Epidemiology of sarcopenia and insight into possible therapeutic targets

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**Abstract**

Musculoskeletal ageing is a major public health concern owing to demographic shifts in the population. Sarcopenia, generally defined as the age-related loss of muscle mass and function, is associated with considerable risk of falls, loss of independence in older adults, and hospitalization with poorer health outcomes. This condition is associated with increased morbidity and health care costs. As with bone mass, muscle mass and strength increase in late adolescence and early adulthood, but then begin to decline substantially from the age of around 50 years. Sarcopenia is characterised by many features, which include loss of muscle mass, altered muscle composition, infiltration with fat and fibrous tissue and alterations in innervation. A better understanding of these factors might help us develop strategies to target these effects. To date, however, methodological challenges and controversies regarding how best to define the condition, in addition to uncertainty about what outcome measures to consider, have delayed research into possible therapeutic options. Most pharmacological agents investigated to date are hormonal, although new developments have seen the emergence of agents that target myostatin signalling to increase muscle mass.

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**Introduction**

Demographic shifts in the population have meant that the number of older adults in society has expanded hugely; the population aged over 60 years is predicted to rise from 841 million in 2013 to more than 2 billion by 2050 worldwide (1). Musculoskeletal disease places a substantial burden on the ageing population, contributing 7.5% of the disease burden in those over 60 years of age (2). The development of both osteoporosis and sarcopenia in later life (3,4) is a common problem encountered as part of musculoskeletal ageing, and contributes substantially to this burden on both personal and societal levels. Research into sarcopenia has perhaps been hampered by uncertainty regarding how best to define the condition (4) (Table 1); indeed, the very term sarcopenia, derived from Greek meaning ‘loss of flesh’, was only first suggested in 1989 (5), and the incorporation of the concept of loss of muscle function as well as muscle mass with age has been a more recent development over the last decade. However, controversy remains on how best to define this condition.

Muscle mass and strength peak in early adulthood, followed by a gradual decline (loss of ~1% lean muscle mass per year) after age 40 years (6), then a more substantial decline from the fifth decade onwards where muscle mass is lost at a rate of 1-2% per year and strength at a slightly greater rate of 1.5-3% per year (7) . Total muscle mass decreases by nearly 50% from the age of 20 years to 90 years (6). On average, ~30% of strength is lost between the age of 50 and 70 years, and another 30% of residual strength is lost during each subsequent decade (8, Figure 1). Lifestyle factors play an important role in the prevention of sarcopenia (Figure 2). Adoption of a more sedentary lifestyle among the general population, and an extended life expectancy, would suggest that the prevalence of sarcopenia and associated health consequences will become much more common in the coming years.

Sarcopenia is associated with a number of adverse outcomes including falls, fractures, frailty and mortality (3). Impaired physical function (but not multimorbidity) is predictive of mortality in older community-dwellers, as shown by results from the ilSIRENTE prospective cohort study (9). The physical frailty phenotype operationalized by Fried, and defined as possessing three or more criteria of the following: weakness (assessed by grip strength), slowness (assessed by gait speed), low levels of physical activity, low levels of energy (self-reported) and unintentional weight loss, predicts many of the negative outcomes described above, and indeed muscle loss is thought to be the mediator of this association (10). Given the interconnection between sarcopenia and frailty, the emergence of a large amount of literature from studies designed to identify strategies to prevent the progression of these twin pathologies is not surprising. Perhaps inevitably, this literature presents the case for use of biomarkers to identify those at greatest risk, although to date no single biomarker has been identified (11). This review considers the current definitional approaches to sarcopenia; the epidemiology of the condition and its pathogenesis (Figure 2), and possible therapeutic advances in its treatment.

