GUIDELINES

Sarcopenia: revised European consensus on definition and diagnosis

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Abstract

Background: in 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) published a sarcopenia definition that aimed to foster advances in identifying and caring for people with sarcopenia. In early 2018, the Working Group met again (EWGSOP2) to update the original definition in order to reflect scientific and clinical evidence that has built over the last decade. This paper presents our updated findings.
Objectives: to increase consistency of research design, clinical diagnoses and ultimately, care for people with sarcopenia.
Recommendations: sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime; sarcopenia is common among adults of older age but can also occur earlier in life. In this updated consensus paper on sarcopenia, EWGSOP2: (1) focuses on low muscle strength as a key characteristic of sarcopenia, uses detection of low muscle quantity and quality to confirm the sarcopenia diagnosis, and identifies poor physical performance as indicative of severe sarcopenia; (2) updates the clinical algorithm that can be used for sarcopenia case-finding, diagnosis and

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confirmation, and severity determination and (3) provides clear cut-off points for measurements of variables that identify and characterise sarcopenia.

Conclusions: EWGSOP2's updated recommendations aim to increase awareness of sarcopenia and its risk. With these new recommendations, EWGSOP2 calls for healthcare professionals who treat patients at risk for sarcopenia to take actions that will promote early detection and treatment. We also encourage more research in the field of sarcopenia in order to prevent or delay adverse health outcomes that incur a heavy burden for patients and healthcare systems.

Introduction: sarcopenia 2018

In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) published a sarcopenia definition that was widely used worldwide; this definition fostered advances in identifying and caring for people at risk for or with sarcopenia [1]. In early 2018, the Working Group met again (EWGSOP2) to determine whether an update to the definition of sarcopenia was justified. This meeting took place 10 years after the gathering of the original EWGSOP, and an update was deemed necessary to reflect scientific evidence that has accumulated since then.

In the decade since EWGSOP's initial work, researchers and clinicians have explored many aspects of sarcopenia. Expert groups worldwide have published complementary definitions of sarcopenia [2–4], and researchers have made remarkable strides in understanding muscle and its roles in health and in disease [5, 6]. Sarcopenia is now formally recognised as a muscle disease with an ICD-10-MC Diagnosis Code that can be used to bill for care in some countries [7, 8].

Even though healthcare professionals today are better at recognising sarcopenia, many research findings have not yet been translated into clinical practice. To this end, EWGSOP2 uses the newest evidence to delineate clear criteria and tools that define and characterise sarcopenia in clinical practice and in research populations. EWGSOP2 emphasises that practitioners have ever-increasing possibilities for preventing, delaying, treating, and sometimes even reversing sarcopenia by way of early and effective interventions.

Health and healthcare costs of untreated sarcopenia

Optimal care for people with sarcopenia is essential because the condition has high personal, social and economic burdens when untreated [9]. In terms of human health, sarcopenia increases risk of falls and fractures [10, 11]; impairs ability to perform activities of daily living [12]; is associated with cardiac disease [13], respiratory disease [14] and cognitive impairment [15]; leads to mobility disorders [2]; and contributes to lowered quality of life [16], loss of independence or need for long-term care placement [17–19], and death [20]. In financial terms, sarcopenia is costly to healthcare systems. The presence of sarcopenia increases risk for hospitalisation and increases cost of care during hospitalisation [21]. Among older adults who are hospitalised, those with sarcopenia on admission were more than 5-fold more likely to have higher hospital costs than those without sarcopenia [22]. Results of a large, community-based study in the Czech Republic showed that direct healthcare costs were more than 2-fold higher for older people with sarcopenia than for those without [23]. In a study of older people in the community, in assisted-living facilities, or in residential living facilities, researchers found that lower gait speed and chair stand were potential drivers of disability in activities of daily living (ADL) and that such disability was associated with lower quality of life (QoL) and higher healthcare costs in these target groups [9]. In another study, patients with sarcopenia had significantly elevated costs of care during hospitalisation—regardless of whether they were younger or older than 65 years [24].

Filling the gaps for sarcopenia awareness, care and research design

Many aspects of the epidemiology and pathophysiology of sarcopenia are better understood today than 10 years ago. Researchers have identified links between muscle pathology and adverse health outcomes, and studies have also provided evidence that certain treatment strategies can help prevent or delay adverse consequences.

Such new insights led EWGSOP2 to review, 'What is new?' and 'How can we use this knowledge to improve care for people with sarcopenia and to guide future research studies?' These insights include:

- First, sarcopenia has long been associated with ageing and older people, but the development of sarcopenia is now recognised to begin earlier in life [25], and the sarcopenia phenotype has many contributing causes beyond ageing [26, 27]. These insights have implications for interventions that prevent or delay development of sarcopenia.
- Second, sarcopenia is now considered a muscle disease (muscle failure), with low muscle strength overtaking the role of low muscle mass as a principal determinant [11, 28–30]. This change is expected to facilitate prompt identification of sarcopenia in practice.
- Third, sarcopenia is associated with low muscle quantity and quality, but these parameters are now used mainly in research rather than in clinical practice. Muscle mass and muscle quality are technically difficult to measure accurately [31–34].

- Fourth, sarcopenia has been overlooked and undertreated in mainstream practice [35], apparently due to the complexity of determining what variables to measure, how to measure them, what cut-off points best guide diagnosis and treatment, and how to best evaluate effects of therapeutic interventions [36]. To this end, EWGSOP2 aims to provide clear rationale for selection of diagnostic measures and cut-off points relevant to clinical practice.

To enhance awareness and care for sarcopenia, the EWGSOP2 has updated its definition and diagnostic strategies in 2018. Specific goals for the updates were to: (1) build a sarcopenia definition that reflects recent advances in scientific, epidemiological, and clinical knowledge about skeletal muscle, (2) identify variables that best detect sarcopenia and predict outcomes, and determine best tools for measuring each variable, (3) advise cut-off points for measured variables and (4) recommend an updated screening and assessment pathway that is easy to use in clinical practice.

EWGSOP2 meetings, methods and endorsement by scientific organisations

EWGSOP2 was organised by the European Geriatric Medicine Society (EuGMS) to include two groups of participants—a 16-member writing group and a 13-member extended group. Original members of the EWGSOP were invited to participate, and other relevant European researchers in the field were identified and recruited by feedback from involved experts and societies. The writing group met face-to-face 1–2 February 2018 near Madrid to identify how the definition and diagnostic characteristics needed to be updated, to begin the process of seeking consensus on key diagnostic and care strategies, and to designate topical areas for additional literature searches.

Following this meeting, literature searches were conducted, and a preliminary draft of the manuscript was prepared and circulated for review among members of the writing and extended groups. Feedback was provided by email, and content was revised. Then a second face-to-face meeting of the writing group took place on 4 June 2018 in Amsterdam to discuss open questions and to achieve further consensus for final recommendations. This second draft was again opened for discussion by members of the Writing Group and Extended Group to produce the final draft.

All EWGSOP2 members participated in manuscript content review throughout the process, and all were polled for consensus agreement on the final content. Once completed, the manuscript was reviewed and endorsed by scientific societies: EuGMS, the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), the European Society for Clinical Nutrition and Metabolism (ESPEN), International Association of Gerontology and Geriatrics European Region (IAGG-ER) and the International Osteoporosis Foundation (IOF).

Sarcopenia: operational definition

Sarcopenia is a progressive and generalised skeletal muscle disorder that is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality. The original operational definition of sarcopenia by EWGSOP was a major change at that time, as it added muscle function to former definitions based only on detection of low muscle mass [1]. In these revised guidelines, muscle strength comes to the forefront, as it is recognised that strength is better than mass in predicting adverse outcomes [11, 28, 29, 37]. Muscle quality is also impaired in sarcopenia; this term has been used to describe micro- and macroscopic aspects of muscle architecture and composition. Because of technological limits, muscle quantity and muscle quality remain problematic as primary parameters to define sarcopenia [31, 32, 34]. Detection of low physical performance predicts adverse outcomes, so such measures are thus used to identify the severity of sarcopenia.

In its 2018 definition, EWGSOP2 uses low muscle strength as the primary parameter of sarcopenia; muscle strength is presently the most reliable measure of muscle function (Table 1). Specifically, sarcopenia is probable when low muscle strength is detected. A sarcopenia diagnosis is confirmed by the presence of low muscle quantity or quality. When low muscle strength, low muscle quantity/quality and low physical performance are all detected, sarcopenia is considered severe.

Techniques for evaluating muscle quantity are available in many but not all clinical settings. As instruments and methods to evaluate muscle quality are developed and refined in the future, this parameter is expected to grow in importance as a defining feature of sarcopenia. Physical performance was formerly considered part of the core definition of sarcopenia, but others have used it as an outcome measure. We now propose using physical performance to categorise the severity of sarcopenia.

To apply this definition in practice, this EWGSOP2 paper reviews tests and tools used for assessing muscle properties and performance, and it presents an updated algorithm for sarcopenia case-finding, diagnosis and severity determination.

