



## Conference on ‘Nutrition and age-related muscle loss, sarcopenia and cachexia’ Symposium 1: Sarcopenia and cachexia: scale of the problem, importance, epidemiology and measurement

### Ageing well: a review of sarcopenia and frailty

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‘Ageing well’ has been declared a global health priority by the World Health Organisation and the role of sarcopenia and frailty in late-life health is receiving increasing attention. Frailty is the decline in an individual's homeostatic function, strength and physiologic reserves leading to increased vulnerability, while sarcopenia describes the loss of muscle mass and function with age. The conceptual definitions of these conditions have been widely agreed but there is a lack of consensus on how to measure them. We review the different operational definitions described in the literature and the evidence that, whatever definition used, the prevalence and clinical impact of these conditions is high. We also consider the commonality of low physical function to both conditions, a feature which could provide a pragmatic way forward in terms of identifying those at risk. Objective measures of physical function such as usual walking speed are simple and feasible measures, extensively validated against health outcomes. Additionally, clinical applications of sarcopenia and frailty are reviewed with particular consideration to their potential role in the management of older people undergoing surgery. Frailty appears to outperform traditional anaesthetic and surgical risk scores in terms of its association with post-operative complications, length of hospital stay, institutionalisation and mortality. However, even within this sub-specialty area there is wide variation in the approaches used to measure frailty and there is an urgent need for studies to utilise established, validated and reproducible methods to identify sarcopenia and frailty in their study participants, in order to expedite scientific development.

#### Sarcopenia: Frail elderly: Ageing

By 2050 the proportion of the world's population aged  $\geq 60$  years is projected to be 22%, double the proportion recorded at the turn of the new millennium<sup>(1)</sup>. Although population ageing is in one way a great public health success story, with mortality rates among older people continuing to fall<sup>(2)</sup>, in another way it presents significant challenges. For example, in the UK 60% of people

admitted to hospital are  $\geq 65$  years old despite this age-group only comprising 17% of the total UK population<sup>(3)</sup>. This disproportionate use of healthcare services by older people not only demonstrates the significant economic implications of an ageing population<sup>(4)</sup>, but also the morbidity experienced by many older people, reducing quality of life. However, it is not inevitable that

**Abbreviations:** CGA, comprehensive geriatric assessment; FI, frailty index; PFP, physical frailty phenotype.  
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older age will be synonymous with poor health<sup>(5)</sup> and the challenge now is to stay healthy in later life. This statement was echoed by the World Health Organisation, which recently declared 'ageing well' a global health priority (<http://www.who.int/ageing/en/>).

Improving health-related quality of life has traditionally focused on the identification and management of diseases such as CVD, cancer or respiratory disorders. Although the prevalence of most major diseases of adulthood does rise with advancing age, it has been increasingly recognised that the heterogeneity of health and function among older adults cannot be explained by co-morbidity alone<sup>(5)</sup>. As a result, efforts have focused on capturing other factors determining health in later life and through these efforts two new late-life syndromes have been described, termed sarcopenia and frailty<sup>(6–8)</sup>. This review will consider the different definitions of frailty and sarcopenia that have evolved over the past few decades and will also consider issues pertaining to their translation into clinical diagnostic criteria. The prevalence of these conditions and their potential impact on late-life health will also be reviewed alongside potential applications to the clinical care of older people.

### Frailty and sarcopenia: findings from epidemiological studies and consensus reports

#### *Frailty*

There has been wide agreement among experts in the field that frailty is a distinct clinical entity, with a recent consensus statement defining frailty as<sup>(9)</sup>:

'... a medical syndrome with multiple causes and contributors that is characterised by diminished strength, endurance and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death.'

There is also wide agreement that frailty is distinct from disability<sup>(9,10)</sup> and co-morbidity<sup>(9,11)</sup>, although all may co-exist. In general, the commonly used operational definitions of frailty lie on a spectrum between two different conceptual approaches to frailty measurement: summation of health deficits to create a frailty index (FI) and measurement of a physical frailty phenotype (PFP). These approaches are summarised below.

In brief, the FI characterises frailty as an accumulation of deficits across multiple body systems, in line with the general concept of frailty as a multi-system disorder<sup>(6,12)</sup>. Any number of health deficits from 30 to 70 can be included, with each deficit carrying an equal weight. Deficits can be symptoms, signs, disabilities, diseases or even laboratory abnormalities and can cover all aspects of health and wellbeing, although deficits should increase in prevalence with age, not saturate too early and be associated with adverse outcomes<sup>(13,14)</sup>. Frailty is then quantified according to the proportion of deficits present and, although designed to be used as a continuous scale, an index value of about 0.20–0.25 (regardless of age) is

usually accepted as the threshold above which frailty is present<sup>(14)</sup>. The deficit approach to frailty measurement was pioneered by Kenneth Rockwood and Arnold Mitnitski in the Canadian Study of Health and Ageing<sup>(16)</sup> but has since been applied in other cohorts<sup>(15,17–19)</sup>. The components of one FI are exemplified in Fig. 1.

In contrast the PFP characterises frailty as the presence of a constellation of attributes: weakness, slow walking speed, unintentional weight loss, exhaustion and low physical activity<sup>(7)</sup>. Frailty is present when three or more of these characteristics are present and those with just one or two characteristics are termed pre-frail. The PFP was initially operationalised by Linda Fried *et al.* using the infrastructure of the Cardiovascular Health Study, after considering consensus clinical opinion on the most salient hallmarks of frailty in patients (Fig. 2). Other frailty measurement tools such as the FRAIL scale<sup>(20)</sup> and the Gérontopôle Frailty Screening Tool<sup>(21)</sup> are also derived from the concept of the PFP.

(Colour online) The PFP is based on the theory of a vicious cycle of frailty, linking reduced physical activity, chronic undernutrition and loss of muscle mass to reduced resting metabolic rate, reduced strength and low mobility<sup>(22)</sup>. This cycle has remained the most plausible biological explanation for the mechanisms underpinning the frailty syndrome and has provided a standard framework upon which aetiological investigations have been based.

Both characterisations of frailty have face validity. We would expect older adults with more health deficits or older adults who have slowed up, become weaker, less active and more fatigued to be more vulnerable. Additionally, regardless of the definition used, frailty increases with advancing age and female sex providing construct validity<sup>(7,15,17)</sup>. For example, frailty was present in 2.1% of 65–69-year olds compared with 20.1% of 80–84-year olds in a Spanish population and 7.7% of men were frail compared with 9.8% of women<sup>(23)</sup>. Most prevalence estimates of frailty are based on the phenotypic definition of frailty and range from 4.0 to 27.3% in community-based populations of older adults ( $\geq 65$  years old)<sup>(7,23–26)</sup>.

