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Is there a social gradient of sarcopenia? A meta-analysis and systematic review protocol

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ABSTRACT

Introduction Sarcopenia (or loss of muscle mass and function) is a relatively new area within the field of musculoskeletal research and medicine. Investigating whether there is a social gradient, including occupation type and income level, of sarcopenia, as observed for other diseases, will contribute significantly to the limited evidence base for this disease. This new information may inform the prevention and management of sarcopenia and widen the evidence base to support existing and future health campaigns.

Methods and analysis We will conduct a systematic search of the databases PubMed, Ovid, CINAHL, Scopus and EMBASE to identify articles that investigate associations between social determinants of health and sarcopenia in adults aged 50 years and older. Eligibility of the selected studies will be determined by two independent reviewers. The methodological quality of eligible studies will be assessed according to predetermined criteria. Established statistical methods to identify and control for heterogeneity will be used, and where appropriate, we will conduct a meta-analysis. In the event that heterogeneity prevents numerical synthesis, a best evidence analysis will be employed. This systematic review protocol adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols reporting guidelines and will be registered with the International Prospective Register of Systematic Reviews (PROSPERO).

Ethics and dissemination This systematic review will use published data, thus ethical permissions will not be required. In addition to peer-reviewed publication, our results will be presented at (inter)national conferences relevant to the field of sarcopenia, ageing and/or musculoskeletal health and disseminated both electronically and in print.

PROSPERO registration number CRD42017072253.

Strengths and limitations of this study

- This systematic review will focus on the newly defined disease of sarcopenia; a recent addition to the International Classification of Diseases, Tenth Revision, Clinical Modification.
- The selection of eligible studies and methodological assessment will be independently confirmed by two authors.
- Potential confounders and/or mediators of any observed relationship between social determinants and sarcopenia will be highlighted.
- Potential limitations of this review may be a paucity of data due to the 'newness' of sarcopenia and, plausibly, much heterogeneity in available studies.

INTRODUCTION

WHO defines the social determinants of health as the conditions in which a person is born, lives, grows, works and ages[1]: social determinants encompass the distribution of economic and social conditions that influence individual and group differences in health status, and they include factors such as area-level or individual-level socioeconomic status, occupation type and level of income.[1 2] As such, social determinants have a profound influence in compromising health-related behaviours and health outcomes[3]: the musculoskeletal system appears to be no exception to this,[4–6] with the association having already been identified in conditions such as osteoporosis.[7] There is now a strong evidence base for the role played by social disadvantage on an increased susceptibility to many chronic illnesses, lower uptake or engagement in preventative care and earlier mortality.[2 8]

Sarcopenia is defined as a progressive and generalised decline in skeletal muscle mass and deficits of overall strength and functionality.[9–24] Two measures of sarcopenia are currently recommended; a combination of a low level of muscle mass and muscle function (a working definition proposed by the European Working Group on Sarcopenia in Older People)[9 10 12]; or, as an operational definition, muscle mass corrected for height that is two or more SD below that of a young healthy adult is sarcopenia.[13 25 26] Sarcopenia is a relatively new term; although initially coined by Irwin Rosenberg in 1989,[9] it was only added to the International Classification of

Diseases, Tenth Revision, Clinical Modification in 2016.[27] Given the current absence of a universal definition of sarcopenia,[12 28] the nascent literature in this field presents varied estimates of prevalence.[17] Nonetheless, there is agreement that the main consequences of sarcopenia include frailty, falls, hospitalisation, disability and earlier mortality,[9 10] thereby increasing the burden on individuals, communities and healthcare systems.[9 20]

In the context of the 'newness' of sarcopenia and the well-documented role of social determinants in other chronic diseases, we present the protocol for a systematic review, which aims to identify, collate and synthesise the evidence for a social gradient of sarcopenia.

