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Published in:
Journal of Cachexia, Sarcopenia and Muscle

DOI:
10.1002/jcsm.13243

Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

REVIEW

Journal of Cachexia, Sarcopenia and Muscle 2023; **14**: 1228–1243
Published online 4 May 2023 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.13243

Sarcopenia and health-related quality of life: A systematic review and meta-analysis

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Abstract

The decrease of physical abilities and functional decline that can be caused by musculoskeletal conditions such as sarcopenia, can lead to higher levels of dependency and disability. Therefore, it may influence patient reported outcome measures (PROM), such as the health-related quality of life (HRQoL). The purpose of this systematic review and meta-analysis is to provide a comprehensive overview of the relationship between sarcopenia and HRQoL. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were followed throughout the whole process of this work. A protocol was previously published on PROSPERO. The electronic databases MEDLINE, Scopus, Allied and Complementary Medicine (AMED), EMB Review – ACP Journal Club, EBM Review - Cochrane Central of Register of Controlled Trials and APA PsychInfo were searched until October 2022 for observational studies reporting a HRQoL assessment in both sarcopenic and non-sarcopenic individuals. Study selection and data extraction were carried out by two independent researchers. Meta-analysis was performed using a random effect model, reporting an overall standardized mean difference (SMD) and its 95% confidence interval (CI) between sarcopenic and non-sarcopenic individuals. Study quality was measured using the Newcastle-Ottawa Scale and the strength of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool. The search strategy identified 3725 references from which 43 observational studies were eligible and included in this meta-synthesis study. A significantly lower HRQoL was observed for sarcopenic individuals compared with non-sarcopenic ones (SMD −0.76; 95% CI −0.95; −0.57). Significant heterogeneity was associated with the model (I^2 = 93%, *Q* test *P*-value <0.01). Subgroup analysis showed a higher effect size when using the specific questionnaire SarQoL compared with generic questionnaires (SMD −1.09; 95% CI −1.44; −0.74 with the SarQoL versus −0.49; 95% CI −0.63; −0.36 with generic tools; *P*-value for interaction <0.01). A greater difference of HRQoL between sarcopenic and non-sarcopenic was found for individuals residing in care homes compared with community-dwelling individuals (*P*-value for interaction <0.001). No differences were found between age groups, diagnostic techniques, and continents/regions. The level of evidence was rated as moderate using the GRADE assessment. This systematic review and meta-analysis combining 43 observational studies shows that HRQoL is significantly reduced in sarcopenic patients. The use of disease-specific HRQoL instruments may better discriminate sarcopenic patients with respect to their quality of life.

Keywords Sarcopenia; Quality of life; HRQoL; Older people

Received: 18 November 2022; Revised: 8 March 2023; Accepted: 3 April 2023
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Introduction

The normal aging process is accompanied by a progressive degradation of musculoskeletal functions. Indeed, from the age of 60, a decrease in muscle mass (−1% per year) and muscle strength (−2.5 to 3% per year) can be observed.[1] Sarcopenia is not part of the normal aging process, and has recently been defined by the European Work Group on Sarcopenia in Older people (EWGSOP) as 'a progressive and generalized skeletal muscle disorder that is associated with an increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality'.[2] This condition affects older people and is associated with higher mortality and morbidity.[3] Current evidence suggests an impact of sarcopenia on health-related quality of life (HRQoL).[4,5]

The assessment of QoL as a health parameter has been gradually introduced in the measurement of the impact of pathologies and more specifically of chronic diseases.[6] Indeed, with the constant increase in life expectancy, the improvement of medical technologies and better prevention, pathologies tend to become chronic and their assessment cannot be limited to mortality or morbidity.[7] The measurement of patient reported outcomes (PROM), and more specifically HRQoL, has become an important indicator increasingly used in epidemiological studies, particularly encouraged by the numerous validations and adaptations of existing tools. In addition, HRQoL measures have been shown to be significant predictors of hard clinical outcomes, such as hospitalization or mortality, reinforcing the importance of their assessment.[8–12] The reduction in physical capacity and functional decline that can be caused by musculoskeletal disorders such as sarcopenia, can lead to a higher levels of dependency and disability and therefore influence the HRQoL.[13,14] Measurement of this specific PROM is recommended in interventional trials, and HRQoL should be used as co-primary endpoint to evaluate the effectiveness of interventions in sarcopenia.[15] HRQoL tools exist under the form of generic or specific tools. Generic tools can be applied to any population suffering from any disease and offer the possibility to obtain comparisons between populations whereas specific tools are specifically designed for a particular population and offer the advantage of being more sensitive to change. To date, there are only two HRQoL specific questionnaires for sarcopenic patients, the Sarcopenia and Quality of Life (SarQoL) questionnaire[16–18] and the Age-Related Muscle Loss Questionnaire (ARMQL),[19] although the latter is not fully validated.

In 2016, Woo and colleagues published a systematic review on the relationship between biomarkers of sarcopenia (i.e., muscle mass, muscle strength, and physical performance) and HRQoL.[4] The authors searched the literature up to December 2015 and included 20 articles. However, only one study used a consensus definition of sarcopenia. In 2019, the widely used definitions of sarcopenia established by the European Work Group on Sarcopenia in Older people and the Asian Working Group for Sarcopenia were revised.[2,20] These revisions followed the assignment, in 2016, of an International Statistical Classification of Diseases and Related Health Problems – Clinical Modification code (ICD-10-CM) to diagnose sarcopenia.[21] As this is a major advance, a significant number of studies have been published using one of the established diagnostic criteria, making it worthwhile to revisit the question of the association between sarcopenia and HRQoL.

The aim of this systematic review and meta-analysis is therefore to summarize the evidence on the association between primary sarcopenia and HRQoL. More specifically, this meta-research work aims to evaluate whether primary sarcopenia affects HRQoL by comparing HRQoL reported by sarcopenic participants with that reported by non-sarcopenic participants.

Methods

The proposed systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA2020).[22] The completed PRISMA checklist is available in Appendix S1. A protocol has been developed and published in PROSPERO (CRD42020215377). The current article reports results coming from observational studies. Because the researchers' team changed during the realization of the project, an amendment to the protocol was published in October 2022.

The research project can be summarized with the following PICOs format: P (Population): Older people with sarcopenia; I (Intervention/Predictors): NA; C (Comparator): Older people without sarcopenia; O (Outcome): a measure of quality of life; S (Study design): Observational studies (i.e., cross-sectional and longitudinal studies).

Literature search

MEDLINE, Allied and Complementary Medicine (AMED), EMB Review – ACP Journal Club, EBM Review - Cochrane Central of Register of Controlled Trials, APA PsychInfo (via OVID platform for all the mentioned bibliographic databases) and Scopus were searched in October 2022 for any observational studies reporting a measure of HRQoL for sarcopenic individuals in comparison with non-sarcopenic individuals. For convenience of translation, the search was limited to English and French studies.[23] A combination of terms of Medical Subject Headings (MeSH) and keywords was used in the search strategy (the complete search strategies for Ovid and Scopus are available in Appendix S2).

