

Sarcopenia Definition: The Position Statements of the Sarcopenia Definition and Outcomes Consortium

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The position statements were presented, discussed, and voted on by an independent international expert panel at a conference organized by the Sarcopenia Definitions and Outcomes Consortium in November 2018.

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OBJECTIVES: To develop an evidence-based definition of sarcopenia that can facilitate identification of older adults at risk for clinically relevant outcomes (eg, self-reported mobility limitation, falls, fractures, and mortality), the Sarcopenia Definition and Outcomes Consortium (SDOC) crafted a set of position statements informed by a literature review and SDOC's analyses of eight epidemiologic studies, six randomized clinical trials, four cohort studies of special populations, and two nationally representative population-based studies.

METHODS: Thirteen position statements related to the putative components of a sarcopenia definition, informed by the SDOC analyses and literature synthesis, were reviewed by an independent international expert panel (panel) iteratively and voted on by the panel during the Sarcopenia Position Statement Conference. Four position statements related to grip strength, three to lean mass derived from dual-energy x-ray absorptiometry (DXA), and four to gait speed; two were summary statements.

RESULTS: The SDOC analyses identified grip strength, either absolute or scaled to measures of body size, as an important discriminator of slowness. Both low grip strength and low usual gait speed independently predicted falls, self-reported mobility limitation, hip fractures, and mortality in community-dwelling older adults. Lean mass measured by DXA was not associated with incident adverse health-related outcomes in community-dwelling older adults with or without adjustment for body size.

CONCLUSION: The panel agreed that both weakness defined by low grip strength and slowness defined by low usual gait speed should be included in the definition of sarcopenia. These position statements offer a rational basis for an evidence-based definition of sarcopenia. The analyses

that informed these position statements are summarized in this article and discussed in accompanying articles in this issue of the journal. *J Am Geriatr Soc* 00:1-9, 2020.

Keywords: sarcopenia; lean mass cut points; grip strength cut points; mobility disability; consensus definition of sarcopenia

The lack of a consensus definition of sarcopenia as a biomarker that can help identify older adults at risk for mobility disability and other adverse health outcomes has limited the ability of clinicians to diagnose and treat this condition and hindered the development of function-promoting therapies.¹ Many investigators, professional societies, and organizations around the world have proposed various definitions of sarcopenia,²⁻¹⁴ but these definitions were largely based on expert opinion. Although an initiative supported by the Foundation for the National Institutes of Health (FNIH) derived cut points for lean mass and grip strength based on the analysis of largely healthy older adults,⁵ this earlier effort did not evaluate whether the cut points independently predicted important clinical outcomes such as falls, fractures, and mortality. Consequently, an evidence-based definition of sarcopenia with optimal translational potential to the clinical care of older patients has been lacking.

In 2016, the National Institute on Aging (NIA) and the FNIH funded the Sarcopenia Definitions and Outcomes Consortium (SDOC; the consortium), a collaboration among content experts and many cohort studies and clinical populations, to develop evidence-based cut points for lean mass and strength to identify persons at risk for mobility disability and other adverse health outcomes such as falls, self-reported mobility limitation, hip fractures, and death. The SDOC assembled a large body of data from epidemiologic studies, clinical trials, and special populations, and it applied data-driven analytical approaches to generate the cut points. The preliminary findings of the analyses were presented at a meeting on October 2, 2017, in Bethesda, Maryland¹ and included SDOC members, additional content experts from around the world, and program staff from the NIA and FNIH. In addition to specific recommendations on the future direction of the research and the analytical approach, the expert attendees offered several recommendations to advance the goal of turning the analytical findings into a consensus definition of sarcopenia.¹ First, it was recommended that SDOC establish an independent international expert panel to review the final analytical findings and a synthesis of the published evidence. Second, it was recommended that SDOC develop a set of position statements informed by the analytical findings and literature synthesis. Third, expert attendees urged SDOC to have the position statements and the supporting evidence reviewed and voted on by the expert panel in a consensus conference in the fall of 2018.