METHODS

This systematic review protocol has been registered with the International Prospective Register of Systematic Reviews (registration ID: CRD42017072253), and it adheres to the preferred reporting process outlined within the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015 guidelines.[29]

Criteria for considering studies in this review

Articles that investigate, in adult populations aged 50 years or older, the association between social determinants as risk factors and the outcome of sarcopenia (regardless of definition), and are epidemiological cohort, cross-sectional and/or case–control studies by design, available in full text, and published in any language will be eligible for inclusion in this review.

Grey literature, conference presentations, opinions or commentaries and randomised controlled trials (RCTs) will be excluded. However, where possible, baseline data from RCTs that apply to social determinants of health and sarcopenia prior to the RCT intervention will be included, as it may be possible that these data may be able to offer relevant cross-sectional information.

Search strategy and data extraction

An electronic search strategy will be performed to investigate medical, health and the social science databases (PubMed, Ovid, CINAHL and EMBASE) to identify studies that match our eligibility criteria, with no limits set for the year of publication. The following Medical Subject Headings will be applied '[All Fields]: (sarcopenia OR aging OR muscular atrophy)'; and the following search strategy will be implemented '((sarcopenia) OR (aging) OR (muscular atrophy) OR (lean mass) OR (musculoskeletal aging)) AND ((social determinants) OR (ses) OR (income) OR (occupation) OR (socioeconomic))'. Keywords of lean mass and musculoskeletal ageing will also be included. For the complete search strategy, please refer to online supplementary file 1 (PubMed search).

Relevant truncation will be applied to each database. One reviewer will perform the search strategy and identify eligible inclusion literature, and two further reviewers will endorse those articles identified as eligible for inclusion. Professional interpreter assistance will be sought to confirm eligibility for articles written in a language other than English. The eligibility of studies will be checked in a three-step process: (1) assessing titles and abstracts, (2) assessing full-text papers and (3) hand-searching reference lists. The reference lists of the studies that have been deemed eligible will be independently hand-searched by two reviewers. One reviewer will extract data from studies deemed eligible for inclusion, and a further reviewer will cross-check all extracted data. Should disagreement arise regarding those data, a third will provide the final judgement.

Table 1 Criteria list for the assessment of methodological quality, modified from Lievense *et al*[30 31]

Item	Criterion	C/CC/CS
Study population		
1	Uniform point (selection before disease was present)	C/CC/CS
2	Cases and controls drawn from the same population	CC
3	Participation rate >80% for cases/cohort	C/CC/CS
4	Participation rate >80% for controls	CC
Assessment of risk factor		
5	Exposure assessment blinded	C/CC/CS
6	Exposure measure identical for cases and controls	CC
7	Exposure assessed prior to the outcome	C/CC/CS
Assessment of outcome		
8	Outcome assessed identically in studied populations	C/CC/CS
9	Outcome assessed reproducibly	C/CC/CS
10	Outcome assessed according to validated measures	C/CC/CS
Study design		
11	Prospective design used	C/CC
12	Follow-up time >12 months	C
13	Withdrawals <20%	C
Analysis and data presentation		
14	Appropriate analysis techniques used	C/CC/CS
15	Adjusted for at least age and sex	C/CC/CS

C, applicable to cohort studies; CC, applicable to case–control studies; CS, applicable to cross-sectional studies.

Assessment of methodological quality of included articles

A modified scoring system from Lievense *et al*[30 31] will be employed to analyse data extracted from included studies (table 1). Each of the eligible studies will be scored based on the previously mentioned methodological assessment criteria, and the score given will be either positive or negative for each of the criterion within the study. Currently, no validated criteria exist for assessing

the methodological quality of observational studies; the Lievense *et al*[30 31] tool provides a reproducible process and enables both validity and informativeness to be assessed in cohort, case–control and cross-sectional study designs, as we have previously demonstrated in the musculoskeletal research field.[32–34] Those studies deemed eligible will be independently scored by two reviewers using the Lievense *et al*[30 31] scoring system: should any differences in scores be found to be irreconcilable, a third reviewer will be introduced and provide the final judgement. The final score will be calculated (as a percentage) and ranked and deemed as having higher methodological quality if scored above the median of the total scores.