Using both constructs, frailty has also been shown to predict the negative health outcomes we associate with vulnerable older people such as disability, institutionalisation, hospitalisation, falls and death<sup>(7,18,27–29)</sup>. Although the FI arguably predicts these outcomes with increased precision compared with the PFP<sup>(30)</sup>, the PFP has gained the most favour in epidemiological studies<sup>(25,31,32)</sup> because it allows frailty to be easily distinguished from co-morbidity and disability<sup>(11)</sup> facilitating exploration of its determinants and consequences<sup>(33,34)</sup>. In contrast, the FI often contains co-morbidity and disability in its construct making it difficult to disentangle associations (Fig. 1). Thus, the FI has been predominantly used when there is a need to use readily available or retrospectively collected data, e.g. in studies of healthcare utilisation for health-service planning<sup>(35)</sup>.

Walking ½ mile	Preparing meals	Dressing	Reaching Out	Sleepy	Disorder of blood clotting	Hearing	Vision	Mood
Walking 10 steps	Paying bills	Bathing	Gripping	Emphysema	Arrhythmia	SBP >140	DBP >80	Bruising
Heavy work	Using phone	Toilet	Heart Attack	Arthritis	Impaired Speech	Heart failure	Cancer	Abnormal Gait
Shopping	Eating	Lifting	Stroke	PD	Fracture	Diabetes	Angina	Memory problems / Cognition

**Fig. 1.** (Colour online) Components of the frailty index operationalised in the Honolulu-Asia Aging Study.<sup>(15)</sup> SBP, systolic blood pressure; DBP, diastolic blood pressure; PD, Parkinson's disease.

### Sarcopenia

Sarcopenia was first described by Rosenberg as the age-related loss of skeletal muscle mass<sup>(8,36)</sup>. It can be distinguished from cachexia by the more moderate degree of muscle wasting observed and the absence of either associated adipose tissue wasting and/or a high inflammatory state<sup>(37)</sup>. Rosenberg's first observations concluded<sup>(8)</sup>:

'...there is probably no decline in structure and function more dramatic than the decline in lean body mass or muscle mass over the decades of life.'

Although early operational definitions were based on low muscle mass alone<sup>(38)</sup>, research over the past few decades has emphasised the strong predictive relationships between measures of muscle quality i.e. strength and/or physical performance, and health outcomes. In particular, measures of physical capability such as grip strength, usual walking speed, timed chair stands performance and standing balance have been the focus of a wealth of research interest<sup>(39–42)</sup>. Thus, more recent proposals for definitions of sarcopenia recommend including some measure of muscle quality in addition to muscle mass<sup>(43–46)</sup> and these definitions are summarised in Fig. 3.

These definitions are broadly comparable, with all including a combination of low muscle function with low muscle mass. The main differences occur in the detail, with different cut-points suggested in each definition for

the different parameters. This is partly due to variation in normative ranges between populations, particularly with respect to muscle strength and muscle mass<sup>(45,47–50)</sup>. However, there is also ongoing debate about how to define valid cut-points. For example, should low muscle mass be identified using a cut-point 2.5 SD below a young adult population, as low bone density was defined in the context of osteoporosis? Alternatively, others suggest that cut-points should be identified by threshold values beyond which the risk of adverse outcomes significantly increases<sup>(51,52)</sup>.

Sarcopenia according to the European definition has been identified in 13.8% of men and 12.4% of women (mean age 75 years) participating in a Japanese study (using a definition of low muscle mass 2 SD below a young Japanese cohort mean)<sup>(53)</sup>. Additionally, sarcopenia was identified in 4.6 and 7.9% of men and women participating in a UK cohort study (mean age 67 years; low muscle mass defined as the lowest sex-specific tertile of lean mass)<sup>(54)</sup> and in 10.8–14.9 and 7.8–16.6% of older men and women in Taiwan (mean age 73 years), depending on the method used to define low muscle mass<sup>(55)</sup>. Regardless of the definition used, prevalence increases with age but women do not always have a higher prevalence than men<sup>(53–55)</sup>. Early evidence suggests that sarcopenia defined by the European definition is associated with health outcomes including self-reported health, disability and mortality<sup>(54,56,57)</sup>. However, these definitions

<p><b>Cardiovascular Health Study (CHS) Robust: 0; Pre-frail: 1-2; Frail: 3-5</b></p> <ul style="list-style-type: none"> <li>• Exhaustion (self-report of 'feeling everything was an effort or not being able to get going a moderate amount or most of the time over the past week')</li> <li>• Weakness (Grip strength: lowest 20% stratified by sex and body mass index)</li> <li>• Slowness (Usual walking speed: lowest 20% stratified by sex and height)</li> <li>• Low physical activity (lowest 20% of self-reported energy expenditure stratified by sex)</li> <li>• Shrinking (weight loss of <math>\geq 10</math>lbs or <math>\geq 5\%</math> of baseline in the past year)</li> </ul>
<p><b>FRAIL Scale Robust: 0; Pre-frail: 1-2; Frail: 3-5</b></p> <ul style="list-style-type: none"> <li>• Fatigue (are you fatigued?)</li> <li>• Resistance (can you walk up one flight of stairs?)</li> <li>• Aerobic (can you walk one block?)</li> <li>• Illnesses (do you have &gt;5 illnesses?)</li> <li>• Loss of weight (have you lost &gt;5% of your weight in the last 6 months?)</li> </ul>
<p><b>Gérontopôle Frailty Screening Tool (GFST) Robust: 0; Frail: 1-5 AND clinical impression of frailty (designed for use in non-disabled adults <math>\geq 65</math> years old)</b></p> <ul style="list-style-type: none"> <li>• Has your patient been more fatigued in the last 3 months?</li> <li>• Has your patient experienced increased mobility difficulties in the last 3 months?</li> <li>• Does your patient have slow gait speed (&gt;4 seconds to walk 4 meters)?</li> <li>• Does your patient live alone?</li> <li>• Has your patient lost weight in the last 3 months unintentionally?</li> <li>• Has your patients complained of memory problems?</li> <li>• If 'Yes' to any of the above: Do you think your patient is frail? and if 'Yes' is your patient willing to be assessed in the frailty clinic?</li> </ul>

**Fig. 2.** (Colour online) The Cardiovascular Health Study physical frailty phenotype<sup>(7)</sup> and other related frailty measurement tools (the FRAIL scale<sup>(20)</sup> and the Gérontopôle Frailty Screening Tool<sup>(21)</sup>).

are all relatively new and have been little scrutinised. A surprisingly low prevalence of sarcopenia (0.9%) was reported when using the European definition in Finnish older women<sup>(58)</sup>. Additionally, studies comparing the different operational definitions suggest that they only exhibit mild–moderate positive per cent agreement, although negative per cent agreement is high<sup>(55,59)</sup>.