**[H1] Defining sarcopenia**

Considerable debate in ongoing regarding the best approach to defining sarcopenia, owing in part to the different technologies available to inform any definition (for example, dual-energy X-ray absorptiometry or bioimpedance analysis). A particular criticism of defining sarcopenia on the basis of muscle mass is that although loss of muscle strength and muscle mass are often correlated, loss of muscle strength often exceeds muscle loss. A number of international bodies have contributed to have contributed to the debate regarding how best to define the condition (Table 1), including The International Osteoporosis Foundation (IOF) and the European Society for the Clinical and Economic aspects of Osteoarthritis and Osteoporosis (ESCEO), and the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project. A report from the FNIH, using data from nine sources of community-dwelling older persons from the USA, Iceland and Europe, highlights numerous priorities for sarcopenia research, specifically the evaluation of the clinical impact of applying a more clinical definition that requires fewer tests, epidemiological data reporting rates of change in lean mass over time, and interventions that might retard muscle loss (such as lifestyle and pharmacological interventions)(8). Similar cut-points for grip strength (<27kg in men, <16kg in women) have been used in another study, which took a life course approach to describing grip strength over adult life by use of normative data from 12 UK studies (49,964 participants) (12), work triggered by a growing understanding of early developmental origins of sarcopenia (13). One of the latest contributions to the debate around definitional approaches to sarcopenia has been from the Asian working group for sarcopenia, which recommends cut-off values for muscle mass measurements, handgrip strength, and usual gait speed (14). Taken together, the recent literature suggests that there is great motivation worldwide to develop a definition of sarcopenia that can be used in a clinical and research setting.

**[H1] Epidemiology and outcomes**

Current definitions of sarcopenia are only newly developed and still not fully accepted. Varying approaches to defining sarcopenia (such as those described in Table 1) inevitably affect its estimated prevalence. Estimates range from 9% to 18% in individuals >65 years of age, rising to 30%in men over 80 (8,15). Applying the European Working Group on Sarcopenia (EWGSOP) definition of sarcopenia in a community dwelling population (the UK-based Hertfordshire Cohort Study), researchers reported that sarcopenia was present in 4.6% of men and 7.9% of women at a mean age of 67 years (16).

Unlike for osteoporosis, the clear consequence of which condition is fragility fracture, an outcome associated with sarcopenia that is important and quantifiable in terms of public health is much harder to define. One important outcome to consider is loss of independence, which may result as a consequence of loss in reserve capacity, defined as an individual’s resources for responding effectively to challenging conditions. In the neuromuscular system, a 30% reduction in reserve capacity limits its normal function, and a loss of 70% results in system failure(17). For example, previous studies have illustrated that sarcopenia in older men and women predicts loss of independence in activities of daily living, (18,19); for example, ability to walk (which may be limited by sarcopenia) is associated with increased healthcare costs (20), and sarcopenia is associated with a higher risk of falling, which leads to loss of independence and hospitalisation costs (21). Sarcopenia is also a predictor of poor outcomes in patients who are undergoing surgery or have other serious co-morbidities (22-24).One of the few studies that have attempted to estimate the economic costs associated with sarcopenia in any country reported a direct cost of approximately $18.5 billion ($10.8 billion in men and $7.7 billion in women) in the USA in 2000, accounting for about 1.5% of the country’s total health expenditure (25); these costs are incurred by hospitalisation, nursing home admissions and home-based health care expenditure. An important research goal, in the USA and elsewhere, is to provide up-to-date estimates of the costs associated with sarcopenia, perhaps also attempting to quantify the indirect costs, such as home-based health care, outlined above. Given that sarcopenia might also be associated with other health care costs, such as lack of productivity, reduced quality of life and psychological problems, research in this area is also timely, especially with the development of a quality of life questionnaire specifically designed for use in subjects with sarcopenia (26).

**[H1] Aetiology of sarcopenia**

Muscle cells are probably influenced by the same fundamental processes of ageing that affect all living cells. These processes include replicative senescence (a limitation in the number of times that cells can divide) and impaired stem cell regeneration; accumulation of cell damage; autophagy (reduced clearance of cell damage) and reduced mitochondrial energy generation. A full discussion of the biology of ageing as applied to muscle is outside the scope of this review, and has been reviewed elsewhere (27-30). However, research into the aetiology of age-related muscle loss is important to the development of therapeutic strategies to retard or prevent muscle loss (31).

Sarcopenia involves negative protein turnover, characterised by a reduction in myofibrillar and mitochondrial protein synthesis (27). Because mitochondria are important in energy provision, redox homeostasis and regulation of cell death, many recent articles over the last 5 years have focused on age-related alterations in mitochondrial function and their role in the aetiology of sarcopenia. For example, one review (28) postulates that defective redox signalling might be important in reducing the integrity of the ageing neuromuscular system, and a better understanding of the causes of defective mitochondrial homeostasis provides an opportunity to identify targeted interventions. Another review, published in 2016 (29), highlights the progressive reduction in the regenerative capacity of the skeletal muscle stem cells (called satellite cells), which are critical for muscle repair in response to trauma or damage. Decreased capacity for muscle regeneration and increased apoptosis in muscle might play an important role in sarcopenia aetiology, an assertion supported by the observation that apoptotic signalling correlates with slow walking speed and reduced muscle volume (30). Loss of muscle strength (32) and neuromuscular impairment (through loss of motor units and loss of motor neurons) accompanies skeletal atrophy with ageing. Finally, as reviewed by Blau *et al.,* a better understanding of the interplay between satellite cell extrinsic and intrinsic factors in sarcopenia might reveal therapeutic opportunities (33).

