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Muscle Loss: The New Malnutrition Challenge in Clinical Practice

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Abstract

Recent definitions of malnutrition include low muscle mass within its diagnostic criteria. In fact, malnutrition is one of the main risk factors of skeletal muscle loss contributing to the onset of sarcopenia. However, differences in the screening and diagnosis of skeletal muscle loss, especially as a result of malnutrition in clinical and community settings, still occur mainly as techniques and thresholds used vary in clinical practice.

The objectives of this position paper are firstly to emphasize the link between skeletal muscle loss and malnutrition-related conditions and secondly to raise awareness for the timely identification of loss of skeletal muscle mass and function in high risk populations. Thirdly to recognize the need to implement appropriate nutritional strategies for prevention and treatment of skeletal muscle loss and malnutrition across the healthcare continuum. Malnutrition needs to be addressed clinically as a muscle-related disorder and clinicians should integrate nutritional assessment with muscle mass measurements for optimal evaluation of these two interrelated entities to tailor interventions appropriately. The design of monitoring/evaluation and discharge plans need to include multimodal interventions with nutrition and physical exercise that are key to preserve patient’s muscle mass and function in clinical and community settings.

Keywords: lean mass loss, skeletal muscle mass, malnutrition, sarcopenia, ageing, continuum of care

1. Ageing, successful ageing, and nutritional status

The world population is ageing [1] and many people experience frailty, disability and chronic disease as they get older, which is linked to impaired skeletal muscle and bone health. Ageing and disease both result in the continuing but progressive decrease in muscle mass, which can limit the ability to remain independent [2]. Today, healthcare professionals can help patients prolong the period of good health across the lifespan by advising individuals how to maintain wellness and good quality of life in addition to providing effective medical management. This can be achieved by encouraging individuals to maintain physical activity and by providing dietary advice to ensure their nutritional needs are met [3].

Problems with nutrition are common in older individuals but malnutrition is not an inevitable part of ageing as the modifiable lifestyle factors of diet and physical activity can be effectively addressed for prevention and treatment in clinical practice [4]. Therefore, creating the social, clinical and lifestyle conditions which improve quality of life will help people to stay independent and active longer.

2. Muscle as a metabolically active organ

Skeletal muscle is vital to mobility, posture, strength and balance and allows the performance of exercise and activities of daily living [5, 6]. Moreover, muscle has been identified as a key metabolic and homeostatic organ via crosstalk between body organs [7]. Muscle plays a central role in protein metabolism acting as a reservoir of amino acids when the protein needs of the body are not met by dietary intake, and enables maintenance of the protein content of other essential tissues and organs [7, 8]. When dietary protein intake is not sufficient, muscle is broken down leading to loss of lean mass (LM) with potentially serious health consequences. LM, or lean body mass (LBM), is a fat-free and bone mineral-free component that includes muscle and other components such as skin, tendons, and connective tissues [9].

LM is therefore important during illness, both for its role in balancing the metabolic needs of other organs and for its reserves of protein for use as energy intermediate substrates. Loss of LM is also associated with muscle weakness and impaired physical function [10] and importantly, is exponentially linked to morbidity and mortality (Figure 1).

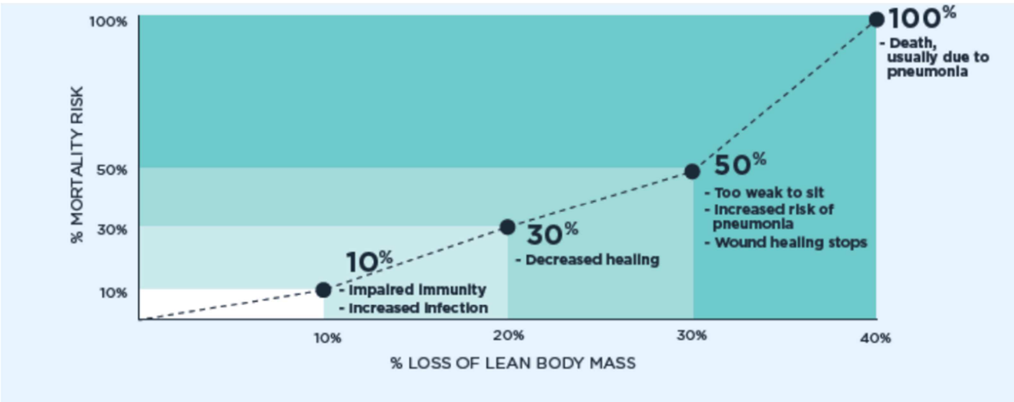

Figure 1. Complications increase with greater lean mass loss. Assuming no preexisting loss. Adapted from Demling et al 2009 [10].

3. Malnutrition contributes to skeletal muscle mass loss

Malnutrition is an increasingly prevalent condition that is the result of lack of intake or uptake of nutrients (protein, vitamins and minerals) leading to altered body composition (decreased muscle) and body cell mass [11]. This results in diminished physical and mental function, and impaired clinical outcomes [11], which can delay recovery from disease and increase mortality [10]. Malnutrition further contributes to acute or chronic loss of muscle mass and function, in both the community and hospitalized individuals. Indeed, the latest definition of malnutrition by The European Society for Clinical Nutrition and Metabolism (ESPEN) has incorporated low fat free mass (specifically fat free mass index) into the diagnostic criteria [12].