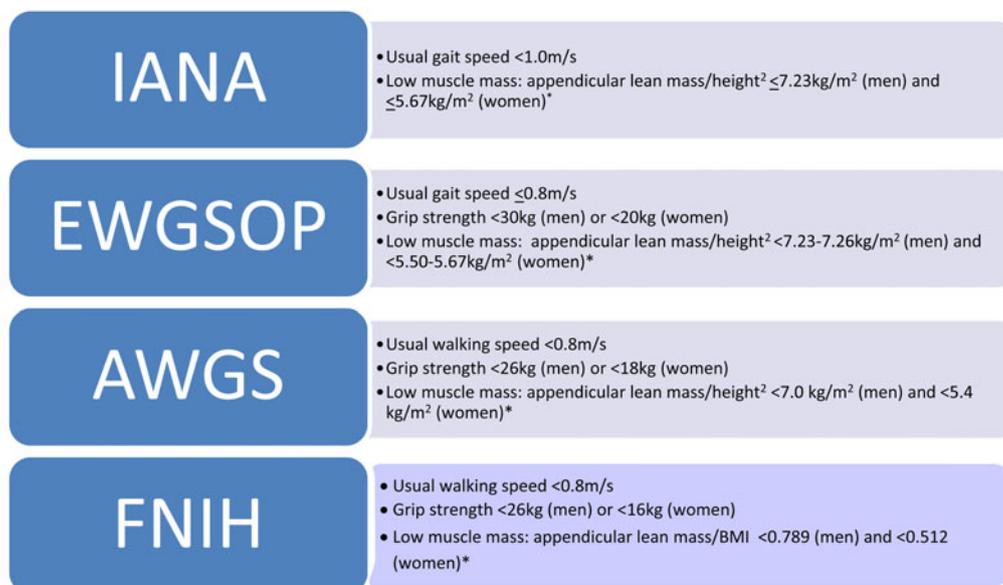
#### *Relationship between sarcopenia and frailty*

The aetiology of sarcopenia is unclear but it is unlikely to be attributable to a single cause. Evidence suggests that loss of motor units as a result of motor axonal degeneration, dysregulation of cell-signalling pathways, persistent low-grade inflammation ('inflammaging'), low habitual physical activity and endocrine dysfunction all contribute to the pathophysiology of sarcopenia<sup>(60)</sup>. Indeed, the likely significant role of motor neuron degeneration in the pathophysiology of sarcopenia has led some investigators to re-characterise it as a primary neurogenic disease, influenced by a multitude of systemic factors, rather than a primary disease of muscle<sup>(61)</sup>.

In similarity with sarcopenia, the aetiology of frailty is also likely to be multi-factorial<sup>(7)</sup> and it is possible that both frailty and sarcopenia are the final common

pathway of many pathological processes. In addition, frailty (certainly physical frailty) also shares with sarcopenia the appearance of skeletal muscle decline as a key feature. Therefore, both conditions share low physical capability as a common attribute<sup>(62)</sup> and almost all definitions of both sarcopenia and frailty include low physical function as a component, either measured by self-report or using objective measures such as usual walking speed (Fig. 4).

Furthermore, weakness has been identified as the most common first manifestation of the PFP<sup>(63)</sup> and low mobility has been associated with organism fragility (e.g. premature mortality) in animal models, emphasising the fundamental importance of mobility for survival<sup>(64)</sup>. Indeed, Schrack *et al.* provided evidence that the decline in walking speed with increasing age reflects the need to conserve energy to support essential metabolic functions such as homeostasis, which become less efficient and increase their metabolic cost as we age<sup>(65)</sup>. Therefore, physical function is not just a marker of musculoskeletal health but encapsulates (or is an epiphenomenon of) the health of the whole organism<sup>(61)</sup> and it is not surprising that measures of low physical function such as low grip strength and slow walking speed have been established as important independent predictors of mortality and



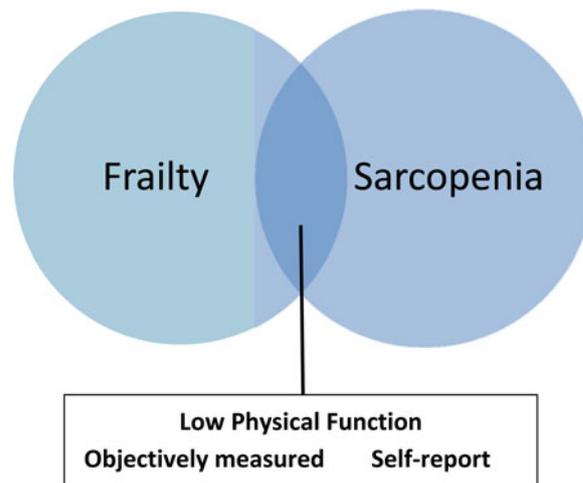
**Fig. 3.** (Colour online) Sarcopenia is defined by international working groups as the presence of low muscle mass with low muscle strength and/or low physical performance. International Academy on Nutrition and Aging: International working group on sarcopenia<sup>(43)</sup>; EWGSOP, European working group on sarcopenia in older people<sup>(44)</sup>; AWGS, Asian working group for sarcopenia<sup>(45)</sup>; FNIH, Foundation for the National Institutes of Health Sarcopenia project<sup>(46)</sup>. \*Measured by dual X-ray absorptiometry.

morbidity in their own right<sup>(40,41,66)</sup>. These measures have also been recommended as biomarkers of the healthy ageing phenotype by the National Institutes for Health, being included in the National Institutes for Health toolbox<sup>(67)</sup>. Indeed some have suggested that markers of low function such as low grip strength could be used as single clinical markers of frailty<sup>(68)</sup> and usual walking speed has been postulated as the sixth vital sign of health due to its association with a wide range of health states, e.g. cognitive function, mood, motivation, musculoskeletal health and cardiovascular fitness<sup>(69)</sup>.

The present consensus opinion still holds the view that frailty is broader than just low function and sarcopenia alone<sup>(9)</sup> and it is unclear to what extent sarcopenia and frailty overlap as clinical syndromes<sup>(62)</sup>. However, it is generally agreed that low physical function is a feature common to both conditions and a range of simple and validated measures of physical function are available, which could be used in the clinical setting to identify those at risk of these conditions<sup>(62)</sup>.

**Evidence that sarcopenia and frailty are potentially reversible conditions**

In a longitudinal study of community-based older persons (≥70 years old), who were non-disabled at baseline, frailty was measured at 18 month intervals over 54 months<sup>(32)</sup>. Over the course of the study, 57.6 % of participants had at least one transition between non-frail, pre-frail and frail states. Although transitions to greater frailty states were more commonly observed (up to



**Fig. 4.** (Colour online) Low physical function is common to both frailty and sarcopenia (adapted from<sup>(62)</sup>).

43 % of transitions at any time interval), a significant number of transitions occurred as participants became less frail (up to 23 % of transitions at any time interval). Thus, frailty is a dynamic process with evidence of reversibility and it should be possible to design interventions to ameliorate or improve frailty.