Systemic inflammation also might be important in the pathogenesis of muscle loss in later life; for example, increased production of proinflammatory cytokines could affect all the mechanisms outlined above. Age-related inflammation (also referred to as ‘inflammaging’,) first proposed as a phenomenon in 2000, is a possible underlying cause of muscle loss (34). Inflammaging is thought to result from lifetime exposure to both clinical and subclinical infections, as well as exposure to noninfective antigens, leading to high antigenic load (35). The inflammatory response to this antigenic load leads to tissue damage and the production of reactive oxygen species, resulting in the release of additional cytokines (36). This vicious cycle favours a chronic proinflammatory state (37), but might be amenable to therapeutic manipulation (38).

**[H1] Risk factors for sarcopenia**

Just as for bone loss, factors that affect muscle can do so from an early age, by influencing the development of peak muscle mass and/or rates of muscle loss. For instance, peak muscle mass is attained in youth but could be a determent of function later in life and is influenced by both genetic and environmental factors. As an example, grip strength over the life course is illustrated in Figure 1. Genetic and environmental factors are major determinants of muscle strength; the latter can also influence muscle, and are potentially amenable to modification. For example, lifestyle factors, such as those displayed in Figure 2, can influence muscle mass in later life. Comorbidities are common in older adults, and may co-exist with, or contribute to, loss of muscle mass and function. Pharmacological intervention, for example with corticosteroid therapy, in patients with co-morbidities such as polymyalgia rheumatic may also contribute to muscle loss.

***[H2] Body composition***

An individual’s body weight and composition is one factor to consider. With increasing age, body fat increases and muscle mass decreases, which can result in a stable body weight but altered body composition. The term sarcopenic obesity  describes the condition where sarcopenia and obesity coexist, resulting in a disproportionate amount of fat mass relative to lean muscle mass. The estimated prevalence of sarcopenic obesity ranges from 0% to 41% in older populations, owing to the varying definitions of both sarcopenia and obesity (39). However, these two conditions might share common aetiologic pathways; for example, both show an accompanying increase in adipokines and inflammation that might adversely affect muscle quality (40). Further research into sarcopenic obesity is important, as highlighted in the review by Cauley *et al* (39). Although obese or overweight adults often have a higher muscle mass compared with non-obese adults, their muscle quality and functional status is lower (41). This may reflect common pathways in the development of sarcopenia and obesity, and may lead to a multiplicative effect in the development of adverse health consequences of both conditions as raised adipokines in obesity may further negatively affect muscle quality. Substantial weight loss has been associated with loss of grip strength, although coexisting comorbidity could be a confounding factor (42).

Physical activity is well known to affect muscle mass and strength. Studies have previously shown that inactivity leads to loss of muscle mass and strength, irrespective of age; during extended bed rest muscle strength decreases before the subsequent decrease in muscle mass is observed (43). By contrast, lifelong physical exercise preserves muscle structure and function (44). Specifically, the risk of mobility impairment in older adults decreases with increased mid-life leisure time physical activity, although conversely occupational activity might actually have the reverse effect (45). A systematic review in 2014 also highlighted the studies that have suggested benefits for exercise on muscle health in later life (46); for example, Law et al (47) provide an overview of the evidence for the role of resistance exercise in the prevention and treatment of sarcopenia, and highlights certain critical factors (namely exercise intensity, volume and progression) that are key to optimizing the resistance exercise prescription.

***[H2] Diet and smoking***

Cigarette smoking might have direct effects on muscle, as well as be associated with other detrimental lifestyle factors. For example, the Minos study (48) demonstrated that current smokers have lowered appendicular muscle mass compared with non-smokers, results that showed a dose-effect relationship. However, other studies have reported no such association (49). Alcohol consumption might also affect muscle health. Although the Minos study found no association between muscle mass and moderate alcohol intake (48), one might speculate that heavy consumption of alcohol could conceivably lower muscle mass via effects on nutrition, physical activity and hormone levels (50), although moderate alcohol consumption does not appear to be harmful to muscle (51)**.**

