Original Article

Start with muscle mass or muscle strength in diagnosis and management of sarcopenia? A systematic review of guidance documents

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Background and Objectives: Sarcopenia has garnered extensive attention in clinical practice since its high prevalence and significant impact on clinical outcomes. Multiple organizations have published guidance documents on sarcopenia, offering evidence-based recommendations for clinical practice and/or research. We aimed to appraise the methodological quality of the included documents and synthesize available recommendations for the screening, diagnosis, and intervention of sarcopenia. **Methods and Study Design:** We conducted a search on PubMed, Embase, Scopus, Cochrane Library, China National Knowledge Infrastructure, guideline database, and guideline organizations and professional societies websites for clinical practices, consensus statements and position papers in terms of sarcopenia, muscle atrophy or muscle loss published before April 17, 2023. The AGREE II instrument was used by three independent reviewers to assess the methodological quality of these documents. **Results:** Thirty-six guidance documents published between 2010 and 2023 were included. Seven documents fulfilled ≥ 50% of all the AGREE II domains. Seven underwent a Delphi process and six graded the strength of the recommendations. The process of screening (n=21), early diagnosis of sarcopenia (n=12), diagnosis of sarcopenia and severe sarcopenia (n=10), and management (n=21) were increasingly recommended. SARC-F (n=14) was the most recommended screening tool, and the assessment of muscle function was considered the first step in diagnosing sarcopenia. The management strategy for both age-related and disease-related sarcopenia mainly focused on exercise and nutrition intervention. **Conclusions:** The guidance documents have provided referential recommendations that have great guiding significance. But the inconsistency in recommendations and variation in methodological rigour suggests that high-quality evidence is lacking yet.

Key Words: sarcopenia, diagnosis, management, guidance, systematic review

INTRODUCTION

Sarcopenia was recognized as a disease entity with an ICD-10-CM (M62.84) code in 2016,[1] significant strides have been made in this field over these years. It is recognized that sarcopenia is a progressive and generalized skeletal muscle disorder characterized by loss of muscle strength, muscle mass and /or low physical performance.[2,3] Sarcopenia caused by aging itself rather than other causes can be considered primary or age-related, while specific medical conditions such as malnutrition, lack of physical activity, chronic obstructive pulmonary disease, diabetes, and neuro-degenerative can be the cause of secondary or disease-related sarcopenia.[4,5,6] A systematic review and meta-analysis including 151 studies from all over the world estimated that the prevalence of sarcopenia ranged from 10% to 27% using different diagnostic criteria including Consensus of Asian Working Group for Sarcopenia in 2014 (AWGS), Consensus of International Working Group on Sarcopenia (IWGS), consensus of Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project (FNIH), and muscle mass with different cut-off points.[7] Both age-related and disease-related sarcopenia are strongly associated with short-term and long-term clinically relevant adverse outcomes including poor quality of life,[8] higher cardiovascular disease risk,[9] falls and fractures,[10] and higher mortality.[11] Sarcopenia foists a significant but changeable economic burden on individuals and governments. Although data on sarcopenia-related costs worldwide are absent, a study reported that the total cost of hospitalization for sarcopenia patients was 40.4 billion dollars in the United States from 1999 to 2004, which was estimated using the Healthcare Cost and Utilization Project-National Inpatient Sample (HCUP-NIS, 2014) dataset and cost-to-charge ratios provided by Agency for Healthcare Research and Quality.[12]

To date, sarcopenia is not recognized sufficiently as a

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preventable and treatable disease across healthcare settings by clinicians, although it has come of age to a certain extent with an ICD-10-CM code, relatively complete case finding tools, diagnostic approach, and effective treatment. Studies indicated that assessment of sarcopenia remains inadequate by dietitians and other professionals, which may be owing to a lack of education and training, inadequate resources and support for healthcare professionals, insufficient patient awareness and medical behavior, and most importantly, the absence of a unified diagnostic and management approach and may result in the vicious cycle of muscle disorder and inflammation, deteriorated function, and decreased quality of life.[13,14] Hence, high quality guidance documents that meet several standards such as the rigorous process of systematic review, a multidisciplinary development group, and a formal development process are needed to be developed and applied.[15]

In recent years, there have been plenty of guidance documents published among countries and regions targeting different populations and issues on sarcopenia. However, inconsistencies still exist between the documents due to differences in the evidence referenced, the different professional groups, and the chosen main indicator of diagnosis. The focus and strategy of diagnosis and treatment may vary across different documents. For instance, some documents prioritize the assessment of muscle mass, while others focus on muscle function, additionally, there are differences in assessment tools and cut-off values. Regarding the management strategy, some documents recommended that exercise needs to be combined with nutrition,[16,17,18] while others considered it unnecessary.[19] Although the unanimous view is that protein supplementation is required, the dosage of supplementation is different. And there is no unified formulation scheme for exercise intervention. These inconsistencies in diagnosis and management may lead to increased confusion in clinical practice.

Thus, the purpose of our study is to collect and summarize guidance documents on sarcopenia to appraise their quality, as well as to synthesize their content and consistency. This work may promote the application of sarcopenia diagnosis and management, as well as call for more related research in the future.

METHODS

Inclusion and exclusion criteria

We included the documents that meet the following criteria: 1) guidance documents of sarcopenia, 2) guidance documents with specific recommendations for screening, diagnosis, and management of sarcopenia. For the discard of articles, the following criteria were considered: 1) articles are not guidance documents, 2) documents are not designed for or relevant to screening, diagnosis, and management of sarcopenia, 3) documents do not contain pragmatical recommendations that are specific and can guide the clinical practice, 4) articles are unpublished draft, abstracts, protocols, editorial comments or personal opinions, 5) documents are not developed by sarcopenia related professional associations, institutes, societies, or communities.

Search methods

We gathered literature from the inception date to April 17, 2023 by conducting a systematic search in PubMed, Embase, Scopus, Cochrane Library, and China National Knowledge Infrastructure without language restriction. We primarily utilize translation software to comprehend the overall content of articles in languages other than English and Chinese, and engage in discussions with individuals who have expertise in the respective languages. The selection of search terms is initially derived from the mesh vocabulary, subsequently, we have compiled the key phrases from a variety of guiding document titles, and lastly, we have consulted other pertinent literature. Search terms consist of “sarcopenia”, “muscle atrophy”, “muscle loss”, “screen”, “diagnose”, “intervention”, “treatment” “guideline”, “consensus”, “position statement”, “recommendation”, “statement”, and “working group”. We also searched guideline databases, and guideline organizations and professional societies websites using the term “sarcopenia”, relevant reviews and all references were screened as well. The full search strategies along with guideline databases are listed in Supplemental Table 1.

Two reviewers (ZY and GJY) independently screened titles, abstracts, and full texts of all searched documents and decided on documents to be included based on inclusion and exclusion criteria, and inconsistencies were discussed with the third reviewer (W.F.). All searched articles were imported into and screened in EndNote (Version X9.1) reference manager software.

Data extraction

Reviewer ZY extracted data from documents including basic characteristics (e.g., development group, year, country/region, development process), scope and purpose (e.g., target population, target user, target condition), and recommendation statements for definition, diagnosis, assessment, and management of sarcopenia. The data extracted were checked by reviewer GJY, and any discrepancies were addressed through consultation.

Appraisal of the quality of documents

Three reviewers (ZY, GJY, and WF) independently assessed the quality of eligible guidance documents using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument,[20] which consists of 23 items rated on a seven-point scale from strongly disagree to strongly agree and was divided into 6 domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence. All three reviewers had an AGREE II training and discussion on the scoring criteria before appraising based on the User’s Manual (www.cmaj.ca/cgi/content/full/cmaj.090449/DC1).

The domain scores were calculated using the formula provided by the AGREE II User’s Manual and the median and interquartile range (IQR) were calculated for each domain. The analysis process was done in SPSS 26.0 software.

RESULTS

Search results and the characteristics of guidance documents

The report of the systematic review was formed using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We retrieved 6933 articles through database searching and a further 12 through hand-searching. We screened titles and abstracts of 3982 articles after de-duplication and full-texts of 59 articles after the former screening. Ultimately, we identified 36 documents (Figure 1).

Table 1 shows the general characteristics of the included guidance documents. Thirty were documents relating to diagnosis, including 23 documents [2,3,4,16,17,18,19,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36] focused on age-related sarcopenia and 7 on disease-related sarcopenia.[37,38,39,40,41,42,43] Management was addressed in 21 documents [16,17,18,19,27,28,29,31,32,33,38,40,41,42,43,44,45,46,47,48,49] with 5 documents centered on disease-related sarcopenia.[38,40,41,42,43] The documents were published between 2010 and 2023 by 7 international groups and 29 national regional working groups or organizations from Europe, Asia, Oceania, and America covering patients of middle and high-income countries.