To date the most evidence has accrued to support exercise interventions for both frailty and sarcopenia. In particular, interventions that are delivered at least three times per week, include resistance exercise training and become progressively more challenging may be effective. For example, progressive resistance exercise training has

been shown to improve physical performance in many studies of older adults<sup>(70,71)</sup> and also to reduce the common clinical manifestations of frailty and sarcopenia, e.g. falls<sup>(72)</sup>.

Nutritional interventions have also been considered but the evidence is less consistent. In particular for all the considered nutritional interventions, e.g. protein, vitamin D and antioxidant supplementation, there is a disparity between observational and experimental evidence. For example, nutritional intake declines during older age and reductions in protein intake may reduce muscle protein synthesis, both through reduced substrate availability and reduced anabolic stimulation (leucine, an amino acid, stimulates muscle protein synthesis)<sup>(73)</sup>. In support of this hypothesis, observational evidence from longitudinal cohort studies has shown that those with the lowest protein intake have the highest rates of muscle mass decline<sup>(74)</sup>. However, protein supplementation studies have failed to consistently demonstrate benefit<sup>(75)</sup> although investigation of the role of protein supplementation as part of a multifactorial intervention is ongoing<sup>(76)</sup>. Additionally, although vitamin D receptors are found on skeletal muscle cells and myopathy is a feature of vitamin D deficient diseases, low serum vitamin D is not always associated with low physical function<sup>(77–81)</sup> in observational studies and supplementation studies also show mixed results<sup>(72,82,83)</sup>.

However, the recognition of sarcopenia and frailty as important medical syndromes has fuelled interest in the development of effective interventions and it is likely that this will be an area of change over the coming few years. In particular, sarcopenia research is stimulating new drug discovery and several novel pharmaceutical interventions are being explored. These both consider new roles for existing drugs, e.g. angiotensin-converting enzyme inhibitors and the development of novel pharmaceutical agents, e.g. myostatin inhibitors<sup>(84)</sup>.

### Sarcopenia and frailty in clinical practice

The prevalence of sarcopenia and frailty is higher in patient populations than community-based cohorts. For example, 40 % of the older emergency medical admissions (mean age 83 years) were identified as frail according to the Cardiovascular Health Study phenotype definition in a Belgium study<sup>(85)</sup> and a recent prospective study in the UK identified 28 % of older patients (mean age 77 years) attending three acute surgical admission units as frail<sup>(86)</sup>. In the outpatient setting, 26 % of urology, surgical oncology and general surgery patients in the USA (mean age 62 years) were deemed frail or pre-frail<sup>(87)</sup> and 37.0 % of men and 29.3 % of women (mean age 64 years) attending a dialysis unit in Korea had sarcopenia (defined as low muscle mass and strength)<sup>(88)</sup>. Presently many studies of prevalence in the clinical setting do not use internationally recognised definitions to identify cases and some caution must be used when comparing the results between clinical and epidemiological studies. For example, in studies of sarcopenia in surgical patients there has been a tendency to

identify cases by the presence of low muscle mass alone<sup>(89,90)</sup>. This tends to produce higher estimates of sarcopenia prevalence than definitions, including both muscle mass and muscle quality parameters.

However, it is likely that sarcopenia and frailty will be more prevalent in patient populations compared with community-based cohorts. Therefore, given the known associations of sarcopenia and frailty with negative health outcomes, it is not surprising that the estimated healthcare cost of these conditions is high. For example, in 2000 \$18.5 billion dollars of spending on healthcare in the USA were attributed to sarcopenia<sup>(91)</sup>. Similarly, one study calculated the absolute costs associated with elective surgical procedures in frail patients to be three times higher (\$76 363 (SD 48 495) per patient) than non-frail patients (\$27 731 (SD 15 693) per patient)<sup>(92)</sup>.

These high estimates, of prevalence and cost, have led to calls for these conditions to be considered more routinely in clinical practice<sup>(93)</sup>. Case-finding has been suggested in the acute medical setting<sup>(94)</sup>, in the care of older adults being considered for aggressive oncological treatments<sup>(95)</sup>, in elective and acute surgery<sup>(96,97)</sup> and in primary care<sup>(93)</sup>. In the primary care setting, there is evidence that frailty may be important when considering treatment of traditional disease risk factors, such as hypertension, which may behave differently in frail patients<sup>(98,99)</sup>. Additionally, there is scope for early intervention to prevent or delay late-life disability since both frailty and sarcopenia often precede disability but are potentially reversible conditions. In contrast, disability is difficult to reverse once it has occurred<sup>(11)</sup>. For example, frailty could be used to identify those older people presenting to medical services who might benefit the most from comprehensive geriatric assessment (CGA). CGA is a multi-dimensional and inter-disciplinary review of the medical, functional and psycho-social needs of an older person in order to formulate a personalised plan for treatment and long-term follow-up. It has been shown to improve the likelihood of older people being alive and in their own home 1 year following an emergency hospital admission<sup>(100)</sup> but present clinical resources are not sufficient to provide CGA for all older people. Therefore, frailty could help to promote equity of access to CGA services.

With respect to medical practice in secondary care, one particular area that has recently received a great deal of interest is frailty in the older surgical patient. Presently a growing number of prospective studies evaluating the associations of frailty with surgical outcomes have been published (Supplementary Material, Table S1).

It is clear from these studies that frailty adds a new dimension to the surgical assessment. Preliminary evidence suggests that frailty measurement can aid risk prediction and outperform traditional anaesthetic or surgical risk scores, in terms of prediction of post-operative complications, longer in-patient stay, discharge to institutional care and mortality<sup>(87)</sup>. Therefore, adding frailty to the assessment of older surgical patients could aid decision making and improve patients' (and their families') understanding of the operative risks, in order to make a more



informed choice regarding treatment options<sup>(97)</sup>. Secondly, if frailty (and/or sarcopenia) was identified, optimisation interventions to reduce or reverse frailty could result in improved outcomes. For example, CGA has also been associated with improved outcomes when applied to the management of older surgical patients<sup>(101)</sup> and the pre-operative identification and treatment of anaemia, a common condition associated with frailty, has been found to be beneficial in older patients presenting for elective orthopaedic surgery<sup>(102)</sup>. Additionally, the concept of 'pre-habilitation' has been suggested<sup>(103)</sup>. This would involve the design of multifaceted interventions to improve the fitness and nutritional health of older patients prior to surgery. However, to date few trials have evaluated exercise or nutritional interventions peri-operatively and this is an area in urgent need of further research.