Different psycho-social, physiological, and pathological conditions lead to inadequate dietary intake, and failure to meet energy and protein requirements in certain populations, especially in advancing age or in those with complex disease. In individuals, the causes of insufficient dietary intake and malnutrition are complex and multi-factorial. Ageing, dementia and depression, chronic illness, multiple hospitalizations (immobilization) or decreased appetite occurring alone or in combination all contribute [13, 14].

Consequences of malnutrition are also multi-faceted, leading to loss of muscle mass and function, which is associated with adverse health outcomes such as mobility-disability, illness and infections, increased recovery time, poor quality of life and mortality [11, 14] (Figure 2).

This is a vicious cycle where muscle reduced mass and a decline in strength and/or function represents either a cause or a consequence of metabolic dysfunction and disease development especially in older adults [15] (Figure 2).

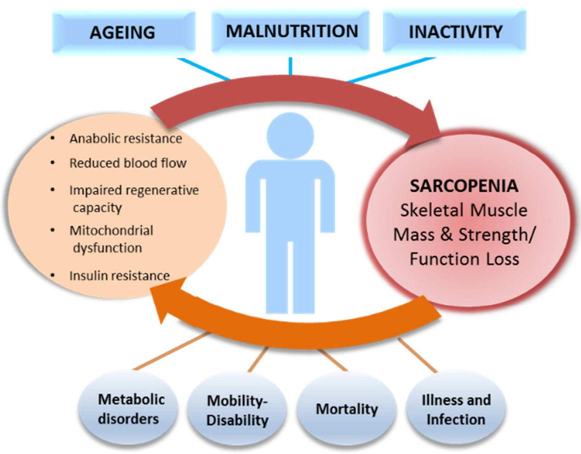

Figure 2. Relationship between malnutrition, and loss of skeletal muscle mass and function.

Therefore, early recognition of malnutrition, and timely administration of nutritional care can also help improve patient’s lives while reducing healthcare costs [13].

Since malnutrition is so strongly associated with loss of muscle mass and strength, this is emerging as the new malnutrition challenge in clinical practice.

Malnutrition is one of the main risk factors of sarcopenia, and acts as a driver of loss of muscle mass and function, which are the main features [16]. Malnutrition and sarcopenia are common and overlapping in older adults. In fact, both entities are prevalent among older adults aged 65 years and over, especially in those hospitalized or living in nursing homes [17]. Therefore, evaluation of muscle mass is crucial for the diagnosis of both conditions.

Another challenge that needs to be taken into account is the presence of malnutrition among obese persons, especially in light of the growing prevalence of obesity worldwide [18] and the presence of sarcopenic obesity [19]. Sarcopenic obesity is the presence of a low proportion of LM despite the presence of obesity [20] and has been independently associated with worse morbidity and disability than either sarcopenia or obesity alone [21]. This can occur in older individuals, in those with Type 2 Diabetes Mellitus (T2DM), COPD, and in obese patients with malignant disorders and post organ transplantations at all ages. Mechanisms include inflammation and/or inactivity induced muscle catabolism [20, 22].

Representatives of the four largest global Parenteral and Enteral Nutrition (PEN)-societies from Europe, North and Latin America, and Asia (The European Society for Clinical Nutrition and Metabolism, ESPEN, American Society for Parenteral and Enteral Nutrition, ASPEN, Federacion Latinoamericana de Terapia Nutricional, Nutricion Clinica y Metabolismo, FELANPE, and The Parenteral and Enteral Nutrition Society of Asia, PENSA comprising the Global Leadership Initiative on Malnutrition, GLIM), have collaborated to create a consensus on the diagnostic criteria for malnutrition that has been recently published [23]. This consensus group provided criteria for the diagnosis of malnutrition that can be used for all patients and in all clinical settings based on a two-step model for risk screening and diagnosis assessment, which requires at least one etiological criterion (weight loss, low BMI, or reduced muscle mass) and one phenotypic criterion (reduced food intake or assimilation, or inflammation) [23].

Importantly, low muscle mass has been proposed as part of the definition of malnutrition [23].

4. Factors affecting rate of skeletal muscle mass and function loss

Muscle accretion and muscle loss have a noticeable life trajectory, i.e. depending on an individual's age [24]. Loss of muscle mass and strength is a natural part of ageing [25]. Peak muscle mass and strength are achieved around the age of 25 years [26] but after the age of 40-50, loss of skeletal muscle mass accelerates due to decreased physical activity and altered protein metabolism [25]. More significantly, during the ageing process a greater decrease in muscle strength and function is observed [25]. Therefore, building muscle before 40 years and preserving muscle as much as possible during adulthood is a key strategy for healthy ageing.

Illness, injury, bed rest and malnutrition (inactivity) can accelerate the natural, age-related progression of LM loss [7, 10, 27]. Patients who suffer such episodes may experience progressive declines in muscle mass, strength and functional capacity. Immobilization and bed rest, and subsequent skeletal muscle loss, can have negative effects on functional capacity, such as walking or climbing stairs. Whether bed rest is prolonged or acute, the loss of muscle is rapid and profound. Most of the skeletal muscle loss occurs during the early part of the bed rest period [28, 29].