Identifying sarcopenia in clinical practice and in research

Validated tests and tools for current use

A wide variety of tests and tools are now available for characterisation of sarcopenia in practice and in research (Table 2) [38, 39]. Tool selection may depend upon the patient (disability, mobility), access to technical resources in the healthcare test setting (community, clinic, hospital or research centre), or the purpose of testing (progression monitoring, or monitoring rehabilitation and recovery). In the next sections, general descriptions of validated tests and tools are provided, and pros and cons for use of each method are noted.

Finding sarcopenia cases

In clinical practice, case-finding may start when a patient reports symptoms or signs of sarcopenia (i.e. falling, feeling weak, slow walking speed, difficulty rising from a chair or weight loss/muscle wasting). In such cases, further testing for sarcopenia is recommended [2].

EWGSOP2 recommends use of the SARC-F questionnaire as a way to elicit self-reports from patients on signs that are characteristic of sarcopenia. SARC-F can be readily used in community healthcare and other clinical settings. The SARC-F is a 5-item questionnaire that is self-reported by patients as a screen for sarcopenia risk [12]. Responses are based on the patient's perception of his or her limitations in strength, walking ability, rising from a chair, stair climbing and experiences with falls. This screening tool was evaluated in three large populations—the African American Health Study, Baltimore Longitudinal Study of Aging and

Table 1. 2018 operational definition of sarcopenia

Probable sarcopenia is identified by Criterion 1.
Diagnosis is confirmed by additional documentation of Criterion 2.
If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe.
(1) Low muscle strength
(2) Low muscle quantity or quality
(3) Low physical performance

Table 2. Choosing tools for sarcopenia case finding and for measurement of muscle strength, muscle mass and physical performance in clinical practice and in research

Variable	Clinical practice	Research studies	Video for practical instruction, reference
Case finding	SARC-F questionnaire	SARC-F	Malmstrom *et al.* (2016) [12]
	Ishii screening tool		Ishii *et al.* (2014) [40]
Skeletal muscle strength	Grip strength	Grip strength	Roberts *et al.* (2011) [41]
	Chair stand test (chair rise test)	Chair stand test (5-times sit-to-stand)	American Academy of Orthotists & Prosthetists
			https://www.youtube.com/watch?v=_jPl-IuRJ5A
Skeletal muscle mass or Skeletal muscle quality	Appendicular skeletal muscle mass (ASMM) by Dual-energy X-ray absorptiometry (DXA)*	ASMM by DXA	Schweitzer (2015) [42]
			Mitsiopoulos (1998) [43]
	Whole-body skeletal muscle mass (SMM) or ASMM predicted by Bioelectrical impedance analysis (BIA)*	Whole-body SMM or ASMM by Magnetic Resonance Imaging (MRI, total body protocol)	Shen (2004) [44]
			Sergi (2017) [45]
			Maden-Wilkinson (2013) [46]
			Heymsfield (1990) [47]
			Kim (2002) [48]
			Yamada (2017) [49]
		Mid-thigh muscle cross-sectional area by Computed Tomography (CT) or MRI	Lee (2004) [50]
	Lumbar muscle cross-sectional area by CT or MRI	Lumbar muscle cross-sectional area by CT or MRI	Van der Werf (2018) [51]
			Derstine (2018) [52]
		Muscle quality by mid-thigh or total body muscle quality by muscle biopsy, CT, MRI or Magnetic resonance Spectroscopy (MRS)	Goodpaster (2000) [53]
			Reinders (2016) [54]
			Grimm (2018) [55]
			Distefano (2018) [56]
			Ruan (2007) [57]
Physical performance	Gait speed	Gait speed	NIH Toolbox 4 Meter Walk Gait Speed Test
			https://www.nia.nih.gov/research/labs/leps/short-physical-performance-battery-sppb
			https://www.youtube.com/watch?v=xLScK_NXUN0
	Short physical performance battery (SPPB)	SPPB	Short Physical Performance Battery Protocol
			https://research.ndorms.ox.ac.uk/prove/documents/assessors/outcomeMeasures/SPPB_Protocol.pdf
			NIH Toolbox
			https://www.nia.nih.gov/research/labs/leps/short-physical-performance-battery-sppb
	Timed-up-and-go test (TUG)	TUG	Mathias (1986) [40]
	400-meter walk or long-distance corridor walk (400-m walk)	400-m walk	Newman (2006) [41]

*Sometimes divided by height^2 or BMI to adjust for body size.

the National Health and Nutrition Examination study [12], and was likewise used in a study of Chinese men and women [58]. In these populations, the SARC-F was valid and consistent for identifying people at risk of sarcopenia-associated adverse outcomes.

SARC-F has a low-to-moderate sensitivity and a very high specificity to predict low muscle strength [59]. As such, SARC-F will mostly detect severe cases. We recommend SARC-F as a way to introduce assessment and treatment of sarcopenia into clinical practice. SARC-F is an inexpensive and convenient method for sarcopenia risk screening. A project is underway to translate and validate SARC-F in multiple different world languages [60]. Since SARC-F is self-reported by the patient, results reflect perceptions of adverse outcomes that matter to the patient.

Alternatively, clinicians may prefer a more formal case-finding instrument for use in clinical populations where sarcopenia is likely [61]. For example, the Ishii screening test is a method that estimates the probability of sarcopenia using an equation-derived score based on three variables—age, grip strength and calf circumference [40].

Measuring sarcopenia parameters

Muscle strength Measuring grip strength is simple and inexpensive. Low grip strength is a powerful predictor of poor patient outcomes such as longer hospital stays, increased functional limitations, poor health-related quality of life and death [28, 29]. Accurate measurement of grip strength requires use of a calibrated handheld dynamometer under well-defined test conditions with interpretive data from appropriate reference populations [41]. Grip strength correlates moderately with strength in other body compartments, so it serves as a reliable surrogate for more complicated measures of arm and leg strength. Because of its ease of use, grip strength is advised for routine use in hospital practice, in specialty clinical settings, and in community health-care [28, 29, 62–64]. The Jamar dynamometer is validated and widely used for measuring grip strength, although use of other brands is being explored [65]. When measurement of grip is not possible due to hand disability (e.g. with advanced arthritis or stroke), isometric torque methods can be used to measure lower limb strength [66].

The chair stand test (also called chair rise test) can be used as a proxy for strength of leg muscles (quadriceps muscle group). The chair stand test measures the amount of time needed for a patient to rise five times from a seated position without using his or her arms; the timed chair stand test is a variation that counts how many times a patient can rise and sit in the chair over a 30-second interval [64, 67, 68]. Since the chair stand test requires both strength and endurance, this test is a qualified but convenient measure of strength.

Muscle quantity Muscle quantity or mass can be estimated by a variety of techniques, and there are multiple methods of adjusting the result for height or for BMI [46, 69, 70]. Muscle quantity can be reported as total body Skeletal Muscle Mass (SMM), as Appendicular Skeletal Muscle Mass (ASM), or as muscle cross-sectional area of specific muscle groups or body locations.

Magnetic resonance imaging (MRI) and computed tomography (CT) are considered to be gold standards for non-invasive assessment of muscle quantity/mass [64]. However, these tools are not commonly used in primary care because of high equipment costs, lack of portability, and the requirement for highly-trained personnel to use the equipment [64]. Moreover, cut-off points for low muscle mass are not yet well defined for these measurements.

Dual-energy X-ray absorptiometry (DXA) is a more widely available instrument to determine muscle quantity (total body lean tissue mass or appendicular skeletal muscle mass) non-invasively, but different DXA instrument brands do not give consistent results [31, 32, 71]. DXA is presently favored by some clinicians and researchers for measuring muscle mass [31]. Fundamentally, muscle mass is correlated with body size; i.e. individuals with a larger body size normally have larger muscle mass. Thus, when quantifying muscle mass, the absolute level of SMM or ASM can be adjusted for body size in different ways, namely using height squared ($ASM/height^2$), weight (ASM/weight) or body mass index (ASM/BMI) [72]. There is an ongoing debate about the preferred adjustment and whether the same method can be used for all populations.

An advantage of DXA is that it can provide a reproducible estimate of ASM in a few minutes when using the same instrument and cut-off points. A disadvantage is that the DXA instrument is not yet portable for use in the community, as needed for care in countries that favor ageing-in-place. DXA measurements can also be influenced by the hydration status of the patient.

Bioelectrical impedance analysis (BIA) [62] has been explored for estimation of total or ASM. BIA equipment does not measure muscle mass directly, but instead derives an estimate of muscle mass based on whole-body electrical conductivity. BIA uses a conversion equation that is calibrated with a reference of DXA-measured lean mass in a specific population [49, 73–75]. BIA equipment is affordable, widely available and portable, especially single-frequency instruments. Since estimates of muscle mass differ when different instrument brands and reference populations are used, we advise use of raw measures produced by the different devices along with the cross-validated Sergi equation for standardisation [74, 76]. BIA prediction models are most relevant to the populations in which they have been derived, and the Sergi equation is based on older European populations. Age, ethnicity and other related discrepancies between those populations and patients should be considered in the clinic. In addition, BIA measurements can also be influenced by hydration status of the patient. For affordability and portability, BIA-based determinations of muscle mass may be preferable to DXA; however, more study is necessary to validate prediction equations for specific populations [75, 77].