Only 6 documents[26,28,32,37,50,51] clearly reported a systematic literature review as part of the development process. Moreover, there were only 4 documents[16,24,32,39] that gathered views and preferences from patients. Seven documents reported that consensus was achieved via Delphi or modified Delphi process.[16,17,25,31,32,34,49] Only 6 documents[16,31,32,43,45,48] rated the evidence and/or strength of the recommendations, and only 4 of them provided rating criteria.[16,31,32,48]

Appraisal of guidance documents

Figure 2 shows the AGREE II domain scores for each document (details are presented in Supplemental Table 2). The quality of documents assessed by the AGREE II tool was mixed, and the scores varied vastly among documents as well as domains. Based on a systematic review, a cut-off value of 50% was frequently applied to differentiate between high- and low-quality guidelines.[52] In this study, only 4 documents attained scores ≥50% for all of the domains, and 20 documents attained scores of ≥50% for rigour of development which is considered the most important domain.[52] The domain with the highest score was clarity of presentation, with a median score of 80% (IQR 17%). The domain with the lowest score was applicability, with a median score of 40% (IQR 30%). The lower score of stakeholder involvement was mainly attributed to the absence of views and preferences from the target population. In the majority of the included documents, the search strategy of the literature used was often unclear, as were the inclusion and exclusion criteria, the evidence evaluation, the development process, and the updating procedure, consequently, the scores in rigour of development were inferior. Subsequently, the facilitators and barriers to application, advice and/or tools on rec-

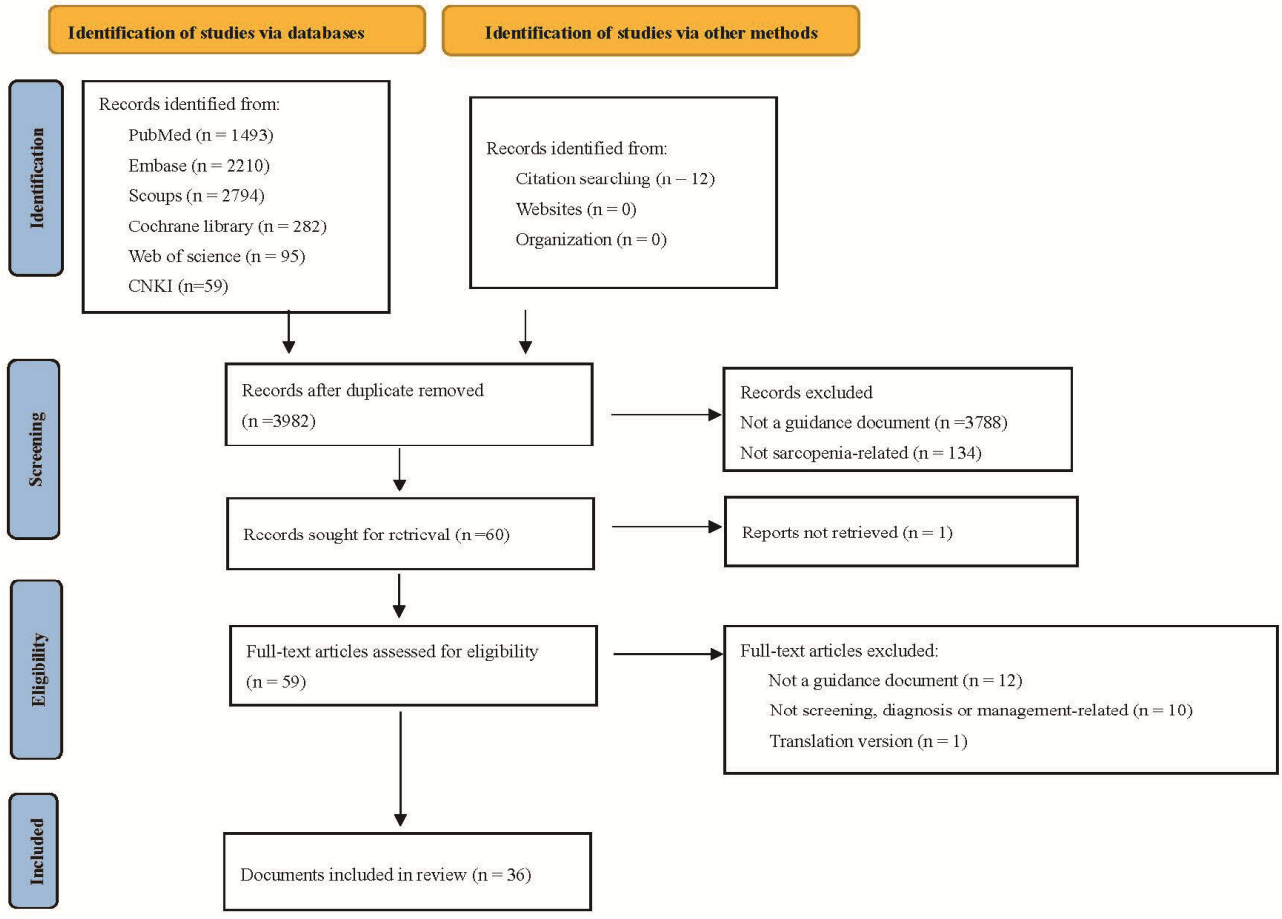

Figure 1. Flow diagram of the identification process for guidance document

Table 1. Characteristics of 36 available sarcopenia guidance documents

First author, Year	Country / Region	Developer	Target Population	Target Users	Delphi	Evidence Base	Evidence level	Recommendation level	Screening
Age-related									
Muscaritoli, 2010[36]	Europe	SIG	People with sarcopenia	Health professionals and care givers		NS			
Cruz-Jentoft, 2010[4]	Europe	EWGSOP	Older people with age-related sarcopenia	NS		Literature reviews			Gait speed
Morley, 2010[49]	International	SCWD	People with sarcopenia	NS	+	Systematic literature review			
Fielding, 2011[22]	International	IWGS	People with sarcopenia	NS		NS			Gait speed
Studenski, 2014[23]	America	FNIH	Older adults	NS		Selected studies			Grip strength
Chen, 2014[21]	Asia	AWGS	Community-dwelling older people with sarcopenia	NS		Best available evidence			Gait speed, grip strength
Iolascon, 2014[27]	Italy	OrtoMed	Older people with sarcopenia	NS		NS			
Shi, 2015[47]	China	Chinese Society of Nutritional Oncology	Older people with sarcopenia	NS		NS			
Sun, 2015[48]	China	The Elderly Nutrition Branch of the Chinese Nutrition Society, the Clinical Nutrition Branch of the Chinese Nutrition Society, Elderly Nutrition Support Group, Parenteral and Enteral Nutrition Branch, Chinese Medical Association	People with sarcopenia	Health professionals and ordinary residents		Best available evidence		+	
Liao, 2016[29]	China	Sarcopenia Consensus Editing Group	Older people with sarcopenia	NS		NS			Gait speed
Beaudart, 2016[19]	Europe	ESCEO	People with sarcopenia	NS		Literature reviews			SARC-F, SMI method, Red Flag method, different prediction equations

SIG: Special Interest Groups, EWGSOP: European Working Group on Sarcopenia in Older People, SCWD: Society of Sarcopenia, Cachexia and Wasting Disorders, IWGS: International Working Group on Sarcopenia, FNIH: Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, AWGS: Asian Working Group for Sarcopenia, OrtoMed: The Italian Society of Orthopaedics and Medicine, ESCEO: Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, SMI: skeletal muscle index, ICFSR: International Conference on Sarcopenia and Frailty Research, ANZSSFR: Australian and New Zealand Society for Sarcopenia and Frailty Research, CC: Calf Circumference, SDOC: Sarcopenia Definition and Outcomes Consortium, SWAG-SARCO: South Asian Working Action Group on SARCOpenia, KWGS: Korean Working Group on Sarcopenia, JSH: Japan Society of Hepatology, COSA: Clinical Oncology Society of Australia, AASLD: American Association for the Study of Liver Diseases, NS: Not stated. CC: Calf Circumference.

Table 1. Characteristics of 36 available sarcopenia guidance documents (cont.)

First author, Year	Country / Region	Developer	Target Population	Target Users	Delphi	Evidence Base	Evidence level	Recommendation level	Screening
Age-related									
Cruz-Jentoft, 2018[3]	Europe	EWGSOP	Older people with sarcopenia	Scientific and clinical evidence		Literature searches			SARC-F
Akishita, 2018[26]	Japan	Japanese Association on Sarcopenia and Frailty	People with sarcopenia (primary and secondary)	NS		Systematic review			Yubi-Wakka test
Dent, 2018[51]	International	ICFSR	Older adults with sarcopenia	Clinicians and allied health professionals	+	Systematic review	+	+	Gait speed, SARC-F
Zanker, 2019[25]	Australia and New Zealand	ANZSSFR	People with sarcopenia	Clinicians and researchers	+	Agreement			SARC-F
Landi, 2018[44]	International	ICFSR	People with sarcopenia	NS		NS			
Arai, 2018[50]	Japan	Japanese Association on Sarcopenia and Frailty	People with sarcopenia	NS		Systematic review	+	+	
Chen, 2019[2]	Asia	AWGS	Older people with sarcopenia	NS		Expert knowledge and research evidence			SARC-F, SARC-CalF, CC
Bauer, 2019[18]	International	SCWD	People with sarcopenia (primary and secondary)	NS		NS			SARC-F
Yang, 2019[46]	China	Geriatrics Branch Chinese Medical Association	Older people with sarcopenia	Medical staff engaged in geriatrics		Review			
Bhasin, 2020[24]	International	SDOC	People with sarcopenia	NS		Literature review and SDOC's analyses of 20 studies			
Chew, 2021[17]	Singapore	multidisciplinary working group	Older adults (muscle health)	Healthcare Professionals	+	In-depth literature review			SARC-F

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Table 1. Characteristics of 36 available sarcopenia guidance documents (cont.)