Additionally, bibliographies of all included studies were manually checked for other potentially relevant publications.

Moreover, references retrieved from previous systematic reviews and review articles performed on the same or similar topic were hand searched and included to search for additional references matching our selection criteria. We also contacted experts in the field to obtain their opinions about our search strategy and the included papers. They were also proposed to provide us any missing studies or grey literature they knew about.

The search results from the electronic sources and hand searching were imported in Covidence software for data management, as recommended by the Cochrane collaboration.

Study selection

Inclusion criteria (Table 1) guided the first step of references selection based on title and abstract. Three reviewers (C. B., C. D. and M. L.) performed this screening independently to exclude irrelevant articles with every single reference screened by two different reviewers. In the second step, the reviewers read the full texts of each non-excluded articles to determine eligibility for inclusion in this systematic review. Disagreements during both stages were resolved by consensus between the two reviewers.

Both cross-sectional studies and longitudinal studies were accepted if those studies provided a HRQoL assessment for both a sarcopenic and a non-sarcopenic group. To be consistent with the objectives of the present systematic review and meta-analysis, only cross-sectional data from longitudinal studies were used (i.e., HRQoL for sarcopenic and non-sarcopenic individuals at a certain time; longitudinal changes in HRQoL for both populations were not used).

Studies were excluded if they included individuals with acute sarcopenia (i.e., development of sarcopenia within a short amount of time after a stressor event such as hospitalization or illness[2]); sarcopenia was diagnosed on the basis of a single biomarker (e.g., muscle mass only); only a screening tool (e.g., the SARC-F) was applied without further diagnosing the condition; hospitalized, pre-/post-operative or disease-specific participants were recruited; only sarcopenic obesity was diagnosed in the study; HRQoL was examined using qualitative research methods; and/or no original data was reported (i.e., exclusion of commentaries, editorials, and letters to the editor).

Data extraction

Data were independently extracted by two reviewers and encoded in a standardized Excel file, pre-tested on a sample of 5 studies. The following information were extracted: article information (e.g., title and year of publication), population characteristics (e.g., description of the population and sarcopenia diagnosis), outcomes (e.g., HRQoL instrument and results), funding, conflict of interest and conclusion.

Disagreements were resolved by consensus or with the help of an additional reviewer (O. B.). When full text was not available or data were missing, authors were contacted.

Quality appraisal

Quality assessment of studies was performed with Newcastle-Ottawa Quality Assessment Scale (NOS). Initially, the NOS has been developed for longitudinal studies, but we used an adapted version for cross-sectional studies (accessed online on August 2022: https://www.kcgg.ugent.be/pdf/NEWCASTLE-OTTAWA_QUALITY_ASSESSMENT_SCALE.pdf). This adapted version has already been used by several other studies that have felt the need to adapt the NOS scale to appropriately assess the quality of cross-sectional studies.[24] This scale consists of three items: selection, comparability and outcome. According to different criteria, a maximum number of stars can be attributed for each item with a maximum total number of 7 stars for cross-sectional studies. Concerning the item 'comparability', we assigned a score of 0 when a significant difference in age of sarcopenic and non-sarcopenic participants was identified without being integrated in a multivariate analysis.

Each study was evaluated independently by the two reviewers. Disagreements were resolved by consensus or with the help of a third reviewer.

Table 1 Inclusion criteria

Inclusion criteria	
Design	Observational studies (i.e., cross sectional studies or longitudinal studies)
Language	English
Participants	Community-dwelling or residents in assisted living facilities, ≥60 years of age or the mean or median age of the sample is ≥60 years. A diagnosis of sarcopenia should be performed (based on at least 2 biomarkers) and participants should be divided in two groups according to the presence of sarcopenia.
Outcome	Quality of life in a quantitative format (i.e., a scale), measured with a validated instrument specifically designed to measure quality of life. Quality of life measurement should be reported for sarcopenic and non-sarcopenic participants.

Grading the evidence

We used the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) method[25] to rate the certainty of the evidence and to summarize the overall quality of the evidence from the pooled studies. The evidence score started with a high-quality evidence and was downgraded by one or two levels if any of the following pre-specified criteria was present: (1) risk of bias (RoB) (i.e., high risk of bias in more than 75% of the included studies; (2) inconsistency (i.e., unexplained substantial heterogeneity $I^2 > 50\%$); (3) indirectness (i.e., presence of factors that limit the generalizability of the results); (4) imprecision (i.e., large 95% confidence interval (CI) recommendation altered if 95% CI represents the true effect); (5) publication bias (i.e., small study effect $P > 0.05$ and significant impact on the estimator). Each meta-analysis outcome assessed was determined to be of very low, low, moderate or high certainty.

Data synthesis

A random effect model was chosen given the expected heterogeneity of protocols and sarcopenia diagnosis across individual studies. To provide a comparison between outcomes reported by the different studies, effect size as standardized mean difference with 95% CIs were measured for each outcome. We extracted mean and standard deviations (SDs) HRQoL values of both groups (i.e., sarcopenic and non-sarcopenic) in each individual study. When data were not available in the right format or incomplete, we first contacted authors of individual studies to obtain missing values. If the missing data could not be obtained from the authors, we used different strategies to obtain the missing information, or an estimation of the missing information, to be sure to include the study in our analyses and maintain an exhaustivity to our research. We used the following techniques: (1) We referred to the methods described in section 7.7.3 of the Cochrane Handbook for Systematic Review to obtain missing SDs from *P*-values or 95% confidence intervals; (2) when only median and interquartile ranges were available, we used the formula proposed by Hozo et al.[26] to convert them into mean and SDs.

When a study reported multiple results for HRQoL according to different sarcopenia diagnosis, we used preferentially first the revised version of the EWGSOP criteria (EWGSOP2 criteria).[2] When different scales were used to measure HRQoL within the same study, we extracted, preferentially first, the results of specific HRQoL questionnaire (e.g., the SarQoL), then the SF-36 Physical Component Scale, then the SF-36 Physical function, then the EQ-5D and then any other scales/subscales for measuring HRQoL.

Subgroup analyses were performed according on the HRQoL instrument used (individual tool or generic vs. specific), on the diagnostic criteria for sarcopenia (EWGSOP1 vs. EWGSOP2 vs. Asian Working Group on Sarcopenia (AWGS)) and on age of participants (>75 years or <75 years). Meta-regression was also performed on age of participants, treated as a continuous variable and on quality of study (number of stars obtained to the NOS scale).

