ($n = 7$) followed the EWGSOP criteria, while no included study followed the EWGSOP2 criteria. Thus, the muscle mass, assessed by Skeletal Muscle Mass Index (SMI), and the muscle strength, assessed by the hand grip test, were the most used criteria to characterize sarcopenia (n = 7). Physical performance using the Short Physical Performance Battery (SPPB) was also analysed in the included studies ($n = 3$). The characteristics of the included studies are reported in Appendix G. The description of the different interventions carried out in the included studies, results achieved in each study, as well as within-group changes and between groups changes, are reported in Appendix H. Within-group, and between-groups effect sizes of each study, the summary of the risk of bias, as well as the level of evidence per outcome according to GRADE criteria are showed in Table 1. Exercise effects during the intervention and follow-ups in sarcopenia outcomes are available in Appendix I.

3.2. Methodological quality

The risk of bias of included RCTs is shown in Appendix J. In summary, two studies (50%) reported a low risk of bias, and two studies (50%) showed an unclear risk of bias. Selection bias (50%), performance bias (100%) and detection bias (75%) were usual across the included RCTs. The risk of bias of non-randomised interventional studies is reported in Appendix K. In summary, three studies (100%) reported a low risk of bias. Detection bias (100%) were usual across the non-randomised interventional studies. The level of evidence according to the GRADE criteria of each sarcopenia outcome is shown in Appendix L. Using GRADE criteria, overall these RCTs and non-randomised interventional studies showed a low level of evidence in muscle mass, a low or moderate level of evidence in muscle strength, and a high level of evidence in physical performance.

3.3. Meta-analysis

Additional forest plots and the effects sizes of exercise on sarcopenia outcomes can also be seen in Appendix M.

3.3.1. Muscle mass (SMI)

Exercise did not appear to improve muscle mass measured with SMI when compared to other control groups, most of which also applied exercise. Thus, the meta-analysis did not show differences between exercise interventions and the control groups in muscle mass [Cohen's d = 0.28 95%CI (−0.17,0.73), $p = 0.22$] (Appendix M.1). Meta-analyses also showed no effect of exercise on muscle mass when only the within changes from the RCTs were included [Cohen's d = 0.35 95%CI (−0.01,0.72), $p = 0.06$] (Fig. 1A) or when the within changes from both RCTs and non-randomised interventional studies were included [Cohen's d = 0.27 95%CI (−0.05,0.58), $p = 0.10$] (Fig. 1B).

3.3.2. Muscle strength (hand grip)

Exercise experimental interventions improved muscle strength measured as hand grip strength compared to the control groups, in most of which a different modality of exercise was applied. Thus, the meta-analysis showed a small effect size [Cohen's d = 0.40 95%CI (0.06,0.73), $p = 0.02$] (Fig. 2A). The meta-analyses of exercise within-group effects showed a medium effect when the RCTs and non-randomised interventional studies were analysed as a whole [Cohen's d = 0.51 95%CI (0.25,0.76), $p < 0.001$] (Fig. 2B). When the effect of exercise on muscle strength was analysed in RCTs and non-randomised interventional studies separately, the meta-analysis reported a medium effect size in RCTs [Cohen's d = 0.55 95%CI (0.21,0.89), $p = 0.002$] (Fig. 2C) and a small effect size in non-randomised interventional studies [Cohen's d = 0.45 95%CI (0.07–0.83), p = 0.02] (Appendix M.2).

3.3.3. Physical performance (SPPB)

The meta-analysis showed a large effect size of exercise on physical performance assessed with the SPPB when within-group changes in RCTs and non-randomised interventional studies were analysed together [Cohen's d = 1.21 95%CI (0.79,1.62), $p < 0.001$] (Fig. 3A). When the effect of exercise on physical performance was analysed in non-randomised interventional studies separately, the meta-analysis also reported a large effect size [Cohen's d = 1.27 95%CI (0.63,1.91), p < 0.001] (Fig. 3B).

3.3.4. Five sit to stand (5-STS) time

Exercise reduced the time which patients take to stand up and sit from a chair five times. Thus, the meta-analysis showed a large effect size when the effect of exercise on 5-STS time was analysed in RCTs and non-randomised interventional studies together [Cohen's d = −0.79 95%CI (−1.13, −0.45), p < 0.001] (Appendix M.3). The effect size reported by the meta-analysis was even larger when only information from non-randomised interventional studies was analysed [Cohen's d = −0.84 95%CI (−1.24, −0.44), p < 0.001] (Appendix M.4).

3.3.5. 4 meters (m) gait speed

Exercise could not improve the gait speed according to the meta-analysis results, which showed that exercise had no effect on gait speed when RCTs and non-randomised interventional studies were analysed together [Cohen's d = 1.30 95%CI (−0.74,3.34), $p = 0.21$] (Appendix

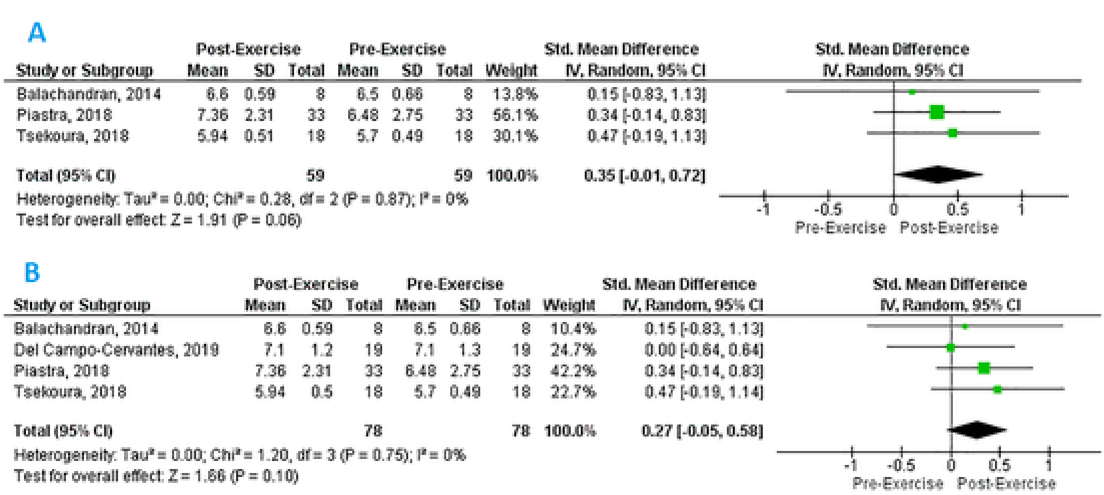

Fig. 1. A) Forest Plot illustrating the effects sizes of exercise on Muscle Mass (SMI) in RCTs; B) Forest Plot illustrating the effects sizes of exercise on Muscle Mass (SMI) in RCTs and non-randomised interventional studies.