The rate of skeletal muscle loss varies across hospital settings. The severity of the illness or injury, coupled with increases in inflammation and catabolic hormones, hallmarks of the stress response, contribute to the progressive and rapid skeletal muscle loss that occurs in patients who are critically ill [30]. In a study evaluating the rate of skeletal muscle wasting in 63 critically ill patients, it was reported that within 10 days of admission an average 18% reduction in muscle mass (*rectus femoris* cross sectional area) was reported [31]. This shows that skeletal muscle loss occurs early, within days of hospitalization, and rapidly in ICU patients. In addition, more severe skeletal muscle loss was observed in patients with multi-organ failure as compared with patients with single organ failure.

Altogether, these data show how hospitalization and illness accelerate skeletal muscle loss and functional decline, and the need for early identification and nutritional intervention.

5. Clinical conditions associated with skeletal muscle loss

Beyond ageing, muscle decline is associated with pathological states and chronic diseases, such as malnutrition, cancer, neurodegenerative disease, chronic kidney disease, chronic obstructive pulmonary disease (COPD), sepsis, and immune disorders. On top of this, hospital immobilization and bed rest are devastating to patients who suffer from these conditions [32-34]. Most of these pathological conditions are associated with various degrees of chronic inflammation, which plays a critical role in the onset of muscle atrophy and malnutrition.

The main factors underlying malnutrition in well-developed regions are disease and its treatment, which can modify the drive to eat and impact the absorption, metabolism, or assimilation of nutrients. In such cases, malnutrition is referred to as "disease-related malnutrition" (DRM) [11]. DRM is characterized by a deficit of energy, protein and other nutrients, loss of appetite, and disease-related catabolism. DRM is a frequent problem in all healthcare settings, including hospitals, home care, and sheltered housing [35], and is highly prevalent in rehabilitation settings [36, 37]. DRM with inflammation is characterized by an inflammatory response with altered body composition, impaired function and adverse health outcomes [38, 39]. Finally, DRM with inflammation can be sub-classified into chronic or acute disease- or injury-related malnutrition.

Cachexia

DRM with inflammation could be considered as synonymous with cachexia [11]. This condition occurs frequently in patients with cancer, COPD, liver disease, congestive heart failure and chronic kidney disease. The cachectic phenotype is characterized by both weight loss (caused by decreased muscle mass and fat mass) and loss of function due to a catabolic inflammatory response from the underlying disease [40]. In cancer, pre-cachexia, cachexia and refractory cachexia can be found dependent on the stage of the disease [41]. While most patients with cachexia are also sarcopenic, not all individuals with sarcopenia have cachexia [24]. The presence or recurrence of systemic inflammation is key for the diagnosis of cachexia. In addition, anorexia, weight loss and reduced fat mass are three elements that can help differentiate between cachexia and sarcopenia [40].

Acute disease- or injury-related malnutrition

Patients in the Intensive Care Unit (ICU) display significant nutritional challenges and are nutritionally compromised. Rates of malnutrition on admission to the ICU are reported to be as high as 60% depending on the patient population and screening tool used [42, 43]. Malnutrition in ICU patients has been associated with worse outcomes [42, 43] and low muscle mass specifically has been associated with higher mortality and longer stays length on ventilation machines [30, 44]. Once in the ICU, these patients experience a rapid and profound loss of LBM. Rates can be as high as 2% per day, with the highest rates being seen in those with worse severity of illness [31]. Although the pathophysiology of this muscle wasting is poorly understood, it is clear that the release of multiple pro-inflammatory cytokines as well as other catabolic hormones lead to an overall net catabolic balance [31]. In addition, organizational factors leading to significant underfeeding likely also contribute. The consequences of muscle wasting in this population are severe, being reported as a contributing factor to post-ICU functional impairment [45] and self-reported physical function [46]. There are no currently agreed objective criteria for diagnosis of malnutrition in ICU patients, although early nutritional intervention is essential in such patients to support lean mass given the above [47, 48].

DRM without inflammation is also called non-cachectic DRM [11]. This is a form of disease-driven malnutrition in which inflammation is not the major causal mechanism e.g. as a consequence of dysphagia, neurologic disorders or dementia/cognitive dysfunction. Advanced ageing contributes to DRM without inflammation due to the presence of anorexia or lack of appetite, named as “anorexia of ageing”, which is caused by non-inflammatory related mechanisms Although, the mechanisms are not fully understood, a range of physiological, psychological and social factors that may influence appetite and food intake in older adults have been proposed [49].

6. Measurement of skeletal muscle loss in malnutrition

Skeletal muscle loss should be appropriately identified in malnourished individuals using validated tools that allow screening, diagnosis, intervention, and monitoring of overall patient health even after discharge [24, 50] (Figure 3).