Dietary factors might also have a role in maintaining muscle mass and strength. Studies have suggested that poor nutrition or reduced physical activity in older people reduces their rate of muscle protein synthesis by 30%, independent of ageing itself, and that this is particularly evidence with mitochondrial protein synthesis in human skeletal muscle (52-55) . Multiple studies have demonstrated a positive association between protein intake and preservation of lean bone mass in older adults (56,57). However, past studies of protein supplementation, most of which used a combination of supplementation and resistance training, have shown mixed results (58). Vitamin D status is thought to be relevant to all areas of musculoskeletal ageing; low vitamin D levels have been associated with poor balance and an increased risk of falls (59). A raised parathyroid hormone level often accompanies low vitamin D levels, and is also associated with sarcopenia and risk of falling independently of vitamin D status (60). Given the above findings, a review from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) included dietary recommendations for the prevention of age-related deterioration of the musculoskeletal system, including optimal intake of dietary protein and vitamin D (53). However, a systematic review published in 2014 reported moderate quality evidence that exercise interventions improve muscle strength and physical performance whereas the benefits of nutritional interventions were more equivocal (61). Further research is required to determine which of these factors is predominant in the development of sarcopenia.

**[H1] Pharmacological therapy**

The management of any common health problem typically includes two possible approaches; identification of individuals at high risk of having, or developing the condition (in this case those with sarcopenia or pre-sarcopenia) or trying to improve the general health of the whole population, through lifestyle measures (that in the case of sarcopenia might include dietary intervention and physical activity). Drugs designed to treat sarcopenia are now starting to emerge. When considering the patients selected to enter studies of novel therapies to prevent or retard development of sarcopenia, it is helpful to be aware of the industry regulatory processes surrounding drug development. The IOF have published recommendations specifically addressing this issue,that suggest possible trial endpoints and selection criteria for individuals who might participate in such studies (62), and highlight the notion that prevention of sarcopenia in high-risk pre-sarcopenic individuals could be possible, as might the treatment of individuals in whom sarcopenia has already developed. Therapeutic targets for the treatment of sarcopenia might include components of the anabolic and catabolic signalling pathways. Hormonal manipulation has formed the basis of many of therapies for sarcopenia investigated to date. Supplementation with testosterone (a well-known androgen) increases skeletal muscle volume by promoting hypertrophy of myofibres (63); however, testosterone is also associated with notable adverse effects and whether its benefits translate to improved muscle function has not been clearly demonstrated in clinical trials. Atkinson *et al.* demonstrated that in pre-frail and frail elderly men, daily treatment with a transdermal testosterone gel (50mg) increased testosterone levels from 11.6 nmol/l (SD 3.5 nmol/l) to 18.0 nmol/l (SD 8.1 nmol/l) , and preserved muscle thickness, whereas a decreased muscle thickness was observed in the placebo group (63). In Phase II trials, treatment with the selective androgen receptor modulator (SARM) enbosarm, resulted in a dose-dependent increase in total lean body mass, in addition to improvements in physical function, in both male and female participants in their seventh decade (64). Furthermore, administration of enbosarm did not seem to be associated with an increased risk of adverse effects. Results of a Phase II trial of another SARM, MK-0773, were published in 2013 (65); in this double blind, placebo-controlled trial involving 170 women with sarcopenia, lean body mass significantly increased in MK-0773-treated patients at 6 months, without evidence of androgenization. Physical performance showed a trend towards improvement over the follow-up period; however, this finding was not statistically significant. Several patients in the treatment group had elevated levels of transaminases but this clinical feature resolved on study discontinuation.

Myostatin is an inhibitor of muscle growth and hence a potential target for preventing or reversing muscle loss; several studies have presented evidence for the potential benefits of targeting the myostatin pathway for improving muscle function. For example, recent work in 2015 into a humanised monoclonal myostatin antibody that binds and neutralizes myostatin suggests that treatment with this antibody can increase lean mass and might also improve functional measures of muscle power (66). In a phase II trial conducted on patients aged 75 years or older who had fallen in the past year, patients treated with this antibody reported a higher muscle mass (0.43kg, 95% CI 0.192–0.660) after 24 weeks when compared with the placebo group, in addition to demonstrating significant improvements in stair climbing time, chair rise with arms and fast gait speed (66). These results follow previous approval for the use of this therapy in the treatment of inclusion body myositis (IBM); in patients with IBM a single dose of therapy increased their 6 min walking distance by 52 m compared with placebo (67). Myostatin signalling is mediated by the transmembrane kinase receptor activin type IIB receptor (ActRIIB) (68), a molecule that might also be a promising therapeutic target. ActRIIB is highly expressed in mammalian skeletal muscle, and postnatal blockade of ActRIIb leads to rapid and massive muscle hypertrophy. One therapeutic approach has involved the systemic delivery of a soluble recombinant form of the receptor that acts as a decoy, thus disrupting the interaction between the receptor and its ligands (68). Having previously been trialled in patients with muscular dystrophy, which is characterised by progressive muscle weakening and wasting, a 2015 study of the effect of receptor blockade in wild-type mice demonstrated that blockade of ActRIIB with a soluble receptor for 8 weeks increased absolute force-generating capacity and reduced mitochondrial function in glycolytic gastrocnemius muscle without compromising energy status during sustained activity (68). This suggests that this agent may be considered for trial in sarcopenic subjects in the future.