First author, Year	Country / Region	Developer	Target Population	Target Users	Delphi	Evidence Base	Evidence level	Recommendation level	Screening
Age-related									
Liu, 2021[28]	China	Editorial Committee of Chinese Journal of Geriatrics, Geriatrics Branch, Chinese Medical Association	Older people with sarcopenia	Geriatrician		NS			SARC-CalF
Dhar, 2022[30]	South Asia	SWAG-SARC	People with sarcopenia	NS		Latest available evidence			clinical suspicion +CC, SARC-F, SARC-CalF
Lim, 2022[31]	Singapore	Clinical Practice Guidelines workgroup convened by the Chapter of Geriatricians and the Society for Geriatric Medicine Singapore.	Community-dwelling older adult	Clinicians and allied health professionals	+	Literature review	+	+	SARC-F, SARC-CalF, CC
Daly, 2022[33]	Australia and New Zealand	ANZSSFR	Hospitalized Older Adults	Clinicians and healthcare professionals		Narrative review			
Huang, 2022[35]	China	Expert Consensus Committee on Osteoporosis and Osteoporosis under the China Health Promotion Foundation	People with sarcopenia-osteoporosis	Medical and scientific research institutions		NS			SARC-F, SARC-CalF, CC, Ishii
Zanker, 2023[32]	Australia and New Zealand	ANZSSFR	Adults aged ≥55 years and/or with medical comorbidities	Health professionals and researchers	+	Systematic review		+	SARC-F, Clinical suspicion
Baek, 2023[34]	Korea	KWGS	Korean community-dwelling older adults	NS	+	NS			SARC-F, CC, Finger ring test, CST, HGGS, GS, TUG

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Table 1. Characteristics of 36 available sarcopenia guidance documents (cont.)

First author, Year	Country / Region	Developer	Target Population	Target Users	Delphi	Evidence Base	Evidence level	Recommendation level	Screening
Disease-related									
Morley, 2011[37]	International	SCWD	Sarcopenia (older people) With Limited Mobility	NS		Consensus conference			
Nishikawa, 2016[39]	Japan	JSH	Liver disease patients with sarcopenia	NS		Review			
Carey, 2019[41]	North American	North American Working Group on Sarcopenia in Liver Transplantation	Patients with cirrhosis	NS		Medical literature			
Kiss, 2020[38]	Australia	COSA	Patients with cancer-related malnutrition and sarcopenia	Health professionals and health services		Literature review			SARC-F, SARC-F+CC
Lai, 2021[40]	America	AASLD	Cirrhosis Patients with Sarcopenia	Clinicians		Formal review and analysis of the literature			
Nagano, 2021[42]	Japan	Japanese Working Group of Respiratory Sarcopenia of the Japanese Association of Rehabilitation Nutrition	People with respiratory decline and sarcopenia	NS		Narrative review			
Shi, 2022[43]	China	Chinese Society of Nutritional Oncology	Cancer-related sarcopenia patients	Clinical medical staff		Systematic review and consensus	+	+	SARC-F, SARC-CalF, CC

SIG: Special Interest Groups, EWGSOP: European Working Group on Sarcopenia in Older People, SCWD: Society of Sarcopenia, Cachexia and Wasting Disorders, IWGS: International Working Group on Sarcopenia, FNIH: Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, AWGS: Asian Working Group for Sarcopenia, OrtoMed: The Italian Society of Orthopaedics and Medicine, ESCEO: Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, SMI: skeletal muscle index, ICFSR: International Conference on Sarcopenia and Frailty Research, ANZSSFR: Australian and New Zealand Society for Sarcopenia and Frailty Research, CC: Calf Circumference, SDOC: Sarcopenia Definition and Outcomes Consortium, SWAG-SARCO: South Asian Working Action Group on SARCOpenia, KWGS: Korean Working Group on Sarcopenia, JSH: Japan Society of Hepatology, COSA: Clinical Oncology Society of Australia, AASLD: American Association for the Study of Liver Diseases, NS: Not stated. CC: Calf Circumference.

ommendations practice, potential resource implications, and the monitoring and/or auditing criteria were all not presented well, making domain 5 a lower score.

Screening for sarcopenia

Screening to identify potential sarcopenia high-risk population is of great significance. Routine screening for sarcopenia in community-dwelling older adults was recommended by numerous documents. Furthermore, sarcopenia screening was also recommended in the following situations: 1) functional decline or impairment and decline in strength and "health" status which may indicate the loss of muscle mass and function, 2) unintentional body weight loss (>5% in a month) because muscle loss is an important component of weight loss, 3) depressive mood or cognitive impairment which is highly associated with sarcopenia, 4) repeated falls which has a close relationship with sarcopenia and mutually influences and promotes each other, 5) malnutrition which is an important cause of sarcopenia, 6) post-hospitalization which may lead to changes in lifestyle and prolonged bedrest and result in promote muscle loss, and 7) chronic conditions which is one of the etiologies of sarcopenia.[2,16,21] Only 3 documents clearly stated that the elderly should be screened for sarcopenia annually or after major health diseases. [16,17,32]

By now, several screening tools for sarcopenia have been developed (Table 1). SARC-F full life questionnaire is the most widely used tool and was recommended as a formal tool by 14 guidance documents[2,3,16,17,18,19,25,30,31,32,34,35,38,43] with a cut-off value ≥4. With a cut-off value ≥11, SARC-CalF was recommended by 7 documents.[2,28,30,31,35,38,43] "Yubi-Wakka" test recommended by the Japanese Association on Sarcopenia and Frailty (JASF) and Korean Working Group on Sarcopenia (KWGS) [26,34] was also alluded to in AWGS2019 as an effective alternative.[2] Ishii screening test was recommended by Chinese experts[35] and involved in the European Working Group on Sarcopenia in Older People in 2018 (EWGSOP2)[3] as an alternative screening test to be used in clinical practice. It was likewise mentioned by the other 2 documents but was not recommended given that the test contains the measure of muscle strength namely grip strength and lacks validation in independent cohorts, respectively.[18,19]

Before screening-specific tools were developed, gait speed, grip strength, and calf circumference (CC) were also commonly used for screening, and some are still recommended now.[2,34] In addition, suspicion of clinicians based on the clinical conditions could be considered as screening as well in health care or clinical research settings.[2,3,28,34]

It is noteworthy that a document regarding hospitalized patients suggested that there are currently no suitable screening tools for this population, and it is recommended to conduct an assessment directly.[33]

Diagnosis of sarcopenia

Age-related sarcopenia

Eighteen documents covered the diagnosis of age-related sarcopenia, and key issues addressed included the approach and threshold for diagnosis, severity determination, and measurement tools selection.

The diagnostic approach consists of 3 parameters muscle mass, muscle strength, and physical performance, and different combinations and sequences of these parameters were recommended by different documents (Table 2).

Table 3 shows the methods and corresponding cut-off values for muscle mass, muscle strength, and physical performance respectively. Muscle mass can be measured directly or indirectly by imaging methods or bioimpedance analysis and anthropometric measurements respectively. Computed tomography (CT) and magnetic resonance imaging (MRI) were recommended and even deemed to be gold standards for assessing muscle mass in 8 documents,[3,4,16,25,27,30,40,43] but were not recommended as routine measurements. Dual-energy X-ray absorptiometry (DXA) was recommended as the preferred alternative method for measuring muscle mass in 20 documents,[2,3,4,16,17,18,19,21,22,23,25,26,27,28,29,30,31,32,34,35] and even as the gold standard by a Chinese working group.[29] However, the Sarcopenia Definition and Outcomes Consortium (SDOC) did not consider DXA as the measurement method of lean mass[24]. Bioelectrical impedance analysis (BIA) was recommended as a portable alternative method to DXA in 16 documents.[2,3,4,17,19,21,23,25,26,27,28,29,30,32,34,35] CC was recommended by the Singapore multidisciplinary working group and Australian and New Zealand Society for Sarcopenia and Frailty Research Expert Working Group (ANZSSFR) as a surrogate in patients without edema, obesity and risk of sarcopenic obesity.[17,33] And it was explicitly deprecated by EWGSOP, but was mentioned that it could be used in the settings when no other method was available in EWGSOP2. Other anthropometric measures including mid-upper arm circumference, skin fold thickness, total or partial body potassium per fat-free soft tissue, and creatine dilution test were not recommended by any documents.