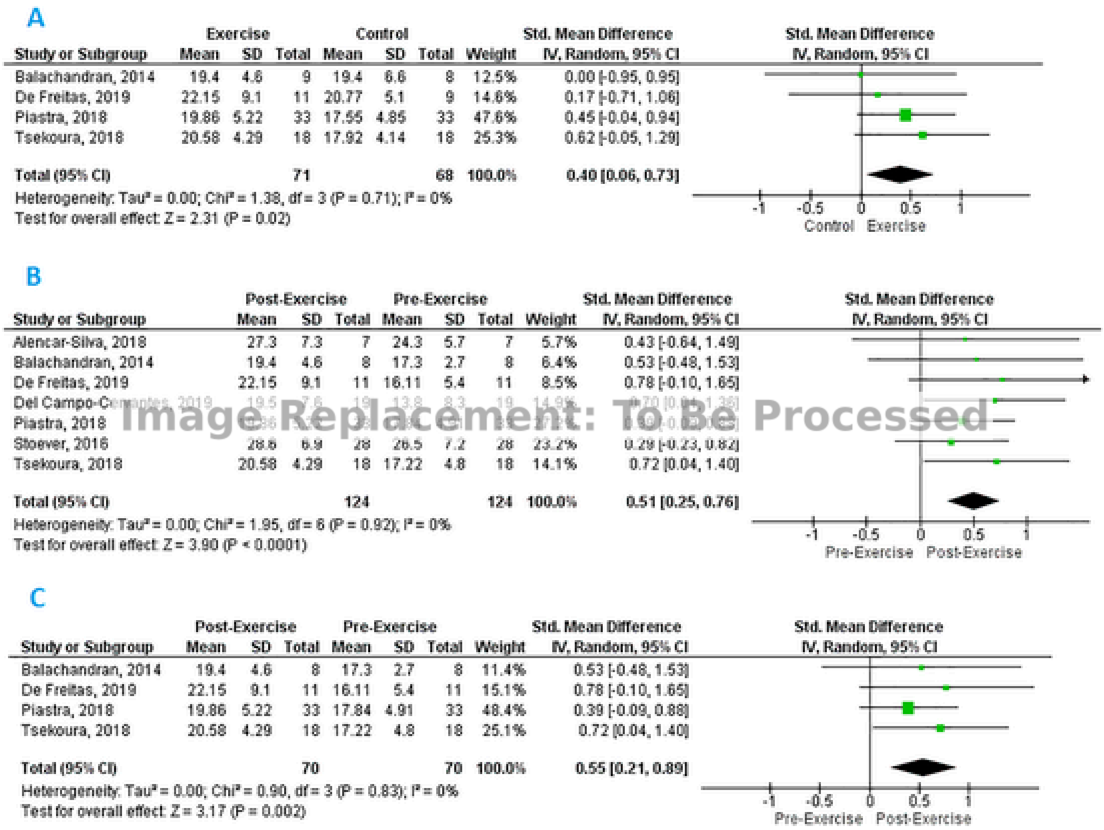

Fig. 2. A) Forest Plot illustrating differences and their effects sizes between exercise groups and control groups on Muscle Strength (Hand Grip) in RCTs; B) Forest Plot illustrating the effects sizes of exercise on Muscle Strength (Hand Grip) in RCTs and non-randomised interventional studies; C) Forest Plot illustrating the effects sizes of exercise on Muscle Strength (Hand Grip) in RCTs.

M.5). However, the meta-analysis of non-randomised interventional studies reported that exercise could reduce the time patients take to perform the 4 m gait speed test [Cohen's d = −1.15 95%CI (−1.77, −0.56), $p < 0.001$] (Appendix M.6).

3.4. Descriptive quantitative analysis

Balachandran et al. (2014) reported that exercise improved physical performance assessed by the SPPB. Thus, the exercise group showed a large effect size compared to a control exercise group (Cohen's d = 0.82). Moreover, Tsekoura et al. (2018) also reported that exercise improved physical performance, assessed in their case by the Timed Up and Go test (TUG). Thus, the time to perform the TUG was decreased in the exercise group compared to the control group (Cohen's d = −1.24), and the effect was sustained 12 weeks after finishing the exercise programme (Cohen's d = −0.88). Del Campo-Cervantes et al. (2019)reported that exercise improved physical performance assessed as SPPB in the first month (Cohen's d = 0.57), first improving balance and 5-STS because the exercise intervention was able to increase the time that patients held in unbalanced positions (Cohen's d = 0.46) and to reduce the time patients take to stand up and sit from a chair five times (Cohen's d = −0.50). Del Campo-Cervantes et al. (2019) also reported that exercise improved muscle strength (hand grip strength) after eight weeks of exercise training (Cohen's d = 0.47). Moreover, at this time, the exercise intervention showed a very large effect on physical performance assessed by the SPPB (Cohen's d = 1.04), improving the balance (Cohen's d = 0.84) and the time needed to perform the 4 m gait speed test (Cohen's d = −0.82), but not the time patients take to stand up and sit from a chair five times (5-STS) (Cohen's d = −0.13).

4. Discussion

This study aimed to summarise and synthesise the evidence about the effect of therapeutic exercise on sarcopenia, applying the diagnostic criteria of the EWGSOP and EWGSOP2 for the selection of studies. The main finding of this review was that exercise programmes produce significant effects on the main characteristics of sarcopenia (decreased strength and physical performance). However, the evidence is not yet strong to support an effect on muscle mass. These results are supported by previous systematic reviews (Bao et al., 2020; Šarabon et al., 2020; Wu et al., 2020). Another relevant finding was that few studies used the EWGSOP diagnostic criteria to recruit older adults with sarcopenia. Although there are significant similarities between both versions of the EWGSOP criteria, none of the articles included strictly fulfilled the EWGSOP2 criteria, evidencing the need to continue increasing the scientific literature in this field following this new update of the consensus.