Preventative and therapeutic strategies are required in the management of sarcopenia. Marzetti *et al.* have previously reviewed this topic, and specifically considered mitochondrial dysfunction (69), highlighting the potential challenges and risks of such a study, as well as suggesting possible study populations. They discuss safety considerations when designing such a trial; what outcome measures to consider, and the use of biomarkers; the optimal timing and duration of the intervention and the selection of a target population. Unfortunately, to date no such agent has become available for trial in a clinical setting.

# [H1] Conclusions

Due to ageing of the population, conditions that emerge later in life and that are associated with considerable morbidity and public health costs are of great consequence. Sarcopenia, which is linked to frailty, is perhaps one of the most important of these conditions and a strong research agenda has emerged to consider the aetiological factors that might prevent or retard the development or progression of sarcopenia. An understanding of the biology of ageing as applied to muscle might help us to identify those at risk of sarcopenia, and to identify potential therapeutic targets; hence, a partnership between basic biologists, the pharmaceutical industry and clinicians is critical. Given the substantial personal, societal and economic burdens associated with sarcopenia, it is essential that we identify ways to detect those at greatest risk, and use strategies for lifestyle modification to retard or prevent muscle loss at a population level. However, many individuals are likely to also benefit from a tailored pharmacological approach and although methodological challenges regarding how best to define the condition, and what outcome measure to consider, have delayed research into possible therapeutic options, promising pharmacological agents have nonetheless emerged. To date, these treatments have largely been hormone-based approaches (such as treatment with testosterone and SARMs) although new developments have seen the emergence of a promising monoclonal antibody to myostatin and ActRIIB blockade agents.

A particular challenge for clinicians who treat patients with sarcopenia is that even though diagnostic tools have been developed that are accurate and reliable in research settings, many are not easily applied in clinical practice, and simpler diagnostic criteria have instead been proposed [62]. A particular criticism of defining sarcopenia on the basis of muscle mass is that although loss of muscle strength and muscle mass are often correlated, loss of muscle strength often exceeds muscle loss. This phenomenon is of considerable relevance when considering approaches to defining sarcopenia and clinical outcomes for pharmacological trials. Analogous to bone mineral density and fracture risk, if preservation of functional performance is the goal of sarcopenia treatment, study designers should be cognizant of the clinical outcome of choice.

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**Author contributions**

E.M.D researched data for the article and wrote the manuscript. A.A.S and C.C. both contributed substantially to the discussion of the content, and reviewed and edited the manuscript before submission.

**Competing interests statement**

C.C. declares that he has received consultancy fees and honoraria from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB. E.M.D. declares that she has received speaker’s fees from Lilly. A.S. declares no competing interests.

**Key points:**

1. Sarcopenia, the age-related loss of muscle mass and function, is associated with considerable morbidity and health care costs
2. Approaches to defining sarcopenia remain controversial, although several groups have proposed ways of defining the condition
3. Moderate-quality evidence suggests that exercise interventions improve muscle strength and physical performance in patients with sarcopenia, whereas the benefits of nutritional interventions are more equivocal
4. Most pharmacological agents for sarcopenia investigated to date are hormonal (testosterone and selective androgen receptor modulators) although therapies targeting myostatin signalling are emerging as new developments.

**Figure 1 Grip strength across the lifecourse**

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*Figure Legend*

Factors that affect muscle can do so from an early age, by influencing the development of peak muscle mass and/or rates of muscle loss. Peak muscle mass is attained in youth, and followed by decline in grip strength in later life. Grip strength over the life course is illustrated here.