Muscle strength can be measured through grip strength measuring, knee flexion/extension strength measuring, and chair stand test. Grip strength was recommended predominantly by 20 documents followed by a 5-time chair stand test by 7 documents as a substitution. Knee flexion/extension could be utilized in research settings recommended by 3 documents.[4,28,30]

There are numerous methods to measure the level of physical performance including gait speed (4-m/6-m), the Short Physical Performance Battery (SPPB), Timed Up and Go test (TUG), 5-time chair stand test, 400 m walk test, and Stair Climb Power Test (SCPT). Most documents recommended (usual) gait speed of 4 meters or 6 meters as a measure of physical performance.[2,3,4,16,17,19,21,22,24,26,27,28,29,30,31,32,34,35,43] SPPB was recommended by 12 documents,[2,3,4,19,27,28,30,31,32,34,35,43] and was recommended as a standard measurement both for research and clinical practice by EWGSOP. TUG was recommended by 6 documents.[3,28,30,32,34,43] SCPT and 400 m walk test were recommended by EWGSOP in 2010 and 2018 respectively.

Organizations and working groups provided different cut-off values based on evidence. Only 5 documents published original diagnostic cut-off values for low muscle mass.[2,3,21,22,23] The cut-off values recommended to con-

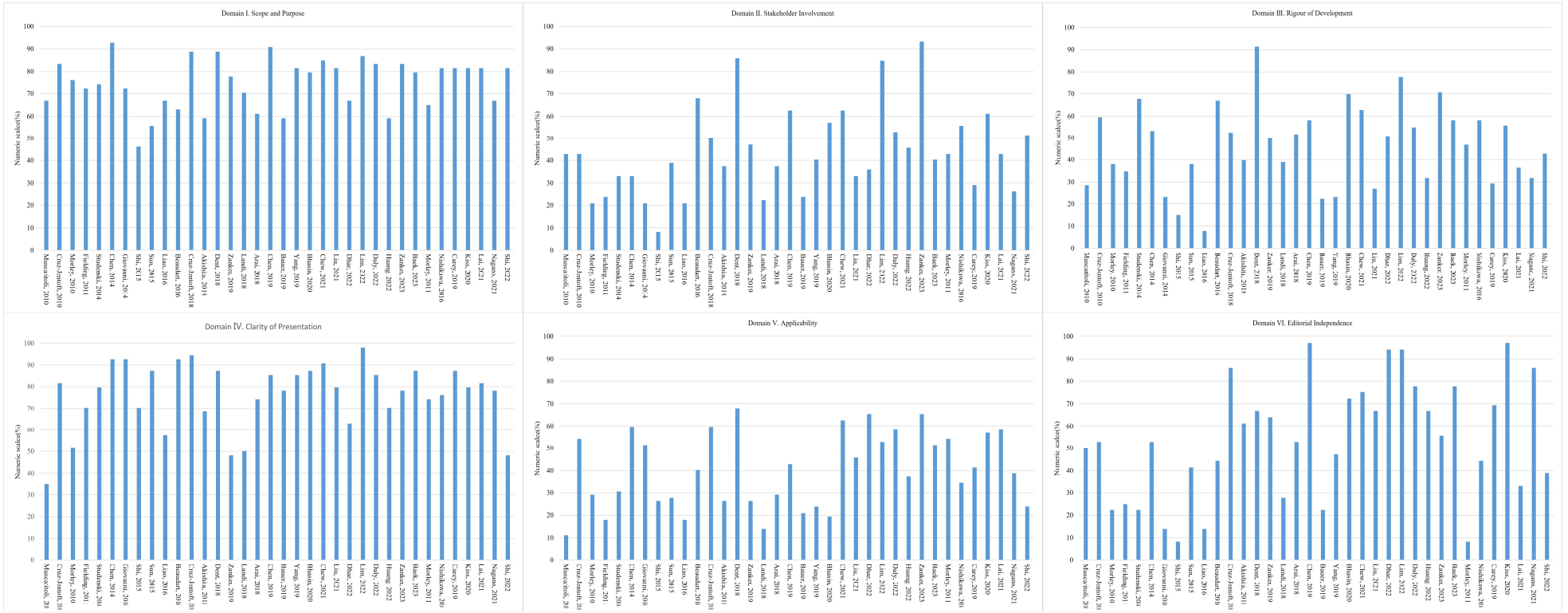

Figure 2. Guidance documents appraisal according to the Appraisal of Guideline for Research and Evaluation II (AGREE II) instrument

Table 2. Diagnosis approaches of sarcopenia

Documents	Sarcopenia	Prophase of sarcopenia	Severe sarcopenia
Age-related sarcopenia			
Cruz-Jentoft, 2010[4]	Low muscle mass + low muscle strength / Low physical performance	Presarcopenia: low muscle mass	Low muscle strength + Low muscle mass+ Low physical performance
Muscaritoli, 2010[36]	Low muscle mass + Low physical performance		
Fielding, 2011[22]	Low physical performance+ Low muscle mass		
Studenski, 2014[23]	Weakness\Low lean mass		
Chen, 2014[21]	Low muscle strength / Low physical performance+ Low muscle mass		
Iolascon, 2014[27]	Low muscle mass + Low muscle strength / Low physical performance		
Liao, 2016[29]	Low muscle strength / Low physical performance+ Low muscle mass		
Cruz-Jentoft, 2018[3]	Low muscle strength + Low muscle mass	Probable sarcopenia: low muscle strength	low muscle strength + low muscle mass+ Low physical performance
Akishita, 2018[26]	Low muscle strength / Low physical performance+ Low muscle mass		
Dent, 2018[16]	EWGSOP[4]/FNIH[23]/IWGS[22]/AWGS[21]		
Zanker, 2019[25]	EWGSOP[4]		
Chen, 2019[2]	Low muscle strength / Low physical performance+ Low muscle mass	Possible sarcopenia: low muscle strength / low physical performance	low muscle strength + low muscle mass+ Low physical performance
Bauer, 2019[18]	Low muscle strength + Low muscle mass		
Liu, 2021[28]	AWGS2019[2]		
Dhar, 2022[30]	Low muscle mass + Low muscle strength /Low muscle mass + Low physical performance/ Low muscle strength + Low physical performance		
Lim, 2022[31]	AWGS2019[2]		
Huang, 2022[35]	Low muscle mass + Low muscle strength / Low physical performance	Suspected sarcopenia: short CC/SARC-F≥4+low grip strength/low physical performance	low muscle strength + low muscle mass+ Low physical performance
Zanker, 2023[32]	EWGSOP[23]		
Baek, 2023[34]	Low muscle mass + Low muscle strength / Low physical performance	Functional sarcopenia: low muscle strength + low physical performance	low muscle strength + low muscle mass+ Low physical performance
Disease-related sarcopenia			
Morley, 2011[37]	Low muscle mass		
Nishikawa 2016[39]	Low muscle strength + Low muscle mass		
Carey, 2019[41]	Low muscle mass		
Kiss, 2020[38]	EWGSOP[4]/FNIH[23]/EWGSOP[23]		
Nagano, 2021[42]	EWGSOP[23]/AWGS2019[2]		
Lai, 2021[40]	Low muscle mass		
Shi, 2022[43]	Low muscle strength / Low physical performance+ Low muscle mass	Presarcopenia: low muscle strength	low muscle strength + low muscle mass+ Low physical performance

EWGSOP: Consensus of European Working Group on Sarcopenia in Older People in 2010, FNIH: Consensus of Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, IWGS: Consensus of International Working Group on Sarcopenia, AWGS: Consensus of Asian Working Group for Sarcopenia in 2014, AWGS2019: Consensus of Asian Working Group for Sarcopenia in 2019, CC: Calf Circumference, EWGSOP2: Consensus of European Working Group on Sarcopenia in Older People in 2018.

Table 3. Diagnostic methods and cut-off points values of sarcopenia

Documents	Muscle mass	Cut-off values	Muscle strength	Cut-off values	Physical performance	Cut-off values
Age-related sarcopenia						
Cruz-Jentoft, 2010[4]						
	CT		HGS		SPPB	
	MRI		Knee flexion/extension		Usual GS(6m)	
	DXA				TUG	
	BIA				SCPT	
Fielding, 2011[22]						
	DXA	M/F: 7.23/5.63 kg/m^2			GS(4m)	1m/s
Studenski, 2014[23]						
	DXA	M/F: 19.75/15.02 kg	HGSMAX	M/F: 26/16 kg		
	BIA	M/F(BMI): 0.789/0.512	HGS(BMI)	M/F: 1.0/0.56		
Chen, 2014[21]						
	DXA	M/F: 7.0/5.4 kg/m^2	HGS	M/F: 26/18 kg	GS(6m)	0.8m/s
	BIA	M/F:7.0/5.7 kg/m^3				
Iolascon, 2014[27]						
	CT	M/F: 7.23/5.67 kg/m^2	HGS		SPPB	
	MRI		Leg extension		TUG	
	DXA				GS	
	BIA					
Beaudart, 2016[19]						
	DXA	EWGSOP[4]/FNIH[23]	HGS		GS (4m)	0.8m/s
	Anthropometric measurements		Lower limb muscle strength		TUG	
	CT		CST		Balance test	
	MRI				6-min walk test	
	BIA				400 m walk test	
Liao, 2016[29]						
	DXA	2SD lower than the peak value of reference young healthy people	HGS	M/F: 25/18 kg	GS	0.8m/s
	MRI					
	CT					
	BIA					

HGS: Handgrip Strength, GS: Gait Speed, CC: Calf Circumference, M: male, F: Female, CST:5- time Chair Stands Test TBF: Total body fat, ALM: Arm lean mass, BW: Body weight, AWGS: consensus of Asian Working Group for Sarcopenia in 2014, EWGSOP: consensus of European Working Group on Sarcopenia in Older People in 2010, MAC: mid-arm circumference, USG-M, skeletal muscle ultrasound, MAMC: mid-arm muscular circumference, FNIH: consensus of Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, AWGS2019: consensus of Asian Working Group for Sarcopenia in 2019, EWGSOP2: consensus of European Working Group on Sarcopenia in Older People in 2018.