As stated previously, muscle mass is correlated with body size, so SMM or ASM can be adjusted for body size in different ways, i.e. using height squared ($ASM/height^2$),

weight (ASM/weight) or body mass index (ASM/BMI) [72]. The authors make no recommendation to adjust for body size, but adjustment can be made if data are available for a relevant normative population.

Although anthropometry is sometimes used to reflect nutritional status in older adults, it is not a good measure of muscle mass [78]. Calf circumference has been shown to predict performance and survival in older people (cut-off point <31 cm) [79]. As such, calf circumference measures may be used as a diagnostic proxy for older adults in settings where no other muscle mass diagnostic methods are available.

Physical performance Physical performance has been defined as an objectively measured whole-body function related to locomotion. This is a multidimensional concept that not only involves muscles but also central and peripheral nervous function, including balance [80]. Physical performance can be variously measured by gait speed, the Short Physical Performance Battery (SPPB), and the Timed-Up and Go test (TUG), among other tests. It is not always possible to use certain physical performance measures, such as when a patient's test performance is impaired by dementia, gait disorder or a balance disorder.

Gait speed is considered a quick, safe and highly reliable test for sarcopenia, and it is widely used in practice [81]. Gait speed has been shown to predict adverse outcomes related to sarcopenia—disability, cognitive impairment, need for institutionalisation, falls and mortality [82–85]. A commonly used gait speed test is called the 4-m usual walking speed test, with speed measured either manually with a stopwatch or instrumentally with an electronic device to measure gait timing [86, 87]. For simplicity, a single cut-off speed ≤0.8 m/s is advised by EWGSOP2 as an indicator of severe sarcopenia.

The SPPB is a composite test that includes assessment of gait speed, a balance test, and a chair stand test [88]. The maximum score is 12 points, and a score of ≤ 8 points indicates poor physical performance [1, 64].

The TUG evaluates physical function. For the TUG test, individuals are asked to rise from a standard chair, walk to a marker 3 m away, turn around, walk back and sit down again [89].

The 400-m walk test assesses walking ability and endurance. For this test, participants are asked to complete 20 laps of 20 m, each lap as fast as possible, and are allowed up to two rest stops during the test.

Each of these physical performance tests (gait speed, SPPB, TUG, 400-m walk) can be performed in most clinical settings. In terms of its convenience to use and ability to predict sarcopenia-related outcomes, gait speed is advised by EWGSOP2 for evaluation of physical performance [67]. The SPPB also predicts outcomes [90], but it is more often used in research than in clinical assessment because the battery of tests takes at least 10 min to administer. Likewise, the 400-m walk test predicts mortality but requires a corridor more than 20 m long to set up the testing course [91]. The TUG has also been found to predict mortality [92].

Alternative or new tests and tools

A variety of methods are being used or evaluated to determine the quantity and quality of muscle and impact of sarcopenia on the patient's QoL. These diagnostic measures are being tested for validity, reliability and accuracy and may play a relevant role in the future. For use in practice, tools need to be cost-effective, standardised and repeatable by practitioners in a variety of clinical settings and across different patient populations [78, 93].

Lumbar 3rd vertebra imaging by computed tomography

For patients with cancer, computed tomography (CT) has been used to image tumors and their response to treatment, and this technique has also been shown to give practical and precise measures of body composition. In particular, CT images of a specific lumbar vertebral landmark (L3) correlated significantly with whole-body muscle [94, 95]. As a result, this imaging method has been used to detect low muscle mass, even in patients with normal or high body weights, and it can also predict prognosis [96, 97]. L3-CT imaging is not limited to patients with cancer; this parameter has been used as a predictor of mortality and other outcomes in the intensive care unit [98] and in those patients affected by liver disease [99]. Quantification of lumbar L3 cross-sectional area has also been done by MRI [42].

With ever-increasing needs to quantify muscle and detect sarcopenia in early stages, high-resolution imaging is expected to be more widely used in the future—initially in research studies, and ultimately in clinical practice.

Mid-thigh muscle measurement

Mid-thigh imaging (by MRI or CT) has also been used in research studies, as it is a good predictor of whole-body skeletal muscle mass and very sensitive to change [50, 94, 96, 100]. Mid-thigh muscle area is more strongly correlated with total body muscle volume than are lumbar muscle areas L1–L5 [42].

Psoas muscle measurement with computed tomography

CT-based measurement of the psoas muscle has also been reported as simple and predictive of morbidities in certain conditions (cirrhosis, colorectal surgery) [101, 102]. However, because psoas is a minor muscle, other experts argue that it is not representative of overall sarcopenia [103, 104]. Further studies are needed to verify or reject use of this method.

Muscle quality measurement

Muscle quality is a relatively new term, referring both to micro- and macroscopic changes in muscle architecture and composition, and to muscle function delivered per unit of muscle mass [33]. Highly-sensitive imaging tools such as

MRI and CT have been used to assess muscle quality in research settings, e.g. by determining infiltration of fat into muscle and using the attenuation of the muscle [54, 93, 105].

Alternatively, the term muscle quality has been applied to ratios of muscle strength to appendicular skeletal muscle mass [106, 107] or muscle volume [108]. In addition, muscle quality has been assessed by BIA-derived phase angle measurement [93].

As yet, there is no universal consensus on assessment methods for routine clinical practice. In the future, assessments of muscle quality are expected to help guide treatment choices and monitor response to treatment.

Creatine dilution test

Creatine is produced by the liver and kidney and is also ingested from a diet rich in meat. Creatine is taken up by muscle cells, where a portion is irreversibly converted each day to phosphocreatine, a high-energy metabolite. Excess circulating creatine is changed to creatinine and excreted in urine. The excretion rate of creatinine is a promising proxy measure for estimating whole-body muscle mass.

For a creatine dilution test, an oral tracer dose of deuterium-labelled creatine (D_3-creatine) is ingested by a fasting patient; labelled and unlabelled creatine and creatinine in urine are later measured using liquid chromatography and tandem mass spectrometry [109]. Total body creatine pool size and muscle mass are calculated from D_3-creatinine enrichment in urine. Creatine dilution test results correlate well with MRI-based measures of muscle mass and modestly with measures from BIA and DXA [110, 111]. The creatine dilution test is mostly used in research at this time, so further refinement is needed to make this methodology practical for use in clinical settings.

Ultrasound assessment of muscle

Ultrasound is a widely used research technique to measure muscle quantity, to identify muscle wasting, and also as a measure of muscle quality. It is reliable and valid and is starting to be used at the bedside by trained clinicians. Ultrasound is accurate with good intra- and inter-observer reliability, even in older subjects [112]. Assessment of pennate muscles such as the quadriceps femoris can detect a decrease in muscle thickness and cross-sectional area within a relatively short period of time, thus suggesting potential for use of this tool in clinical practice, including use in the community [112, 113].

The use of ultrasound has recently been expanded in clinical practice to support the diagnosis of sarcopenia in older adults. The EuGMS sarcopenia group recently proposed a consensus protocol for using ultrasound in muscle assessment, including measurement of muscle thickness, cross-sectional area, fascicle length, pennation angle and echogenicity [114]. Echogenicity reflects muscle quality, since non-contractile tissue associated with myosteatosis shows hyper-echogenicity [115, 116]. Thus, ultrasound has

the advantage of being able to assess both muscle quantity and quality.

A systematic review on the use of ultrasound to assess muscle in this population concluded that the tool was reliable and valid for the assessment of muscle size in older adults, including those with comorbid conditions such as coronary artery disease, stroke, and chronic obstructive pulmonary disease [117]. Ultrasound was shown to have good validity to estimate muscle mass as compared to DXA, MRI and CT. While data are available for older adults, more research is needed to validate prediction equations for those with varying health conditions and functional status [116–119].

Specific biomarkers or panels of biomarkers

The development and validation of a single biomarker might be an easy and cost-effective way to diagnose and monitor people with sarcopenia. Potential biomarkers could include markers of the neuromuscular junction, muscle protein turnover, behaviour-mediated pathways, inflammation-mediated pathways, redox-related factors and hormones or other anabolic factors [120]. However, because of the complex pathophysiology of sarcopenia, it is unlikely that there will be a single biomarker that can identify the condition in the heterogeneous population of young and old people [78]. The development of a panel of biomarkers must instead be considered, including potential serum markers and tissue markers [120, 121]. The implementation of a multidimensional methodology for the modelling of these pathways could provide a way to stratify risk for sarcopenia, facilitate the identification of a worsening condition and provide monitoring of treatment effectiveness [121].

SarQoL questionnaire

From a patient's perspective, it is important to have sarcopenia treatment plans that address QoL issues. To this end, the SarQoL tool is a self-administered questionnaire for people with sarcopenia [16, 122–124]. SarQoL identifies and predicts sarcopenia complications that may later impact the patient's quality of life. SarQoL assists the healthcare provider in assessing a patient's perception of his or her physical, psychological and social aspects of health. The SarQoL tool has been validated as consistent and reliable, and it can be used in clinical care and in research studies [16]. The sensitivity of SarQoL to patient status changes over time needs validation in longitudinal studies. Once validated, SarQoL may serve as a proxy measure of treatment efficacy. To facilitate widespread use of the SarQoL tool, it has been translated into multiple languages.