**Table 1**

**Diagnostic criteria for sarcopenia: elements included in different definitions**

|  |  |  |
| --- | --- | --- |
| Study group | Definitions | Criteria |
| Low Muscle Mass | Low Muscle Strength | Reduced Physical performance |
| ESPEN Special Interest Groups  | Loss of muscle mass and muscle strengthOften associated with comorbidity | Low muscle mass (<2SD below young normal mean) | Not included | Reduced gait speed (<0.8 m/s in 4 min test) or reduced performance in any functional test used for the comprehensive geriatric assessment |
| European Working Group on Sarcopenia in Older People  | Loss of muscle mass and strengthRisk of adverse outcomesOften associated with comorbidity | Low muscle mass (<2SD below young normal mean) | Low hand grip strength (<2 SD below young normal mean) | Low gait speed (< 2SD below young normal mean) |
| International Working Group on Sarcopenia  | Loss of muscle mass and function with age | Reduced muscle mass e.g. Appendicular lean mass relative to height squared ≤7.23 kg/m2 in men and ≤5.67 kg/m2 in women  |  Not included | Gait speed <1 m/s  |
| Society of Sarcopenia, Cachexia and Wasting Disorders  | Loss of muscle mass with reduced mobility | A lean appendicular mass relative to height squared < 2SD below young adult mean |  Not included | Walking speed ≤1 m/s  |
| Foundation for the National Institutes of Health Sarcopenia Project (FNIH) | Loss of muscle mass and muscle weakness | Appendicular lean mass adjusted for body mass index <0.789 in men and <0.512 in women  | Hand grip strength <26kg in men and in <16kg women  | Gait speed ≤0.8 m/s |
| Asian working group for sarcopenia | Low muscle mass with low muscle strength and/ or low physical performance | Muscle mass of 7.0 kg/m2 for men and 5.4 kg/m2 for women when measured by dual X-ray absorptiometry or 7.0 kg/m2 for men and 5.7 kg/m2 for women when measured by bioimpedance analysis | Hand grip strength <26 kg for men and <18 kg for women | Gait speed <0.8 m/s |

|  |
| --- |
|  Risk factors for muscle aging NEW FIGURE**Intrinsic factors*** Age
* Sex hormone deficiency
* Co-morbidity (e.g. diabetes)
* Genetic factors (e.g. myostatin and vitamin D receptor genes)
* Early life

**Body Composition*** Significant weight loss
* Sarcopenic obesity

**Lifestyle habits*** Cigarette smoking
* Excessive alcohol consumption
* Prolonged immobilisation and/or low physical activity

**Diet*** Low protein intake
* Vitamin D deficiency

**Pharmacological therapy** * Use of ACE inhibitors
* Use of steroids
 |

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**Author biographies**

Professor Elaine Dennison is professor of Musculoskeletal Epidemiology and honorary consultant in Rheumatology within Medicine at the MRC Lifecourse Epidemiology Unit, University of Southampton. Having worked as a principal investigator of the Hertfordshire Cohort Study for many years, her research interest centres around musculoskeletal aging. She is particularly interested in how early events in life interact with adult lifestyle factors to determine how we age.

Professor Avan Aihie Sayer is Professor of Geriatric Medicine and Director of the NIHR Newcastle Biomedical Research Centre. Her research involves a life course approach to understanding ageing syndromes such as sarcopenia, frailty and multimorbidity with translation of the findings into new approaches to diagnosis, treatment and prevention.

Cyrus Cooper is professor of Rheumatology and director of the MRC Lifecourse Epidemiology Unit; Vice-Dean of the Faculty of Medicine at the University of Southampton; and professor of Epidemiology at the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford. Professor Cooper leads an internationally competitive programme of research into the epidemiology of musculoskeletal disorders, most notably osteoporosis.

**Competing interests**

Professor Cyrus Cooper has received consultancy fees and honoraria from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB. Professor Dennison has received speaking fees from Lilly. Professor Aihie Sayer has no conflicts to declare.

**Subject ontology terms**

[Health sciences / Rheumatology / Musculoskeletal system / Muscle / Skeletal muscle](http://subjects.npd.nature.com/products/nrrheum#692/4023/1671/1668/1973)
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[Health sciences / Risk factors](http://subjects.npd.nature.com/products/nrrheum#692/499)
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**ToC blurb**

With the aging population, sarcopenia is becoming a public health concern. However, controversy remains on how it can be best defined. This review discusses the various approaches to defining sarcopenia, its prevalence and potential lifestyle modifications and therapies for its treatment.