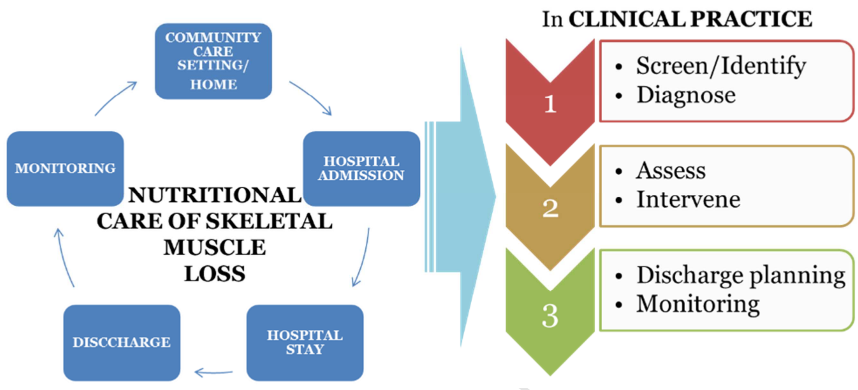

Figure 3. Skeletal muscle loss as a consequence of malnutrition is observed across the continuum of care and should be appropriately addressed in clinical practice.

Currently, all muscle mass measures are indirect and none are perfect. Indeed, the literature does not establish consensus on the best technique for measuring muscle mass, but a recent publication considers dual X-ray absorptiometry (DXA) as a reference standard (but not a gold standard) [9].

Existing criteria for the identification of malnutrition are mainly based on observations of recent weight loss and body mass index (BMI), yet, BMI does not always reflect skeletal muscle loss. BMI as well as muscle mass varies with ethnicity and race and these differences need to be considered. In addition, individuals with the same BMI can have different proportions of lean and fat mass [51]. Therefore, it is fundamental to stress the importance of measuring body composition to evaluate muscle mass and strength loss when making assessments of malnutrition and sarcopenia in clinical practice.

It is important to realize that malnutrition screening and many assessment tools may not take LM into account, as they were developed before muscle was included in the definition of malnutrition. BMI has its limitations since it cannot distinguish between fat, muscle, bone mass, or the distribution of fat across the body. As another limitation of BMI, it might be important that the change in height associated with aging has implications for interpretation of the BMI, a commonly used index of nutritional status. So, clinicians need to assess and measure not only weight, but also muscle mass to tailor interventions appropriately.

Among body composition measurements anthropometry, like calf and arm circumference and skin-fold thickness [52], as well as bioelectrical impedance analysis (BIA) and ultrasound are valuable when used taken sequentially over time. According to the EWGSOP consensus document on the definition and diagnosis of sarcopenia, screening for sarcopenia is recommended from age 65 years onwards by measuring gait speed, and handgrip strength, and/or muscle mass [24]. Very recently, a revised European consensus on definition and diagnosis of sarcopenia has been published to update the original definition (EWGSOP2) [53]. The EWGSOP2 consensus paper now focuses on low muscle strength as a key feature of sarcopenia (primary indicator of probable sarcopenia), uses detection of low muscle quantity and quality to diagnose and identifies physical performance to determine severity. In addition, simple, specific cut-off points are recommended for measures aimed at facilitating early detection and treatment in clinical practice [53]. Different techniques currently exist for the measurement of muscle mass, strength and physical performance, and have been described by their suitability for use in research and/or clinical practice [24-53] (Table 1). We can expect new emerging devices and techniques for muscle mass measurements, e.g. ultrasound [53-54].

Variable	Research	Clinical practice
Skeletal muscle strength	Grip strength Chair stand test (chair rise test) Knee flexion/extension Peak expiratory flow	Grip strength Chair stand test (chair rise test)
Skeletal muscle mass	Dual energy X-ray absorptiometry (DXA) Computed tomography (CT) Magnetic resonance imaging (MRI) Bioelectrical impedance analysis (BIA) Ultrasound	DXA BIA Lumbar muscle cross-sectional area by CT Anthropometry
Physical performance	Short Physical Performance Battery (SPPB) Gait speed Timed-up-and-go test (TUG) 400-meter walk or long-distance corridor walk Stair climb power test	SPPB Gait speed TUG 400-m walk

Table 1. Methods routinely available to assess muscle-related outcomes in research and clinical practice. Adapted from Cruz-Jentoft et al 2010 [24] and 2018 [53].

These techniques can help determine whether the three diagnostic criteria for sarcopenia are met.

Another important issue to consider is sarcopenic obesity [11]. Although, there are currently no commonly accepted criteria for diagnosing sarcopenic obesity beyond those for sarcopenia and obesity separately, muscle function assessed by strength can serve as a useful indicator of the condition [11].

For all these reasons, a sensitive screening approach is needed to capture all individuals considered to be at risk of malnutrition, followed by a diagnostic assessment using a combination of physical examination and biochemical analyses [55].

7. Role of diet and enteral nutrition to prevent lean mass loss across the continuum of care

Across the healthcare continuum, it is important to ensure that patients are able to access and consume nutritious foods which provide sufficient energy and protein, as well as micronutrients. Lifestyle interventions factors such as good nutrition and physical exercise are key to maintaining muscle or slowing muscle decline [29-31]. Growing evidence links nutrition to muscle health suggesting it is important to maintain an optimal nutritional status to prevent muscle mass and strength loss in older adults [56]. In fact, optimal nutrition combined with exercise has been shown to act synergistically against skeletal muscle loss in aging population [57].

