

# Effectiveness of Exercise on Osteosarcopenia in Elderly People: A Protocol Systematic Review

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## Protocol

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# Abstract

**Background:** Osteosarcopenia is defined as the concomitant occurrence of sarcopenia and osteopenia or osteoporosis. Older adults with this syndrome have greater fragility and chances of mortality compared to those without these conditions. Exercise has been recommended as a treatment for osteosarcopenia based on interventions with sarcopenic and osteoporotic individuals separately. However, there is no evidence that physical exercise can really be an effective treatment for osteosarcopenia. Our objective is to identify whether physical exercise can improve the osteosarcopenia in older adults and lead to good health outcomes.

**Methods:** We will perform a systematic review on the follow databases: PubMed, Embase, Cochrane, and Scopus. The criterion of inclusion will be clinical trial studies in which the interventions were physical exercises in older adults diagnosed with osteosarcopenia. To assess the risk of bias, the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) and the Black and Downs tools will be used. For each search result, the quality of the evidence will ultimately receive one of four grades: high quality, moderate quality, low quality, or very low quality.

**Discussion:** Through this systematic review protocol, an article on physical exercise recommendations for osteosarcopenia in older adults will be prepared. The results of this study may lead to recommendations for physical exercise as a non-pharmacological treatment or complementary therapy for the prevention of osteosarcopenia.

**Systematic review registration:** Ongoing on Prospero.

**Ethics and dissemination:** Protocol written according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA).

## Background

Osteosarcopenia is a recent syndrome [1], defined as the presence of sarcopenia plus osteopenia or osteoporosis in the same individual [2]. The diagnosis of osteopenia / osteoporosis provides an assessment of bone mineral density (BMD) through the absorption of double energy by X-rays (DEXA) [3, 4]. Sarcopenia, on the other hand, is characterized by low muscle strength, with the diagnosis confirmed through the detection of low muscle quality and it is identified as severe sarcopenia through weak physical performance [5].

Osteosarcopenia in elderly people in Germany had a prevalence of 28% [6], while in a study carried out with elderly people from the Australian community, the rates were 37% [7]. In addition, when compared to the presence of isolated conditions, i.e., sarcopenia, osteopenia, or osteoporosis, elderly people with osteosarcopenia have more fractures [8] and a 15.1% higher chance of mortality [9].

Physical exercise (PE) has been recommended in recent reviews as a prevention strategy or non-pharmacological therapeutic approach for osteosarcopenia [10, 11]. However, the prescriptions prescribed for sarcopenia and osteoporosis alone [11–13], consider that there is a consensus in the literature about the effectiveness of PE for elderly people with sarcopenia and osteoporosis [14–17].

Regarding osteosarcopenia, no literature review was found that addressed the effects of regular PE practice on osteosarcopenia for elderly people. Therefore, our aim is to develop a systematic review of the literature that can answer the following question: “What are the influences of regular PE practice on osteosarcopenia in elderly people?” The results of this study may promote the application of PE as a form of non-pharmacological or complementary therapy for the prevention or treatment of osteosarcopenia.

## Methods

This systematic review will be prepared according to the criteria of the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols - PRISMA-P [18, 19]. We adopted the “PICO” structure and defined it as follows: “P” represents elderly people, “I” represents physical exercise, “C” represents without physical exercise, and “O” represents osteosarcopenia.

## Eligibility criteria

Controlled, randomized, blind, or open clinical trials will be included that performed an intervention with any modality of physical exercise with a minimum time of four weeks, conducted with elderly people (age  $\geq 65$  years) of both sexes, diagnosed with osteosarcopenia, i.e., individuals with osteopenia (T-score  $-2.5$  to  $<-1$ ) and osteoporosis (T-score  $\leq -2.5$ ) according to the World Health Organization (WHO) diagnostic criteria [3], and sarcopenia according to a grant from the European Working Group on Sarcopenic in Older People (EWGSOP) [5, 20], without language restrictions and period of publication.

Studies with hospitalized elderly people, which focused on specific conditions, e.g., stroke, will be excluded. Observational studies, opinion articles, editorials, narrative reviews, case series and comments, duplicate studies and publications that present data unavailability even after asking the authors.