Results were examined for heterogeneity using Cochran's Q statistic and the I^2 statistic. Potential publication bias was explored by means of a contour-enhanced funnel plot. We used the Egger's regression asymmetry test to detect publication bias. In case of significant publication bias, the Trim and Fill method was applied to assess the impact of potential missing studies on the pooled effect size.

We also conducted one-way sensitivity analyses to evaluate the stability of our results when one study is removed at a time. Because it was feasible for all studies using the same HRQoL questionnaire (i.e., the SarQoL), we also performed a sensitivity analysis by changing the effect size within this meta-analysis. Therefore, for all studies measuring HRQoL using the SarQoL, the difference between sarcopenic and non-sarcopenic participants was also measured using the Mean Difference and its 95% CI.

For all results, a two-sided *P*-value of 0.05 or less were considered as significant. All analyses were performed using R Software (R-4.2.1) and appropriate packages (meta, metafor, tidyverse, devtools, esc, mathjax, and dmetar).

Results

A total of 3725 references were identified using the search strategies applied on to the databases in October 2022. After removing duplicates, 2293 references were assessed for eligibility based on their title/abstract and 188 of these were further assessed based on their full text. From these 188 studies, 39 met our inclusion criteria and four additional studies were further identified through a manual search. The list of excluded studies and their respective reasons of exclusion is available on our Open Science Framework deposit (https://osf.io/rqhvy/). Therefore, a total of 43 observational studies were included in this systematic review, 42 cross-sectional studies[5,27–67] and one prospective study[68] for which baseline values of HRQoL for the sarcopenic and non-sarcopenic groups were used (Figure 1).

Cross-sectional studies

The total of the 43 studies combined data from 30 322 participants, 4108 sarcopenic and 26 214 non-sarcopenic. The characteristics of the included studies are shown in Table 2. The EWGSOP criteria were used in 34 (79.1%) of the studies (EWGSOP1: *n* = 19; EWGSOP2: *n* = 15) whereas the AWGS criteria were used in the remaining 9 studies (20.9%). About

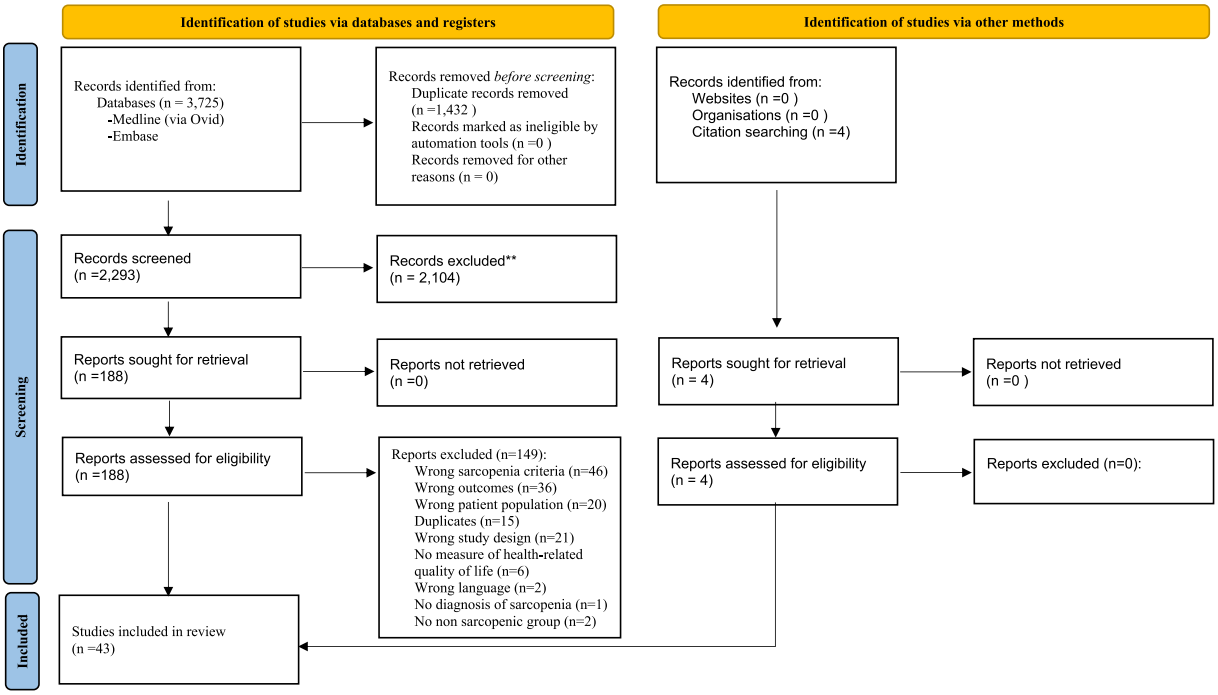

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) flowchart of study selection.

46.5% of the studies used the specific HRQoL questionnaire SarQoL (n = 20) and the others used generic questionnaires (i.e., SF-36 n = 11, EQ 5D n = 8, CASP n = 2, OHIP-14 n = 1, OPQoL n = 1, WHOQoL n = 1). The calculated median age of the participants was 74.6 years. Regarding the quality of the studies, out of a total of 7 points on the NOS scale, 3 studies received 3 points, 14 studies received 4 points, 18 studies received 5 points, 7 studies received 6 points and only one study received the maximum value of 7 points. The quality assessment of each study is shown in Table 3.

Authors of 14 papers were contacted because the data were not usable in the format presented in the paper and 11 authors responded to provide the data in the correct format. Therefore, imputations (i.e., transformation of 95% CI into SD and transformation of median and interquartile range into mean and SD) were only necessary for 3 out of the 43 studies (6.98%).[32,39,60]

A general forest plot including the 43 observational studies is shown in Figure 2 and highlights a significantly important reduced HRQoL for sarcopenic participants compared with non-sarcopenic ones (SMD −0.76; 95% CI −0.95; −0.57). The model was associated with significant heterogeneity (I^2 = 93%, Q test P-value <0.01). The leave one analysis removing some outliers (e.g., Alekna, 2019, Le, 2021, Mahmoodi, 2022 or Yoo, 2020) did not affect the global results (SMD −0.71 [−0.87; −0.54] when removing Mahmoodi, 2022; SMD −0.73 [−0.92; −0.54] when removing any of the three at that time).

Asymmetry was observed in the funnel plot (Figure 3), which was further confirmed by the Egger's test (t = −4.56, df = 43, P-value<0.01), indicating significant publication bias in the model. The Trim and Fill method applied to all studies identified 18 potentially missing studies. After applying the Trim and Fill method to the data, the HRQoL of sarcopenic participants was still reduced compared with non-sarcopenic participants but in a moderate manner (SMD recalculated with 18 imputed studies: −0.31, 95% CI −0.55; −0.07).