Intervening early with nutrition is vital to preserve and re-build muscle that may be lost as a result of ageing, disease, bed rest, or inadequate food intake. The impact of early nutritional therapy and physical rehabilitation on LM and self-sufficiency has been assessed in hospitalized older patients with acute illness [32]. Results showed that early intervention preserved and built LM and prevented declines in functional performance [32].

Currently, the most researched nutrition intervention to prevent skeletal muscle loss in clinical populations is protein supplementation. Achieving adequate protein intake through diet alone can be challenging in the presence of illness and disease, so oral nutritional supplements, (ONS) or enteral tube feeding can be helpful in preserving and preventing skeletal muscle loss in both the hospital and community healthcare settings.

The benefits of high quality protein-enriched ONS have been extensively demonstrated [58]. Research shows that ONS can increase total energy and protein intake without reducing spontaneous food intake and lead to weight gain and prevention of weight loss in both hospital and community patients, including older people [14, 58-61]. Furthermore, ONS can be more effective than food-based snacks of equal energy content to improve micronutrient intake in older hospitalized patients [62], and provide greater energy and protein intake in post-operative patients [63].

Branched chain amino acids have been shown to increase skeletal muscle protein synthesis and net protein balance. In particular, supplementation with leucine, isoleucine, and valine has been shown to increase skeletal muscle protein synthesis to preserve skeletal muscle loss in the elderly [64]. Although dietary supplementation with leucine remains controversial, two recent systematic reviews and meta-analyses concluded that leucine intake significantly increases the muscle protein fractional synthetic rate and exerts beneficial effects on body weight and LM in older persons and may be of benefit to address sarcopenia [65, 66]. Results from a recent study suggest that provision of a supplement containing vitamin D, leucine-enriched whey protein and a mixture of micronutrients may be important to increase gains in appendicular LM (aLM) and improved functionality in sarcopenic older adults, as compared to a control group [67].

More recently, β-hydroxy-β-methyl-butyrate (HMB), an active metabolite of the essential amino acid leucine, has attracted interest, with reported anabolic and anticatabolic effects on muscle. Recent research has been focused on the use of HMB to maintain or rebuild muscle mass in older populations, especially those at risk of LM loss. Some studies have demonstrated the benefits of HMB supplementation, alone or in combination with other amino acids, for preserving and rebuilding LM in older adults [27, 68, 69]. A recent study conducted by Kuriyan et al. [70] revealed an age-related decline in endogenous plasma HMB levels, which was positively correlated with appendicular aLM and muscle grip strength in young and older adults. This indicates that HMB supplementation may be beneficial especially for individuals with or at risk of LM loss, such as older adults or those with disease-related loss of LM. Moreover, a recent meta-analysis of clinical studies conducted using HMB alone, or combined with other amino acids, in older populations demonstrated that HMB supplementation was significantly associated with an increased muscle mass [71]. Even though research on the effects of HMB in muscle health mainly is limited by the small number of studies, heterogeneous methodological approaches, and the interaction of HMB with other nutrients and with exercise, HMB has been documented to prevent muscle mass loss, improve muscle mass, and increase muscle function and physical performance [72, 73]. Moreover, the NOURISH study [74], which is one of the largest clinical studies of its kind, showed that administration of two servings of an ONS containing CaHMB reduced the risk of mortality by 50% through 90 days post-hospital discharge in malnourished, cardiopulmonary patients, 65 years or older, as compared to standard nutritional care and placebo. This clinical trial, including over 600 patients, also demonstrated improved nutritional status, body weight, and vitamin D levels over standard care within 90 days of hospital discharge in those individuals receiving the ONS containing CaHMB.

Other nutrients that also work as important anabolic stimuli, such as some minerals and vitamins, also warrant discussion [75]. Regarding the role of minerals, a recent systematic review [76] evaluated the scientific evidence linking dietary intake of minerals and muscle mass, muscle strength, and physical performance in older adults. This review highlighted calcium, potassium, and sodium as important micronutrients for muscle health and nerve activity, and magnesium, which is known to participate in muscle relaxation and muscle function [77]. Low levels of some other minerals such as iron, phosphorus and selenium are related to poor physical performance, muscle weakness, or muscular diseases, respectively and zinc is able to delay oxidative processes, which are known to contribute to disuse muscle atrophy.

Dietary intake of vitamin D has also been linked to improved muscle health and decreased risk of falls and fractures in the elderly. Vitamin D levels are known to decline with age [78, 79]. Effects of vitamin D supplementation on improving muscle health have been controversial through diverse findings observed in different deficient populations. A recent systematic-review and meta-analysis including community-dwelling adults concluded that no improvement in muscle strength after the administration of vitamin D with or without calcium supplements were observed [80]. However, a large body of evidence suggests that vitamin D supplementation seems to improve muscle-related parameters particularly in vitamin D-deficient individuals and especially among older adults. In fact, a further systematic review that included 13 studies in adults aged 60 years and older, found that vitamin D supplementation at varying doses is associated with beneficial effects on muscle strength and balance, compared with placebo or standard treatment [81]. These results were consistent with a newer meta-analysis which included 29 RCTs involving 5,615 individuals across a wide age range (mean age: 61.1 years) [82].