4.1. Muscle mass (SMI)

According to this study results, exercise does not improve muscle mass measured as SMI compared to other interventions because the meta-analysis of this outcome did not show differences between exercise interventions and the control groups (Appendix M.1). However, this could be since most control groups of the included studies that analysed muscle mass applied a different exercise modality than the intervention group, but exercise anyhow (Balachandran et al., 2014; de Freitas et al., 2019; Piastra et al., 2018; Tsekoura et al., 2018). In this sense, the only study that compared the effects of exercise versus a control group without exercise, applying an educational intervention, found significant differences in favour of a group-based exercise programme (Cohen's d = 0.63, $p < 0.001$) (Tsekoura et al., 2018). There-

Table 1
Effect size, risk of bias, and level of evidence per outcome.

Author and year	Outcome	Effect Sizes		Risk of Bias	Level of Evidence (GRADE)
		Within	Between		
Balachandran et al., 2014	Muscle Mass SMI Muscle Strength Hand Grip Physical Performance SPPB	Muscle Mass HSC Cohen's d = 0.16 SH Cohen's d = 0.23 Muscle Strength HSC Cohen's d = 0.56 SH Cohen's d = 0.23 Physical Performance HSC Cohen's d = 1.18 SH Cohen's d = 0.29	Muscle Mass HSC VS SH Cohen's d = −0.39 Muscle Strength HSC VS SH Cohen's d = 0 Physical Performance HSC VS SH Cohen's d = 0.82	Low	Muscle Mass Low (intervention vs control) Low (exercise effect) Muscle Strength Low (intervention vs control) Moderate (exercise effect) Physical Performance Not reported
Piastra et al., 2018	Muscle Mass SMI Muscle Strength Hand Grip	Muscle Mass Resistance Group Cohen's d = 0.35 Postural Group Cohen's d = −0.030 Muscle Strength Resistance Group Cohen's d = 0.40 Postural Group Cohen's d = −0.057	Muscle Mass Resistance Group VS Postural Group Cohen's d = 0.31 Muscle Strength Resistance Group VS Postural Group Cohen's d = 0.46	Unclear	Muscle Mass Low (intervention vs control) Low (exercise effect) Muscle Strength Low (intervention vs control) Moderate (exercise effect)
Tsekoura et al., 2018	Muscle Mass SMI Muscle Strength Hand Grip Knee Muscle Strength Physical Performance 4 m Gait Speed TUG 5-STS	Muscle Mass at 12 weeks Group-Based Exercise Cohen's d = 0.48 Home-Based Exercise Cohen's d = 0.13 Control Group Cohen's d = −0.015 Muscle Strength at 12 weeks Group-Based Exercise Cohen's d = 0.74 Home-Based Exercise Cohen's d = 0.032 Control Group Cohen's d = 0.12 Physical Performance at 12 weeks 4 m Gait Speed Group-Based Exercise Cohen's d = 2.42 Home-Based Exercise Cohen's d = 1.41 Control Group Cohen's d = 0.074 TUG Group-Based Exercise Cohen's d = −0.74 Home-Based Exercise Cohen's d = −0.96 Control Group Cohen's d = 0.076 5-STS Group-Based Exercise Cohen's d = −0.65 Home-Based Exercise Cohen's d = −0.78 Control Group Effect Size Cohen's d = −0.13	Muscle Mass at 12 weeks Group-Based Exercise VS Home-Based Exercise Cohen's d = 0.44 Group-Based Exercise VS Control Group Cohen's d = 0.63 Home-Based Exercise VS Control Group Cohen's d = 0.23 Muscle Strength at 12 weeks Group-Based Exercise VS Home-Based Exercise Cohen's d = 0.28 Group-Based Exercise VS Control Group Cohen's d = 0.63 Home-Based Exercise VS Control Group Cohen's d = 0.33 Physical Performance at 12 weeks 4 m Gait Speed Group-Based Exercise VS Home-Based Exercise Cohen's d = 0.87 Group-Based Exercise VS Control Group Cohen's d = 1.93 Home-Based Exercise VS Control Group Cohen's d = 1.07 TUG Group-Based Exercise VS Home-Based Exercise Cohen's d = −0.12 Group-Based Exercise VS Control Group Cohen's d = −1.24 Home-Based Exercise VS Control Group Cohen's d = −1.46 5-STS Group-Based Exercise VS Home-Based Exercise Cohen's d = −0.04 Group-Based Exercise VS Control Group Cohen's d = −1 Home-Based Exercise VS Control Group Cohen's d = −1.31	Low	Muscle Mass Low (intervention vs control) Low (exercise effect) Muscle Strength Low (intervention vs control) Moderate (exercise effect) Physical Performance Not reported
De Freitas et al., 2019	Muscle Mass SMM Muscle Strength Hand Grip mean Hand Grip max	Muscle Mass LP Cohen's d = 0.07 NP Cohen's d = 0.15 Muscle Strength Hand Grip mean LP Cohen's d = 0.83 NP Cohen's d = 0.98 Hand Grip max LP Cohen's d = 0.67 NP Cohen's d = 0.90	Muscle Mass LP VS NP Cohen's d = 0.15 Muscle Strength Hand Grip mean LP VS NP Cohen's d = 0.19 Hand Grip max LP VS NP Cohen's d = 0.23	Unclear	Muscle Mass Low (intervention vs control) Low (exercise effect) Muscle Strength Low (intervention vs control) Moderate (exercise effect)

(continued on next page)

Table 1 (*continued*)