The results of the subgroups analyses are shown in Table 4. A significant difference in HRQoL found in sarcopenic populations was found when using a specific HRQoL questionnaire compared with a generic one. The specific HRQoL questionnaire SarQoL better discriminated sarcopenia in terms of HRQoL (SMD of −1.09 [−1.44; −0.74] using the SarQoL versus −0.49 [−0.63; −0.36] using generic tools [P-value for interaction <0.01]). Because all studies using a specific HRQoL used the same tool, the SarQoL questionnaire (n = 20), it was also possible to perform a post-hoc sensitivity analysis (not specified in the protocol) by changing the SMD estimate with a Mean Difference (MD) estimate. A MD of −15.01 points/100 (95% CI of −19.00; −11.01) on the SarQoL questionnaire was found for sarcopenic compared with non-sarcopenic participants.

A subgroup interaction was also found regarding clinical setting. A larger difference of HRQoL between sarcopenic individuals and non-sarcopenic ones was found among those living in care homes (n = 2, SMD of −1.29, 95% CI −1.51;

Table 2 Characteristics of included studies

First author's name, year	Country	Participants (type of population, sample size, age, sex ratio)	Sarcopenia ratio	Definition of sarcopenia	Tool used to access sarcopenia	Tool to assess HRQoL
Alekna, 2019[53]	Lithuania	Community dwelling older adults, Sample size: 176, Age: 78.2 (74.1–82.6), Women: 59.7%	58 (32.9%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* SPPB	SarQoL
Beaudart, 2015[36]	Belgium	Community dwelling older adults, Sample Size: 534, Age: 73.5 ± 6.16, women: 60.3%	73 (13.7%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* SPPB	SF-36 EQ-5D
Beaudart, 2017[38]	Belgium	Community dwelling older adults, Sample size: 296, Age: 73.3 (68.9–78.6), Women: 57.1%	43 (14.5%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* SPPB	SarQoL
Beaudart, 2017[51]	UK	Community dwelling participants of the Hertfordshire Cohort Study, Sample size: 297, Age: 79.5 ± 2.62, Women: 46.1%	14 (4.7%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Beaudart, 2018[34]	Belgium	Community dwelling older adults, Sample size: 387, Age: 74.02 ± 5.99, Women: 58.5%	50 (12.9%) 48 (12.4%) 17 (4.4%) 38 (9.8%)	EWGSOP1 IWGS SSCWD FNIH	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Chew, 2020[54]	Singapore	Community-dwelling older adults, Sample size: 200, Age: 67.9 ± 7.86, Women: 68.5%	31 (15.5%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	EQ-5D
De Souza Orlandi, 2018[60]	Brazil	Community dwelling older adults, Sample size: 226, Age: 69.97 ± 6.82	43 (19%)	EWGSOP1	NR	EQ-5D SF-36
De Souza Orlandi, 2022[24]	Brazil	Community dwelling older adults, Sample size: 221, Women: 68.3%	55 (36.4%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Erdogan, 2019[41]	Turkey	Community dwelling older adults, Sample size: 100, Age: 74.7 ± 6.1, Women: 71.0%	27 (27.0%)	EWGSOP2	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Fábrega-Cuadros, 2020[33]	Spain	Community dwelling older adults, Sample size: 252, Age: 74.00 (70.00–78.00), Women: 82.54%	66 (26.2%)	EWGSOP2	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer	SarQoL
Fábrega-Cuadros, 2021[43]	Spain	Community dwelling older adults, Sample size: 304, Age: 72.04 ± 7.88, Women: 83.88%	72 (28.23%)	EWGSOP2	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
Gasparik, 2017[22]	Romania	Community dwelling older adults recruited in hospital, Sample size: 100, Age: 72 (67–79), Women: 69%	13 (13.0%)	EWGSOP1	*Muscle mass:* Lee equation *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL

(*Continues*)

Table 2 (continued)

First author's name, year	Country	Participants (type of population, sample size, age, sex ratio)	Sarcopenia ratio	Definition of sarcopenia	Tool used to access sarcopenia	Tool to assess HRQoL
Geerinck, 2018[31]	Belgium	Community dwelling older adults, Sample size: 92, Age: 82 (73–85), Women: 43.5%	30 (32.6%)	EWGSOP1	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Geerinck, 2020[50]	Belgium	Community dwelling older adults, Sample size: 296, Age: 73.3 (68.9–78.6)	13 (4.4%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer	SarQoL
Geerinck, 2021[28]	Belgium	Community dwelling older adults, Sample size:214, Age: 76 (73–81), Women: 63.1%	21 (9.8%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer	SF-36 SarQoL
Guillamon-Escudero, 2022[42]	Spain	Community dwelling older adults, Sample size: 202, Age: 73 ± 7, Women: 164 (81.2%)	54 (26.7%)	EWGSOP2	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Ilhan, 2019[5]	Turkey	Community dwelling older adults, Sample size: 408, Age: 77.1 ± 6.8, Women: 69.0%	11 (2.7%)	EWGSOP1	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	EQ-5D
Imai, 2022[40]	Japan	Community dwelling older adults, Sample size: 113, Age: 76.3 ± 5.6	22 (19.5%)	AWGS	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	EQ-5D
Kitamura, 2022[29]	Japan	Community older people covered by long term care insurance attending rehabilitation in a one-day care centre, Sample size: 64, Age: 79.3 ± 8.8, Women: 67.3%	24 (55.8%)	AWGS	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer	EQ 5D-3L
Konstantynowicz, 2018[52]	Poland	Community dwelling older adults, Sample size: 106, Age: 73.3 ± 5.94, Women: 65.1%	60 (56.6%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Le, 2021[49]	China	Community-dwelling older adults and outpatient department of geriatrics, Sample size: 159, Women: 46.5%	51 (32.01%)	AWGS	*Muscle mass:* Lee equation *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Lee, 2022[61]	Taïwan	Community dwelling older adults, Sample size: 100, Age: >65 years, Women: 28%	50 (50.0%)	AWGS	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed or SPBB	SarQoL
Losa-Reyna, 2020[45]	Spain	Community dwelling older adults, Sample size: 1189, Age: 75.8 ± 5.9, Women: 53.7%	97 (8.16%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	EQ-5D
Mahmoodi, 2022[23]	Iran	Community dwelling older adults, Sample size: 128, Women: 41.4%	88 (68.5%)	AWGS	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL

(*Continues*)

Table 2 (continued)