Defining cut-off points for sarcopenia tests

Cut-off points depend on the measurement technique and on the availability of reference studies and populations. The original EWGSOP consensus paper did not advise specific cut-off points, and disputes over cut-off points have

hampered research and development in the field due to lack of study consistency. More recently, the Asian Working Group on Sarcopenia developed an EWGSOP-based consensus that specified cut-off points for diagnostic variables [4]. The cut-off points in the Asian consensus proved to be very useful for implementation of recommended sarcopenia care. Thus, EWGSOP2 has opted to provide recommendations for cut-off points for different parameters to increase harmonisation of sarcopenia studies (Table 3).

The current EWGSOP recommendations focus on European populations and use of normative references (healthy young adults) [26] whenever possible, with cut-off points usually set at −2 standard deviations compared to the mean reference value. In specific circumstances, we advise use of −2.5 standard deviations for more conservative diagnosis [26]. For measures such as gait speed and strength, results depend upon stature, so we recommend use of regional normative populations when available. For EWGSOP2 cut-off points, we opted to use round figures, with the confidence that the minor reduction in accuracy will be overcome by ease of use.

Practical algorithm: sarcopenia case-finding, diagnosis and severity

Here, EWGSOP2 updates its algorithm for sarcopenia case-finding, diagnosis and severity determination. The reasoning for this update is logical and practical—to make the algorithm consistent with our 2018 updated sarcopenia definition, and to make it straightforward in order to foster its use in clinical settings. Specifically, we recommend a pathway of Find-Assess-Confirm-Severity (F-A-C-S; Figure 1) for use across clinical practices and in research studies.

In clinical practice, EWGSOP2 advises use of the SARC-F questionnaire to find individuals with probable sarcopenia. We advise use of grip strength and chair stand measures to identify low muscle strength. To generate evidence that confirms muscle of low quantity or quality, we recommend evaluation of muscle by DXA and BIA methods in usual clinical care, and by DXA, MRI or CT in research and in specialty care for individuals at high risk of adverse outcomes. We advise measures of physical performance (SPPB, TUG and 400-m walk tests) to assess severity of sarcopenia.

Sarcopenia development

Time course

Muscle mass and strength vary across a lifetime—generally increasing with growth in youth and young adulthood, being maintained in midlife and then decreasing with ageing. In young adulthood (up to ~40 years of age), maximal levels, which are higher in men than in women, are reached (Figure 2) [26]. Beyond the age of 50 years, loss of leg muscle mass (1–2% per year) and loss of strength (1.5–5% per year) have been reported [129].

Interestingly, there is a positive association between birth weight and muscle strength, which is maintained across the life course [130]. In the initial stages of sarcopenia development, an individual may be above the threshold of low physical performance and is very likely to be above the threshold of disability. While genetic and lifestyle factors can hasten muscle weakening and progression toward functional impairment and disability, interventions including nutrition and exercise training seem to slow or reverse these processes [131]. Therefore, to prevent or delay sarcopenia, the aim is to maximise muscle in youth and young adulthood, maintain muscle in middle age and minimise loss in older age (Figure 3) [25].

Categories of sarcopenia and sarcopenia-like conditions

Primary and secondary sarcopenia

In some individuals, sarcopenia is largely attributable to ageing; in many cases, other causes can be identified. Thus, the categories of primary sarcopenia and secondary sarcopenia may be useful in clinical practice (Figure 4) [1]. Sarcopenia is considered 'primary' (or age-related) when no other specific cause is evident, while sarcopenia is considered 'secondary' when causal factors other than (or in addition to) ageing are evident. Sarcopenia can occur secondary to a systemic disease, especially one that may invoke inflammatory processes, e.g. malignancy or organ failure. Physical inactivity also contributes to development of sarcopenia, whether due to a sedentary lifestyle or to disease-related immobility or disability [132]. Further, sarcopenia can develop as a result of inadequate intake of energy or protein, which may be due to anorexia, malabsorption, limited access to healthy foods or limited ability to eat.

Acute and chronic sarcopenia

EWGSOP2 newly identifies subcategories of sarcopenia as acute and chronic. Sarcopenia that has lasted less than 6 months is considered an acute condition, while sarcopenia lasting ≥6 months is considered a chronic condition. Acute sarcopenia is usually related to an acute illness or injury, while chronic sarcopenia is likely to be associated with chronic and progressive conditions and increases the risk of mortality. This distinction is intended to underscore the need to conduct periodic sarcopenia assessments in individuals who may be at risk for sarcopenia in order to determine how quickly the condition is developing or worsening. Such observations are expected to facilitate early intervention with treatments that can help prevent or delay sarcopenia progression and poor outcomes.

Sarcopenic obesity

Sarcopenic obesity is a condition of reduced lean body mass in the context of excess adiposity [133]. Sarcopenic obesity is most often reported in older people, as both risk and prevalence increase with age [134]. Obesity exacerbates sarcopenia, increases the infiltration of fat into muscle, lowers physical function and increases risk of mortality [135–138].

Table 3. EWGSOP2 sarcopenia cut-off points

Test	Cut-off points for men	Cut-off points for women	References
EWGSOP2 sarcopenia cut-off points for low strength by chair stand and grip strength			
Grip strength	**<27 kg**	**<16 kg**	Dodds (2014) [26]
Chair stand	**>15 s for five rises**		Cesari (2009) [67]
EWGSOP2 sarcopenia cut-off points for low muscle quantity			
ASM	**<20 kg**	**<15 kg**	Studenski (2014) [3]
ASM/height^2	**<7.0 kg/m^2**	**<6.0 kg/m^2**	Gould (2014) [125]
EWGSOP2 sarcopenia cut-off points for low performance			
Gait speed	**≤0.8 m/s**		Cruz-Jentoft (2010) [1]
			Studenski (2011) [84]
SPPB	**≤8 point score**		Pavasini (2016) [90]
			Guralnik (1995) [126]
TUG	**≥20 s**		Bischoff (2003) [127]
400 m walk test	**Non-completion or ≥6 min for completion**		Newman (2006) [128]
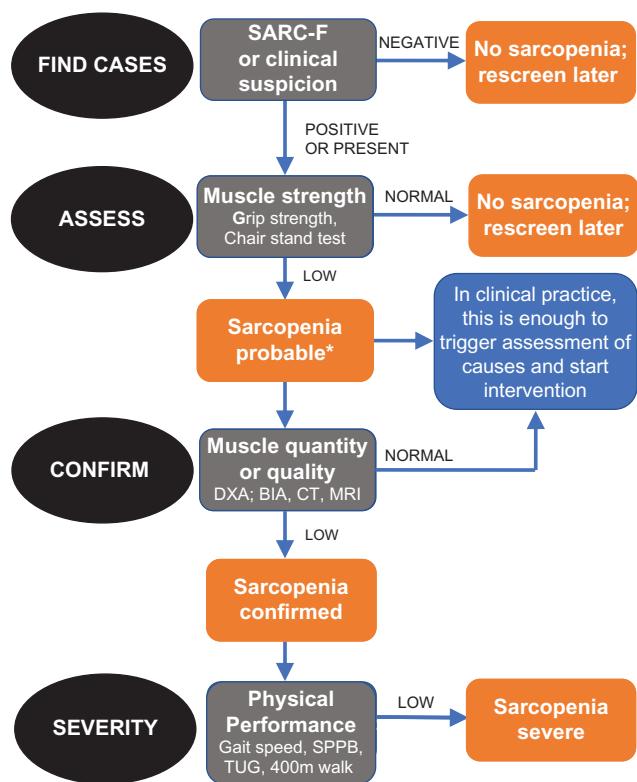
Figure 1. Sarcopenia: EWGSOP2 algorithm for case-finding, making a diagnosis and quantifying severity in practice. The steps of the pathway are represented as Find-Assess-Confirm-Severity or F-A-C-S. *Consider other reasons for low muscle strength (e.g. depression, sroke, balance disorders, peripheral vascular disorders).

Sarcopenic obesity is a distinct condition, and there are ongoing initiatives to improve its definition. Sarcopenic obesity is therefore outside of the scope of this article.

Frailty

Frailty is a multidimensional geriatric syndrome that is characterised by cumulative decline in multiple body systems or functions [139, 140], with pathogenesis involving physical as well as social dimensions [141]. Frailty increases vulnerability to poor health outcomes such as disability, hospital admission, reduced quality of life and even death [141, 142].

The physical phenotype of frailty, described by Fried and co-workers [143], shows significant overlap with sarcopenia; low grip strength and slow gait speed are characteristic of both. Weight loss, another diagnostic criterion for frailty, is also a major etiologic factor for sarcopenia. Treatment options for physical frailty and for sarcopenia likewise overlap—provision of optimal protein intake, supplementation of vitamin D, and physical exercise [19, 144, 145].

Taken together, frailty and sarcopenia are still distinct—one a geriatric syndrome and the other a disease. While sarcopenia is a contributor to the development of physical frailty, the syndrome of frailty represents a much broader concept. Frailty is seen as the decline over a lifetime in multiple physiological systems, resulting in negative consequences to physical, cognitive, and social dimensions. Frailty's diagnostic tools reflect these multiple dimensions, e.g. the Groningen Frailty Indicator, the Frailty Index of Rockwood *et al.* and others [146–149].