### Challenges to clinical translation

Presently neither sarcopenia nor frailty are recognised with International Classification of Diseases codes and debate over the exact definitions and diagnostic criteria of both sarcopenia and frailty has been a major limiting factor with respect to clinical appetite to incorporate these conditions into practice<sup>(104)</sup>. As demonstrated, the lack of consistency when defining sarcopenia or frailty even extends to within sub-specialty areas of the research field. For example, a striking observation from Table S1 (Supplementary Material) is the variety of tools used to measure frailty and the different ways even the same measure is operationalised. For example, the PFP definition proposed by Fried is sometimes operationalised incorrectly as a continuous score (from 0 to 5) rather than a three-level category (frail (0), pre-frail (1–2) and robust ( $\geq 3$ ))<sup>(105)</sup>. Additionally, while consensus meetings often agree on the concepts of frailty and sarcopenia they often fail to achieve agreement on diagnostic criteria<sup>(10)</sup>, including methods to identify low muscle mass<sup>(46)</sup> and the choice of appropriate cut-points. A particular problem has been the use of cohort-specific cut-points in research studies, e.g. low muscle mass defined as the 'lowest tertile' of muscle mass in the cohort under investigation. While use of different percentile groups to explore correlations and trends within cohorts can provide useful observations, it makes findings of different studies hard to compare and replication of results more difficult. This will be especially true when sarcopenia and frailty are the subjects from interventional studies. For example, in absolute terms the lowest 'tertile' cut-point of one cohort may be very different from another. Thus, if the same intervention was applied in two study populations and the results differed, then this difference may be attributed to the inherent differences between the cases included in each study. Doubt would be cast that the same people, and thus the same underlying condition, were identified by each interventional study. This problem was exemplified in a report from the Leiden Longevity Study which considered seven proposed operational definitions of sarcopenia and found that only one

individual in their cohort of 654 older men and women was sarcopenic by all definitions<sup>(106)</sup>.

Additionally, the operational definitions that have worked well in epidemiological studies do not always function as smoothly in the clinical context. For example, although a FI can be derived from standard clinical assessments such as the CGA<sup>(107)</sup>, it is not feasible to conduct a CGA on every older person presenting to healthcare services and one of the main indications for identifying frailty in clinical practice would be as an indication for CGA. Even the PFP has proved difficult to execute in busy clinical settings, since it requires measurement of attributes which are not part of the routine examination and which require additional equipment, e.g. dynamometer to measure grip strength. To this end several other frailty scales have been developed in recent years, which may be more feasible, e.g. the FRAIL scale (exemplified in Fig. 3) or the SHARE-FI75+<sup>(108)</sup>. Rockwood *et al.* also developed a Clinical Frailty Scale based on clinical judgement that is simple to use and performs well in comparison with the multiple deficits based FI<sup>(109)</sup>.

With respect to sarcopenia, the main area of the present debate resides in the necessity to measure muscle mass in clinical practice. Compared with measures of strength or performance, relationships between muscle mass and health outcomes are weaker<sup>(52,110,111)</sup>. Additionally, low muscle mass does not always correlate well with low strength or performance<sup>(58)</sup> and it is not clear how best to measure muscle mass in clinical practice or whether it would be feasible<sup>(112)</sup>. Dual X-ray absorptiometry is widely regarded as the safest and most accurate measure for clinical practice but equipment is bulky, with limited availability in many healthcare settings. Additionally, bioelectrical impedance analysis, while more portable and potentially feasible in primary as well as secondary care, is not clearly superior to simple anthropometric methods of body composition assessment<sup>(113)</sup>, which are themselves not endorsed due to concerns over accuracy<sup>(44)</sup>.

The challenges of measuring muscle mass in the clinical setting have led to proposals for function-based sarcopenia screening tools. For example, SARC-F measures risk of sarcopenia based upon responses to questions pertaining to lifting or carrying, rising from a chair, assistance with walking, stair climbing and falls and has been validated for use<sup>(114–116)</sup>.

Thus, in the clinical setting we may need to adapt what has been used in research and take a pragmatic approach<sup>(117)</sup>. For example, we could take advantage of the commonality of low physical function to both frailty and sarcopenia in order to utilise simple tests, such as usual walking speed, to identify those at risk of both conditions. Whether further assessment would then be warranted, e.g. with tests to identify low muscle mass, would depend on the further development of interventions. At present the exercise interventions with the best evidence base work equally well in frail patients, sarcopenic patients or simply those patients identified to have low physical function. Therefore, until more specific treatment is available, more specific identification and differentiation of sarcopenia and frailty in the clinical

setting will not be justified in terms of cost or resource allocation. However, the pragmatic assessment of frailty and sarcopenia in clinical practice and research will be justified as long as it adds value to help explain the observed heterogeneity in risk among older people.

### Conclusions

Frailty and sarcopenia are important medical syndromes that are associated with high morbidity, mortality and healthcare costs. Recognition of these syndromes in clinical practice has the potential to improve the assessment and management of older patients in many different clinical settings. However, it is particularly important that we expand the research-based evaluating potential interventions for sarcopenia and frailty and show that these interventions add clinical value and improve patient outcomes, in order to move forward. The specific choice of tools to identify frailty and sarcopenia needs to be done pragmatically and tailored to the particular research or clinical scenario. However, it is of vital importance that studies utilise established, validated and reproducible methods to identify sarcopenia and frailty in their study participants. This will aid comparison between studies and subsequent research synthesis, expediting scientific development. An exciting time lies ahead.

### Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S0029665115002037>

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### Conflicts of Interest

None.