Author and year	Outcome	Effect Sizes		Risk of Bias	Level of Evidence (GRADE)
		Within	Between		
Del Campo-Cervantes et al., 2019	Muscle Mass SMI Muscle Strength Hand Grip Physical Performance SPPB	Muscle Mass Cohen's d = 0 Muscle Strength Cohen's d = 0.72 Physical Performance Cohen's d = 1.68 Balance Cohen's d = 1.31 5-STS Cohen's d = −0.78 4 m Gait Speed Cohen's d = −1.32		Low	Muscle Mass Very Low (exercise effect) Muscle Strength Low (exercise effect) Physical Performance High (exercise effect)
De Alencar-Silva et al., 2018	Muscle Strength Hand Grip Physical Performance 4 m Gait Speed 5-STS	Muscle Strength Cohen's d = 0.49 Physical Performance 4 m Gait Speed Cohen's d = −1.16 5 STS Cohen's d = −0.57		Low	Muscle Strength Low (exercise effect) Physical Performance High (4 m gait speed exercise effect) High (5-STS exercise effect)
Stoever et al., 2018	Muscle Mass SMI Muscle Strength Hand Grip Physical Performance SPPB 4 m Gait Speed 5-STS	Muscle Mass Cohen's d = 0.050 Muscle Strength Cohen's d = 0.30 Physical Performance SPPB Cohen's d = 1 4 m Gait Speed Cohen's d = 0.29 5-STS Cohen's d = −0.99		Low	Muscle Mass Very Low (exercise effect) Muscle Strength Low (exercise effect) Physical Performance High (SPPB exercise effect) High (4 m gait speed exercise effect) High (5-STS exercise effect)

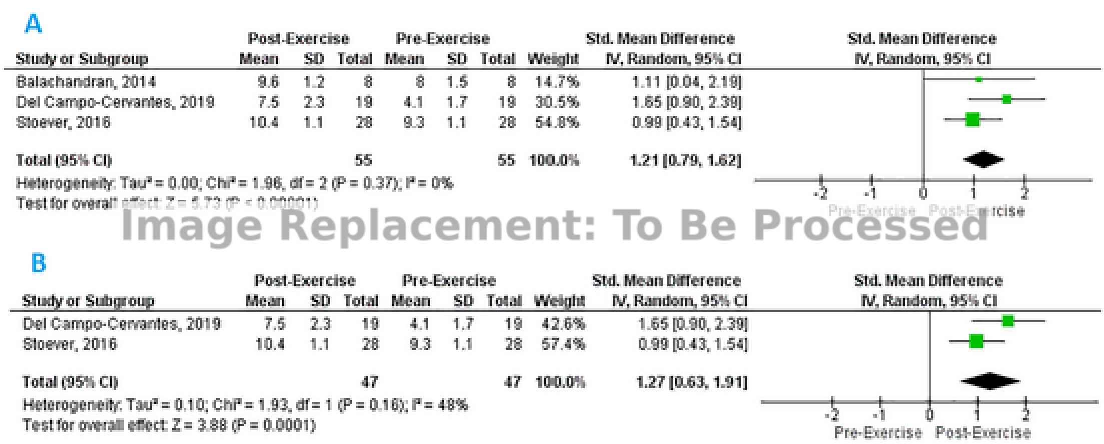

Fig. 3. A) Forest Plot illustrating the effects sizes of exercise on Physical Performance (SPPB) in RCTs and non-randomised interventional studies; B) Forest Plot illustrating the effects sizes of exercise on Physical Performance (SPPB) in non-randomised interventional studies.

fore, exercise intervention effects may be hidden if only differences between groups are analysed due to a predominance of studies comparing similar exercise interventions. The meta-analyses of the within-group changes showed a small but non-significant effect size of exercise on muscle mass when the results of the RCTs were included in isolation from the non-randomised interventional studies [Cohen's d = 0.35, p = 0.06] (Fig. 1A) (Balachandran et al., 2014; Piastra et al., 2018; Tsekoura et al., 2018), or when non-randomised interventional studies were also included (del Campo-Cervantes et al., 2019), with or without the inclusion of RCTs. These results are in accordance with previous reviews suggesting that whole-body muscle mass gains are difficult to obtain in older patients with sarcopenia (Bao et al., 2020; Šarabon et al., 2020; Vlietstra et al., 2018), although some positive results have been found in leg muscle mass when it is studied in isolation (Šarabon et al., 2020). The feasibility of increasing muscle mass in older people has been a subject of great controversy in the last decade. While some studies have found similar hypertrophic responses in young, middle-aged and older untrained subjects (Ivey et al., 2000; Roth et al., 2001), many authors suggest that adaptations are greater among younger subjects (Kosek et al., 2006; Welle et al., 1996). Based on current evidence, it appears that exercise does produce hypertrophic adaptations in older people (Peterson et al., 2011; Roth et al., 2001; Welle et al., 1996), but perhaps it does so in an attenuated manner (Kosek et al., 2006; Welle et al., 1996). Thus, previous analyses have found that resistance training can increase approximately 1 kg of lean body mass in older people (Peterson et al., 2011), which should be enough to contrast the 0.18 kg that has been determined as the annual loss of muscle mass that occurs in people over 50 years with a sedentary lifestyle (Melton et al., 2000). Insufficient duration of exercise programmes to observe changes in an outcome such as muscle mass that requires more extended periods of training (Francaux and Deldicque, 2019), or the need for the application of higher doses and intensities (Peterson et al., 2011; Strasser et al., 2018) as well as the benefits of starting at as young an age as possible (Peterson et al., 2011), have been proposed as possible causes for the lack of results in this outcome in older adults. Also, continuous manipulation of volumes and intensity seems beneficial to avoid the accommodation of stimuli in older people (Peterson et al., 2010). Some studies suggest the need to support exercise with nutritional supplementation

(Anton et al., 2018; Cruz-Jentoft et al., 2014). However, the effects of exercise applied in isolation on muscle mass need to be further elucidated.