First author's name, year	Country	Participants (type of population, sample size, age, sex ratio)	Sarcopenia ratio	Definition of sarcopenia	Tool used to access sarcopenia	Tool to assess HRQoL
Manrique-Espinoza, 2017[59]	Mexico	Community dwelling older adults, Sample size: 543, Age: 76.1 ± 3.1, Women: 52.7%	198 (36.5%)	EWGSOP1	*Muscle mass:* Calf circumference *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
Marques, 2018[37]	Brazil	Community dwelling older adults, Sample size: 604, Women: 65.2%	37 (6.1%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer	CASP-16
Matijević, 2020[48]	Serbia	Community dwelling older adults, Sample size: 699, Age: 70 (67–74), Women: 72.7%	12 (1.7%)	EWGSOP2	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Mijnarends, 2016[56]	Netherlands	Community dwelling older adults, Sample size: 227, Age: 74.9 ± 7.2	53 (23.3%)	EWGSOP1	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	EQ-5D EQVAS
Montero-Errasquín, 2022[46]	Spain	Community dwelling older adults, Sample size: 86, Age: 77.6 ± 5.3, Women: 80.2%	16 (18.6%) 13 (15.1%)	EWGSOP1 FNIH	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer	SarQoL
Mori, 2019[57]	Japan	Community-dwelling adults aged ≥60 years, Sample size: 331, Age: 71.5 ± 5.1, Women: 71.9%	19 (5.7%)	AWGS	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
Öztürk, 2018[39]	Turkey	Community dwelling geriatric population referred to outpatient clinic, Sample size: 423, Age: 71.8 ± 6.01, Women: 56.7%	61 (14.4%)	EWGSOP1	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
Patel, 2013[27]	United-Kingdom	Community dwelling older adults, Sample size: 103, Age: 72.4 ± 4.4, Women: 0.00%, 100% of men	7 (6.8%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
SilvaNeto, 2016[32]	Brazil	Community dwelling older adults, Sample size: 70, Age: 65.58 ± 6.67, Women: 55.7%	7 (10%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
Simsek, 2022[44]	Turkey	Nursing home residents, Sample size: 172, Age: 81.78 ± 7.03, Women: 57.6%	88 (51.2%)	EWGSOP2	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer	EQ-5D
Singhal, 2019[26]	India	Community dwelling people, outpatients of the Department of Geriatric Medicine, Sample size: 100, Age: 72.5 ± 6.4, Women: 31%	53 (53%)	AWGS	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	OPQoL
Smith, 2022[62]	Multicentre	Community dwelling older adults, Sample size: 14 585, Age: 72.6 ± 11.5, Women: 55.0%	1750 (12.0%)	EWGSOP2	*Muscle mass:* Lee equation*Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	WHOQoL

(*Continues*)

Table 2 (continued)

First author's name, year	Country	Participants (type of population, sample size, age, sex ratio)	Sarcopenia ratio	Definition of sarcopenia	Tool used to access sarcopenia	Tool to assess HRQoL
Takahashi, 2018[58]	Japan	Community dwelling older adults, dental clinic outpatients, Sample size: 279, Age: 76 ± 7.5, Women: 62.0%	86 (30.8%)	AWGS	*Muscle mass:* Calf circumference *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	OHIP-14
Tsekoura, 2020[30]	Greece	Community dwelling older adults, Sample size: 176, Age: 71.19 ± 7.95, Women: 77.27%	50 (28.4%)	EWGSOP1	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SarQoL
Umegaki, 2022[63]	Japan	Community dwelling older adults attending a memory clinic, Sample size: 23, Age: NR 1-year follow-up	23 (100%)	AWGS	*Muscle mass:* BIA*Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	EQ-5D
Veronese, 2022[47]	Italy	Community dwelling older adults, Sample size: 4044, Age: 70.7 ± 7.6, Women: 55.1%	375 (9.3%)	EWGSOP2	*Muscle mass:* Lee equation *Muscle strength:* handgrip dynamometer	CASP-19
Woo, 2018[25]	Australia	Community dwelling older adults, Sample size: 727, Age: 73.9 ± 6.2 for men, 73.2 ± 6 for women, Women: 50.9%	71 (9.77%)	EWGSOP1	*Muscle mass:* DXA *Muscle strength:* handgrip dynamometer	SF-36
Yalcin, 2017[35]	Turkey	Residents of a Turkish nursing home, $N = 241$, 83.27 ± 5.65, women: (52.1%)	12393 (38.6%)	EWGSOP1	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer *Physical performance:* gait speed	SF-36
Yoo, 2020[55]	Korea	Community dwelling older adults, Sample size: 450, Age: 73.9 ± 6.6, Women: 87.7%	53 (11.8%)	EWGSOP2	*Muscle mass:* BIA *Muscle strength:* handgrip dynamometer	SarQoL

AWGS, Asian Working Group on Sarcopenia; BIA, bioelectrical impendance analysis; CASP-19 (or 16), Quality of Life Scale; DXA, dual energy X-ray absorptiometry; EQ-5D, EuroQol five-dimensions; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project; HRQoL, health-related quality of life; NR, not reported; OHIP-14, Oral Health Impact Profile-14; SarQoL, Sarcopenia and Quality of life questionnaire; SF-36, Short-Form 36; SPPB, Short Physical Performance Battery; WHOQoL, World Health Organization Quality of Life questionnaire.

Table 3 Quality appraisal of included studies

First author's name, year	Selection	Comparability	Outcome	Total score*
Alekna, 2019	★☆☆	★★	★★	★★★★★☆☆
Beaudart, 2015	★★☆	★★	★★	★★★★★★☆
Beaudart, 2017	★☆☆	★★	★★	★★★★★☆☆
Beaudart, 2017	★★☆	★☆	★★	★★★★★☆☆
Beaudart, 2018	★☆☆	★★	★★	★★★★★☆☆
Chew, 2020	★☆☆	★★	★☆	★★★★☆☆☆
De Souza Orlandi, 2018	★☆☆	☆☆	★★	★★★☆☆☆☆
De Souza Orlandi, 2022	★☆☆	☆☆	★★	★★★☆☆☆☆
Erdogan, 2019	★☆☆	★☆	★★	★★★★☆☆☆
Fábrega-Cuadros, 2020	★★☆	★☆	★★	★★★★★☆☆
Fábrega-Cuadros, 2021	★☆☆	★☆	★★	★★★★☆☆☆
Gasparik, 2017	★★★	★★	★★	★★★★★★★
Geerinck, 2018	★★☆	★☆	★★	★★★★★☆☆
Geerinck, 2020	★☆☆	★★	★★	★★★★★☆☆
Geerinck, 2021	★☆☆	★☆	★★	★★★★☆☆☆
Guillamon-Escudero, 2022	★☆☆	★☆	★★	★★★★☆☆☆
Ilhan, 2019	★☆☆	★☆	★★	★★★★☆☆☆
Imai, 2022	★☆☆	★★	★★	★★★★★☆☆
Kitamura, 2022	★☆☆	★★	★★	★★★★★☆☆
Konstantynowicz, 2018	★☆☆	★★	★★	★★★★★☆☆
Le, 2021	★☆☆	★★	★★	★★★★★☆☆
Lee, 2022	★★☆	★★	★★	★★★★★★☆
Losa-reyna, 2020	★★☆	★★	★★	★★★★★★☆
Mahmoodi, 2022	★★☆	★★	★★	★★★★★★☆
Manrique-Espinoza, 2017	★☆☆	★★	★★	★★★★★☆☆
Marques, 2018	★☆☆	★★	★★	★★★★★☆☆
Matijević, 2020	★★☆	☆☆	★★	★★★★☆☆☆
Mijnarends, 2016	★★☆	★★	★★	★★★★★☆☆
Montero-Errasquín, 2022	★☆☆	★★	★★	★★★★★☆☆
Mori, 2019	★☆☆	★★	★★	★★★★★☆☆
Öztürk, 2018	★☆☆	★☆	★★	★★★★☆☆☆
Patel,	★★☆	★☆	★★	★★★★★☆☆
SilvaNeto, 2016	★☆☆	★☆	★★	★★★★☆☆☆
Simsek, 2022	★★☆	★☆	★★	★★★★★☆☆
Singhal, 2019	★☆☆	★☆	★★	★★★★☆☆☆
Smith, 2022	★★☆	★★	★★	★★★★★★☆
Takahashi, 2018	★★☆	☆☆	★★	★★★★☆☆☆
Tsekoura, 2020	★☆☆	★☆	★★	★★★★☆☆☆
Umegaki, 2022[a]	★☆☆	★☆	★★	★★★★☆☆☆
Veronese, 2022	★★☆	★★	★★	★★★★★★☆
Woo, 2018	★★☆	★☆	★☆	★★★★☆☆☆
Yalcin, 2017	★★☆	★★	★★	★★★★★★☆
Yoo, 2020	★☆☆	☆☆	★★	★★★☆☆☆☆

