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Muscle Loss: The New Malnutrition Challenge in Clinical Practice

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1 Muscle Loss: The New Malnutrition Challenge in Clinical Practice

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35 **Abstract**

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

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

52

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

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61 1. Ageing, successful ageing, and nutritional status

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

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

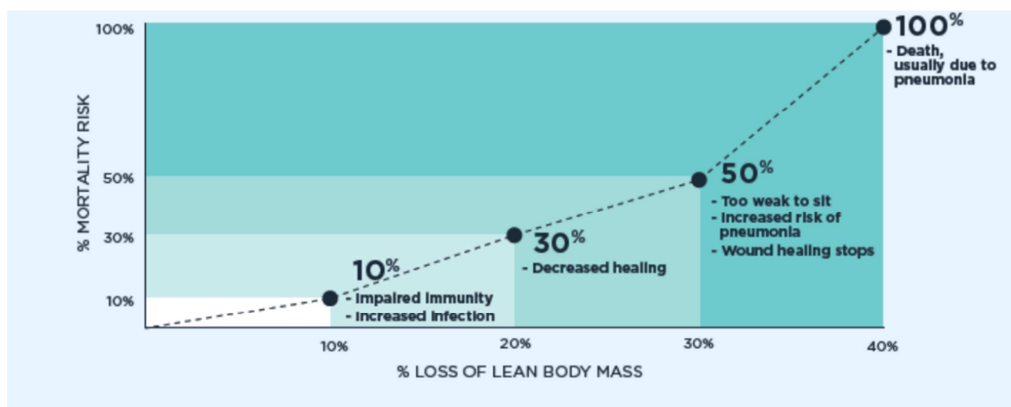
75

76 2. Muscle as a metabolically active organ

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

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

90



91

92 Figure 1. Complications increase with greater lean mass loss. Assuming no preexisting loss.

93 Adapted from Demling et al 2009 [10].

94

95 3. Malnutrition contributes to skeletal muscle mass loss

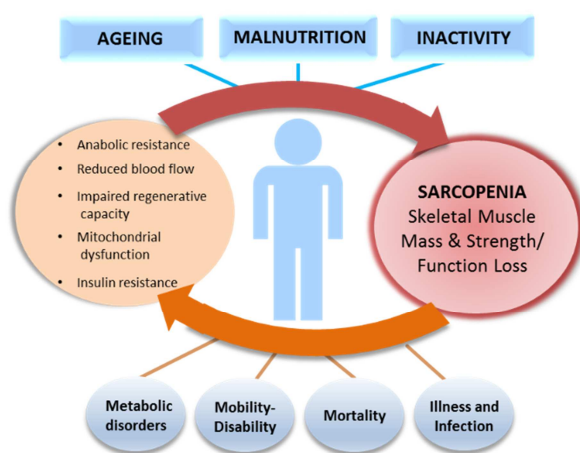
96 Malnutrition is an increasingly prevalent condition that is the result of lack of intake or uptake
 97 of nutrients (protein, vitamins and minerals) leading to altered body composition (decreased
 98 muscle) and body cell mass [11]. This results in diminished physical and mental function, and
 99 impaired clinical outcomes [11], which can delay recovery from disease and increase mortality
 100 [10]. Malnutrition further contributes to acute or chronic loss of muscle mass and function, in
 101 both the community and hospitalized individuals. Indeed, the latest definition of malnutrition
 102 by The European Society for Clinical Nutrition and Metabolism (ESPEN) has incorporated low
 103 fat free mass (specifically fat free mass index) into the diagnostic criteria [12].

104 Different psycho-social, physiological, and pathological conditions lead to inadequate dietary
 105 intake, and failure to meet energy and protein requirements in certain populations, especially

106 in advancing age or in those with complex disease. In individuals, the causes of insufficient
 107 dietary intake and malnutrition are complex and multi-factorial. Ageing, dementia and
 108 depression, chronic illness, multiple hospitalizations (immobilization) or decreased appetite
 109 occurring alone or in combination all contribute [13, 14].

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

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



116
 117 Figure 2. Relationship between malnutrition, and loss of skeletal muscle mass and function.

118
 119 Therefore, early recognition of malnutrition, and timely administration of nutritional care can
 120 also help improve patient's lives while reducing healthcare costs [13].