To implement these recommendations of the October 2017 meeting,¹ the SDOC held a Sarcopenia Position Statement Conference in Boston, Massachusetts, in November 2018. Before the conference, draft position statements related to the putative components of the sarcopenia definition were developed by the SDOC team based on literature review and SDOC analyses of the data from eight epidemiologic studies, six randomized clinical trials and four cohort studies of special populations, and two nationally representative population-based studies. A summary of the analyses and the position statements were presented to the expert panel, other content experts, and stakeholders. These 13 position statements reviewed by the expert panel and the evidence that formed the basis of these positions are summarized in this article, and they are described in detail in a series of linked articles in this issue of the journal.¹⁵⁻¹⁸

METHODS

The Analytic Approach

The detailed methods and results of the analyses are presented in several accompanying articles in this issue of the journal¹⁵⁻¹⁸ and described only briefly here. The SDOC team assembled eight observational studies that included 18 831 community-dwelling older adults (13 683 men and 5148 women), eight carefully characterized clinical populations (randomized trials and additional cohort studies of patients with hip fracture and human immunodeficiency virus [HIV]), and two nationally representative population-based cohorts (the Health and Retirement Survey [HRS], with 7370 subjects [3170 men and 4200 women]; and the National Health and Aging Trends Survey [NHATS], with 5614 subjects [2460 men and 3154 women]).¹⁹⁻³³ Among 18 831 community-dwelling older adults in the eight observational studies, 3143 (17%) had self-reported mobility limitation defined as any difficulty walking two to three blocks or climbing 10 steps.

The SDOC team assembled a comprehensive set of 36 candidate sarcopenia variables related to dual-energy x-ray absorptiometry (DXA)-derived body composition measures and grip strength. In the epidemiologic cohorts, the lean mass measurements by DXA were harmonized across studies and calibrated to the National Health and Nutrition Examination Survey (NHANES) standard using validated equations.³⁴ We also evaluated the impact of body size using allometric scaling³⁵; neither harmonization nor allometric scaling, however, had substantial effects on the results.

The candidate variables were assessed for their ability as discriminators for slowness (defined as usual walking speed <.8 m/s) cross-sectionally in two parallel analyses. Receiver operating characteristic (ROC) and the associated area under the ROC curves (AUC) from logistic regression were used to screen several putative sarcopenia variables derived from grip strength, lean mass, body size, and their combinations against the outcome of slowness. In addition, these variables were also entered into Classification and Regression Tree (CART) models to identify those variables that most strongly discriminated those with slowness from

those without and to derive cut points for these variables as discriminators of slowness.

Using cut points for lean mass and grip strength identified by the CART and ROC/AUC models, we assessed whether the candidate sarcopenia variables were associated with adverse clinical outcomes such as mortality, falls, self-reported mobility limitation, and hip fracture using proportional hazards and logistic regression. In addition, we determined the prevalence of weakness defined by the cut points derived from the CART and ROC/AUC analyses and evaluated the sensitivity and specificity of these cut points in clinical populations, randomized trials, and in nationally representative samples from the NHATS and HRS.

The Expert Panel

The SDOC convened an independent expert panel that included content experts from around the world and representatives of pharmaceutical and nutritional companies, major professional societies, and patient advocacy groups experienced with sarcopenia and older adults with functional limitations

(Table 1). The potential financial or professional conflicts disclosed by the panelists were reviewed. Members of the expert panel were not involved in the development of the SDOC analysis plan or in the analyses.

The Process of Position Statement Development, Vetting, and Approval

The SDOC established three task forces consisting of two or three SDOC members each to assemble the analytical results, perform a literature review, and develop proposals for position statements for consideration by the expert panel. The SDOC team synthesized the analytical findings and literature review to craft 13 position statements grouped in these four categories: statements related to grip strength (four statements), lean mass measured using DXA (three statements), gait speed (four statements), and summary statements (two statements) (Table 2).

Members of the expert panel reviewed the analytical findings and literature evidence presented by the SDOC task forces in conference calls between May and November 2018, and