Table 3. Diagnostic methods and cut-off points values of sarcopenia (cont.)

Documents	Muscle mass	Cut-off values	Muscle strength	Cut-off values	Physical performance	Cut-off values
Age-related sarcopenia						
Cruz-Jentoft, 2018[3]						
	MRI	ASM: M/F:20/15 kg ASM/height2: M/F:7.0/5.5kg/m^2	HGS	M/F: 27/16 kg	GS (4m)	0.8m/s
	CT		CST	15s	SPPB	8point score
	DXA				TUG	20s
	BIA				400 m walk test	Non-completion/≥6 min
	CC	31cm				
Akishita, 2018[26]						
	AWGS[21]					
Dent, 2018[16]						
	DXA	Diagnosis of Sarcopenia according to International Working Groups	HGS	other documents	GS	other documents
	MRI					
	CT					
Zanker, 2019[25]						
	EWGSOP[4]					
Chen, 2019[2]						
	DXA	M/F: 7.0/5.4 kg/m^2	HGS	M/F: 28/18 kg	6-metre walk	1.0m/s
	BIA	M/F: 7.0/5.7 kg/m^2			CST	12s
Bauer, 2019[18]					SPPB	9
	DXA		HGS			
			CST			
Bhasin, 2020[24]						
			HGS	GS(max):M/F:35.5 /20.0kg GS(BMI):M/F: 1.05/0.79 GS(TBF): M /F: 1.66/0.65 GS (ALM):M/F: 6.1/3.26 GS(BW):M/F: 0.45/0.34	GS	
				M/F:28/18 kg	Usual GS	

HGS: Handgrip Strength, GS: Gait Speed, CC: Calf Circumference, M: male, F: Female, CST:5- time Chair Stands Test TBF: Total body fat, ALM: Arm lean mass, BW: Body weight, AWGS: consensus of Asian Working Group for Sarcopenia in 2014, EWGSOP: consensus of European Working Group on Sarcopenia in Older People in 2010, MAC: mid-arm circumference, USG-M, skeletal muscle ultrasound, MAMC: mid-arm muscular circumference, FNIH: consensus of Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, AWGS2019: consensus of Asian Working Group for Sarcopenia in 2019, EWGSOP2: consensus of European Working Group on Sarcopenia in Older People in 2018.

Table 3. Diagnostic methods and cut-off points values of sarcopenia (cont.)

Documents	Muscle mass	Cut-off values	Muscle strength	Cut-off values	Physical performance	Cut-off values
Age-related sarcopenia						
Chew, 2021[17]						
	BIA	M/F: 7.0/5.7 kg/m^2	HGS			1.0 m/s
	DXA	M/F: 7.0/5.4 kg/m^2	CST	10s	CST	12s
	CC	M/F: 34/33 cm				
Liu, 2021[28]						
	DXA	AWGS2019[2]	Knee flexion/extension	AWGS2019[2]	GS(6m)	AWGS2019[2]
	BIA	AWGS2019[2]	CST		SPPB	
					TUG	
					Long distance walking	
Dhar, 2022[30]						
	CC	M/F: 34/33 cm	HGS	M/F: 27.5/18 kg	GS(6m)	0.8/0.96 m/s
	MAC		Lower limb muscle strength	2.29 (0.5-10.0) /AWGS[21]	Sit-to-stand	AWGS[21]
	Thigh/Waist circumference				CST	
	BMI				SPPB	
	DXA	M/F: 7.0/5.7 kg/m^2/			TUG	10.2s
	BIA					
	CT					
	USG-M					
Lim, 2022[31]						
	DXA	AWGS2019[2]	HGS	AWGS2019[2]	CST	AWGS2019[2]
					Usual GS (6m)	
					SPPB	
Huang, 2022[35]						
	DXA	M/F: 7.0/5.4 kg/m	HGS	M/F:28/18 kg	GS(6m)	1.0m/s
	BIA:	M/F:7.0/5.7 kg/m2	CST	12s	SPPB	9
Daly, 2022[33]						
	CC (surrogate)	M/F: 34/33 cm				
Zanker, 2023[3]2						
	EWGSOP[23]					

HGS: Handgrip Strength, GS: Gait Speed, CC: Calf Circumference, M: male, F: Female, CST:5- time Chair Stands Test TBF: Total body fat, ALM: Arm lean mass, BW: Body weight, AWGS: consensus of Asian Working Group for Sarcopenia in 2014, EWGSOP: consensus of European Working Group on Sarcopenia in Older People in 2010, MAC: mid-arm circumference, USG-M, skeletal muscle ultrasound, MAMC: mid-arm muscular circumference, FNIH: consensus of Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, AWGS2019: consensus of Asian Working Group for Sarcopenia in 2019, EWGSOP2: consensus of European Working Group on Sarcopenia in Older People in 2018.

Table 3. Diagnostic methods and cut-off points values of sarcopenia (cont.)

Documents	Muscle mass	Cut-off values	Muscle strength	Cut-off values	Physical performance	Cut-off values
Age-related sarcopenia						
Baek, 2023[34]						
	DXA	M/F: 7.0/5.4 kg/m	HGS	M/F:28/18 kg	SPPB	9
	BIA	M/F:7.0/5.7 kg/m2			GS(4/6m)	1.0 m/s
					TUG	12s
					CST	10 s (standing position)
						11 s (sitting position)
					Chair stand (30-sec):	M/F: 17/15
					400-m walk test:	non-completion/ 6 min
Disease-related sarcopenia						
Morley, 2011[37]						
	DXA					
	MRI					
	CT					
	MAMC/Calf circumference					
	Ultrasound					
	13C-creatine dilution					
Nishikawa, 2016[39]						
	CT	M/F: 42/38 cm^2/m^2				
	BIA	M/F:7.0/5.7 kg/m^2				
Carey, 2019[41]						
	CT/MRI	SMI:M/F: 50/39 cm^2/m^2				
Kiss, 2020[38]						
	EWGSOP[4]/FNIH[22]/EWGSOP[23]					
Nagano, 2021[42]						
	EWGSOP[23]/AWGS2019[2]					
Lai, 2021[40]						
	CT		HGS		6-min walk test / GS(4m)	
Shi, 2022[43]						
	CT	M/F: 40.8/34.9 cm^2/m^2	HGS	M/F:27/16 kg	GS	8 m/s
	DXA	M/F: 7.0/5.4 kg/m^2	CST	15s	SPPB	8
	BIA	M/F: 7.0/5.7 kg/m^2			TUG	20s

HGS: Handgrip Strength, GS: Gait Speed, CC: Calf Circumference, M: male, F: Female, CST:5- time Chair Stands Test TBF: Total body fat, ALM: Arm lean mass, BW: Body weight, AWGS: consensus of Asian Working Group for Sarcopenia in 2014, EWGSOP: consensus of European Working Group on Sarcopenia in Older People in 2010, MAC: mid-arm circumference, USG-M, skeletal muscle ultrasound, MAMC: mid-arm muscular circumference, FNIH: consensus of Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project, AWGS2019: consensus of Asian Working Group for Sarcopenia in 2019, EWGSOP2: consensus of European Working Group on Sarcopenia in Older People in 2018.

firm low muscle mass ranged from 7.0 to 7.23kg/m^2 for men and 5.4 to 5.7 kg/m^2 for women or 19.75 to 20 kg for men and 15 to 15.02 kg for women measured by DXA or BIA based on different reference population. Only AWGS and AWGS 2019 provided different cut-off values for DXA and BIA.

Different cut-off values of grip strength have been offered to characterize low muscle strength, ranging from 16 to 20 kg for women and 26 to 35.5 kg for men. Two documents[23,24] proposed cut-off values adjusted by BMI and other factors. When using the 5-time chair stand test to measure muscle strength, the cut-off values suggested by EWGSOP2, Chinese experts, and the Singapore multidisciplinary working group were 15s, 12s, and 10s, respectively.