Malnutrition-associated sarcopenia

The sarcopenia phenotype is also associated with malnutrition, regardless of whether the malnourished condition is rooted in low dietary intake (starvation, inability to eat), reduced nutrient bioavailability (e.g. with diarrhea, vomiting) or high nutrient requirements (e.g. with inflammatory diseases such as cancer or organ failure with cachexia) [150, 151]. Low muscle mass has recently been proposed as part of the definition of malnutrition [152]. Also in malnutrition, low fat mass is usually present, which is not necessarily the case in sarcopenia [151, 152].

Looking ahead: gaps in sarcopenia research

There are still many gaps in our knowledge about sarcopenia—its initiation and progression, diagnostic tools and cut-off points, and outcomes.
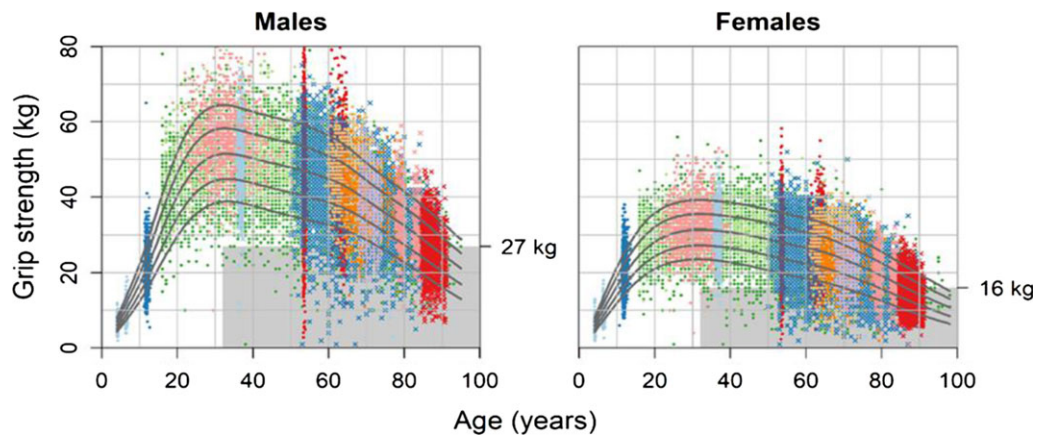
9

Figure 2. Normative data for grip strength across the life course in men and women in the UK (Dodds RM, *et al.* PLoS One. 2014;9:e113637). Centiles shown are 10th, 25th, 50th, 75th and 90th. Cut-off points based on *T*-score of ≤ -2.5 are shown for males and females (≤27 kg and 16 kg, respectively). Color-coding represents different birth cohorts used for the study (Figure adapted with permission from R Dodds and PLOS One).
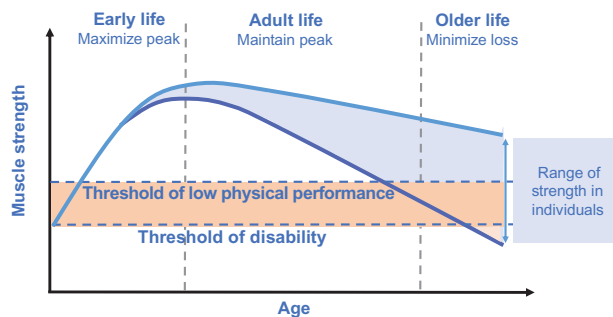

Figure 3. Muscle strength and the life course. To prevent or delay sarcopenia development, maximise muscle in youth and young adulthood, maintain muscle in middle age and minimise loss in older age
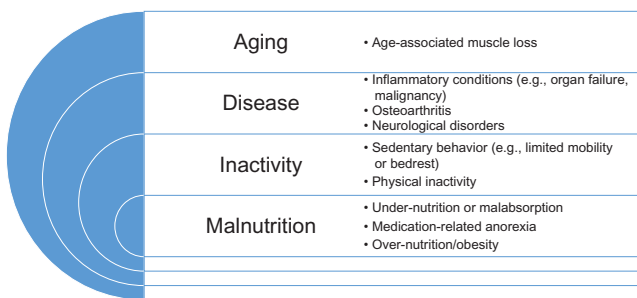
Figure 4. Factors that cause and worsen muscle quantity and quality, sarcopenia, are categorised as primary (ageing) and secondary (disease, inactivity, and poor nutrition). Because a wide range of factors contribute to sarcopenia development, numerous muscle changes seem possible when these multiple factors interact.

Some suggested areas for further study are listed below.

• What are the influences operating to cause and worsen sarcopenia, and what are the opportunities for intervention across the life course?

• How can we identify older persons at high risk of sarcopenia, and what preventive actions are preferred?
• For sarcopenia diagnosis, some cut-off points are arbitrary at this time; the development of validated cut-off points will depend on normative data and their predictive value for hard end-points—a high priority for research studies.
• For stature-dependent measures of sarcopenia and its risk (gait speed, muscle strength), studies are needed to establish if gender-specific and region-specific threshold values for sarcopenia diagnosis improve prediction of outcomes.
• What muscle quality indicators best predict outcomes? How can we best assess muscle quality? What tools and measurements are accurate and affordable?
• What are the kinetics of muscle loss in different people and circumstances, as detected by multiple measurements? What are differences in causes and consequences of gradual versus rapid loss?
• What outcomes are best used as sensitive measures of response to sarcopenia treatments?

Summary and call-to-action

Sarcopenia, i.e. muscle failure, is a muscle disease rooted in adverse muscle changes that accrue across a lifetime; sarcopenia is common among adults of older age but can also occur earlier in life. Sarcopenia is defined by low levels of measures for three parameters: (1) muscle strength, (2) muscle quantity/quality and (3) physical performance as an indicator of severity.

Although research findings over the last decade have answered many questions, other findings raised more areas for researchers to address in the future. Thus, a clear definition of sarcopenia, as well as clear diagnostic criteria, are necessary to guide both clinical practice and research design for the future.

> **For screening and diagnosis of sarcopenia, EWGSOP recommends following the pathway: Find cases-Assess-Confirm-Severity (F-A-C-S).**
>
> **Find-cases:** To identify individuals at risk for sarcopenia, EWGSOP advises use of the SARC-F questionnaire or clinical suspicion to find sarcopenia-associated symptoms.
>
> **Assess:** To assess for evidence of sarcopenia, EWGSOP recommends use of grip strength or a chair stand measure with specific cut-off-points for each test. For special cases and for research studies, other methods for measurement of strength (knee flexion/extension) can be used.
>
> **Confirm:** To confirm sarcopenia by detection of low muscle quantity and quality, DXA is advised in clinical practice, and DXA, BIA, CT or MRI in research studies.
>
> Determine **Severity**: Severity can be evaluated by performance measures; gait speed, SPPB, TUG and 400-m walk tests can be used.

EWGSOP2's updated recommendations aim to increase awareness of sarcopenia and its risk. With these new recommendations, EWGSOP2 calls for healthcare professionals who treat patients at risk for sarcopenia to take actions that will promote early detection and treatment. We also encourage more research in the field of sarcopenia in order to prevent or delay adverse outcomes that also incur a heavy burden for patients and healthcare systems.

Key points

- In the updated definition of sarcopenia, EWGSOP2 elevates low strength to the forefront as a primary indicator of probable sarcopenia.
- Sarcopenia is now defined as a muscle disease that may be acute or chronic.
- We recommend an algorithm for case-finding, diagnosis, and severity determination for systematic and consistent identification of people with sarcopenia or its risk.
- We recommend simple, specific cut-off points for measures that identify and characterize sarcopenia.
- These new recommendations are aimed at facilitating early detection and better treatment of sarcopenia in clinical practice.