*Total score is on 7 points for cross-sectional studies (adapted NOS scale for cross-sectional studies)
[a]Umegaki et al.[63] is a longitudinal study. However, for the present paper, only baseline values of the sarcopenic and non-sarcopenic groups were used in analyses. This study was therefore used as a cross-sectional one. As a matter of consistence between studies, we decided to apply the same NOS scale than the other cross-sectional studies.

−1.08) compared with those living in the community (n = 41, SMD of −0.73, 95% CI −0.93; −0.54).

No other differences were found in subgroups defined by diagnostic techniques, age, and continents or regions.

Results of meta-regressions performed on age and RoB are shown in Table 5. No significant effect of age and RoB of individual studies on the association between HRQoL and sarcopenia was observed.

Using GRADE assessment, the meta-analysis which included 43 observational studies with 30 322 participants, was rated as moderate level of evidence. No serious risk of bias, no serious indirectness and no serious imprecision were observed for the association. We did not downgrade the publication bias item because, even if publication bias appears to be significant, the Trim and Fill method showed that the impact on this publication bias on the results is moderate. The level of evidence was downgraded only because inconsistency of results (unexplained heterogeneity $I^2 > 50\%$) was observed.

Discussion

The aim of this study was to qualitatively and quantitatively summarize all data on the relationship between sarcopenia and HRQoL in order to provide a clear assessment of the impact of sarcopenia on this health parameter. Understanding

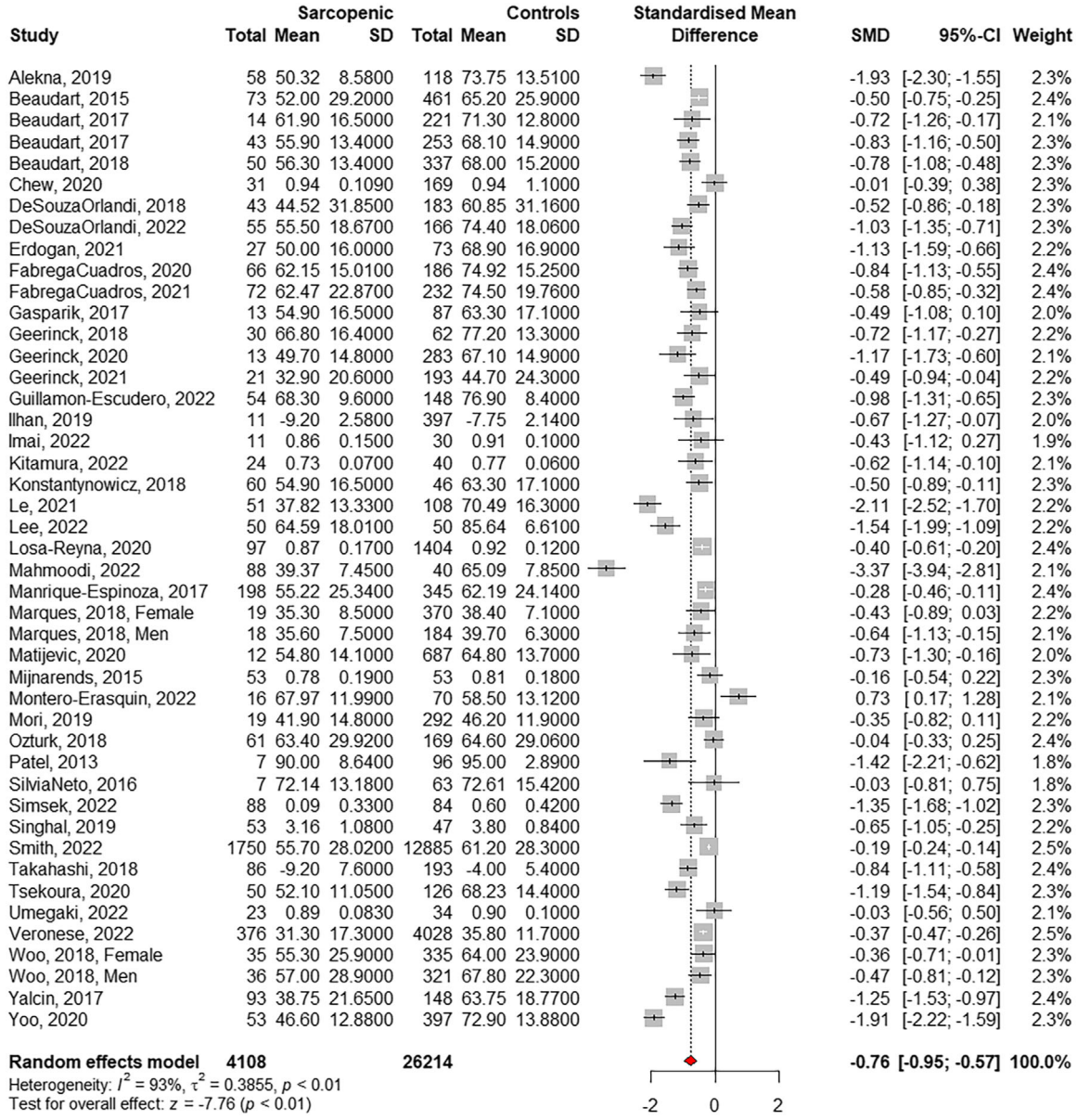

Figure 2 Quality of life in sarcopenia – Forest plot including 43 observational studies published until October 2022. CI, confidence interval; SD, standard deviation; SMD, standardized mean difference.

the impact of sarcopenia on HRQoL is important for healthcare providers and regulators and may guide the development of care strategies for sarcopenic patients.