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

123 Malnutrition is one of the main risk factors of sarcopenia, and acts as a driver of loss of muscle
 124 mass and function, which are the main features [16]. Malnutrition and sarcopenia are
 125 common and overlapping in older adults. In fact, both entities are prevalent among older

126 adults aged 65 years and over, especially in those hospitalized or living in nursing homes [17].
127 Therefore, evaluation of muscle mass is crucial for the diagnosis of both conditions.
128 Another challenge that needs to be taken into account is the presence of malnutrition among
129 obese persons, especially in light of the growing prevalence of obesity worldwide [18] and the
130 presence of sarcopenic obesity [19]. Sarcopenic obesity is the presence of a low proportion of
131 LM despite the presence of obesity [20] and has been independently associated with worse
132 morbidity and disability than either sarcopenia or obesity alone [21]. This can occur in older
133 individuals, in those with Type 2 Diabetes Mellitus (T2DM), COPD, and in obese patients with
134 malignant disorders and post organ transplantations at all ages. Mechanisms include
135 inflammation and/or inactivity induced muscle catabolism [20, 22].
136 Representatives of the four largest global Parenteral and Enteral Nutrition (PEN)-societies from
137 Europe, North and Latin America, and Asia (The European Society for Clinical Nutrition and
138 Metabolism, ESPEN, American Society for Parenteral and Enteral Nutrition, ASPEN, Federacion
139 Latinoamericana de Terapia Nutricional, Nutricion Clinica y Metabolismo, FELANPE, and The
140 Parenteral and Enteral Nutrition Society of Asia, PENSA comprising the Global Leadership
141 Initiative on Malnutrition, GLIM), have collaborated to create a consensus on the diagnostic
142 criteria for malnutrition that has been recently published [23]. This consensus group provided
143 criteria for the diagnosis of malnutrition that can be used for all patients and in all clinical
144 settings based on a two-step model for risk screening and diagnosis assessment, which
145 requires at least one etiological criterion (weight loss, low BMI, or reduced muscle mass) and
146 one phenotypic criterion (reduced food intake or assimilation, or inflammation) [23].
147 Importantly, low muscle mass has been proposed as part of the definition of malnutrition [23].

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

149 Muscle accretion and muscle loss have a noticeable life trajectory, i.e. depending on an
150 individual's age [24]. Loss of muscle mass and strength is a natural part of ageing [25]. Peak

151 muscle mass and strength are achieved around the age of 25 years [26] but after the age of 40-
152 50, loss of skeletal muscle mass accelerates due to decreased physical activity and altered
153 protein metabolism [25]. More significantly, during the ageing process a greater decrease in
154 muscle strength and function is observed [25]. Therefore, building muscle before 40 years and
155 preserving muscle as much as possible during adulthood is a key strategy for healthy ageing.

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

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

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

174

175 **5. Clinical conditions associated with skeletal muscle loss**

176 Beyond ageing, muscle decline is associated with pathological states and chronic diseases,
177 such as malnutrition, cancer, neurodegenerative disease, chronic kidney disease, chronic
178 obstructive pulmonary disease (COPD), sepsis, and immune disorders. On top of this, hospital
179 immobilization and bed rest are devastating to patients who suffer from these conditions [32-
180 34]. Most of these pathological conditions are associated with various degrees of chronic
181 inflammation, which plays a critical role in the onset of muscle atrophy and malnutrition.

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

192 *Cachexia*

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

201 addition, anorexia, weight loss and reduced fat mass are three elements that can help
202 differentiate between cachexia and sarcopenia [40].

203 *Acute disease- or injury-related malnutrition*

204 Patients in the Intensive Care Unit (ICU) display significant nutritional challenges and are
205 nutritionally compromised. Rates of malnutrition on admission to the ICU are reported to be as
206 high as 60% depending on the patient population and screening tool used [42, 43].
207 Malnutrition in ICU patients has been associated with worse outcomes [42, 43] and low muscle
208 mass specifically has been associated with higher mortality and longer stays length on
209 ventilation machines [30, 44]. Once in the ICU, these patients experience a rapid and profound
210 loss of LBM. Rates can be as high as 2% per day, with the highest rates being seen in those with
211 worse severity of illness [31]. Although the pathophysiology of this muscle wasting is poorly
212 understood, it is clear that the release of multiple pro-inflammatory cytokines as well as other
213 catabolic hormones lead to an overall net catabolic balance [31]. In addition, organizational
214 factors leading to significant underfeeding likely also contribute. The consequences of muscle
215 wasting in this population are severe, being reported as a contributing factor to post-ICU
216 functional impairment [45] and self-reported physical function [46]. There are no currently
217 agreed objective criteria for diagnosis of malnutrition in ICU patients, although early
218 nutritional intervention is essential in such patients to support lean mass given the above [47,
219 48].