4.2. Muscle strength (hand grip)

The results of the different meta-analyses carried out for the strength outcome (measured with the hand grip test) support the application of exercise to increase strength in older adults with sarcopenia. Again, the highest effect was obtained when exercise was evaluated versus a control group without exercise ($p < 0.05$) (Tsekoura et al., 2018). However, in this case, the set of experimental exercise programmes did obtain significant differences compared to the set of control interventions (Cohen's d = 0.40; $p = 0.02$) (Balachandran et al., 2014; de Freitas et al., 2019; Piastra et al., 2018; Tsekoura et al., 2018). Within-group analyses showed medium effect sizes when RCTs and non-randomised interventional studies were analysed together (Cohen's d = 0.51; $p < 0.0001$) (Balachandran et al., 2014; de Alencar-Silva et al., 2018; de Freitas et al., 2019; del Campo-Cervantes et al., 2019; Piastra et al., 2018; Stoever et al., 2018; Tsekoura et al., 2018) and when RCTs were analysed separately (Cohen's d = 0.55; $p = 0.002$) (Balachandran et al., 2014; de Freitas et al., 2019; Piastra et al., 2018; Tsekoura et al., 2018), while the meta-analysis of the non-randomised interventional studies reported a small effect size (Cohen's d = 0.45; p = 0.02) (de Alencar-Silva et al., 2018; del Campo-Cervantes et al., 2019; Stoever et al., 2018). In general, it seems that the potential of the exercise on this variable is sufficiently important to show significant differences in the different analyses. These differences between RCTs and non-randomised interventional studies were also observed in the analysis of the evidence using GRADE: the RCTs obtained a moderate level of evidence while the non-randomised interventional studies reported a low level of evidence. These results are in accordance with previous literature, which suggests that exercise training is generally effective for increasing the muscle strength of healthy older adults regardless of exercise methodology (Bao et al., 2020; Šarabon et al., 2020; Vlietstra et al., 2018). However, given the evidence of the existence of different dose-responses through different exercise methodologies in healthy older adults (Borde et al., 2015; Sbardelotto and Pedroso, 2017), the effect of different exercise methodologies should be studied to maximise its effectiveness in people diagnosed with sarcopenia.

4.3. Physical performance (SPPB, 5-STS time, 4-m gait speed)

In general, the different physical performance outcomes analysed showed a positive response to exercise. Thus, both the SPPB and the time invested in the 5-STS test showed large effect sizes in the different meta-analyses of the within-group differences. In this case, these outcomes mainly were evaluated in non-randomised interventional studies (Balachandran et al., 2014; del Campo-Cervantes et al., 2019; Stoever et al., 2018), so they are mainly influenced by the results of these studies. For these outcomes, the non-randomised interventional studies showed a high level of evidence in GRADE. Physical performance outcomes (e.g., gait speed, 5-STS) have shown similar results in previous reviews (Bao et al., 2020; Šarabon et al., 2020; Wu et al., 2020) to those found in the present review. Tsekoura et al. (2018) reported that exercise improved physical performance assessed using the TUG test, and the effect was sustained 12 weeks after finishing the exercise programme (Cohen's d = −0.88). Again, these results also support previous evidence showing the beneficial effects of exercise on this physical performance (Bao et al., 2020; Wu et al., 2020). However, the lack of effect on this outcome in some previous reviews suggests the need to continue studying this relationship (Šarabon et al., 2020). As far as strength concerns, exercise seems to be a valuable tool to achieve significant physical performance improvements in older adults with sarcopenia.

Two studies made intermediate measurements during the exercise programme (de Freitas et al., 2019; del Campo-Cervantes et al., 2019). The results of the study of del Campo-Cervantes et al. (2019) suggest that in the short term (4 weeks), it is already possible to produce some improvement in physical performance variables such as balance and 5-STS (measured in the SPPB). At eight weeks, it was also possible to find a significant improvement in hand grip strength and an even greater increase in balance. However, the 5-STS did not show differences in comparison to gains from the first four weeks. These findings could indicate that while some outcomes, such as muscle mass, may require extended training times, other functional variables may require shorter interventions.

4.4. What does this review contribute?

This study reported the effect of therapeutic exercise on patients who fulfilled specific criteria of sarcopenia established by consensus (EWGSOP). Including patients with sarcopenia according to different criteria could bias the results and hide the actual effect of exercise on each of the accepted phenotypes of sarcopenia. Previous reviews have previously outlined a similar research question (Bao et al., 2020; De Mello et al., 2019; Gonzalez et al., 2021; Liao et al., 2019; Montoro et al., 2015; Šarabon et al., 2020; Talar et al., 2021; Wu et al., 2020). However, this is the first review to use specific criteria (EWGSOP) for sarcopenia without mixing with other criteria or syndromes. Additionally, to our knowledge, this systematic review and meta-analysis is the first study to report the quality and the strength of the evidence on the effect of therapeutic exercise on each of the dimensions that characterize the sarcopenia, according to GRADE criteria.

4.5. Implications for clinical practice

The current findings show that exercise should be a therapeutic option in handling sarcopenic older adults, diagnosed according to the EWGSOP criteria.

4.6. Future research

Future research should conduct more RCTs in which sarcopenia is diagnosed according to EWGSOP criteria but especially the new EWGSOP2 criteria. Likewise, additional studies are necessary that use control groups implementing interventions other than exercise, thus allowing evaluating the isolated effect of exercise. Furthermore, future RCTs should carry out exercise programmes of longer duration to assess the effect of exercise on muscle mass.

4.7. Strengths and limitations of the study

The strengths of this systematic review and meta-analysis included the use of a pre-specified protocol registered on PROSPERO, the PRISMA checklist, the Cochrane Collaboration's Tools to determine the risk of bias of included RCTs and the MINORS to determine the risk of bias of included non-randomised interventional studies, the GRADE criteria to assess the overall quality and the strength of the evidence per outcome, a robust search strategy complemented by a manual search, so that all studies that met the eligibility criteria should have been identified, and the rigid selection criteria applied only including those studies that based their recruitment on the EWGSOP criteria. Another strength could also be the detailed analysis of the between and within-group effects of all outcomes, carrying out numerous meta-analyses to obtain extensive data. Moreover, the use of the standardised mean difference and random effects represent a conservative approach that adds even more value to the effects found. However, several limitations should be mentioned. First, the lack of more RCTs including a control group in which an intervention other than exercise is performed to determine the superiority of exercise over other interventions. Second, the lack of more studies in which sarcopenia is diagnosed using the same diagnostic criteria, the EWGSOP criteria. Exercise-based interventions should be of longer duration in order to determine the effect of exercise on muscle mass. Finally, although one of the strengths of the current review is the use of homogeneous criteria in selecting studies based on the EWGSOP criteria, this approach could limit the generalizability of the conclusions drawn.

5. Conclusion

Exercise is a valid therapeutic option in handling sarcopenic older adults, diagnosed according to the EWGSOP criteria. The application of exercise programmes in this population seems to counteract some of the main effects of this syndrome, such as decreased strength and physical performance. However, the evidence is not sufficient yet to support an effect on muscle mass.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2021.111420.