When gait speed is used to measure physical performance, the cut-off values were 0.8m/s recommended by 3 documents,[3,21,30] 1m/s recommended by 4 documents,[2,22,34,35] 0.96m/s by 1 document,[30] and 8 m/s recommended by 1 documents which was highly suspected to be a clerical error by the authors.[43] Documents gave thresholds of 8/9-point score, 20/10.2s, and non-completion/6 min for completion for SPPB, TUG, and 400 m walk test, respectively. About the chair stand test, the recommended threshold were 12s, 10s (standing position), 11s (sitting position), as well as 17 times for men and 15 times for women within 30 seconds.[2,34]

Disease-related sarcopenia

In terms of diagnosing or assessing sarcopenia in the presence of comorbidities, seven organizations and working groups developed guidance documents targeting 4 diseases namely sarcopenia with liver disease, sarcopenia with limited mobility, cancer-related sarcopenia, and respiratory sarcopenia.[37,38,39,40,41,42,43]

Three documents on sarcopenia with liver disease, two of which were respectively specific to cirrhosis and liver transplantation, recommended assessing sarcopenia via measuring muscle mass,[40,41] and the other recommended measuring both muscle strength and muscle mass.[39] In addition, the Japan Society of Hepatology (JSH)[39] and North American Working Group on Sarcopenia in Liver Transplantation[41] provided cut-off values of CT-measured total muscle mass at the third lumbar (L3) vertebra adjusted by height squared depending studies in Japan and North America respectively. The BIA technique was recommended by JSH as well with the cut-off values proposed by AWGS.

The documents concerning sarcopenia with limited mobility recommended that sarcopenia was defined as lean appendicular mass corrected for height squared below 2 SD of the mean value of healthy persons of the same ethnicity age 20 to 30, and muscle mass was recommended to be measured by DXA, CT, MRI, ultrasound but not BIA.

With regard to diagnosing cancer-related sarcopenia, the Clinical Oncology Society of Australia (COSA) recommended using the CT-measured SMI (skeletal muscle area/ height squared at L3) method or methods submitted by EWGSOP, FNIH, and EWGSOP2. CSNO suggested using the methods and tools for usual sarcopenia (age-related sarcopenia).

The Japanese Working Group of Respiratory Sarcopenia recommended using methods proposed by EWGSOP2 or AWGS2 to diagnose sarcopenia when diagnosing respiratory sarcopenia.

Management of sarcopenia

Table 4 shows the three ways recommended by documents to manage sarcopenia including nutrition, exercise, and pharmacotherapy. To start with, it would be essential to manage sarcopenia in a multidisciplinary team embracing multi-professional clinicians and healthcare providers which was highlighted in 2 documents already.[16,17]

To treat sarcopenia, the combination of nutrition and exercise was strongly or conditionally recommended by 14 documents.[16,17,18,27,28,29,31,32,33,43,45,47,48,49] In addition, the International Conference on Frailty and Sarcopenia Research Task Force44 concluded that nutrition needs to be combined with physical activity and pharmacotherapy to have a profound impact on improving muscle health. Only one document 19 recommended patient-centered management for sarcopenia involving physical activity (resistance and aerobic exercise) with or without nutrition intake.

While recommending active nutrition intervention, documents also emphasized optimizing the structure of nutrition intake, including adequate protein and energy intake. And more consumption of proteins rich in essential amino acids especially leucine was recommended in some documents.[29,45,47,48,49] Seven documents provided specific dose recommendations for protein supplementation, five of which were 1-1.5g/kg/day[18,47,49] with high-quality protein ≥50%[48], two was 1.2-1.5g/kg/day,[28,32] and at least 1.5g/kg/day if complicated by severe malnutrition.28 In addition, protein intake was recommended to be distributed throughout the day.[28,37,48]

Recommendations for vitamin D were inconsistent across documents. Three documents held that existing evidence was insufficient to support vitamin D intervention in sarcopenia patients.16,18,45 Nevertheless, seven documents recommended that vitamin D deficiency should be screened and treated in sarcopenia patients,[17,19,29,31,47,48,49] four of which[17,47,48,49] supported that the daily intake of vitamin D could be 600-800 IU.

One document provided recommendations on the application of oral nutritional supplementation (ONS) in elderly sarcopenia patients including the selection criteria of supplements, protein sources, intake methods, the timing of administration, intolerance treatment, and nutrition evaluation scenario in the implementation process.46 And 1 document recommended more supplementation of foods rich in n-3 polyunsaturated fatty acid and antioxidant nutrients.[48]

Eleven documents discussed specific types of exercise of which resistance exercise was the most recommended.[16,17,18,19,27,28,31,32,33,43,48,49] Six documents recommended resistance exercise combined with other types of exercise.[19,27,28,33,48,49] Detailed exercise modes were recommended in 4 documents.[27,47,48,49] Some drugs, such as testosterone, growth hormone, ghrelin agonist, and anti-myostatin antibodies were not recommended.[16,18,45]

Five documents gave recommendations on the management of disease-related sarcopenia.[38,40,41,42,43] Multi-

Table 4. Management of sarcopenia

First author Year	Strategy	Nutrition	Exercise	Pharmacotherapy
Morley, 2010[49]	Exercise + Nutrition	1. Total protein intake: 1 -1.5 g/kg/day 2. Add leucine-enriched balanced essential amino acid mix 3. Measure 25(OH) vitamin D concentrations, and supplement it when < 100 nmol/L	1. Resistance + aerobic exercise 20 to 30 minutes, 3 times a week	NA
Iolascon, 2014[27]	Exercise + Nutrition	NS	1. Aerobic Exercise: moderate intensity (≥30 min/day, ≥5 days/week)/ vigorous intensity (≥20 min/day, 3 days/week) 2. Both multiple- and single-joint exercises (free weights and machines), with slow-to-moderate lifting velocity, for 1-3 sets per exercise, with 60-80% of 1 RM, for 8-12 repetitions, with 1-3 min of rest among sets, for 2-3 days/week, 3. Both single-and multiple-joint exercises for 1-3 sets per exercise using light to moderate loading (30-60% of 1 RM) for 6-10 repetitions with high repetition velocity	NA
Shi, 2015[47]	Exercise + Nutrition	1. Total protein intake: 1 -1.5 g/kg/day 2. Add leucine-enriched balanced essential amino acid mix 3. Measure 25(OH) vitamin D concentration, and supplement it when < 100 nmol/L	1. Resistance + aerobic exercise 20 to 30 minutes, 3 times a week	NA
Sun, 2015[48]	Exercise + Nutrition	1.Protein: 1.0-1.5 g/(kg · d), the proportion of high-quality protein≥50%, distribute evenly among three meals 2. ADMR for EPA+DHA is 0.25-2.00 g/d 3. Measurement and treatment of vitamin D deficiency, the recommended dose is 600 ~ 800IU/d (Vitamin D2 or vitamin D3) 4. Encourage an increase in the intake of foods or dietary supplements rich in antioxidant nutrients 5. Supplementing nutritional supplements twice a day between meals or after exercise, consuming 15-20 g of protein rich in essential amino acids or leucine and around 200 kcal	1. Moderate to high intensity exercise for 40-60 min every day with resistance exercise lasting 20-30 minutes and ≥ 3 days per week	NA
Liao, 2016[29]	NS	1. Balanced diet, adequate nutrition, and supplement protein/EAA when necessary 2. Screening and treatment of vitamin D deficiency	NS	NS

NS: Not Stated, NA: Not applicable.

Table 4. Management of sarcopenia (cont.)

First author Year	Strategy	Nutrition	Exercise	Pharmacotherapy
Beaudart, 2016[19]	Exercise +/- Nutrition	2. Adequate energy and dietary protein intake. 1. Treatment and prevention of vitamin D deficiency	1. Resistance + Aerobic exercise	NA
Dent, 2018[16]	Exercise + Nutrition	1. adequate calorie 2. Protein supplementation/a protein-rich diet	1. Resistance based training	NA
Landi, 2018[44]	Nutrition+ Exercise + Pharmacotherapy	NS	NS	NS
Arai, 2018[45]	Exercise + Nutrition	1. Intake of essential amino acids	NS	NA
Bauer, 2019[18]	Exercise + Nutrition	1. Protein intake of 1.0 - 1.5 g/kg/day	1. Resistance exercise	NA
Yang, 2019[46]	Nutrition	Oral nutrition supplementation	NA	NA
Chew, 2021[17]	Exercise + Nutrition	1. Adequate energy and protein intake 2. Source: whole foods and/or high protein oral nutrition supplements 3. Meeting the recommended daily intake of vitamin D (600–800 IU)	1. Progressive resistance/weight-based exercise training	NA
Liu, 2021[28]	Exercise + Nutrition	1. Screen for nutritional risk, and give active nutritional intervention, especially adequate protein supplementation. 2. The sarcopenia patients having malnutrition or nutritional risk should be supplemented with Oral nutrition supplementation.	1. Resistance training combined with aerobic, stretching, and balance exercise	NA
Lim,2022[31]	Exercise + Nutrition	1. Advise on the importance of a quality diet with adequate caloric and protein intake. 2. Consider nutritional intervention with protein supplementation 3. Consider vitamin D supplementation for sarcopenic older adults with Vitamin D insufficiency (<30 mg/L)	1. Encourage to participate in resistance-based exercises	NA
Daly, 2022[33]	Exercise + Nutrition	1. Assess and monitor by a dietitian to determine the most appropriate nutritional support and correct any deficiencies. 2. Nutrition support interventions should be escalated in patients who do not meet nutritional goals during the first 3–5 days of admission. 3. Nutritional interventions delivered via whole food should aim to provide at least 30 kcal/kg energy and 1.2–1.5 g/kg protein per day	1. Multicomponent exercise programs(elements of resistance, challenging balance, and functional training mimicking ADLs) should be implemented as early as possible following hospital admission	NA

NS: Not Stated, NA: Not applicable.