Forty-three observational studies evaluating the association between sarcopenia and HRQoL were identified in the literature. The results showed a significant decrease in HRQoL in sarcopenic compared with non-sarcopenic elderly. It is not surprising to observe a reduced HRQoL in sarcopenic patients as sarcopenia has already been shown to be responsible for many adverse health outcomes such as mobility decline, disability, falls, fractures, hospitalization and death.[3,69–71]

Regarding the magnitude of the effect size, an even larger SMD was found when the analyses focused on the studies using a specific HRQoL questionnaire compared with a generic one. These results suggest that a specific HRQoL may better discriminate sarcopenic participants in terms of their HRQoL and thus may be more appropriate to accurately assess the impact of sarcopenia on HRQoL. Of the 20 studies that used a specific HRQoL questionnaire, all used the SarQoL. This is not surprising because the SarQoL is currently the only validated specific HRQoL questionnaire for sarcopenia. This questionnaire is available in more than 35 languages and has already been validated in multiple populations. In the SarQoL questionnaire, as in all disease-specific questionnaires, the vast majority of items are directly related to the disease. In the case of sarcopenia, the items included in

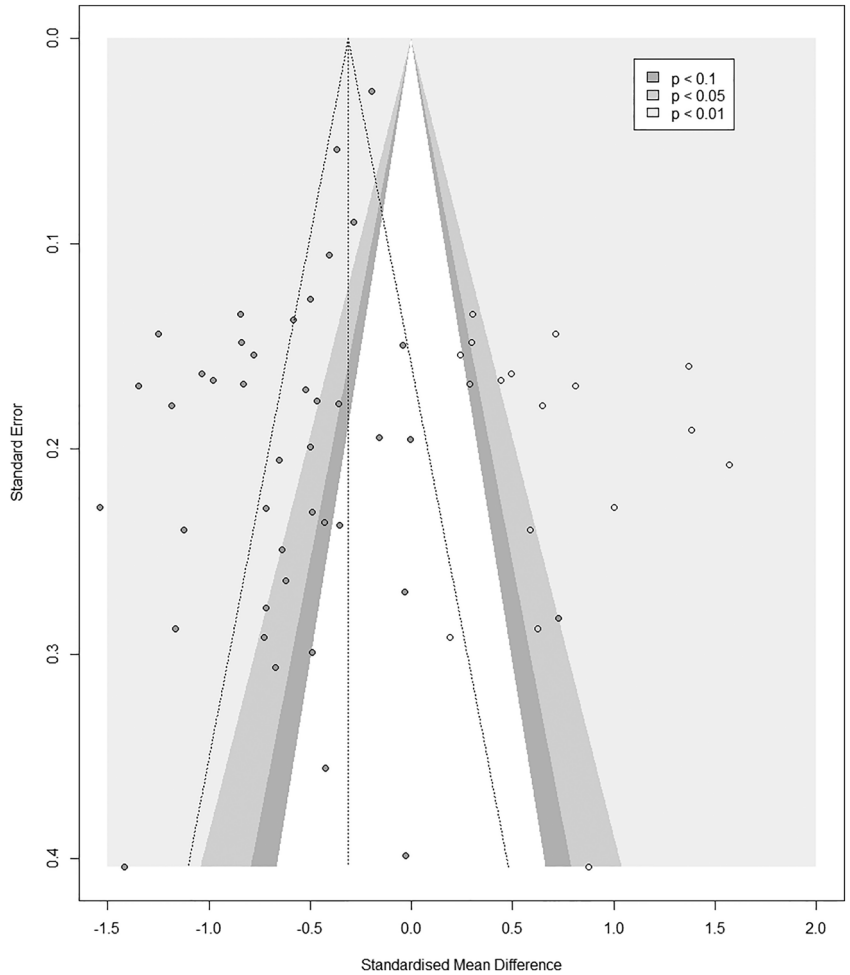

Figure 3 Contour Enhanced funnel plot for cross-sectional studies on sarcopenia and quality of life – Trim and Fill method (the 18 imputed studies are represented by circles that have no filled colour).

SarQoL are therefore muscle oriented.[16] The use of such a questionnaire may more accurately reflect the added value of a targeted intervention for sarcopenia, as all items may be affected. Generic tools may therefore not be able to detect subtle effects of a specific condition on HRQoL, in contrast to specific instruments. In regards to this, a recent publication on the SarQoL questionnaire revealed that this questionnaire has a higher responsiveness than common generic tools such as the SF-36 or the EQ 5D.[72] Therefore, the use of this specific questionnaire in clinical trials evaluating treatments for the management of sarcopenia should be recommended, as patient-related outcomes are encouraged to be included as co-primary endpoints in such trials.[73]

The results also revealed a larger difference of HRQoL between sarcopenic and non-saropenic for individuals living in care facilities compared with those living in the community. While these results may indicate that individuals in institutions may have a more severe status of sarcopenia and therefore a greater impact on HRQoL, they should nevertheless be taken with caution as only two studies (n = 413) reported results on individuals in care facilities compared with 41 studies (n = 29 909) reporting results on community-dwelling individuals.

The results did not highlight any difference in regards of the strength of association between sarcopenia and HRQoL for different age groups, for different sarcopenia diagnoses, or for different regions/countries/continents. Regarding the ethnicity of participants, although the difference between groups was not significant, we still observed nevertheless a larger SMD for studies conducted in Asia or using the AWGS criteria for sarcopenia diagnoss. However, this association may be biased by the results of some outliers, such as Mahmoodi et al.,[28] Lee et al.,[66] Le et al.[54] and Yoo et al.[60] who reported larger SMD compared with other studies. Sensitivity analyses revealed that these individual studies did not impact the global estimated effect size. Unfortunately, the association between gender of sarcopenic participants and HRQoL could not be measured in the present analyses. In