Declaration of sources of funding

The study had no source of funding.

Declaration of competing interest

All authors declare that they have no conflict of interest.

Acknowledgements

Escriche-Escuder is supported by the University Teaching Training Programme (FPU) of the Ministry of Science, Innovation and Universities of Spain. Grant number: FPU17/00161.

References

Akune, T., Muraki, S., Oka, H., Tanaka, S., Kawaguchi, H., Nakamura, K., Yoshimura, N., 2014. Exercise habits during middle age are associated with lower prevalence of sarcopenia: the ROAD study. Osteoporos. Int. 25, 1081–1088. https://doi.org/10.1007/s00198-013-2550-z.

Anton, S.D., Hida, A., Mankowski, R., Layne, A., Solberg, L.M., Mainous, A.G., Buford, T., 2018. Nutrition and exercise in sarcopenia. Curr. Protein Pept. Sci. 19, 649–667. https://doi.org/10.2174/1389203717666161227144349.

Atkins, D., Best, D., Briss, P.A., Eccles, M., Falck-Ytter, Y., Flottorp, S., Guyatt, G. H., Harbour, R.T., Haugh, M.C., Henry, D., Hill, S., Jaeschke, R., Leng, G., Liberati, A., Magrini, N., Mason, J., Middleton, P., Mrukowicz, J., O'Connell, D., Oxman, A.D., Phillips, B., Schünemann, H.J., Edejer, T.T.-T., Varonen, H., Vist, G.E., Williams, J.W., Zaza, S., GRADE Working Group, 2004. Grading quality of evidence and strength of recommendations. BMJ 328, 1490. https://doi.org/10.1136/bmj.328.7454.1490.

Balachandran, A., Krawczyk, S.N., Potiaumpai, M., Signorile, J.F., 2014. High-speed circuit training vs hypertrophy training to improve physical function in sarcopenic obese adults: a randomized controlled trial. Exp. Gerontol. 60, 64–71. https://doi.org/10.1016/j.exger.2014.09.016.

Bao, W., Sun, Y., Zhang, T., Zou, L., Wu, X., Wang, D., Chen, Z., 2020. Exercise programs for muscle mass, muscle strength and physical performance in older adults with sarcopenia: a systematic review and meta-analysis. Aging Dis. 11, 863–873. https://doi.org/10.14336/AD.2019.1012.

Beaudart, C., Reginster, J.Y., Slomian, J., Buckinx, F., Dardenne, N., Quabron, A., Slangen, C., 2015. Estimation of sarcopenia prevalence using various assessment tools. Exp. Gerontol. 61, 31–37. https://doi.org/10.1016/j.exger.2014.11.014.

Bhasin, S., Travison, T.G., Manini, T.M., Patel, S., Pencina, K.M., Fielding, R.A., Magaziner, J.M., Newman, A.B., Kiel, D.P., Cooper, C., Guralnik, J.M., Cauley, J.A., Arai, H., Clark, B.C., Landi, F., Schaap, L.A., Pereira, S.L., Rooks, D., Woo, J., Woodhouse, L.J., Binder, E., Brown, T., Shardell, M., Xue, Q.-L., D'Agostino, R.B., Orwig, D., Gorsicki, G., Correa-De-Araujo, R., Cawthon, P.M., 2020. Sarcopenia definition: the position statements of the sarcopenia definition and outcomes consortium. J. Am. Geriatr. Soc. 68, 1410–1418. https://doi.org/10.1111/jgs.16372.

Borde, R., Hortobágyi, T., Granacher, U., 2015. Dose-response relationships of resistance training in healthy old adults: a systematic review and meta-analysis. Sports Med. 45, 1693–1720. https://doi.org/10.1007/s40279-015-0385-9.

Cohen, J., 1968. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol. Bull. 70, 213–220. https://doi.org/10.1037/h0026256.

Cohen, J., 1988. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. L. Erlbaum Associates, Hillsdale, N.J.

Cruz-Jentoft, A.J., Baeyens, J.P., Bauer, J.M., Boirie, Y., Cederholm, T., Landi, F., Martin, F.C., Michel, J.-P., Rolland, Y., Schneider, S.M., Topinková, E., Vandewoude, M., Zamboni, M., European Working Group on Sarcopenia in Older People, 2010a. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing 39, 412–423. https://doi.org/10.1093/ageing/afq034.

Cruz-Jentoft, A.J., Landi, F., Topinková, E., Michel, J.-P., 2010b. Understanding sarcopenia as a geriatric syndrome. Curr. Opin. Clin. Nutr. Metab. Care 13, 1–7. https://doi.org/10.1097/MCO.0b013e328333c1c1.

Cruz-Jentoft, A.J., Landi, F., Schneider, S.M., Zúñiga, C., Arai, H., Boirie, Y., Chen, L.-K., Fielding, R.A., Martin, F.C., Michel, J.-P., Sieber, C., Stout, J.R., Studenski, S.A., Vellas, B., Woo, J., Zamboni, M., Cederholm, T., 2014. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing 43, 748–759. https://doi.org/10.1093/ageing/afu115.

Cruz-Jentoft, A.J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A.A., Schneider, S.M., Sieber, C.C., Topinkova, E., Vandewoude, M., Visser, M., Zamboni, M., 2019. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 48, 16–31. https://doi.org/10.1093/ageing/afy169.

de Alencar-Silva, B.S., Lira, F.S., Rossi, F.E., de Freitas, M.C., Freire, A.P.C.F., dos Santos, V.R., Gobbo, L.A., 2018. Elastic resistance training improved glycemic homeostasis, strength, and functionality in sarcopenic older adults: a pilot study. J. Exerc. Rehabil. 14, 1085–1091. https://doi.org/10.12965/jer.1836412.206.

de Freitas, M.C., de Souza Pereira, C.G., Batista, V.C., Rossi, F.E., Ribeiro, A.S., Cyrino, E.S., Cholewa, J.M., Gobbo, L.A., 2019. Effects of linear versus nonperiodized resistance training on isometric force and skeletal muscle mass adaptations in sarcopenic older adults. J. Exerc. Rehabil. 15, 148–154. https://doi.org/10.12965/jer.1836534.267.

del Campo-Cervantes, J.M., Habacuc Macías Cervantes, M., Monroy Torres, R., 2019. Effect of a resistance training program on sarcopenia and functionality of the older adults living in a nursing home. J. Nutr. Health Aging 23, 829–836. https://doi.org/10.1007/s12603-019-1261-3.