Table 1. International Expert Panel

Name	Position(s)	Role
Cyrus Cooper, DM, FMedSci	Director of the MRC Lifecourse Epidemiology Unit; Vice Dean of Medicine, University of Southampton; Professor of Rheumatology, Honorary Consultant Rheumatologist, University of Oxford	Chairperson of the international expert panel
Hidenori Arai, MD, PhD	Professor, Department of Human Health Sciences, Kyoto University; Leader, Asian Working Group for Sarcopenia	Member of the international expert panel
Brian C. Clark, PhD	Harold E Clybourne, D.O., Endowed Research Chair; Executive Director, Ohio Musculoskeletal and Neurological Institute; Professor of Physiology and Neuroscience, Department of Biomedical Sciences, Ohio University, Athens, OH	Member of the international expert panel
Jane A. Cauley, DrPH	Distinguished Professor of Epidemiology, Executive Vice Chair, Epidemiology, University of Pittsburgh, Pittsburgh, PA	Member of the international expert panel
Jack Guralnik, MD, PhD, MPH	Professor, Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD	Member of the international expert panel
Francesco Landi, MD, PhD	Associate Professor of Internal Medicine, Catholic University of Sacred Heart, Rome, Italy	Member of the international expert panel
Suzette Pereira, PhD	Associate Research Fellow, Strategic Research, Abbott Nutrition	Member of the international expert panel
Daniel Rooks, PhD	Head, Muscle group, Translational Medicine, Novartis	Member of the international expert panel
Laura Schaap, PhD	Faculty of Science, Nutrition and Health, Free University Amsterdam	Member of the international expert panel
Jean Woo, MD, PhD	Henry G. Leong Research Professor of Gerontology and Geriatrics; Director, CUHK Jockey Club Institute of Aging, The Chinese University of Hong Kong	Member of the international expert panel

Table 2. Approved Position Statements**Grip strength**

1. Muscle weakness in older adults can be conveniently defined using grip strength.
2. Muscle weakness, as defined by low grip strength, is a predictor of adverse health-related outcomes such as mobility limitation, falls, ADL [activities of daily living] disability, and mortality in community-dwelling older adults.
3. Muscle weakness, as defined by low grip strength, should be included in the definition of sarcopenia.
4. The performance characteristics of a sex-specific cut point for low grip strength may vary by age, race, disease condition, and other factors.

Lean mass by DXA

5. Appendicular lean mass measured by dual-energy X-ray absorptiometry (DXA), either absolute or after scaling for body size, is not a good predictor of adverse health-related outcomes such as mobility limitation, falls, ADL disability, and mortality in community-dwelling older adults.
6. The highly variable risk associations found between appendicular lean mass by DXA and adverse health-related outcomes in community-dwelling older adults limit the utility of lean mass assessed by DXA as a predictor or prognostic risk factor for adverse health-related outcomes.
7. Lean mass measured by DXA should not be included in the definition of sarcopenia.

Gait speed

8. Slowness, defined by low usual gait speed, is a predictor of adverse health-related outcomes, such as self-reported mobility limitation, falls, ADL disability, hospitalization, and mortality in older adults.
9. Strength is one of the many factors that influence usual gait speed.
10. Usual gait speed is an indicator of walking ability and should be included in the definition of sarcopenia.
11. The performance characteristics of a cut point for low usual gait speed may vary by age, sex, race, disease condition, and other factors.

Summary statements

12. Low grip strength and low usual gait speed independently predict adverse health-related outcomes such as mobility limitation, falls, ADL disability, and mortality in community-dwelling older adults.
13. Both weakness defined by low grip strength and slowness defined by low usual gait speed should be included in the definition of sarcopenia.

they provided comments and suggestions. The interactive discussions between the expert panel and the SDOC task forces enabled a comprehensive review of the position statements and multiple revisions based on the expert panel's feedback.

The Sarcopenia Position Statement Conference was held on November 13, 2018, in Boston, Massachusetts, and attended by the SDOC investigators, the expert panel, and other content experts and stakeholders from around the world. During the conference, after discussion of the position statements in which all conference attendees took part, the expert panel voted on each of the 13 position statements. Each expert panel member voted to approve or disapprove each position statement on a scale of 1 to 9 (1-3 approve; 4-6 uncertain; and 7-9 disapprove). The expert panel could indicate uncertainty about a position statement in one of two ways: an average score of 4 to 6 or a substantial dispersion of

scores, for example, some panelists voting 1 to 3 and some voting 7 to 9. After the November 2018 conference, these position statements were posted on a website for a 4-week comment period. A summary of the supporting evidence and the discussion are provided here.