Table 4 Subgroup analyses

	No. studies	No. patients	SMD (95% CI)	I^2	*P* for heterogeneity	*P* for interaction
HRQoL scale (n = 44)[a]						<0.01
Generic	24	26 143	−0.49 (−0.63; −0.36)	83%	<0.01	
Specific[b]	20	4475	−1.09 (−1.44; −0.74)	91%	<0.01	
Age of participants (n = 42)[c]						0.48
<75 years	27	25 463	−0.78 (−1.02; −0.53)	93%	<0.01	
>75 years	15	4268	−0.76 (−1.11; −0.40)	92%	<0.01	
Sarcopenia diagnosis (n = 45)[d]						0.16
EWGSOP2	15	23 826	−0.86 (−1.16; −0.57)	95%	<0.01	
EWGSOP1	19	5257	−0.54 (−0.72; −0.36)	79%	<0.01	
AWGS	9	1239	−1.11 (−1.79; −0.42)	94%	<0.01	
FNIH	2	473	−0.73 (−1.65; 0.19)	88%	<0.01	
EWGSOP diagnosis vs. others (n = 45)						0.15
EWGSOP	34	29 083	−0.68 (−0.85; −0.51)	92%	<0.01	
Others	11	1712	−1.03 (−1.61; −0.46)	93%	<0.01	
Settings (n = 43)						<0.01
Community dwelling	41	29 909	−0.73 (−0.93; −0.54)	93%	<0.01	
Care homes	2	413	−1.29 (−1.51; −1.08)	0%	0.66	
Continent (n = 42)[e]						0.08
Europe	20	10 269	−0.70 (−0.91; −0.48)	85%	<0.01	
America	5	1651	−0.53 (−0.79; −0.26)	72%	<0.01	
Asia	16	3040	−1.02 (−1.46; −0.58)	94%	<0.01	
Australia	1	727	−0.41 (−0.66; −0.17)	NA	NA	
Europe region (n = 20)						0.26
Northern Europa	11	2545	−0.81 (−1.11; −0.52)	83%	<0.01	
Southern Europa	9	7724	−0.56 (−0.89; −0.23	85%	<0.01	

[a]For the general Forest Plot, when a study presented results for multiple HRQoL scale, the specific scale was used for analyses. One out of the 43 included studies presented results for both generic and specific scale. Therefore, it was possible to add an additional study in the subgroup of generic scale (n = 44).
[b]Because all the 20 studies assessing HRQoL using a specific HRQoL questionnaire used the same HRQoL questionnaire (i.e., the SarQoL), a post-hoc sensitivity analysis was performed changing the SMD estimate with a MD estimate. A MD of −15.01 (95% CI −19.00; −11.01), I^2 92%, $P < 0.01$ between sarcopenic and non-sarcopenic participants was found.
[c]Age was missing in one study, therefore subgroup on age of participants included only 42 out of the 43 observational studies (n = 42).
[d]For the general Forest Plot, when a study presented results for multiple definition of sarcopenia, the EWGSOP2 definition was used for analyses. Two out of the 43 included studies presented results for different diagnosis criteria. Therefore, it was possible to add a subgroup of FNIH definition (n = 45). Given the data obtained we also developed a subgroup analysis to compare EWGSOP definitions (version 1 or 2 combined) versus others (n = 45).
[e]The study of Smith et al. was removed from the analyses per continent (n = 42) as this study is composed with participants from different countries and different continents. Authors did not provide separate analyses per country.
AWGS, Asian Working Group on Sarcopenia; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project; HRQoL, health-related quality of life; SMD, standardized mean difference.

Table 5 Meta-regressions model between HRQoL and sarcopenia and age and risk of bias in univariate analysis

Covariates	Level	β-coefficient	Std.err. (β)	Z	*P*-value
Mean age	Years	−0.0475	0.0286	−1.6603	0.097
Risk of bias	Points	0.1826	0.1147	1.5925	0.111

fact, most of the individual studies were composed of a sample of men and women together (women/men ratio ranging from 28% to 87.7% of women), and separate analyses for gender were not performed.

Strength and limitations

This is the very first time that a meta-analysis has been performed to measure the association between sarcopenia and HRQoL. We were able to include a large amount of evidence in this systematic review and all of the available studies were also included in the meta-analysis, which also ensures the exhaustivity of the statistical synthesis. Of course, our study also contains some methodological limitations. First, it is important to highlight an important heterogeneity observed in the forest plot, which downgrades the certainty of evidence (GRADE of evidence is 'Moderate'). We investigated this heterogeneity by performing additional subgroup analyses and meta-regressions, but were unable to explain the remaining heterogeneity. Because sarcopenia is a multifactorial disease that may be associated with various comorbidities, studies performed on sarcopenia are always complex to interpret. Moreover, even if we tried to standardize the diagnostic criteria, the device used to measure the biomarkers of sarcopenia and the cut-offs used for the diagnosis may have introduced an important heterogeneity in the condition of interest, as previously reported.[74,75]

Therefore, the characteristics of sarcopenic participants may vary from one study to another, which could have led to some variations in the results of HRQoL. It is important to raise that all but one study (97.7%) agreed on the fact that HRQoL was reduced in sarcopenic participants compared with non-sarcopenic. There was no inconsistency in the direction of the estimates but only in their magnitude. Second, only cross-sectional data were included, which does not allow to investigate the causal relationship between sarcopenic and HRQoL. The present systematic review allowed the inclusion of both cross-sectional studies and prospective studies as long as these studies included two groups that could be compared in terms of their HRQoL. Surprisingly, only one prospective study was identified, which means that data on the evolution of HRQoL in sarcopenic individuals are almost inexistant. Prospective studies, who would allow to investigate deeply the causal relationship between sarcopenia and HRQoL, are therefore needed. Finally, as a last limitation, we regret not being able to run sex-specific analyses. Indeed, given the different body composition profile between men and women, it would have been relevant to provide analyses of the impact of sarcopenia on HRQoL stratified by sex. However, published evidence with sex-stratified analyses was so limited that it was simply not possible to perform subgroup analyses in our meta-analysis. Authors of further studies are encouraged to provide separate analyses by gender.

Conclusion

This systematic review and meta-analysis of observational studies highlighted a large decrease in HRQoL in sarcopenic compared with non-sarcopenic older adults. The results also revealed that using disease-specific HRQoL instruments may better discriminate sarcopenic patients with regard to their quality of life. Although a large amount of evidence was included in the meta-analytic model, the final association was rated as 'moderate level of evidence' according to the GRADE assessment because important unexplained heterogeneity was observed in the results. As poor quality of life in older people has been shown to be associated with several negative health outcomes such as falls, hospitalizations and mortality, these findings allowed us to suggest that diagnosis of sarcopenia in community-dwelling and institutionalized older people should be considered as a priority in clinical practice. The earlier sarcopenia is detected, the earlier programs for the prevention and treatment of this condition can be initiated to prevent the important impact that sarcopenia can have on HRQoL.

Conflict of interest

C.B., O.B. and J.-Y.R. are shareholder of SARQOL SRL, a spin-off of the University of Liege. The other co-authors have no conflicts of interest to declare. This is a systematic review. No ethical approval, consent to participate or consent to publish is required.[76]

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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