In addition to providing adequate levels of macro- and micronutrients, follow-up is essential to ensure continuity of care between healthcare settings. Appropriate monitoring should be instigated to confirm that nutritional needs are being met and ensure patients receive nutritional support for the correct duration of time.

8. Conclusions

Skeletal muscle loss is one of the main features of malnutrition in community dwelling and hospitalized patients and dramatically impacts on their need for care and quality of life. Early identification of malnutrition in high risk populations is essential, yet current tools to screen/diagnose malnutrition based on measures of body weight do not reflect skeletal muscle loss**.** Malnutrition needs to be addressed as a muscle-related disorder across the continuum of care in clinical practice (Table 2)**.**

Target	Key message
MUSCLE ROLE	Muscle plays a vital structural and metabolic role in maintaining overall individual's health, quality of life and longevity
SKELETAL MUSCLE MAINTANANCE	For optimal maintenance of skeletal muscle with aging, it is important to build muscle when young, maintain it in mid-life, and minimize loss in older adulthood
SKELETAL MUSCLE LOSS	Skeletal muscle loss is at the core of malnutrition
MALNUTRITION	Malnutrition acts as a driver of skeletal muscle loss
SKELETAL MUSCLE LOSS ASSESSMENT	BMI is an imperfect measure of body composition and clinicians need to measure not only weight, but also muscle mass, to tailor interventions appropriately
NUTRITION	Nutrition intervention needs to consider skeletal muscle loss and include those nutrients with evidence to have an impact on muscle function

Table 2. Malnutrition needs to be addressed as a muscle-related disorder across the continuum of care in clinical practice. Some key messages are provided to tailor appropriate interventions.

Early intervention is key to prevent or minimise loss of muscle mass and function. Multimodal interventions including nutrition and exercise need to be implemented to counteract malnutrition-related skeletal muscle loss. High protein, vitamin D and other key nutrients, leucine or its active metabolite, HMB, are all valuable approaches to restore muscle anabolism and combat malnutrition in hospital, and in community health and care settings. Monitoring and discharge plans are important to ensure continuity of nutritional care between settings, and to ensure patients receive optimal treatment for the right duration of time to support muscle mass and functional recovery**.** Therefore, this position paper highlights the importance of addressing skeletal muscle loss in malnourished older adults in a timely manner. Some guidance and recommendations are provided to tailor appropriate intervention, which include early identification using validated tools and early use of multimodal therapies including optimal nutrition and exercise to restore muscle anabolism and combat malnutrition in different care settings.

Conflict of interest

FL has received speaker fees and funds for educational activities from Abbott Nutrition. MCR is employed by Abbott Nutrition. DEB has received speaker fees, conference attendance support or consulting fees from Nutricia, Baxter, BBraun, Fresenius Kabi, Abbott Nutrition, Nestle Nutrition and Cardinal Health and grant support through her institution from Corpak MedSystems UK. TC has received unconditional research grants from Nutricia, Nestle and Fresenius-Kabi. VM has received speaker fees, conference attendance support or consulting fees from Nutricia, Abbott Nutrition, Nestle Health Science, Pfizer, Lacer, Rovi, Grünenthal, and has received unconditional research grants from Nutricia. AAW has given lectures organised by Abbott and has received unconditional research grants from Dairy Australia. AJCJ has received funds for educational activities from Abbott Nutrition, Nestle and Nutricia, and research funds by Nutricia.