RESULTS**Supporting Evidence for Position Statements Related to Grip Strength**

The CART analyses identified grip strength, either absolute or scaled to measures of body size (maximal grip strength [<35.5 kg in men; <20.0 kg in women], grip over body mass index [BMI] [<1.05 for men; $.79$ for women], grip strength over total body fat [<1.66 for men; $<.65$ for women], grip over arm lean mass [<6.1 for men; <3.26 for women], and grip over body weight [$<.45$ for men; $<.34$ for women]) as an important discriminator of slowness. Low grip strength, with or without standardization to weight or BMI, was a predictor of adverse health outcomes such as falls, self-reported mobility limitation, hip fracture, and mortality in older adults. Weakness, defined by the grip strength cut points, was common among older Americans. The sensitivity and specificity of these metrics as discriminators of slowness, as well as the proportion of individuals below the diagnostic cut points (prevalence) varied by sex and comorbidity status. In general, the grip strength cut points to define weakness in women had higher sensitivity and lower specificity than in men. The performance of grip strength cut points to define weakness differed substantially in hip fracture and HIV cohorts than in epidemiologic studies of community-dwelling individuals, indicating that the performance of the cut points may vary with the study population.

Discussion Related to Grip Strength

The advantages and disadvantages of using grip strength in the definition of sarcopenia were discussed. Grip strength can be measured easily and reliably, and equipment for measuring grip strength is inexpensive and portable. However, nonmuscle factors such as arthritis, pain, depression, subject motivation and effort, as well as other central neural factors, could influence grip strength measurement. The devices and the procedures used for measuring grip strength vary in different countries; therefore, standardization of the equipment and the procedure for measuring grip strength is necessary for application of cut points across regions. Although grip strength is cross-sectionally associated with lower extremity strength, lower extremity strength is a more important contributor to slowness.³⁶ However, few large epidemiologic studies have included data on rigorously measured lower extremity strength; furthermore, measurement of lower extremity strength requires specialized equipment and skilled personnel, and it may be difficult to perform in a clinic setting. The SDOC analyses used grip strength at one time point consistent with clinical practice where the clinicians often rely on a single measurement at the time of patient encounter.

Voting Results and Strength of Agreement for Position Statements Related to Grip Strength

The expert panel expressed strong agreement with position statements 1 to 4 and unanimously approved these statements (Figure 1).

Supporting Evidence for Position Statements Related to DXA-Derived Lean Mass

The position statements 5, 6, and 7 related to lean mass were informed by the SDOC analyses, literature review, and meta-analyses of studies published from 1998 to 2018.^{37,38} DXA-derived lean mass was harmonized across different models and manufacturers of scanners to the NHANES standard. The harmonization of DXA-derived lean mass did not make a substantial difference in the cut points.

The SDOC team considered scaling factors including body mass, body surface area, height, body fat, percentage fat mass, BMI, and regional lean mass. The team used proportional ratios, allometric scaling, and regression residuals to derive scaling factors. Because all scaling approaches produced similar results, in favor of simplicity, only the unscaled variables were used in the CART analyses.

In the CART analyses, body composition measures (eg, BMI, lean mass by DXA, or body fat) did not emerge as important discriminators of slowness.

The SDOC team reviewed several published meta-analyses that evaluated the relationship between lean mass and adverse health outcomes.³⁸⁻⁴¹ These meta-analyses used

composite measures of sarcopenia that included walking speed and grip strength or combined data from studies that used disparate methods for the assessment of lean mass such as DXA, bioelectrical impedance, and computed tomography. To address the limitations of the published meta-analyses, the SDOC researchers conducted an additional meta-analysis of DXA-derived lean mass and its relationship to disability, physical function, mortality, and falls in a smaller carefully selected subset of published studies (not shown). However, the odds ratios relating lean mass alone to these four outcomes were around 1, consistent with the findings of our analyses.

Discussion Regarding DXA-Derived Lean Mass

Because muscle mass has historically been viewed as an important component of sarcopenia, panelists disagreed about excluding lean mass from the definition of sarcopenia. Lean mass was traditionally measured by DXA as an approximation of muscle mass; the analytical results were based on DXA-derived lean mass and may not apply to all methods of measuring muscle mass. It is possible that other more accurate measures of skeletal muscle mass, such as D3-creatine dilution, may be associated more robustly with health outcomes than DXA and may be used in the future. Regardless of whether lean mass should be included in a definition of sarcopenia, the panelists agreed that DXA-derived lean mass measures were not good predictors of self-reported mobility limitations or other health-related outcomes such as falls, hip fracture, and mortality.