Presenting and reporting results

This systematic review protocol adheres to the PRISMA-P reporting guidelines.[35] An adapted Quality of Reporting of Meta-analyses standards (QUORUM) diagram[36] will be used to present study selection, numbers and reasons for inclusion and exclusion of articles in line with the predetermined eligibility criteria. All relevant studies will have key information regarding sarcopenia and social determinants identified, manually extracted and presented, which will be from the articles eligible for inclusion. The key information to be extracted from eligible papers may include, but will not be limited to, the definition and measures of sarcopenia, lean mass and hand grip strength, socioeconomic status, income and education attainment. Results from the methodological scoring will be presented as a percentage.

Where methodological heterogeneity is low, a meta-analysis will be performed and a numerical synthesis presented. The determination of whether statistical heterogeneity is low enough to conduct a meta-analysis will be assessed using the Cochrane Q statistic and the I^2 statistic: this method will also inform whether we adopt a fixed-effects or random-effects model. We will apply a threshold of an I^2 >50% to classify moderate heterogeneity and, if there is overall consistency in the direction of effect, the potential use of a random-effects model. Sources of heterogeneity will be investigated by removing studies at high risk of bias and comparing summary estimates from different study-level methodological characteristics (such as sarcopenia definitions, study design and age of population), using metaregression where appropriate. Funnel plots will be used to investigate publication bias, whereby the distribution of ORs will be presented according to sample size.

Where missing data are identified and to enable methodological scoring using the Lievense *et al*[30 31] multi-item instrument, we will (1) employ inverse probability weighting and (2) report the number of missing items on which the inferences were based.[37] We will present all available data in the eligible studies, noting where missing data preclude our ability to report.

A 'best evidence syntheses' will be undertaken where a meta-analysis is not possible, due to heterogeneity: this latter method will enable an evaluation of the combined level of evidence; ranging from no evidence to strong evidence (table 2), as previously published in the musculoskeletal field.[33 34]

Table 2 Criteria for determining evidence level for best evidence synthesis: modified from Lievense *et al*[30]

Level of evidence	Criteria for inclusion in best evidence synthesis
Strong evidence	Generally consistent findings in: ► Multiple high-quality cohort studies
Moderate evidence	Generally consistent findings in: ► 1 high-quality cohort study and >2 high-quality case-control studies ► >3 high-quality case–control studies
Limited evidence	Generally consistent findings in: ► A single cohort study ► 1 or 2 case–control studies ► Multiple cross-sectional studies
Conflicting evidence	Inconsistent findings in <75% of the trials
No evidence	No studies could be found

Dissemination

Findings from this review will be published in a peer-reviewed scientific journal and presented at (inter)national conferences relevant to the field of sarcopenia and/or musculoskeletal health.

Ethics

Given that this systematic review will use only published data, ethical permissions will not be required. However, ethical and governance standards with regard to data management and the presentation and discussion of our findings will be strictly abided by within our research processes.

CONCLUSION

To the best of our knowledge, this will be the first review to explore whether there is a social gradient of sarcopenia. Investigating sarcopenia in relation to the social determinants of health is a novel area of enquiry, and these findings will contribute to the current paucity of literature regarding the prevention of sarcopenia, while widening the evidence base to support existing and future health campaigns targeted at sarcopenia.

Contributors DG, GD and SLB-O conceptualised the research question for this protocol. All authors edited and revised the research question. DG and SLB-O contributed to the development of, and confirmed, the research strategy and developed the methodological process. All authors edited, revised and approved the methodological process. DG and SLB-O drafted the manuscript. All authors edited and contributed to the writing of this paper, read and approved the final version and guaranteed the review.

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Competing interests SLB-O has received speaker fees from Amgen. GD has received speaker fees from Amgen, Sanofi and Eli Lilly Australia.

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