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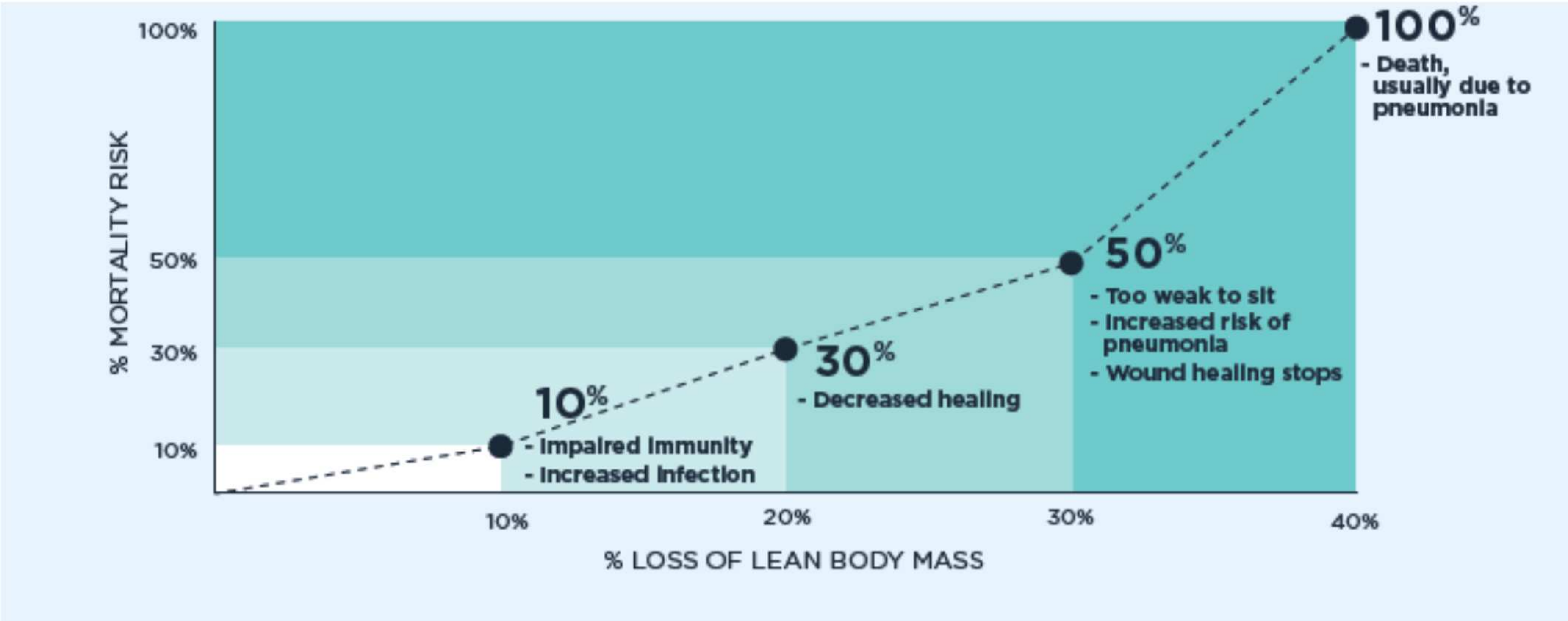
Figure 1. Complications increase with greater lean mass loss*. Adapted from Demling et al 2009 [10].



*Assuming no preexisting loss

Figure 2. Relationship between malnutrition, and loss of skeletal muscle mass and function.

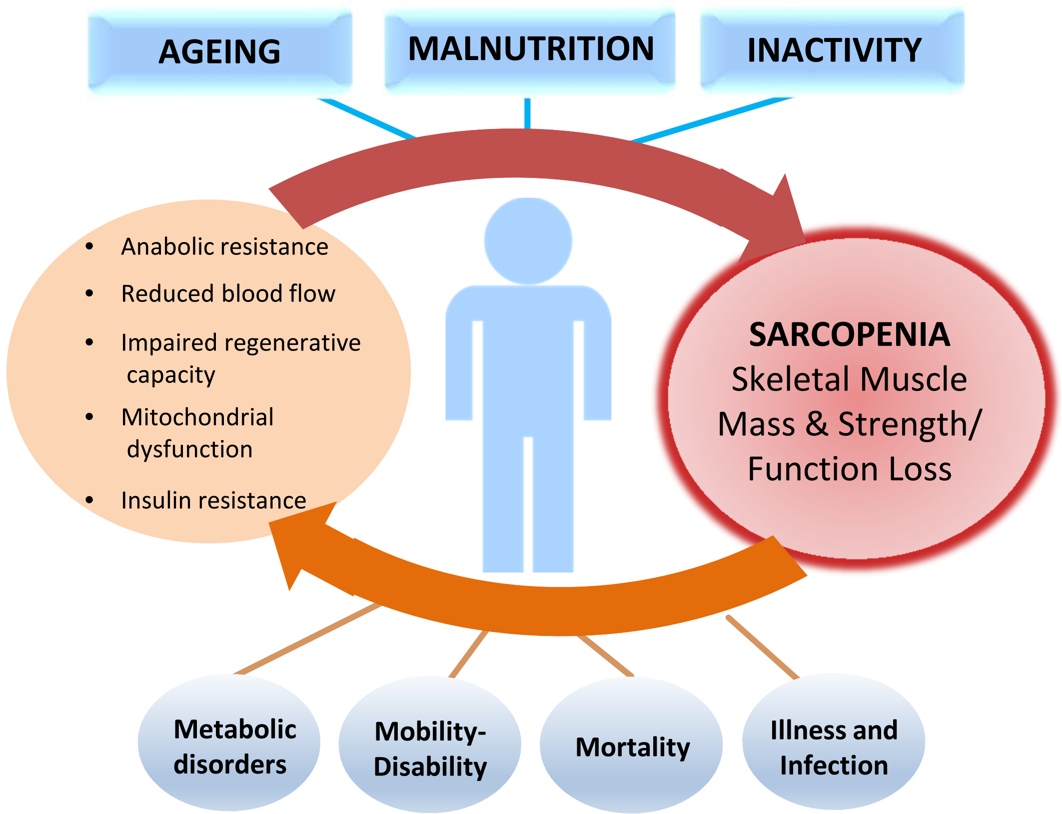


Figure 3. Skeletal muscle loss as a consequence of malnutrition is observed across the continuum of care and should be appropriately addressed in clinical practice.