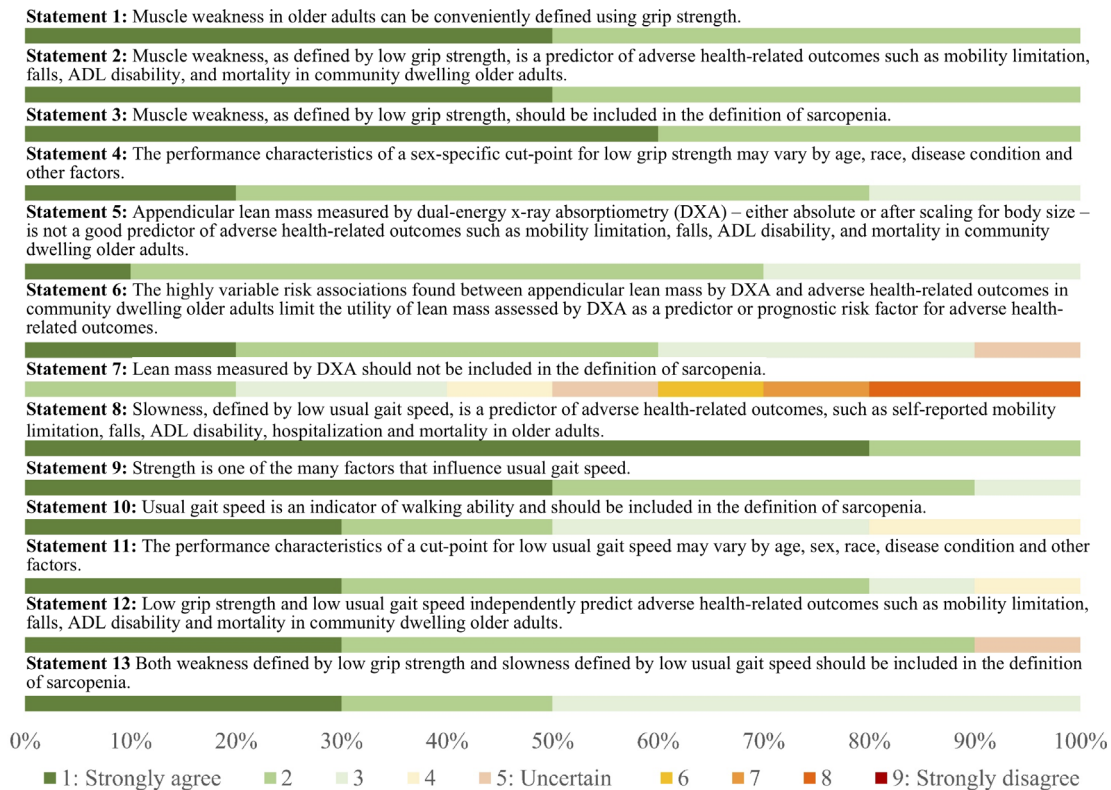


Figure 1. Position statements for the Sarcopenia Definition and Outcomes Consortium (SDOC) and the level of agreement among the international expert panel on the position statements.

Voting Results and Strength of Agreement for Position Statements Related to Lean Mass

The members of the expert panel expressed strong agreement with position statements 5 and 6, but they expressed some uncertainty about statement 7 (Figure 1).

Supporting Evidence for Position Statements Related to Gait Speed

Usual gait speed declines with aging. Because ample data are available in the literature regarding the usefulness of gait speed as a predictor of many relevant outcomes in older adults including physical disability, hospitalization, fall risk, and death,^{39,42} the SDOC did not aim to define new gait speed cut points. In the SDOC analysis, low gait speed was significantly associated with mortality, falls, and instrumental activities of daily living disability, regardless of grip strength and body size, consistent with previous reports. In general, both low grip strength and low usual gait speed were independently associated with adverse health outcomes (increased risk of falls, self-reported mobility limitation, and mortality).

Discussion Related to Gait Speed

Many factors influence gait speed; muscle strength is an important but only one of many determinants of gait speed. Gait speed varies with age, sex, race/ethnicity, and disease condition. Gait speed can be measured in a clinical setting but may vary depending on how it is measured, highlighting the need for standardizing the procedure for measuring it.