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References

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM *et al*. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing 2010; 39: 412–23.
2. Morley JE, Abbatecola AM, Argiles JM *et al*. Sarcopenia with limited mobility: an international consensus. J Am Med Dir Assoc 2011; 12: 403–9.
3. Studenski SA, Peters KW, Alley DE *et al*. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 2014; 69: 547–58.
4. Chen LK, Liu LK, Woo J *et al*. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc 2014; 15: 95–101.
5. Argiles JM, Campos N, Lopez-Pedrosa JM *et al*. Skeletal muscle regulates metabolism via interorgan crosstalk: roles in health and disease. J Am Med Dir Assoc 2016; 17: 789–96.
6. Frontera WR, Ochala J. Skeletal muscle: a brief review of structure and function. Calcif Tissue Int 2015; 96: 183–95.
7. http://www.icd10data.com/ICD10CM/Codes/M00-M99/M60-M63/M62-/M62.84. *2018 ICD-10-CM Diagnosis Code M62.84*. 2018. [cited 2018 March 12].
8. Vellas B, Fielding RA, Bens C *et al*. Implications of ICD-10 for sarcopenia clinical practice and clinical trials: report by the International Conference on Frailty and Sarcopenia Research Task Force. J Frailty Aging 2018; 7: 2–9.
9. Mijnarends DM, Luiking YC, Halfens RJG *et al*. Muscle, health and costs: a glance at their relationship. J Nutr Health Aging 2018; 22: 766–73.
10. Bischoff-Ferrari HA, Orav JE, Kanis JA *et al*. Comparative performance of current definitions of sarcopenia against the prospective incidence of falls among community-dwelling seniors age 65 and older. Osteoporos Int 2015; 26: 2793–802.
11. Schaap LA, van Schoor NM, Lips P *et al*. Associations of sarcopenia definitions, and their components, with the incidence of recurrent falling and fractures: the longitudinal aging study Amsterdam. J Gerontol A Biol Sci Med Sci 2018; 73: 1199–204.
12. Malmstrom TK, Miller DK, Simonsick EM *et al*. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle 2016; 7: 28–36.
13. Bahat G, Ilhan B. Sarcopenia and the cardiometabolic syndrome: a narrative review. Eur Geriatr Med 2016; 6: 220–23.
14. Bone AE, Hepgul N, Kon S *et al*. Sarcopenia and frailty in chronic respiratory disease. Chron Respir Dis 2017; 14: 85–99.
15. Chang KV, Hsu TH, Wu WT *et al*. Association between sarcopenia and cognitive impairment: a systematic review and meta-analysis. J Am Med Dir Assoc 2016; 17: 1164.e7–64.e15.
16. Beaudart C, Biver E, Reginster JY *et al*. Validation of the SarQoL(R), a specific health-related quality of life questionnaire for Sarcopenia. J Cachexia Sarcopenia Muscle 2017; 8: 238–44.
17. Dos Santos L, Cyrino ES, Antunes M *et al*. Sarcopenia and physical independence in older adults: the independent and synergic role of muscle mass and muscle function. J Cachexia Sarcopenia Muscle 2017; 8: 245–50.
18. Akune T, Muraki S, Oka H *et al*. Incidence of certified need of care in the long-term care insurance system and its risk factors in the elderly of Japanese population-based cohorts: the ROAD study. Geriatr Gerontol Int 2014; 14: 695–701.
19. Steffl M, Bohannon RW, Sontakova L *et al*. Relationship between sarcopenia and physical activity in older people: a systematic review and meta-analysis. Clin Interv Aging 2017; 12: 835–45.
20. De Buyser SL, Petrovic M, Taes YE *et al*. Validation of the FNIH sarcopenia criteria and SOF frailty index as predictors of long-term mortality in ambulatory older men. Age Ageing 2016; 45: 602–8.
21. Cawthon PM, Lui LY, Taylor BC *et al*. Clinical definitions of sarcopenia and risk of hospitalization in community-dwelling older men: the osteoporotic fractures in men study. J Gerontol A Biol Sci Med Sci 2017; 72: 1383–89.
22. Antunes AC, Araujo DA, Verissimo MT *et al*. Sarcopenia and hospitalisation costs in older adults: a cross-sectional study. Nutr Diet 2017; 74: 46–50.
23. Steffl M, Sima J, Shiells K *et al*. The increase in health care costs associated with muscle weakness in older people without long-term illnesses in the Czech Republic: results from the Survey of Health, Ageing and Retirement in Europe (SHARE). Clin Interv Aging 2017; 12: 2003–07.
24. Sousa AS, Guerra RS, Fonseca I *et al*. Financial impact of sarcopenia on hospitalization costs. Eur J Clin Nutr 2016; 70: 1046–51.
25. Sayer AA, Syddall H, Martin H *et al*. The developmental origins of sarcopenia. J Nutr Health Aging 2008; 12: 427–32.

26. Dodds RM, Syddall HE, Cooper R et al. Grip strength across the life course: normative data from twelve British studies. PLoS One 2014; 9: e113637.

27. Sayer AA, Syddall HE, Gilbody HJ et al. Does sarcopenia originate in early life? Findings from the Hertfordshire cohort study. J Gerontol A Biol Sci Med Sci 2004; 59: M930–4.

28. Ibrahim K, May C, Patel HP et al. A feasibility study of implementing grip strength measurement into routine hospital practice (GRImP): study protocol. Pilot Feasibility Stud 2016; 2: 27.

29. Leong DP, Teo KK, Rangarajan S et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. Lancet 2015; 386: 266–73.

30. Alley DE, Shardell MD, Peters KW et al. Grip strength cut-points for the identification of clinically relevant weakness. J Gerontol A Biol Sci Med Sci 2014; 69: 559–66.

31. Buckinx F, Landi F, Cesari M et al. Pitfalls in the measurement of muscle mass: a need for a reference standard. J Cachexia Sarcopenia Muscle 2018; 9: 269–78.

32. Masanes F, Rojano ILX, Salva A et al. Cut-off points for muscle mass—not grip strength or gait speed—determine variations in sarcopenia prevalence. J Nutr Health Aging 2017; 21: 825–29.

33. McGregor RA, Cameron-Smith D, Poppitt SD. It is not just muscle mass: a review of muscle quality, composition and metabolism during ageing as determinants of muscle function and mobility in later life. Longev Healthspan 2014; 3: 9.

34. Trevino-Aguirre E, Lopez-Teros T, Gutierrez-Robledo L et al. Availability and use of dual energy X-ray absorptiometry (DXA) and bio-impedance analysis (BIA) for the evaluation of sarcopenia by Belgian and Latin American geriatricians. J Cachexia Sarcopenia Muscle 2014; 5: 79–81.

35. Keller K. Sarcopenia. Wien Med Wochenschr 2018. doi: 10.1007/s10354-018-0618-2 [Epub ahead of print].

36. Han A, Bokshan SL, Marcaccio SE et al. Diagnostic criteria and clinical outcomes in sarcopenia research: a literature review. J Clin Med 2018; 7. doi: 10.3390/jcm7040070.

37. Schaap LA, Koster A, Visser M. Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. Epidemiol Rev 2013; 35: 51–65.

38. Reginster JY, Cooper C, Rizzoli R et al. Recommendations for the conduct of clinical trials for drugs to treat or prevent sarcopenia. Aging Clin Exp Res 2016; 28: 47–58.

39. Mijnarends DM, Meijers JM, Halfens RJ et al. Validity and reliability of tools to measure muscle mass, strength, and physical performance in community-dwelling older people: a systematic review. J Am Med Dir Assoc 2013; 14: 170–8.

40. Ishii S, Tanaka T, Shibasaki K et al. Development of a simple screening test for sarcopenia in older adults. Geriatr Gerontol Int 2014; 14(Suppl 1): 93–101.

41. Roberts HC, Denison HJ, Martin HJ et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 2011; 40: 423–9.

42. Schweitzer L, Geisler C, Pourhassan M et al. What is the best reference site for a single MRI slice to assess whole-body skeletal muscle and adipose tissue volumes in healthy adults? Am J Clin Nutr 2015; 102: 58–65.

43. Mitsiopoulos N, Baumgartner RN, Heymsfield SB et al. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol (1985) 1998; 85: 115–22.

44. Shen W, Punyanitya M, Wang Z et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. J Appl Physiol (1985) 2004; 97: 2333–8.

45. Sergi G, De Rui M, Stubbs B et al. Measurement of lean body mass using bioelectrical impedance analysis: a consideration of the pros and cons. Aging Clin Exp Res 2017; 29: 591–97.

46. Maden-Wilkinson TM, Degens H, Jones DA et al. Comparison of MRI and DXA to measure muscle size and age-related atrophy in thigh muscles. J Musculoskelet Neuronal Interact 2013; 13: 320–8.

47. Heymsfield SB, Smith R, Aulet M et al. Appendicular skeletal muscle mass: measurement by dual-photon absorptiometry. Am J Clin Nutr 1990; 52: 214–8.

48. Kim J, Wang Z, Heymsfield SB et al. Total-body skeletal muscle mass: estimation by a new dual-energy X-ray absorptiometry method. Am J Clin Nutr 2002; 76: 378–83.

49. Yamada Y, Nishizawa M, Uchiyama T et al. Developing and validating an age-independent equation using multi-frequency bioelectrical impedance analysis for estimation of appendicular skeletal muscle mass and establishing a cutoff for sarcopenia. Int J Environ Res Public Health 2017; 14. doi: 10.3390/ijerph14070809.

50. Lee SJ, Janssen I, Heymsfield SB et al. Relation between whole-body and regional measures of human skeletal muscle. Am J Clin Nutr 2004; 80: 1215–21.

51. van der Werf A, Langius JAE, de van der Schueren MAE et al. Percentiles for skeletal muscle index, area and radiation attenuation based on computed tomography imaging in a healthy Caucasian population. Eur J Clin Nutr 2018; 72: 288–96.

52. Derstine BA, Holcombe SA, Ross BE et al. Skeletal muscle cutoff values for sarcopenia diagnosis using T10 to L5 measurements in a healthy US population. Sci Rep 2018; 8: 11369.

53. Goodpaster BH, Kelley DE, Thaete FL et al. Skeletal muscle attenuation determined by computed tomography is associated with skeletal muscle lipid content. J Appl Physiol (1985) 2000; 89: 104–10.

54. Reinders I, Murphy RA, Brouwer IA et al. Muscle quality and myosteatosis: novel associations with mortality risk: the Age, Gene/Environment Susceptibility (AGES)-Reykjavik study. Am J Epidemiol 2016; 183: 53–60.

55. Grimm A, Meyer H, Nickel MD et al. Evaluation of 2-point, 3-point, and 6-point Dixon magnetic resonance imaging with flexible echo timing for muscle fat quantification. Eur J Radiol 2018; 103: 57–64.