### Authorship

V. L. K conducted the literature search and drafted the manuscript. R. R. O reviewed and revised the manuscript.

### References

1. Department of Economic and Social Affairs Population Division United Nations (2013) World Population Ageing 2013. ST/ESA/SER.A/348.
2. Mathers CD, Stevens GA, Boerma T *et al.* (2014) Causes of international increases in older age life expectancy. *Lancet* **6736**, 1–9. World Health Organization. Published by Elsevier Ltd/Inc/BV. All rights reserved.
3. House of Commons Health Committee (2011) Written evidence from the British Geriatrics Society. <http://www.publications.parliament.uk/pa/cm201213/cmselect/cmhealth/6/6vw03.htm> (accessed November 2014).
4. Bloom DE, Chatterji S, Kowal P *et al.* (2014) Macroeconomic implications of population ageing and selected policy responses. *Lancet* **6736**, 1–9. World Health Organization. Published by Elsevier Ltd/Inc/BV. All rights reserved.
5. Lloyd-Sherlock P, McKee M, Ebrahim S *et al.* (2012) Population ageing and health. *Lancet* **379**, 1295–1296. Elsevier Ltd.
6. Mitnitski AB, Mogilner AJ & Rockwood K (2001) Accumulation of deficits as a proxy measure of aging. *Sci World J* **1**, 323–336.
7. Fried LP, Tangen CM, Walston J *et al.* (2001) Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* **56**, M146–M156.
8. Rosenberg IH (1997) Sarcopenia: origins and clinical relevance. *J Nutr* **127**, 990S–991S.
9. Morley JE, Vellas B, van Kan GA *et al.* (2013) Frailty consensus: a call to action. *J Am Med Dir Assoc* **14**, 392–397.
10. Rodriguez-Mañas L, Féart C, Mann G *et al.* (2013) Searching for an operational definition of frailty: a Delphi method based consensus statement: the frailty operative definition-consensus conference project. *J Gerontol A Biol Sci Med Sci* **68**, 62–67.
11. Fried LP, Ferrucci L, Darer J *et al.* (2004) Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* **59**, 255–263.
12. Rockwood K & Mitnitski A (2007) Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* **62**, 722–727.
13. Howlett SE, Rockwood MRH, Mitnitski A *et al.* (2014) Standard laboratory tests to identify older adults at increased risk of death. *BMC Med* **12**, 171.
14. Searle SD, Mitnitski A, Gahbauer EA *et al.* (2008) A standard procedure for creating a frailty index. *BMC Geriatr* **8**, 24.
15. Armstrong JJ, Mitnitski A, Launer LJ *et al.* (2015) Frailty in the Honolulu-Asia aging study: deficit accumulation in a male cohort followed to 90 % mortality. *J Gerontol A Biol Sci Med Sci* **70**, 125–131.
16. Mitnitski AB, Graham JE, Mogilner AJ *et al.* (2002) Frailty, fitness and late-life mortality in relation to chronological and biological age. *BMC Geriatr* **2**, 1.
17. Goggins WB, Woo J, Sham A *et al.* (2005) Frailty index as a measure of biological age in a chinese population. *J Gerontol. A Biol Sci Med Sci* **60**, 1046–1051.
18. Romero-Ortuno R & Kenny RA (2012) The frailty index in Europeans: association with age and mortality. *Age Ageing* **41**, 684–689.
19. Peña FG, Theou O, Wallace L *et al.* (2014) Comparison of alternate scoring of variables on the performance of the frailty index. *BMC Geriatr* **14**, 25.
20. Morley JE, Malmstrom TK & Miller DK (2012) A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* **16**, 601–608.



21. Vellas B, Balardy L, Gillette-Guyonnet S *et al.* (2013) Looking for frailty in community-dwelling older persons: the Gérontopôle Frailty Screening Tool (GFST). *J Nutr Health Aging* **17**, 629–631.
22. Fried LP & Watson J (1998) Frailty and failure to thrive. In *Princ. Geriatr. Med. Gerontol.*, 4th ed., pp. 1387–1402 [W Hazzard, J Blass, W Ettinger, J Halter, J Ouslander, *et al.*, editors]. New York: McGraw Hill.
23. Garcia-Garcia FJ, Gutierrez Avila G, Alfaro-Acha A *et al.* (2011) The prevalence of frailty syndrome in an older population from Spain. The Toledo Study for Healthy Aging. *J Nutr Health Aging* **15**, 852–856.
24. Chen C-Y, Wu S-C, Chen L-J *et al.* (2010) The prevalence of subjective frailty and factors associated with frailty in Taiwan. *Arch Gerontol Geriatr* **50**, Suppl. 1, S43–S47. Elsevier Ltd.
25. Syddall H, Roberts HC, Evandrou M *et al.* (2010) Prevalence and correlates of frailty among community-dwelling older men and women: findings from the Hertfordshire Cohort Study. *Age Ageing* **39**, 197–203.
26. Santos-Eggimann B, Cuénoud P, Spagnoli J *et al.* (2009) Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* **64**, 675–681.
27. Ensrud KE, Ewing SK, Taylor BC *et al.* (2007) Frailty and risk of falls, fracture, and mortality in older women: the study of osteoporotic fractures. *J Gerontol A Biol Sci Med Sci* **62**, 744–751.
28. Rockwood K, Mitnitski A, Song X *et al.* (2006) Long-term risks of death and institutionalization of elderly people in relation to deficit accumulation at age 70. *J Am Geriatr Soc* **54**, 975–979.
29. Bandeen-Roche K, Xue Q-L, Ferrucci L *et al.* (2006) Phenotype of frailty: characterization in the women's health and aging studies. *J Gerontol A Biol Sci Med Sci* **61**, 262–266.
30. Rockwood K, Andrew M & Mitnitski A (2007) A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci* **62**, 738–743.
31. Sirola J, Pitkala KH, Tilvis RS *et al.* (2011) Definition of frailty in older men according to questionnaire data (RAND-36/SF-36): the Helsinki Businessmen Study. *J Nutr Health Aging* **15**, 783–787.
32. Gill TM, Gahbauer EA, Allore HG *et al.* (2006) Transitions between frailty states among community-living older persons. *Arch Intern Med* **166**, 418–423.
33. Gale CR, Cooper C, Deary IJ *et al.* (2014) Psychological well-being and incident frailty in men and women: the English Longitudinal Study of Ageing. *Psychol Med* **44**, 697–706.
34. Baylis D, Bartlett DB, Syddall HE *et al.* (2013) Immune-endocrine biomarkers as predictors of frailty and mortality: a 10-year longitudinal study in community-dwelling older people. *Age (Dordr)* **35**, 963–971.
35. Albaba M, Cha SS & Takahashi PY (2012) The Elders Risk Assessment Index, an electronic administrative database-derived frailty index, can identify risk of hip fracture in a cohort of community-dwelling adults. *Mayo Clin Proc* **87**, 652–658.
36. Rosenberg I (1989) Epidemiologic and methodologic problems in determining nutritional status of older persons. (summary comments). *Am J Clin Nutr* **50**, 1231–1233.
37. Morley JE (2008) Sarcopenia: diagnosis and treatment. *J Nutr Health Aging* **12**, 452–456.
38. Baumgartner RN, Koehler KM, Gallagher D *et al.* (1998) Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* **147**, 755–763.
39. Guralnik JM, Ferrucci L, Simonsick EM *et al.* (1995) Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *NEJM* **332**, 556–561.
40. Studenski S, Perera S, Patel K *et al.* (2011) Gait speed and survival in older adults. *JAMA* **305**, 50–58.
41. Cooper R, Kuh D & Hardy R (2010) Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ* **341**, c4467–c4467.
42. Guralnik JM, Simonsick EM, Ferrucci L *et al.* (1994) A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* **49**, M85–M94.
43. Fielding RA, Vellas B, Evans WJ *et al.* (2011) Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc* **12**, 249–256.
44. Cruz-Jentoft AJ, Baeyens JP, Bauer JM *et al.* (2010) Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. *Age Ageing* **39**, 412–423.
45. Chen L-K, Liu L-K, Woo J *et al.* (2014) Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. *J Am Med Dir Assoc* **15**, 95–101.
46. Studenski SA, Peters KW, Alley DE *et al.* (2014) The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. *J Gerontol A Biol Sci Med Sci* **69**, 547–558.
47. Yoshimura N, Oka H, Muraki S *et al.* (2011) Reference values for hand grip strength, muscle mass, walking time, and one-leg standing time as indices for locomotive syndrome and associated disability: the second survey of the ROAD study. *J Orthop Sci* **16**, 768–777.
48. Andersen-Ranberg K, Petersen I, Frederiksen H *et al.* (2009) Cross-national differences in grip strength among 50+ year-old Europeans: results from the SHARE study. *Eur J Ageing* **6**, 227–236.
49. Keevil V, Mazzuin Razali R, Chin A-V *et al.* (2013) Grip strength in a cohort of older medical inpatients in Malaysia: a pilot study to describe the range, determinants and association with length of hospital stay. *Arch Gerontol Geriatr* **56**, 155–159.
50. Kamarul T, Ahmad TS & Loh WYC (2006) Hand grip strength in the adult Malaysian population. *J Orthop Surg (Hong Kong)* **14**, 172–177.
51. Cesari M, Kritchevsky SB, Penninx BWHJ *et al.* (2005) Prognostic value of usual gait speed in well-functioning older people – results from the Health, Aging and Body Composition Study. *J Am Geriatr Soc* **53**, 1675–1680.
52. Lauretani F, Russo CR, Bandinelli S *et al.* (2003) Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* **95**, 1851–1860.
53. Akune T, Muraki S, Oka H *et al.* (2014) Exercise habits during middle age are associated with lower prevalence of sarcopenia: the ROAD study. *Osteoporos Int* **25**, 1081–1088.
54. Patel HP, Syddall HE, Jameson K *et al.* (2013) Prevalence of sarcopenia in community-dwelling older people in the UK using the European Working Group on Sarcopenia in Older People (EWGSOP) definition: findings from the Hertfordshire Cohort Study (HCS). *Age Ageing* **42**, 378–384.
55. Lee W-J, Liu L-K, Peng L-N *et al.* (2013) Comparisons of sarcopenia defined by IWGS and EWGSOP criteria among