Fielding, R.A., Vellas, B., Evans, W.J., Bhasin, S., Morley, J.E., Newman, A.B., Abellan van Kan, G., Andrieu, S., Bauer, J., Breuille, D., Cederholm, T., Chandler, J., De Meynard, C., Donini, L., Harris, T., Kannt, A., Keime Guibert, F., Onder, G., Papanicolaou, D., Rolland, Y., Rooks, D., Sieber, C., Souhami, E., Verlaan, S., Zamboni, M., 2011. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J. Am. Med. Dir. Assoc. 12, 249–256. https://doi.org/10.1016/j.jamda.2011.01.003.

Francaux, M., Deldicque, L., 2019. Exercise and the control of muscle mass in human. Pflugers Arch. 471, 397–411. https://doi.org/10.1007/s00424-018-2217-x.

Goodpaster, B.H., Study, for the H.A, Park, S.W., Study, for the H.A, Harris, T.B., Study, for the H.A, Kritchevsky, S.B., Study, for the H.A, Nevitt, M., Study, for the H.A, Schwartz, A.V., Study, for the H.A, Simonsick, E.M., Study, for the H. A, Tylavsky, F.A., Study, for the H.A, Visser, M., Study, for the H.A, Newman, A.B., Study, for the H.A, 2006. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J. Gerontol. A Biol. Sci. Med. Sci. 61, 1059–1064. https://doi.org/10.1093/gerona/61.10.1059.

Guyatt, G.H., Oxman, A.D., Vist, G.E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., Schünemann, H.J., GRADE Working Group, 2008. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336, 924–926. https://doi.org/10.1136/bmj.39489.470347.AD.

Haddaway, N.R., Collins, A.M., Coughlin, D., Kirk, S., 2015. The role of Google scholar in evidence reviews and its applicability to Grey literature searching. PLoS One 10, e0138237. https://doi.org/10.1371/journal.pone.0138237.

Hassan, B.H., Hewitt, J., Keogh, J.W.L., Bermeo, S., Duque, G., Henwood, T.R., 2016. Impact of resistance training on sarcopenia in nursing care facilities: a pilot study. Geriatr. Nurs. 37, 116–121. https://doi.org/10.1016/j.gerinurse.2015.11.001.

Higgins, J.P.T., Thompson, S.G., 2002. Quantifying heterogeneity in a meta-analysis. Stat. Med. 21, 1539–1558. https://doi.org/10.1002/sim.1186.

Higgins, J.P.T., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ 327, 557–560. https://doi.org/10.1136/bmj.327.7414.557.

Higgins, J.P.T., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savovic, J., Schulz, K.F., Weeks, L., Sterne, J.A.C., Cochrane Bias Methods Group, Cochrane Statistical Methods Group, 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ d 5928, 343. https://doi.org/10.1136/bmj.d5928.

Ivey, F.M., Roth, S.M., Ferrell, R.E., Tracy, B.L., Lemmer, J.T., Hurlbut, D.E., Martel, G.F., Siegel, E.L., Fozard, J.L., Jeffrey Metter, E., Fleg, J.L., Hurley, B. F., 2000. Effects of age, gender, and myostatin genotype on the hypertrophic response to heavy resistance strength training. J. Gerontol. A Biol. Sci. Med. Sci. 55, M641–M648. https://doi.org/10.1093/gerona/55.11.m641.

Janssen, I., Baumgartner, R.N., Ross, R., Rosenberg, I.H., Roubenoff, R., 2004. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. Am. J. Epidemiol. 159, 413–421. https://doi.org/10.