## Database

Our search strategy will be conducted in four databases (PubMed (National Library of Medicine), Embase, Cochrane, and Scopus). In addition, the GreyNet International platform will be used to locate productions referring to gray literature internationally as well as Google Scholar. To complement the search and ensure the saturation of the literature, the references of the selected articles will also be considered.

Search terms were selected using the MeSH (Medical Subject Headings) for the PubMed database. Search: ((Osteosarcopenia [Title/Abstract]) AND (((((exercise [MeSH Terms]) OR (exercise [Title/Abstract])) OR (physical activity [Title/Abstract])) OR (physical activities [Title/Abstract])) OR (“Physical Fitness”[Title/Abstract]))) AND (((((((aged[MeSH Terms]) OR (aged[Title/Abstract])) OR

(elderly[Title/Abstract])) OR (older adult [Title/Abstract])) OR (older adults [Title/Abstract])) OR (elder[Title/Abstract])) OR (Ageing[Title/Abstract])) OR (aging[Title/Abstract])). The same search strategy model was adapted to Embase, Cochrane, and Scopus databases.

## Review Process

The search for articles will be carried out by two independent researchers (GVS, MN) and a third senior reviewer (EAS). The inclusion of articles will be carried out by reading the titles, and later by reading the abstracts. Finally, the complete content will be analyzed for inclusion.

After executing the search strategy, articles will be collated, and duplicates will be removed using Mendeley Software. Then, two reviewers (GVS and MN) will independently screen the titles and abstracts of all articles identified in the literature search for inclusion. Disagreement regarding inclusion will be discussed and resolved by a third reviewer (EAS). The screening process will be performed for both reviewers using Rayyan Software [21]. Inter-rater reliability for individual component ratings will be determined by calculating the percentage of agreement and the Cohen's Kappa coefficient [22]. The remaining articles will be read in full and evaluated to determine their eligibility based on the inclusion and exclusion criteria. Finally, the eligible articles will be included in the systematic review.

We will prepare a flowchart with information about the screening of studies, the included studies and the reasons for excluding others, the recording and viewing of this process, following the recommendation of PRISMA-P.

## Data extraction and study quality assessment

To extract data from an article, a standardized form prepared by the authors will be used. The following items will be considered: author / year of publication, place of study, age group studied, sample size, intervention performed, time of intervention, and main results.

To assess the risk of bias, the Grading of Recommendations, Assessment, Development and Evaluations - GRADE [23] and Black and Downs [24] tools will be used. For each research result, the quality of the evidence will ultimately receive one of four scores: high quality, moderate quality, low quality, or very low quality [25]. We will also analyze whether the authors of the included studies addressed the impact of possible conflicts of interest and information regarding ethical approval [26].

## Data analysis

The outcome of this study will be the improvement in osteosarcopenia (bone mineral density, appendicular muscle mass, muscle strength, and function) in elderly people. The possibility of meta-analysis will be assessed according to the homogeneity of the studies, using the methods of fixed or random effect. The Chi-square test will be applied to assess heterogeneity, with a significance level of  $p < 0.05$ . The I-square ( $I^2$ ) statistic will be used to assess the magnitude of inconsistency, which will point to high heterogeneity when the results are greater than 75%, moderate heterogeneity when the results are between 25–75%, and an  $I^2$  less than 25% will demonstrate low heterogeneity [27, 28]. Sensitivity

analyses will be performed, and the funnel plot will be used to assess publication bias. The proposed statistical analyses will be performed using the STATA Software, version 14.0.

## Discussion

The prescription of PE has been described based on specific recommendations for osteoporosis and sarcopenia [10, 11]. This is why our investigation will seek to identify and determine which duration, frequency, intensity, and type of PE is the most appropriate for preventing and treating osteosarcopenia. We will seek to broaden the research by addressing the possible evidence of different exercise modalities: low or high impact aerobics, resistance exercise, balance exercises, combined exercises, and whole body vibration.