- older people: results from the I-Lan longitudinal aging study. *J Am Med Dir Assoc* **14**, 528. e1–7. Elsevier Ltd.
56. Landi F, Cruz-Jentoft AJ, Liperoti R *et al.* (2013) Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from iLSIRENTE study. *Age Ageing* **42**, 203–209.
  57. Alexandre T da S & Duarte Y (2014) Sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOP) *versus* dynapenia as a risk factor for disability in the elderly. *J Nutr* **1**–7.
  58. Patil R, Uusi-Rasi K, Pasanen M *et al.* (2013) Sarcopenia and osteopenia among 70–80-year-old home-dwelling Finnish women: prevalence and association with functional performance. *Osteoporos Int* **24**, 787–796.
  59. Dam T-T, Peters KW, Fragala M *et al.* (2014) An evidence-based comparison of operational criteria for the presence of sarcopenia. *J Gerontol A Biol Sci Med Sci* **69**, 584–590.
  60. Matthews GDK, Huang CL-H, Sun L *et al.* (2011) Translational musculoskeletal science: is sarcopenia the next clinical target after osteoporosis? *Ann N Y Acad Sci* **1237**, 95–105.
  61. Kwan P (2013) Sarcopenia, a neurogenic syndrome? *J Aging Res* **2013**, 791679.
  62. Cesari M, Landi F, Vellas B *et al.* (2014) Sarcopenia and physical frailty: two sides of the same coin. *Front Aging Neurosci* **6**, 192.
  63. Xue Q-L, Bandeen-Roche K, Varadhan R *et al.* (2008) Initial manifestations of frailty criteria and the development of frailty phenotype in the Women's Health and Aging Study II. *J Gerontol. A Biol Sci Med Sci* **63**, 984–990.
  64. Fisher AL (2004) Of worms and women: sarcopenia and its role in disability and mortality. *J Am Geriatr Soc* **52**, 1185–1190.
  65. Schrack JA, Simonsick EM & Ferrucci L (2011) The energetic pathway to mobility loss: an emerging new framework for longitudinal studies on aging. *J Am Geriatr Soc* **58**, 1–19.
  66. Cooper R, Kuh D, Cooper C *et al.* (2011) Objective measures of physical capability and subsequent health: a systematic review. *Age Ageing* **40**, 14–23.
  67. Reuben DB, Magasi S, McCreath HE *et al.* (2013) Motor assessment using the NIH Toolbox. *Neurology* **80**, S65–S75.
  68. Syddall H, Cooper C, Martin F *et al.* (2003) Is grip strength a useful single marker of frailty? *Age Ageing* **32**, 650–656.
  69. Fritz S & Lusardi M (2009) White paper: “walking speed: the sixth vital sign”. *J Geriatr Phys Ther* **32**, 46–49.
  70. Liu C-J & Latham NK (2009) Progressive resistance strength training for improving physical function in older adults. *Cochrane Database Syst Rev* CD002759.
  71. Peterson MD, Rhea MR, Sen A *et al.* (2010) Resistance exercise for muscular strength in older adults: a meta-analysis. *Ageing Res Rev* **9**, 226–237.
  72. Gillespie LD, Robertson MC, Gillespie WJ *et al.* (2009) Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* CD007146.
  73. Drummond MJ & Rasmussen BB (2008) Leucine-enriched nutrients and the regulation of mammalian target of rapamycin signalling and human skeletal muscle protein synthesis. *Curr Opin Clin Nutr Metab Care* **11**, 222–226.
  74. Houston DK, Nicklas BJ, Ding J *et al.* (2008) Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. *Am J Clin Nutr* **87**, 150–155.
  75. Milne AC, Potter J, Vivanti A *et al.* (2009) Protein and energy supplementation in elderly people at risk from malnutrition. *Cochrane Database Syst Rev* CD003288.
  76. Romera L, Orfila F, Segura JM *et al.* (2014) Effectiveness of a primary care based multifactorial intervention to improve frailty parameters in the elderly: a randomised clinical trial: rationale and study design. *BMC Geriatr* **14**, 125.
  77. Annweiler C, Beauchet O, Berrut G *et al.* (2009) Is there an association between serum 25-hydroxyvitamin D concentration and muscle strength among older women? Results from baseline assessment of the EPIDOS study. *J Nutr Health Aging* **13**, 90–95.
  78. Bolland MJ, Bacon CJ, Horne AM *et al.* (2010) Vitamin D insufficiency and health outcomes over 5 years in older women. *J Am Geriatr Soc* **25**, 82–89.
  79. Ceglia L, Chiu GR, Harris SS *et al.* (2011) Serum 25-hydroxyvitamin D concentration and physical function in adult men. *Clin Endocrinol (Oxf)* **74**, 370–376.
  80. Bischoff-Ferrari HA, Dietrich T, Orav EJ *et al.* (2004) Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 years. *Am J Clin Nutr* **80**, 752–758.
  81. Visser M, Deeg DJH & Lips P (2003) Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. *J Clin Endocrinol Metab* **88**, 5766–5772.
  82. Stockton KA, Mengersen K, Paratz JD *et al.* (2011) Effect of vitamin D supplementation on muscle strength: a systematic review and meta-analysis. *Osteoporos Int* **22**, 859–871.
  83. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB *et al.* (2009) Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ* **339**, b3692–b3692.
  84. Laosa O, Alonso C, Castro M *et al.* (2014) Pharmaceutical interventions for frailty and sarcopenia. *Curr Pharm Des* **20**, 3068–3082.
  85. Joosten E, Demuyneck M, Detroyer E *et al.* (2014) Prevalence of frailty and its ability to predict in hospital delirium, falls, and 6-month mortality in hospitalized older patients. *BMC Geriatr* **14**, 1.
  86. Hewitt J, Moug SJ, Middleton M *et al.* (2015) Prevalence of frailty and its association with mortality in general surgery. *Am J Surg* **209**, 254–259.
  87. Revenig LM, Canter DJ, Taylor MD *et al.* (2013) Too frail for surgery? Initial results of a large multidisciplinary prospective study examining preoperative variables predictive of poor surgical outcomes. *J Am Coll Surg* **217**, 665–670. e1.
  88. Kim J-K, Choi SR, Choi MJ *et al.* (2014) Prevalence of and factors associated with sarcopenia in elderly patients with end-stage renal disease. *Clin Nutr* **33**, 64–68.
  89. Sheetz K & Waits S (2013) Cost of major surgery in the sarcopenic patient. *J Am Coll Surg* **217**, 1–13.
  90. Jones KI, Doleman B, Scott S *et al.* (2015) Simple psoas cross-sectional area measurement is a quick and easy method to assess sarcopenia and predicts major surgical complications. *Colorectal Dis* **17**, O20–O26.
  91. Janssen I, Shepard DS, Katzmarzyk PT *et al.* (2004) The healthcare costs of sarcopenia in the United States. *J Am Geriatr Soc* **52**, 80–85.
  92. Robinson TN, Wu DS, Stiegmann GV *et al.* (2011) Frailty predicts increased hospital and six-month healthcare cost