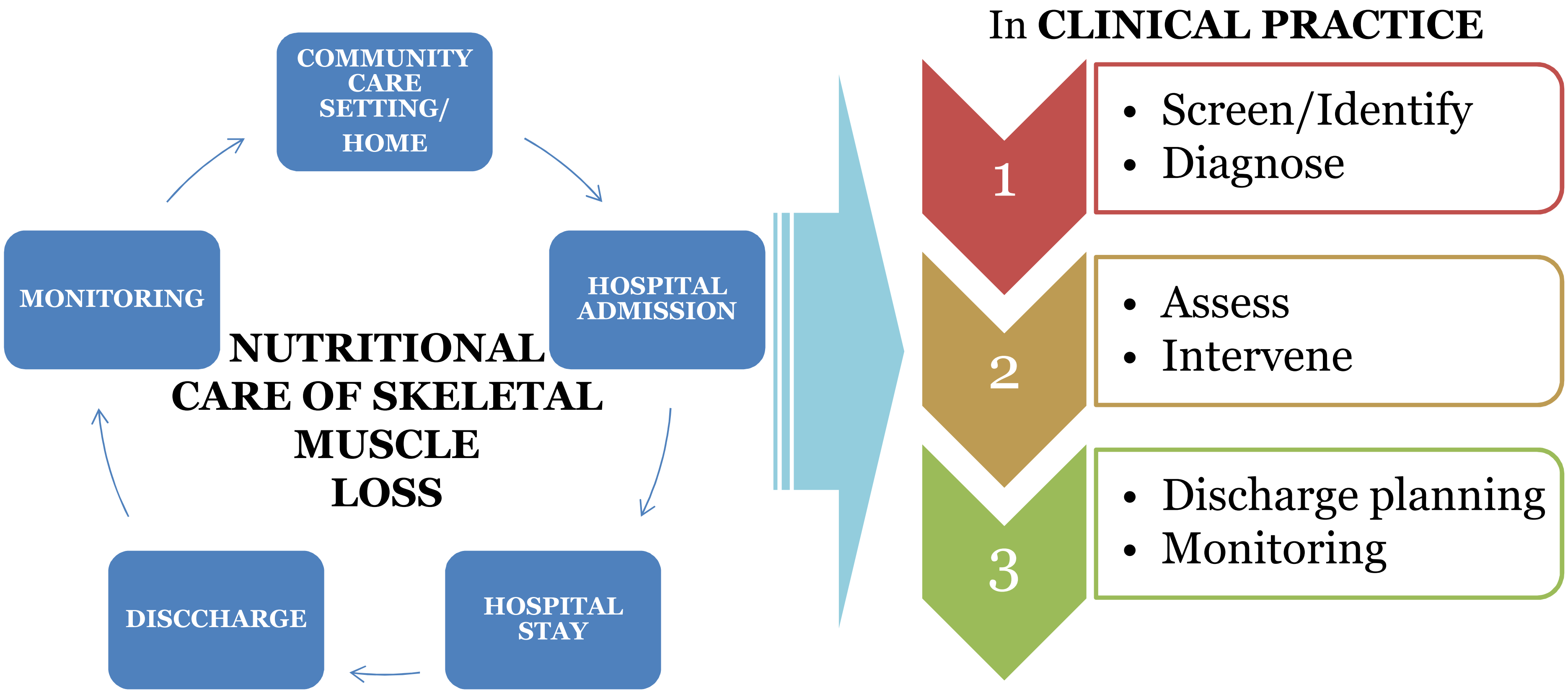


Table 1. Methods routinely available to assess muscle-related outcomes in research and clinical practice. Adapted from Cruz-Jentoft et al 2010 [24] and 2018 [53].

Variable	Research	Clinical practice
Skeletal muscle strength	Grip strength Chair stand test (chair rise test) Knee flexion/extension Peak expiratory flow	Grip strength Chair stand test (chair rise test)
Skeletal muscle mass	Dual energy X-ray absorptiometry (DXA) Computed tomography (CT) Magnetic resonance imaging (MRI) Bioelectrical impedance analysis (BIA) Ultrasound	DXA BIA Lumbar muscle cross-sectional area by CT Anthropometry
Physical performance	Short Physical Performance Battery (SPPB) Gait speed Timed-up-and-go test (TUG) 400-meter walk or long-distance corridor walk Stair climb power test	SPPB Gait speed TUG 400-m walk

Table 2. Malnutrition needs to be addressed as a muscle-related disorder across the continuum of care in clinical practice. Some key messages are provided to tailor appropriate interventions.

Target	Key message
MUSCLE ROLE	Muscle plays a vital structural and metabolic role in maintaining overall individual's health, quality of life and longevity
SKELETAL MUSCLE MAINTANANCE	For optimal maintenance of skeletal muscle with aging, it is important to build muscle when young, maintain it in mid-life, and minimize loss in older adulthood
SKELETAL MUSCLE LOSS	Skeletal muscle loss is at the core of malnutrition
MALNUTRITION	Malnutrition acts as a driver of skeletal muscle loss
SKELETAL MUSCLE LOSS ASSESSMENT	BMI is an imperfect measure of body composition and clinicians need to measure not only weight, but also muscle mass, to tailor interventions appropriately
NUTRITION	Nutrition intervention needs to consider skeletal muscle loss and include those nutrients with evidence to have an impact on muscle function