By carrying out this protocol, a systematic review and possible meta-analysis to elucidate which physical exercises are most effective for the treatment of osteosarcopenia in elderly people will be produced, as well as whether to prevent the problem. Until then, we are not aware of a published systematic review on this topic. Consequently, the results may bring important recommendations for the field of Gerontology. At the conclusion of this project, we aim to clarify the influence of physical exercise on the parameters of osteosarcopenia, to trace paths of recommendations for a possible therapeutic practice, and to identify the need for new studies.

## Declarations

**Ethics approval and consent to participate:** Ethical approval will not be required as only published data will be used.

**Consent for publication:** Consent for publication will not be required as only published data will be used.

**Availability of data and materials:** The data are available upon request from the corresponding author.

**Competing interests:** The authors declare that they have no competing interests.

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**Authors' contributions:** GVS and EAS conceived the study idea. GVS, EAS, and MN contributed to the design of the systematic review. GVS, EAS, and MN contributed to the data analysis plan. All authors contributed to the writing and editing of the manuscript and approved the final manuscript.

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## Abbreviations

BMD – Bone mineral density; DEXA – Absorption of double energy by X-rays; PE – Physical exercise; PRISMA-P – Preferred Reporting Items for Systematic review and Meta-Analysis Protocols; WHO – World

## References

1. Binkley N, Buehring B. Beyond FRAX®: It's Time to Consider "Sarco-Osteopenia." *Journal of Clinical Densitometry* [Internet]. 2009;12:413–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1094695009001541>.
2. 10.1007/s00198-017-4151-8  
Hirschfeld HP, Kinsella R, Duque G. Osteosarcopenia: where bone, muscle, and fat collide. *Osteoporosis International* [Internet]. 2017;28:2781–90. Available from: <http://link.springer.com/10.1007/s00198-017-4151-8>.
3. Who Scientific Group On The Assessment Of. Osteoporosis At Primary Health Care Level Summary Meeting Report. 2004.
4. 10.1007/s00198-015-3037-x  
Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporosis International* [Internet]. 2015;26:2045–7. Available from: <http://link.springer.com/10.1007/s00198-015-3037-x>.
5. 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*. Oxford University Press; 2019. p. 16–31.
6. 10.1007/s40520-015-0494-1  
Drey M, Sieber CC, Bertsch T, Bauer JM, Schmidmaier R. Osteosarcopenia is more than sarcopenia and osteopenia alone. *Aging Clinical and Experimental Research* [Internet]. 2016;28:895–9. Available from: <http://link.springer.com/10.1007/s40520-015-0494-1>.
7. Huo YR, Suriyaarachchi P, Gomez F, Curcio CL, Boersma D, Muir SW, et al. Phenotype of Osteosarcopenia in Older Individuals With a History of Falling. *Journal of the American Medical Directors Association* [Internet]. 2015;16:290–5. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1525861014006963>.
8. Wang Y-J, Wang Y, Zhan J-K, Tang Z-Y, He J-Y, Tan P, et al. Sarco-Osteoporosis: Prevalence and Association with Frailty in Chinese Community-Dwelling Older Adults. *International Journal of Endocrinology* [Internet]. 2015;2015:1–8. Available from: <http://www.hindawi.com/journals/ije/2015/482940/>.
9. Yoo J-I, Kim H, Ha Y-C, Kwon H-B, Koo K-H. Osteosarcopenia in Patients with Hip Fracture Is Related with High Mortality. *Journal of Korean Medical Science* [Internet]. 2018;33. Available from: <https://jkms.org/DOIx.php?id=10.3346/jkms.2018.33.e27>.
10. 10.12968/hmed.2018.79.5.253  
Paintin J, Cooper C, Dennison E. Osteosarcopenia. *British Journal of Hospital Medicine* [Internet]. 2018;79:253–8. Available from:

<http://www.magonlinelibrary.com/doi/10.12968/hmed.2018.79.5.253>.

11. 10.1177/1759720X19867009

Fatima M, Brennan-Olsen SL, Duque G. Therapeutic approaches to osteosarcopenia: insights for the clinician. *Therapeutic Advances in Musculoskeletal Disease* [Internet]. 2019;11:1759720 × 1986700. Available from: <http://journals.sagepub.com/doi/10.1177/1759720X19867009>.

12. Hassan EB, Duque G. Osteosarcopenia. A new geriatric syndrome The role of the Kynurenine Pathway in Osteoblastogenesis View project. 2017.