Voting Results and Strength of Agreement for Position Statements Related to Gait Speed

The expert panel expressed strong agreement with position statements 8, 9, and 11. Statement 10 had good agreement with a few members expressing some uncertainty.

Discussion Related to Summary Position Statements

The panel noted some caveats related to summary statements 12 and 13. First, these position statements are formulated for community-dwelling adults; how they apply to persons with acute or subacute muscle loss due to cancer or sepsis or to hospitalized acutely ill persons is not known. The panel noted that although frailty and sarcopenia may have some overlapping features, such as decreased muscle strength, they are distinct conditions, and these position statements do not apply to frailty or cachexia. Although the grip strength and gait speed cut points may help define sarcopenia, they may not necessarily be responsive to some types of interventions depending on the mechanism of action of the therapeutic intervention. The expert panel discussed whether weakness and slowness represent different stages of the condition and whether older adults who have both weakness and slowness have a more advanced stage of the condition than those who have low grip strength (weakness) but not low gait speed (slowness).

Voting Results and Strength of Agreement for Summary Position Statements

Statement 13 had strong agreement from the expert panel, and statement 12 had good agreement with a few members expressing some uncertainty. The uncertainty was related to the exclusion of DXA-derived lean mass from the definition.

DISCUSSION: SYNTHESIS AND CONCLUSIONS

The SDOC position statements on sarcopenia, vetted and approved by an external independent international expert panel, offer a rational basis for an evidence-based definition of sarcopenia. Several unique attributes of the SDOC processes and position statements distinguish them from some other efforts to develop a consensus definition of sarcopenia. First, these position statements and the cut points described in the linked articles are evidence based rather than opinion based. They were derived from the analyses of data from one of the largest assemblies of observational studies that included large numbers of older adults with mobility complaints. Second, the proposed cut points were evaluated based on their ability to predict patient-important incident health outcomes of public health importance: mobility limitation, mortality, falls, and hip fractures. Both low grip strength and low gait speed were generally predictive of adverse health outcomes. The performance characteristics of cut points (sensitivity, specificity, and predictive value) were evaluated in community-dwelling older adults and in special populations enrolled in randomized clinical trials of function-promoting therapies and special clinical populations (eg, persons with hip fracture or HIV infection), as well as two large nationally representative population-based studies. Third, the SDOC process of generating the position statements facilitated consensus generation while maintaining transparency because it enabled the panelists to express disagreement and their level of uncertainty. The iterative nature of the expert panel's review of the position statements and the supporting analyses and literature synthesis during multiple conference calls over several months leading up to the conference enabled the panel's input to be incorporated into the final position statements.

As described in the accompanying articles,¹⁵⁻¹⁸ the performance characteristics of these cut points vary with age, race/ethnicity, comorbid conditions, and population. Therefore, sex-specific cut points derived in these analyses should be evaluated in additional diverse populations including clinical populations with specific conditions. The estimates of prevalence of weakness, slowness, or sarcopenia based on these cut points in various populations would be a valuable guide to public health policy, to pharmaceutical drug development, and in clinical practice to encourage lifestyle interventions.

There was agreement that developing a clinically useful risk model to predict mobility disability and other patient-important outcomes that integrates these position statements and considers age, sex, and race/ethnicity is a priority research need. Inevitably, the cut points derived from these analyses will be refined over time as they are evaluated prospectively as outcomes or enrollment criteria in randomized

trials and observational studies and as new data become available. The national efforts to generate guidelines for high cholesterol and high blood pressure offer useful historical precedence for the nascent SDOC initiative. The cholesterol guidelines published by the Adult Treatment Panel (ATP) of the National Cholesterol Education Program⁴³ and the Joint National Commission (JNC) guidelines for the treatment of hypertension^{44,45} have undergone multiple revisions over many decades. Analogously, the transformation of SDOC into a sustainable organization based on the ATP and JNC models will enable continual refinement of the risk models and the generation of progressively updated guidelines for the diagnosis, treatment, and prevention of sarcopenia in the general population and in older adults with specific conditions.

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of Osteoporosis and Osteoarthritis working group on frailty and sarcopenia. She is involved in a project on the assessment of muscle function and physical performance in daily clinical practice. Francesco Landi, Todd Manini, Tom Trivison, and Jean Woo declared no conflicts of interest for this article.

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