- following colorectal surgery in older adults. *Am J Surg* **202**, 511–514.
93. Fit for Frailty – consensus best practice guidance for the care of older people living in community and outpatient settings – a report from the British Geriatrics Society (2014) *Fit for Frailty*. Available at [http://www.bgs.org.uk/campaigns/fff/fff\\_full.pdf](http://www.bgs.org.uk/campaigns/fff/fff_full.pdf)
94. The Royal College of Physicians (2012) Acute care toolkit 3 Acute medical care for frail older people. Available at <https://www.rcplondon.ac.uk/sites/default/files/acute-care-toolkit-3.pdf>.
95. Handforth C, Clegg A, Young C *et al.* (2014) The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Ann Oncol* (Epublication ahead of print version).
96. Anaya DA, Johanning J, Spector SA *et al.* (2014) Summary of the panel session at the 38th annual surgical symposium of the association of VA surgeons: what is the big deal about frailty? *JAMA Surg* **149**, 1191–1197.
97. Partridge JSL, Harari D & Dhesei JK (2012) Frailty in the older surgical patient: a review. *Age Ageing* **41**, 142–147.
98. Muller M, Smulders YM, de Leeuw PW *et al.* (2013) Treatment of hypertension in the oldest old: a critical role for frailty? *Hypertension* **63**, 433–441.
99. Odden MC, Peralta CA, Haan MN *et al.* (2012) Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. *Arch Intern Med* **172**, 1162–1168.
100. Ellis G, Whitehead MA, Robinson D *et al.* (2011) Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. *BMJ* **343**, d6553.
101. Harari D, Hopper A, Dhesei J *et al.* (2007) Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. *Age Ageing* **36**, 190–196.
102. Goodnough LT, Maniatis A, Earnshaw P *et al.* (2011) Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. *Br J Anaesth* **106**, 13–22.
103. Gillis C, Li C, Lee L *et al.* (2014) Prehabilitation *versus* rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology* **121**, 937–947.
104. Cooper C, Dere W, Evans W *et al.* (2012) Frailty and sarcopenia: definitions and outcome parameters. *Osteoporos Int* **23**, 1839–1848.
105. Leung J, Tsai T & Sands L (2011) Preoperative frailty in older surgical patients is associated with early postoperative delirium. *Anesth Analg* **112**, 1199–1201.
106. Bijlsma AY, Meskers CGM, Ling CHY *et al.* (2012) Defining sarcopenia: the impact of different diagnostic criteria on the prevalence of sarcopenia in a large middle aged cohort. *Age (Dordr)* **35**, 871–881.
107. Jones D, Song X, Mitnitski A *et al.* (2005) Evaluation of a frailty index based on a comprehensive geriatric assessment in a population based study of elderly Canadians. *Aging Clin Exp Res* **17**, 465–471.
108. Romero-Ortuno R & Soraghan C (2014) A Frailty Instrument for primary care for those aged 75 years or more: findings from the Survey of Health, Ageing and Retirement in Europe, a longitudinal population-based cohort study (SHARE-FI75+). *BMJ Open* **4**, e006645.
109. Rockwood K, Song X, MacKnight C *et al.* (2005) A global clinical measure of fitness and frailty in elderly people. *CMAJ* **173**, 489–495.
110. Janssen I (2006) Influence of sarcopenia on the development of physical disability: the Cardiovascular Health Study. *J Am Geriatr Soc* **54**, 56–62.
111. Newman AB, Kupelian V, Visser M *et al.* (2006) Strength, but not muscle mass, is associated with mortality in the health, aging and Body Composition Study Cohort. *J Gerontol A Biol Sci Med Sci* **61**, 72–77.
112. Keevil VL, Hayat S, Dalzell N *et al.* (2013) The physical capability of community-based men and women from a British cohort: the European Prospective Investigation into Cancer (EPIC)-Norfolk study. *BMC Geriatr* **13**, 93.
113. Elia M (2013) Body composition by whole-body bioelectrical impedance and prediction of clinically relevant outcomes: overvalued or underused? *Eur J Clin Nutr* **67**, Suppl. 1, S60–S70. Nature Publishing Group.
114. Malmstrom TK & Morley JE (2013) SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. *J Am Med Dir Assoc* **14**, 531–532. American Medical Directors Association, Inc.
115. Woo J, Leung J & Morley JE (2014) Validating the SARC-F: a suitable community screening tool for sarcopenia? *J Am Med Dir Assoc* **15**, 630–634.
116. Morley JE & Malmstrom TK (2014) Can sarcopenia be diagnosed without measurements? *Eur Geriatr Med* **5**, 291–293.
117. Martin FC & Brighton P (2008) Frailty: different tools for different purposes? *Age Ageing* **37**, 129–131.