Table 4. Management of sarcopenia (cont.)

First author Year	Strategy	Nutrition	Exercise	Pharmacotherapy
Zanker, 2023[32]	Exercise + Nutrition	1. Accredited healthcare professionals (or degreed, NZ) should provide an accessible explanation of sarcopenia. 2. Clinicians should consider referring persons with sarcopenia to a dietitian 3. Total protein intake: 1–1.5 g/kg/day, except for those with significant kidney disease	1. All persons with sarcopenia should be offered resistance-based training by an accredited healthcare professional, tailored to the individuals' abilities and preferences.	NA
Disease-related sarcopenia				
Carey, 2019[41]	Nutrition+ Exercise + Pharmacotherapy	1. Adiposity-tailored caloric intake 2. A daily protein intake of 1.2-1.5 g/kg 3. Late-evening snack	1. Aerobic and resistance training (ratio favoring the latter), 150-200 min/week	NS
Kiss, 2020[38]	Exercise + Nutrition	NS	NS	NA
Lai, 2021[40]	Nutrition+ Exercise + Pharmacotherapy	1. Calorie intake of at least 35 kcal/kg (non-obese) 2. Protein intake of 1.2 to 1.5 g/kg/d 3. Micronutrient repletion 4. Frequent, small meals and minimized fasting 5. Address barriers to intake 6. Onsult a registered dietitian	1. Aerobic, resistance, flexibility and balance 2. Aerobic 150 min per week (4-7 d/week)/ resistance≥1 day per week (2-3 d/week) 3. Intensity: Use the talk test (be short of breath but can still speak a full sentence),3 sets of 10-15 repetitions at a time 4. Consult a certified exercise physiologist or physical therapist	
Nagano, 2021[42]	Exercise + Nutrition	NS	1. Strength training of respiratory muscles 2. Strength training of the lower limb 3. Resistance training of the whole body 4. Combined aerobic and resistance training	NA
Shi, 2022[43]	Exercise + Nutrition+ Pharmacotherapy	1. Increase protein intake. 2. Supplement vitamin D, HMB, and ω-3 PUFA properly	Resistance training	Hormone drugs

NS: Not Stated, NA: Not applicable.

disciplinary teams were momentous likewise[38,40] and interventions combining nutrition and exercise (aerobic and resistance exercises) were also recommended.[38,40,41,42] However, early and timely intervention should be personalized. Documents proposed that a personalized nutrition formulation should be customized and regularly evaluated according to the patient's nutritional status. Two documents targeting sarcopenia with liver disease supported the determination of the patient's calorie needs by resting energy expenditure calculation, traditional prediction equation, or weight (weight for non-obese, BMI for obese).[40,41] The documents recommended that the protein intake could be 1.2-1.5g/kg ideal body weight per day and 1.2-2.0g/kg ideal body weight per day for critically ill patients.[40,41] Multiple protein sources were recommended, but BCAA supplementation was not.[40] The document on respiratory sarcopenia proposed a strategy of rehabilitation nutrition treatment, which integrated nutritional intervention, strength training of respiratory muscles and the lower limb, whole body endurance training, and aerobic training. And it is worthy of further research to verify its efficacy.[42] CSNO recommended increasing protein intake and supplementing properly vitamin D, β-hydroxy-β-methyl butyrate (HMB) and ω-3 polyunsaturated fatty acid (ω-3 PUFA).[43] Unlike the absence of drugs for age-related sarcopenia, two documents related to sarcopenia with liver disease indicated that testosterone could be used as a treatment for men who exhibit symptoms of hypogonadism or have low testosterone concentrations (total testosterone <12 nmol/L/free testosterone <230 pmol/L).[40,41] But relative contraindications including a history of hepatocellular carcinoma, other malignancy, or thrombosis cannot be neglected. Hormone drug was also recommended by CSNO.[35] The aforementioned recommendations offer direction for guidance for healthcare professionals to develop personalized nutrition management formulation. However, aside from consulting these sarcopenia-related guiding documents, it is imperative to also refer to other pertinent disease treatment and nutrition guidelines. Presently, the guidance documents for sarcopenia do not specify the timing for nutritional assessment, Nevertheless, in clinical practice, the timing for sarcopenia screening and regular nutritional screening for patients with various diseases can serve as a point of reference.

DISCUSSION

We evaluated 36 guidance documents regarding the screening, diagnosis, and treatment of sarcopenia using the AGREE II tool. These documents have great guiding significance in raising awareness of sarcopenia, popularizing diagnosis, standardizing treatment, and promoting related research progress. Nevertheless, we found that the quality of documents was generally heterogeneous. Most documents did not state that there was a systematic review of the available evidence, which is an important part of developing a guideline and can minimize bias.[53] Patients and clinicians may have distant perspectives on treatment effectiveness and risks, and their values and preferences are also different. Therefore, full and reasonable reference to patients' preferences may improve the direction and strength of recommendations.[54] Describing the facilitators and barriers to implementation can improve the utility of documents. Our findings suggested that higher rigour can be achieved by conducting high-quality systematic reviews, stakeholder involvement can be improved by incorporating patient input, and clinical applicability can be enhanced by offering tools or recommendations for application. All these factors could help make a guidance document more trustworthy and meet the needs of guidance document producers and other stakeholders.[55]

The scores of 6 domains are consistent with those of Carmelo Messina et al.[56] which appraised clinical practice guidelines concerning sarcopenia, except that the highest and second highest domains were reversal. However, the scores of each domain of documents are rather lower than those of Carmelo Messina et al. especially in stakeholder involvement and applicability. The reason why divergence exists may be that the included documents are different. We did not incorporate the guidance documents related to clinical trials and biomarkers, and the databases searched were different either. Additionally, different evaluation standards of appraisers may also lead to a discrepancy in scores.

The documents covered the definition, screening, diagnosis, and treatment of sarcopenia, with various recommendations on screening timing and tools, diagnostic approaches, measurement methods, as well as treatment prescriptions. The reasons for proposing different recommendations are multifactorial which may be explained partly by that 1) as the deep study of sarcopenia, the evidence available increased, 2) inadequate high-quality evidence increased the role of expert panel views on recommendations formulating or voting 3) documents was developed by organizations and working groups from different nations and regions via different development process.

The recommended screening tools tend to be rapid, simple, and convenient and can be reported by patients themselves. SARC-F has been validated and well-studied to screen sarcopenia and widely recommended and used.[57] However, documents also pointed out that the low sensitivity of SARC-F may hinder its application. So SARC-CalF, combining SARC-F with CC, was developed to improve the sensitivity of SARC-F.[58] Furthermore, CC and “Yubi-Wakka” test were recommended as one of the screening methods, which were more objective than SARC-F and SARC-CalF and equally simple and convenient. The reference population to obtain the cut-off values of these screening tools were from different populations. When applying the screening tools, the cut-off points provided may not be the optimum, despite good accuracy. Hence, cut-off values appropriate for the target population merit further exploration and verification by researchers.

In addition to the above recommended screening tools, numerous other tools have been developed to screen sarcopenia and are worthy of further research and validation, such as the PUMCHS index,[59] SARC-EBM,[60] and MARSH[61]. The PUMCHS index is a recently developed simple screening tool based on the Asia population that encompassed BMI, grip strength, CC, and age. It has been shown to possess high predictive accuracy and can be

utilized to evaluate sarcopenia in situations where BIA is not accessible (AUC: 0.905 for women, 0.920 for men. SARC-EBM combining EBM (Elderly and BMI) and SARC-F improved the sensitivity and overall diagnostic accuracy of the SARC-F.

At present, the recommended diagnostic approach for sarcopenia is separated into three levels, including early diagnosis of sarcopenia, diagnosis of sarcopenia, and diagnosis of severe sarcopenia. Only the diagnosis of severe sarcopenia has been agreed upon in various guidance documents. There are various methods or techniques for measuring diagnostic parameters of sarcopenia and each has its pros and cons. According to a position paper, the following factors should be considered when selecting measurement and screening tools: patient characteristics, psychometric characteristics of the tool, the availability of required techniques, the applicability in the clinical environment, prognostic reliability of relevant clinical results, and the strengths and limitations of the method.[62] Additionally, based on the AGREE II scores of the documents, the tools recommended by documents with higher quality should also be considered.