1093/aje/kwh058.
Kosek, D.J., Kim, J.-S., Petrella, J.K., Cross, J.M., Bamman, M.M., 2006. Efficacy of 3 days/wk resistance training on myofiber hypertrophy and myogenic mechanisms in young vs. older adults. J. Appl. Physiol. 1985 (101), 531–544. https://doi.org/10.1152/japplphysiol.01474.2005.
Landi, F., Marzetti, E., Martone, A.M., Bernabei, R., Onder, G., 2014. Exercise as a remedy for sarcopenia. Curr. Opin. Clin. Nutr. Metab. Care 17, 25–31. https://doi.org/10.1097/MCO.0000000000000018.
Lee, W.-J., Liu, L.-K., Peng, L.-N., Lin, M.-H., Chen, L.-K., 2013. Comparisons of sarcopenia defined by IWGS and EWGSOP criteria among older people: results from the I-Lan longitudinal aging study. J. Am. Med. Dir. Assoc. 14, 528.e1-528.e7. https://doi.org/10.1016/j.jamda.2013.03.019.
Liao, C., Tsauo, J., Lin, L., Huang, S., Ku, J., Chou, L., Liou, T., 2017. Effects of elastic resistance exercise on body composition and physical capacity in older women with sarcopenic obesity. Medicine (Baltimore) 96.
Ma, L.-L., Wang, Y.-Y., Yang, Z.-H., Huang, D., Weng, H., Zeng, X.-T., 2020. Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: what are they and which is better?. Mil. Med. Res. 7, 7. https://doi.org/10.1186/s40779-020-00238-8.
McHugh, M.L., 2012. Interrater reliability: the kappa statistic. Biochem. Med. (Zagreb) 22, 276–282.
Melton, L.J., Khosla, S., Crowson, C.S., O'Connor, M.K., O'Fallon, W.M., Riggs, B.L., 2000. Epidemiology of sarcopenia. J. Am. Geriatr. Soc. 48, 625–630.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., PRISMA Group, 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J. Clin. Epidemiol. 62, 1006–1012. https://doi.org/10.1016/j.jclinepi.2009.06.005.
Morley, J.E., Baumgartner, R.N., Roubenoff, R., Mayer, J., Nair, K.S., 2001. Sarcopenia. J. Lab. Clin. Med. 137, 231–243. https://doi.org/10.1067/mlc.2001.113504.
Newman, A.B., Kupelian, V., Visser, M., Simonsick, E., Goodpaster, B., Nevitt, M., Kritchevsky, S.B., Tylavsky, F.A., Rubin, S.M., Harris, T.B., 2003. Sarcopenia: alternative definitions and associations with lower extremity function. J. Am. Geriatr. Soc. 51, 1602–1609. https://doi.org/10.1046/j.1532-5415.2003.51534.x.
Peterson, M.D., Rhea, M.R., Sen, A., Gordon, P.M., 2010. Resistance exercise for muscular strength in older adults: a meta-analysis. Ageing Res. Rev. 9, 226–237. https://doi.org/10.1016/j.arr.2010.03.004.
Peterson, M.D., Sen, A., Gordon, P.M., 2011. Influence of resistance exercise on lean body mass in aging adults: a meta-analysis. Med. Sci. Sports Exerc. 43, 249–258. https://doi.org/10.1249/MSS.0b013e3181eb6265.
Piastra, G., Perasso, L., Lucarini, S., Monacelli, F., Bisio, A., Ferrando, V., Gallamini, M., Faelli, E., Ruggeri, P., 2018. Effects of two types of 9-month adapted physical activity program on muscle mass, muscle strength, and balance in moderate Sarcopenic older women [WWW document]. Biomed. Res. Int.. https://doi.org/10.1155/2018/5095673.
Review Manager (RevMan 5.3), 2014. The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen.
Rosenberg, I.H., 1989. Summary comments. Am. J. Clin. Nutr. 50, 1231–1233. https://doi.org/10.1093/ajcn/50.5.1231.
Rosenberg, I.H., 2011. Sarcopenia: origins and clinical relevance. Clin. Geriatr. Med. 27, 337–339. https://doi.org/10.1016/j.cger.2011.03.003.
Roth, S.M., Ivey, F.M., Martel, G.F., Lemmer, J.T., Hurlbut, D.E., Siegel, E.L., Metter, E.J., Fleg, J.L., Fozard, J.L., Kostek, M.C., Wernick, D.M., Hurley, B. F., 2001. Muscle size responses to strength training in young and older men and women. J. Am. Geriatr. Soc. 49, 1428–1433. https://doi.org/10.1046/j.1532-5415.2001.4911233.x.
Šarabon, N., Kozinc, Ž., Löfler, S., Hofer, C., 2020. Resistance exercise, electrical muscle stimulation, and whole-body vibration in older adults: systematic review and meta-analysis of randomized controlled trials. J. Clin. Med. 9, 2902. https://doi.org/10.3390/jcm9092902.
Sbardelotto, M.L., Pedroso, G.S., 2017. The effects of physical training are varied and occur in an exercise type-dependent manner in elderly men. Aging Dis. 8, 887–898. https://doi.org/10.14336/AD.2017.0209.
Slim, K., Nini, E., Forestier, D., Kwiatkowski, F., Panis, Y., Chipponi, J., 2003. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ J. Surg. 73, 712–716. https://doi.org/10.1046/j.1445-2197.2003.02748.x.
Stoever, K., Heber, A., Eichberg, S., Brixius, K., 2018. Influences of resistance training on physical function in older, obese men and women with sarcopenia. J. Geriatr. Phys. Ther. 41, 20–27. https://doi.org/10.1519/JPT.0000000000000105.
Strasser, E.-M., Hofmann, M., Franzke, B., Schober-Halper, B., Oesen, S., Jandrasits, W., Graf, A., Praschak, M., Horvath-Mechtler, B., Krammer, C., Ploder, M., Bachl, N., Quittan, M., Wagner, K.-H., Wessner, B., 2018. Strength training increases skeletal muscle quality but not muscle mass in old institutionalized adults: a randomized, multi-arm parallel and controlled intervention study. Eur. J. Phys. Rehabil. Med. 54, 921–933. https://doi.org/10.23736/S1973-9087.18.04930-4.
Studenski, S.A., Peters, K.W., Alley, D.E., Cawthon, P.M., McLean, R.R., Harris, T. B., Ferrucci, L., Guralnik, J.M., Fragala, M.S., Kenny, A.M., Kiel, D.P., Kritchevsky, S.B., Shardell, M.D., Dam, T.-T.L., Vassileva, M.T., 2014. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J. Gerontol. A Biol. Sci. Med. Sci. 69, 547–558. https://doi.org/10.1093/gerona/glu010.
Su, Y., Hirayama, K., Han, T.-F., Izutsu, M., Yuki, M., 2019. Sarcopenia prevalence and risk factors among Japanese community dwelling older adults living in a snow-covered city according to EWGSOP2. J. Clin. Med. 8, 291. https://doi.org/10.3390/jcm8030291.
Tsekoura, M., Billis, E., Tsepis, E., Dimitriadis, Z., Matzaroglou, C., Tyllianakis, M., Panagiotopoulos, E., Gliatis, J., 2018. The effects of group and home-based exercise programs in elderly with sarcopenia: a randomized controlled trial. J. Clin. Med. 7, 480–498. https://doi.org/10.3390/jcm7120480.
Vlietstra, L., Hendrickx, W., Waters, D.L., 2018. Exercise interventions in healthy older adults with sarcopenia: a systematic review and meta-analysis. Australas. J. Ageing 37, 169–183. https://doi.org/10.1111/ajag.12521.
Welle, S., Totterman, S., Thornton, C., 1996. Effect of age on muscle hypertrophy induced by resistance training. J. Gerontol. A Biol. Sci. Med. Sci. 51, M270–M275. https://doi.org/10.1093/gerona/51a.6.m270.
Wu, S., Ning, H.-T., Xiao, S.-M., Hu, M.-Y., Wu, X.-Y., Deng, H.-W., Feng, H., 2020. Effects of vibration therapy on muscle mass, muscle strength and physical function in older adults with sarcopenia: a systematic review and meta-analysis. Eur. Rev. Aging Phys. Act. 17, 14. https://doi.org/10.1186/s11556-020-00247-5.
Zeng, X., Zhang, Y., Kwong, J.S.W., Zhang, C., Li, S., Sun, F., Niu, Y., Du, L., 2015. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. J. Evid. Based Med. 8, 2–10. https://doi.org/10.1111/jebm.12141.