56. Distefano G, Standley RA, Zhang X et al. Physical activity unveils the relationship between mitochondrial energetics, muscle quality, and physical function in older adults. J Cachexia Sarcopenia Muscle 2018; 9: 279–94.

57. Ruan XY, Gallagher D, Harris T et al. Estimating whole body intermuscular adipose tissue from single cross-sectional magnetic resonance images. J Appl Physiol (1985) 2007; 102: 748–54.

58. Woo J, Leung J, Morley JE. Defining sarcopenia in terms of incident adverse outcomes. J Am Med Dir Assoc 2015; 16: 247–52.

59. Bahat G, Yilmazi O, Kilic C et al. Performance of SARC-F in regard to sarcopenia definitions, muscle mass and functional measures. J Nutr Health Aging 2018. doi:10.1007/s12603-018-1067-8; Epub ahead of print.

60. Bahat G, Yilmaz O, Oren M *et al*. Cross-cultural adaptation and validation of the SARC-F to assess sarcopenia: methodological report from European Union Geriatric Medicine Society Sarcopenia Special Interest Group. Eur Geriatr Med 2018; 9: 23–8.

61. Locquet M, Beaudart C, Reginster JY *et al*. Comparison of the performance of five screening methods for sarcopenia. Clin Epidemiol 2018; 10: 71–82.

62. Rossi AP, Fantin F, Micciolo R *et al*. Identifying sarcopenia in acute care setting patients. J Am Med Dir Assoc 2014; 15: 303.e7–12.

63. Steiber N. Strong or weak handgrip? Normative reference values for the German population across the life course stratified by sex, age, and body height. PLoS One 2016; 11: e0163917.

64. Beaudart C, McCloskey E, Bruyere O *et al*. Sarcopenia in daily practice: assessment and management. BMC Geriatr 2016; 16: 170.

65. Sipers WM, Verdijk LB, Sipers SJ *et al*. The Martin vigorimeter represents a reliable and more practical tool than the Jamar dynamometer to assess handgrip strength in the geriatric patient. J Am Med Dir Assoc 2016; 17: 466.e1–7.

66. Francis P, Toomey C, Mc Cormack W *et al*. Measurement of maximal isometric torque and muscle quality of the knee extensors and flexors in healthy 50- to 70-year-old women. Clin Physiol Funct Imaging 2017; 37: 448–55.

67. Cesari M, Kritchevsky SB, Newman AB *et al*. Added value of physical performance measures in predicting adverse health-related events: results from the Health, Aging And Body Composition Study. J Am Geriatr Soc 2009; 57: 251–9.

68. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. Res Q Exerc Sport 1999; 70: 113–9.

69. Cooper C, Fielding R, Visser M *et al*. Tools in the assessment of sarcopenia. Calcif Tissue Int 2013; 93: 201–10.

70. Cawthon PM, Peters KW, Shardell MD *et al*. Cutpoints for low appendicular lean mass that identify older adults with clinically significant weakness. J Gerontol A Biol Sci Med Sci 2014; 69: 567–75.

71. Hull H, He Q, Thornton J *et al*. iDXA, Prodigy, and DPXL dual-energy X-ray absorptiometry whole-body scans: a cross-calibration study. J Clin Densitom 2009; 12: 95–102.

72. Kim KM, Jang HC, Lim S. Differences among skeletal muscle mass indices derived from height-, weight-, and body mass index-adjusted models in assessing sarcopenia. Korean J Intern Med 2016; 31: 643–50.

73. Kyle UG, Genton L, Hans D *et al*. Validation of a bioelectrical impedance analysis equation to predict appendicular skeletal muscle mass (ASMM). Clin Nutr 2003; 22: 537–43.

74. Sergi G, De Rui M, Veronese N *et al*. Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults. Clin Nutr 2015; 34: 667–73.

75. Gonzalez MC, Heymsfield SB. Bioelectrical impedance analysis for diagnosing sarcopenia and cachexia: what are we really estimating? J Cachexia Sarcopenia Muscle 2017; 8: 187–89.

76. Yu SC, Powell A, Khow KS *et al*. The performance of five bioelectrical impedance analysis prediction equations against dual X-ray absorptiometry in estimating appendicular skeletal muscle mass in an Adult Australian Population. Nutrients 2016; 8: 189.

77. Reiss J, Iglseder B, Kreutzer M *et al*. Case finding for sarcopenia in geriatric inpatients: performance of bioimpedance analysis in comparison to dual X-ray absorptiometry. BMC Geriatr 2016; 16: 52.

78. Tosato M, Marzetti E, Cesari M *et al*. Measurement of muscle mass in sarcopenia: from imaging to biochemical markers. Aging Clin Exp Res 2017; 29: 19–27.

79. Landi F, Onder G, Russo A *et al*. Calf circumference, frailty and physical performance among older adults living in the community. Clin Nutr 2014; 33: 539–44.

80. Beaudart C, Rolland Y, Cruz-Jentoft A *et al*. Assessment of muscle function and physical performance in daily clinical practice. Submitted 2018.

81. Bruyere O, Beaudart C, Reginster J-V *et al*. Assessment of muscle mass, muscle strength and physical performance in clinical practice: an international survey. Eur Geriatr Med 2016; 7: 243–46.

82. Abellan van Kan G, Rolland Y, Andrieu S *et al*. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. J Nutr Health Aging 2009; 13: 881–9.

83. Peel NM, Kuys SS, Klein K. Gait speed as a measure in geriatric assessment in clinical settings: a systematic review. J Gerontol A Biol Sci Med Sci 2013; 68: 39–46.

84. Studenski S, Perera S, Patel K *et al*. Gait speed and survival in older adults. JAMA 2011; 305: 50–8.

85. Guralnik JM, Ferrucci L, Pieper CF *et al*. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000; 55: M221–31.

86. Maggio M, Ceda GP, Ticinesi A *et al*. Instrumental and non-instrumental evaluation of 4-meter walking speed in older individuals. PLoS One 2016; 11: e0153583.

87. Rydwik E, Bergland A, Forsen L *et al*. Investigation into the reliability and validity of the measurement of elderly people's clinical walking speed: a systematic review. Physiother Theory Pract 2012; 28: 238–56.

88. https://www.nia.nih.gov/research/labs/leps/short-physical-performance-battery-sppb. *Short Physical Performance Battery*. [cited 2018 March 19].

89. Podsiadlo D, Richardson S. The timed 'Up & Go': a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991; 39: 142–8.

90. Pavasini R, Guralnik J, Brown JC *et al*. Short physical performance battery and all-cause mortality: systematic review and meta-analysis. BMC Med 2016; 14: 215.

91. Vestergaard S, Patel KV, Bandinelli S *et al*. Characteristics of 400-meter walk test performance and subsequent mortality in older adults. Rejuvenation Res 2009; 12: 177–84.

92. Bergland A, Jorgensen L, Emaus N *et al*. Mobility as a predictor of all-cause mortality in older men and women: 11.8 year follow-up in the Tromso study. BMC Health Serv Res 2017; 17: 22.

93. Heymsfield SB, Gonzalez MC, Lu J *et al*. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. Proc Nutr Soc 2015; 74: 355–66.

94. Mourtzakis M, Prado CM, Lieffers JR *et al*. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 2008; 33: 997–1006.

95. Fearon K, Strasser F, Anker SD *et al.* Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011; 12: 489–95.

96. Kim EY, Kim YS, Park I *et al.* Prognostic significance of CT-determined sarcopenia in patients with small-cell lung cancer. J Thorac Oncol 2015; 10: 1795–9.

97. Baracos V, Kazemi-Bajestani SM. Clinical outcomes related to muscle mass in humans with cancer and catabolic illnesses. Int J Biochem Cell Biol 2013; 45: 2302–8.

98. Moisey LL, Mourtzakis M, Cotton BA *et al.* Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. Crit Care 2013; 17: R206.

99. Montano-Loza AJ, Meza-Junco J, Baracos VE *et al.* Severe muscle depletion predicts postoperative length of stay but is not associated with survival after liver transplantation. Liver Transpl 2014; 20: 640–8.

100. Baracos VE, Reiman T, Mourtzakis M *et al.* Body composition in patients with non-small cell lung cancer: a contemporary view of cancer cachexia with the use of computed tomography image analysis. Am J Clin Nutr 2010; 91: 1133S–37S.

101. Gu DH, Kim MY, Seo YS *et al.* Clinical usefulness of psoas muscle thickness for the diagnosis of sarcopenia in patients with liver cirrhosis. Clin Mol Hepatol 2018; 24: 319–30.

102. Hanaoka M, Yasuno M, Ishiguro M *et al.* Morphologic change of the psoas muscle as a surrogate marker of sarcopenia and predictor of complications after colorectal cancer surgery. Int J Colorectal Dis 2017; 32: 847–56.

103. Baracos VE. Psoas as a sentinel muscle for sarcopenia: a flawed premise. J Cachexia Sarcopenia Muscle 2017; 8: 527–28.

104. Rutten IJG, Ubachs J, Kruitwagen R *et al.* Psoas muscle area is not representative of total skeletal muscle area in the assessment of sarcopenia in ovarian cancer. J Cachexia Sarcopenia Muscle 2017; 8: 630–38.