13. Kirk B, al Saedi A, Duque G. Osteosarcopenia: A case of geroscience. *Aging Medicine* [Internet]. 2019;2:147–56. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/agm2.12080>.

14. <http://doi.wiley.com/10.1111/ajag.12521>

Vlietstra L, Hendrickx W, Waters DL. Exercise interventions in healthy older adults with sarcopenia: A systematic review and meta-analysis. *Australasian Journal on Ageing* [Internet]. 2018;37:169–83. Available from: <http://doi.wiley.com/10.1111/ajag.12521>.

15. 10.3389/fphys.2019.00445/full

Kirk B, Mooney K, Amirabdollahian F, Khaiyat O. Exercise and Dietary-Protein as a Countermeasure to Skeletal Muscle Weakness: Liverpool Hope University – Sarcopenia Aging Trial (LHU-SAT). *Frontiers in Physiology* [Internet]. 2019;10. Available from: <https://www.frontiersin.org/article/10.3389/fphys.2019.00445/full>.

16. 10.1111/sms.13443

Gonzalo-Encabo P, McNeil J, Boyne DJ, Courneya KS, Friedenreich CM. Dose-response effects of exercise on bone mineral density and content in post-menopausal women. *Scandinavian Journal of Medicine & Science in Sports* [Internet]. 2019;sms.13443. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1111/sms.13443>.

17. Matzkin EG, DeMaio M, Charles JF, Franklin CC. Diagnosis and Treatment of Osteoporosis. *Journal of the American Academy of Orthopaedic Surgeons* [Internet]. 2019;27:e902–12. Available from: <http://journals.lww.com/00124635-201910150-00006>.

18. Moher D, Stewart L, Shekelle P. Implementing. PRISMA-P: recommendations for prospective authors. *Systematic Reviews* [Internet]. 2016;5:15. Available from: <http://www.systematicreviewsjournal.com/content/5/1/15>.

19. 10.1186/2046-4053-4-1

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* [Internet]. 2015;4:1. Available from: <https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/2046-4053-4-1>.

20. 10.1093/ageing/afq034

Cruz-Jentoft AJ, Baeyens JP, Bauer JM, 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 [Internet]. 2010;39:412–23. Available from: <https://academic.oup.com/ageing/article-lookup/doi/10.1093/ageing/afq034>.
21. 10.1186/s13643-016-0384-4  
Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Systematic Reviews* [Internet]. 2016;5:210. Available from: <http://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-016-0384-4>.
22. 10.3389/fphys.2016.00246/abstract  
Stefani L, Galanti G, Padulo J, Bragazzi NL, Maffulli N. Sexual Activity before Sports Competition: A Systematic Review. *Frontiers in Physiology* [Internet]. 2016;7. Available from: <http://journal.frontiersin.org/Article/10.3389/fphys.2016.00246/abstract>.
23. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology* [Internet]. 2011;64:401–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S089543561000332X>.
24. 10.1136/jech.52.6.377  
Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology & Community Health* [Internet]. 1998;52:377–84. Available from: <http://jech.bmj.com/cgi/doi/10.1136/jech.52.6.377>.
25. Grading quality of evidence and strength of recommendations. *BMJ* [Internet]. 2004;328:1490. Available from: <http://www.bmj.com/lookup/doi/10.1136/bmj.328.7454.1490>.
26. 10.1136/bmjopen-2015-010442  
Elia N, von Elm E, Chatagner A, Pöpping DM, Tramèr MR. How do authors of systematic reviews deal with research malpractice and misconduct in original studies? A cross-sectional analysis of systematic reviews and survey of their authors. *BMJ Open* [Internet]. 2016;6:e010442. Available from: <http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2015-010442>.
27. 10.1136/bmj.327.7414.557  
Higgins JPT. Measuring inconsistency in meta-analyses. *BMJ* [Internet]. 2003;327:557–60. Available from: <http://www.bmj.com/cgi/doi/10.1136/bmj.327.7414.557>.
28. Kirkwood BR, Sterne JA. *Essential medical statistics*. 2nd ed. Blackwell; 2010.

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