There are various methods or techniques for measuring diagnostic parameters of sarcopenia. Muscle mass measurement tools are diverse and have their own pros and cons. Although CT and MRI were generally regarded as a gold standard with excellent accuracy and reproducibility, their application is finite on account of no explicit threshold, high equipment costs, lack of portability, high radiation exposure, and complicated post-processing. The preferred alternative method DXA has wide availability, simplicity, accuracy, reproducibility, extremely low radiation exposure, and low cost. However, it can only provide bidimensional data, is susceptible to the effects of hydration status, has heterogeneous results between different densitometer brands, and lacks portability for the use in community. Although ultrasound was not recommended widely, it is a very promising tool worth further study to demonstrate its application accuracy and reproducibility.[63] The portable alternative method BIA is an inexpensive, portable, and widely available in both community and healthcare settings method for measuring body composition, and has good consistency with MRI, and a certain correlation with muscle function. Whereas it relies on race-specific prediction equations and the validity may be influenced by hydration status.64 Compared with DXA, BIA may underestimate fat mass and overestimate muscle mass, resulting in a higher prevalence of sarcopenia.65,66 Therefore, separate diagnostic thresholds for BIA and DXA may be more necessary.

Knee flexion and knee extension are measured by isokinetic dynamometry which has been used for the assessment of muscle function, and its use in the clinical setting is astricted by technical challenges, low availability, and high cost.[67] Hand-grip strength is highly responsive and correlated with leg strength and represents limb muscle strength with good test–retest reliability and inter-rater reliability. The grip strength measurement tool handgrip dynamometry has the characteristics of portability, low cost, and simplicity.[62,68,69] Studies showed that grip strength measurements are impressionable to various factors such as hand position, hand size and dominance, body position, verbal encouragement, subject motivation, circadian rhythms, and fatigue.[62,70] However, grip strength cannot be equated with limb strength, especially lower extremity strength.[71] The chair stand test could be used to evaluate both muscle strength and physical performance with good test–retest reliability and only requires simple equipment (chair and a stopwatch) and little training to conduct.[62,72] However, the repetitions of sit-to-stand tests, the height of the seat, the chair with or without armrests, the type of footwear, whether to use a walker and the pace may affect the results and safety of the measurement.[73,74]

Gait speed is a simple, sensitive and highly reproducible, and responsive measure of physical performance with excellent test–retest reliability and inter-rater reliability.[62,75] Some of the variable factors that need to be taken into account during the measurement of gait speed include walking distance, static or dynamic start of walking, usual or maximum gait speed, and the use of walking aids.[76] SPPB can be applied in clinical and research settings, which has excellent reproducibility and responsiveness, and good to excellent test–retest reliability. However, it requires training, time, and space, and potential ceiling effects may exist.[62,77,78] TUG is a reliable, valid, simple, and inexpensive measure to assess physical performance with moderate to good test–retest reliability and excellent inter-rater reliability.[79] It requires no special training but is affected by pace, distance, mechanism of turn, and type of chair.80 SCPT is considered to be clinically feasible, low-technology, and low-cost with high test–retest reliability, but it is controversial because of its lack of standardization (number and height of steps, ascents with or without descents) and patient safety.[81-83] The 400-meter walk test is also a reliable measurement with high test-retest reliability adopted by clinicians and researchers, though it requires training for examiners. It is influenced by walking aids and warm-ups, and its use in clinical settings is precluded because of requirements for more time and space.[76]

As concerns management of sarcopenia, the worldwide consensus has not been arrived upon because high quality RCTs were not enough. Inappropriate interventions may result in adverse outcomes particularly in the elderly with comorbidities as with inappropriate drugs. The intervention strategies recommended in the guidance documents include exercise intervention and exercise combined with nutrition. Studies showed that both nutrition intervention alone and physical activity alone have different degrees of beneficial effects on muscle mass and function of the elderly.[84] Moreover, nutritional supplementation has been discovered to reduce fat mass.[85] Therefore, nutritional intervention alone also has certain recommended value for sarcopenia patients who are unable to engage in physical activity.

The interdisciplinary team to formulate individualized management regimens should, at the very least, consist of the patient's attending and primary care physician, registered dietician, physiotherapists, nurses, and specialists with expertise in managing patients with serious medical conditions.[17,40] Pharmacists, rehabilitation therapists, psychotherapists, patients, community doctors, social workers, and family members could also be part of the close

team. Care and monitoring in the hospital, community, and home are closely connected to establishing a full-life cycle management file for sarcopenia patients. Collaboration with health care policy makers is also required to promote the use of the ICD diagnosis code for sarcopenia in clinical deeds. To make the process of management at all levels closely connected, it is necessary to have an efficient information collection and processing system. A sarcopenia management database could be established using big data technology and could be associated with healthcare information systems and other data sources such as wearable devices. And it could screen and diagnose sarcopenia earlier, improve full-life cycle patient-centered management, and promote research on mechanisms and intervention. Finally, we hope to establish a government health department-hospital-community linkage system to clarify the division of labor of screening, referral, treatment, and post-hospital rehabilitation management, so as to provide the whole process management for sarcopenia patients.

Based on the synthesis of existing guidance documents and high-quality research, we have found that elderly people are affected by various chronic diseases or functional decline. Simply using the evaluation indicators recommended by diagnostic guidelines may mistakenly evaluate the muscle function status of the elderly population. For the elderly with cognitive impairment or peripheral nervous system disease, there may be errors in using grip strength to assess their muscle strength, and for patients with concomitant malignant tumors or chronic obstructive pulmonary disease, using RSMMI alone to evaluate the overall muscle condition may lead to bias. Targeted body composition detection methods and evaluation indicators should be used based on the patient's anamnesis to determine the overall muscle status. For elderly individuals with high BMI, considering muscle alone may overlook the suppression effect of fat on muscle attenuation. Therefore, the metabolic impact of sarcopenic obesity in the elderly population should be comprehensively considered, and biochemical indicators should be used to comprehensively evaluate patients. Therefore, the screening, evaluation, and diagnostic approaches for sarcopenia should be classified and evaluated, with targeted comprehensive evaluations based on the age, gender, cognitive function, and chronic disease comorbidities of the subjects. Changes in the intestinal microecological environment during aging and the host form an inflammatory response loop. Static activity patterns and high fat dietary patterns can lead to chronic inflammatory environments and insulin resistance, becoming important foundations for the occurrence of sarcopenia. Clarifying the pathogenesis of sarcopenia at the molecular level is still an important issue that urgently needs to be addressed.

Apparently, the dearth of original studies, whether on age-related sarcopenia or disease-related sarcopenia, is a significant issue affecting the methodological quality and consistency of the guidance documents. To enhance our knowledge and awareness of sarcopenia and specify more complete guidelines, we still need to 1) measure sarcopenia in epidemiological studies, including chronic disease research, organ oriented disease research, and so forth, 2) explore the best threshold of measurement tools for various populations in clinical practice, 3) investigate the effects of targeted nutritional intervention on sarcopenia, 4) probe the best intervention plan, and its timing and long-term effects in the process of life, 5) conduct research on some available drugs, 6) determine the best monitoring frequency over time after intervention, and 7) explore the pathophysiological mechanism of sarcopenia.[3,4,18,40,41,86]

To our knowledge, this is the first review that attempted to systematically synthesize and appraise guidance documents on sarcopenia. We conducted a comprehensive literature search including database, guideline website searches, and manual searches. We summarized the existing recommendations on diagnosis and management of sarcopenia and evaluated the quality of the guideline development process using AGREE II. We found some defects in the guidance documents development process, which implicated that improvement can be made in aspects associated with stakeholder involvement, rigour of development, applicability, and editorial independence.

The review has some limitations as well. Firstly, although we have conducted a comprehensive literature search, we cannot guarantee that we have obtained all relevant literature. Secondly, the guideline development process is complex, and we may not have access to all the information, which may cause some items to be scored incorrectly when appraising. Thirdly, AGREE II does not provide detailed scoring criteria and allocates equal weight to six domains, which also leads to bias. Finally, we did not appraise the quality of evidence of documents but rather their methodologies during development, making it difficult to identify the reasons for differences between documents.

In conclusion, our review suggests that based on limited evidence, these guidance documents have, to the fullest extent possible, advanced relatively referential recommendations that have certain guiding significance. The screening, the three-level diagnostic process, and the full-life cycle management of sarcopenia have momentous significance in muscle health. Despite that numerous new screening technologies have been developed, SARC-CalF recommended by guidance documents may be the presently most reliable screening tool. According to recent guidance documents, we reckon that the early diagnosis of sarcopenia can be determined based on whether muscle function (muscle strength, physical performance) decreases when there is no significant decrease in muscle mass, while the diagnosis of sarcopenia can be determined based on the decrease in muscle mass plus muscle strength or physical performance. It cannot be ignored that there is currently no clear evidence indicating the order of decline in muscle mass and muscle strength. Therefore, more extensive research is necessary in the future to elucidate this, such as well-designed multicenter cohort studies. Combining exercise and nutritional interventions is still the current best choice for managing sarcopenia. Based on AGREE II, the methodological quality of guidance documents could make further improvement, and a large amount of high-quality research is still needed in the future to facilitate the development of higher-quality guidance documents.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors have no competing interests to declare.

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