105. Hamaguchi Y, Kaido T, Okumura S *et al.* Impact of skeletal muscle mass index, intramuscular adipose tissue content, and visceral to subcutaneous adipose tissue area ratio on early mortality of living donor liver transplantation. Transplantation 2017; 101: 565–74.

106. Lynch NA, Metter EJ, Lindle RS *et al.* Muscle quality. I. Age-associated differences between arm and leg muscle groups. J Appl Physiol (1985) 1999; 86: 188–94.

107. Rolland Y, Lauwers-Cances V, Pahor M *et al.* Muscle strength in obese elderly women: effect of recreational physical activity in a cross-sectional study. Am J Clin Nutr 2004; 79: 552–7.

108. Tracy BL, Ivey FM, Hurlbut D *et al.* Muscle quality. II. Effects Of strength training in 65- to 75-yr-old men and women. J Appl Physiol (1985) 1999; 86: 195–201.

109. Shankaran M, Czerwieniec G, Fessler C *et al.* Dilution of oral D3-creatine to measure creatine pool size and estimate skeletal muscle mass: development of a correction algorithm. J Cachexia Sarcopenia Muscle 2018; 9: 540–46.

110. Clark RV, Walker AC, Miller RR *et al.* Creatine (methyl-d3) dilution in urine for estimation of total body skeletal muscle mass: accuracy and variability vs. MRI and DXA. J Appl Physiol 2018; 124: 1–9.

111. Buehring B, Siglinsky E, Krueger D *et al.* Comparison of muscle/lean mass measurement methods: correlation with functional and biochemical testing. Osteoporos Int 2018; 29: 675–83.

112. Galindo Martin CA, Monares Zepeda E, Lescas Mendez OA. Bedside ultrasound measurement of rectus femoris: a tutorial for the nutrition support clinician. J Nutr Metab 2017; 2017: 2767232.

113. Ticinesi A, Narici MV, Lauretani F *et al.* Assessing sarcopenia with vastus lateralis muscle ultrasound: an operative protocol. Aging Clin Exp Res 2018. doi: 10.1007/s40520-018-0958-1 [Epub ahead of print].

114. SARCUS working group on behalf of the Sarcopenia Special Interest Group of the European Geriatric Medicine Society. Perkisas S, Baudry S *et al.* Application of ultrasound for muscle assessment in sarcopenia: towards standardized measurements. Eur J Med 2018. In press. doi: 10.1007/s41999-018-0104-9.

115. Sipila S, Suominen H. Muscle ultrasonography and computed tomography in elderly trained and untrained women. Muscle Nerve 1993; 16: 294–300.

116. Ismail C, Zabal J, Hernandez HJ *et al.* Diagnostic ultrasound estimates of muscle mass and muscle quality discriminate between women with and without sarcopenia. Front Physiol 2015; 6: 302.

117. Nijholt W, Scafoglieri A, Jager-Wittenaar H *et al.* The reliability and validity of ultrasound to quantify muscles in older adults: a systematic review. J Cachexia Sarcopenia Muscle 2017; 8: 702–12.

118. Ticinesi A, Meschi T, Narici MV *et al.* Muscle ultrasound and sarcopenia in older individuals: a clinical perspective. J Am Med Dir Assoc 2017; 18: 290–300.

119. Abe T, Loenneke JP, Young KC *et al.* Validity of ultrasound prediction equations for total and regional muscularity in middle-aged and older men and women. Ultrasound Med Biol 2015; 41: 557–64.

120. Curcio F, Ferro G, Basile C *et al.* Biomarkers in sarcopenia: a multifactorial approach. Exp Gerontol 2016; 85: 1–8.

121. Calvani R, Marini F, Cesari M *et al.* Biomarkers for physical frailty and sarcopenia. Aging Clin Exp Res 2017; 29: 29–34.

122. Beaudart C, Biver E, Reginster JY *et al.* Development of a self-administrated quality of life questionnaire for sarcopenia in elderly subjects: the SarQoL. Age Ageing 2015; 44: 960–6.

123. Beaudart C, Reginster JY, Geerinck A *et al.* Current review of the SarQoL(R): a health-related quality of life questionnaire specific to sarcopenia. Expert Rev Pharmacoecon Outcomes Res 2017; 17: 335–41.

124. Beaudart C, Locquet M, Reginster JY *et al.* Quality of life in sarcopenia measured with the SarQoL(R): impact of the use of different diagnosis definitions. Aging Clin Exp Res 2018; 30: 307–13.

125. Gould H, Brennan SL, Kotowicz MA *et al.* Total and appendicular lean mass reference ranges for Australian men and women: the Geelong osteoporosis study. Calcif Tissue Int 2014; 94: 363–72.

126. Guralnik JM, Ferrucci L, Simonsick EM *et al.* Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med 1995; 332: 556–61.

127. Bischoff HA, Stahelin HB, Monsch AU *et al.* Identifying a cut-off point for normal mobility: a comparison of the timed 'up and go' test in community-dwelling and institutionalised elderly women. Age Ageing 2003; 32: 315–20.

128. Newman AB, Simonsick EM, Naydeck BL *et al.* Association of long-distance corridor walk performance with mortality,

cardiovascular disease, mobility limitation, and disability. JAMA 2006; 295: 2018–26.

129. Keller K, Engelhardt M. Strength and muscle mass loss with aging process. Age and strength loss. Muscles Ligaments Tendons J 2013; 3: 346–50.

130. Dodds R, Denison HJ, Ntani G *et al*. Birth weight and muscle strength: a systematic review and meta-analysis. J Nutr Health Aging 2012; 16: 609–15.

131. Bloom I, Shand C, Cooper C *et al*. Diet quality and sarcopenia in older adults: a systematic review. Nutrients 2018; 10.

132. Mijnarends DM, Koster A, Schols JM *et al*. Physical activity and incidence of sarcopenia: the population-based AGES-Reykjavik Study. Age Ageing 2016; 45: 614–20.

133. Prado CM, Wells JC, Smith SR *et al*. Sarcopenic obesity: a critical appraisal of the current evidence. Clin Nutr 2012; 31: 583–601.

134. Johnson Stoklossa CA, Sharma AM, Forhan M *et al*. Prevalence of sarcopenic obesity in adults with class II/III obesity using different diagnostic criteria. J Nutr Metab 2017; 2017: 7307618.

135. Kalinkovich A, Livshits G. Sarcopenic obesity or obese sarcopenia: A cross talk between age-associated adipose tissue and skeletal muscle inflammation as a main mechanism of the pathogenesis. Ageing Res Rev 2017; 35: 200–21.

136. Barbat-Artigas S, Pion CH, Leduc-Gaudet JP *et al*. Exploring the role of muscle mass, obesity, and age in the relationship between muscle quality and physical function. J Am Med Dir Assoc 2014; 15: 303.e13–20.

137. Tian S, Xu Y. Association of sarcopenic obesity with the risk of all-cause mortality: A meta-analysis of prospective cohort studies. Geriatr Gerontol Int 2016; 16: 155–66.

138. Newman AB, Haggerty CL, Goodpaster B *et al*. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. J Am Geriatr Soc 2003; 51: 323–30.

139. Morley JE, Vellas B, van Kan GA *et al*. Frailty consensus: a call to action. J Am Med Dir Assoc 2013; 14: 392–7.

140. Clegg A, Young J, Iliffe S *et al*. Frailty in elderly people. Lancet 2013; 381: 752–62.

141. Langlois F, Vu TT, Kergoat MJ *et al*. The multiple dimensions of frailty: physical capacity, cognition, and quality of life. Int Psychogeriatr 2012; 24: 1429–36.

142. Sieber CC. Frailty - From concept to clinical practice. Exp Gerontol 2017; 87: 160–67.

143. Fried LP, Tangen CM, Walston J *et al*. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56: M146–56.

144. Dodds R, Sayer AA. Sarcopenia and frailty: new challenges for clinical practice. Clin Med (Lond) 2015; 15(Suppl 6): s88–91.

145. Cederholm T. Overlaps between frailty and sarcopenia definitions. Nestle Nutr Inst Workshop Ser 2015; 83: 65–9.

146. Steverink N, Slaets J, Schuurmans H *et al*. Measuring frailty: developing and testing the Groningen Frailty Indicator (GFI). Gerontologist 2001; 41: 236–37.

147. Rockwood K, Song X, MacKnight C *et al*. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173: 489–95.

148. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: A review. Eur J Intern Med 2016; 31: 3–10.

149. Roppolo M, Mulasso A, Gobbens RJ *et al*. A comparison between uni- and multidimensional frailty measures: prevalence, functional status, and relationships with disability. Clin Interv Aging 2015; 10: 1669–78.

150. Muscaritoli M, Anker SD, Argiles J *et al*. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) 'cachexia-anorexia in chronic wasting diseases' and 'nutrition in geriatrics'. Clin Nutr 2010; 29: 154–9.

151. Cederholm T, Barazzoni R, Austin P *et al*. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017; 36: 49–64.

152. Cederholm T, Jensen GL, Correia M *et al*. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. Clin Nutr 2018. doi: 10.1002/jpen.1440 [Epub ahead of print].