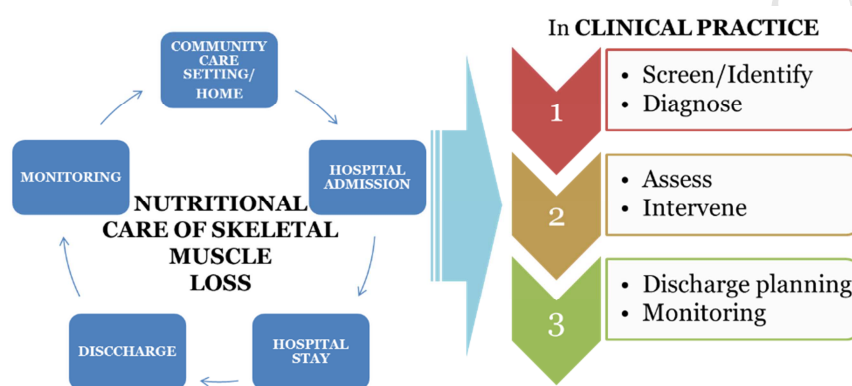
220 DRM without inflammation is also called non-cachectic DRM [11]. This is a form of disease-
221 driven malnutrition in which inflammation is not the major causal mechanism e.g. as a
222 consequence of dysphagia, neurologic disorders or dementia/cognitive dysfunction. Advanced
223 ageing contributes to DRM without inflammation due to the presence of anorexia or lack of
224 appetite, named as “anorexia of ageing”, which is caused by non-inflammatory related
225 mechanisms Although, the mechanisms are not fully understood, a range of physiological,

226 psychological and social factors that may influence appetite and food intake in older adults
 227 have been proposed [49].

228

229 6. Measurement of skeletal muscle loss in malnutrition

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



233

234

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

237

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

242 Existing criteria for the identification of malnutrition are mainly based on observations of
 243 recent weight loss and body mass index (BMI), yet, BMI does not always reflect skeletal muscle
 244 loss. BMI as well as muscle mass varies with ethnicity and race and these differences need to
 245 be considered. In addition, individuals with the same BMI can have different proportions of

246 lean and fat mass [51]. Therefore, it is fundamental to stress the importance of measuring
247 body composition to evaluate muscle mass and strength loss when making assessments of
248 malnutrition and sarcopenia in clinical practice.

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

256 Among body composition measurements anthropometry, like calf and arm circumference and
257 skin-fold thickness [52], as well as bioelectrical impedance analysis (BIA) and ultrasound are
258 valuable when used taken sequentially over time. According to the EWGSOP consensus
259 document on the definition and diagnosis of sarcopenia, screening for sarcopenia is
260 recommended from age 65 years onwards by measuring gait speed, and handgrip strength,
261 and/or muscle mass [24]. Very recently, a revised European consensus on definition and
262 diagnosis of sarcopenia has been published to update the original definition (EWGSOP2) [53].
263 The EWGSOP2 consensus paper now focuses on low muscle strength as a key feature of
264 sarcopenia (primary indicator of probable sarcopenia), uses detection of low muscle quantity
265 and quality to diagnose and identifies physical performance to determine severity. In addition,
266 simple, specific cut-off points are recommended for measures aimed at facilitating early
267 detection and treatment in clinical practice [53]. Different techniques currently exist for the
268 measurement of muscle mass, strength and physical performance, and have been described by
269 their suitability for use in research and/or clinical practice [24-53] (Table 1). We can expect
270 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

271

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

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

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

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

283

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

285 Across the healthcare continuum, it is important to ensure that patients are able to access and
286 consume nutritious foods which provide sufficient energy and protein, as well as
287 micronutrients. Lifestyle interventions factors such as good nutrition and physical exercise are
288 key to maintaining muscle or slowing muscle decline [29-31]. Growing evidence links nutrition
289 to muscle health suggesting it is important to maintain an optimal nutritional status to prevent
290 muscle mass and strength loss in older adults [56]. In fact, optimal nutrition combined with
291 exercise has been shown to act synergistically against skeletal muscle loss in aging population
292 [57].

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

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

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

310 Branched chain amino acids have been shown to increase skeletal muscle protein synthesis
311 and net protein balance. In particular, supplementation with leucine, isoleucine, and valine has
312 been shown to increase skeletal muscle protein synthesis to preserve skeletal muscle loss in
313 the elderly [64]. Although dietary supplementation with leucine remains controversial, two
314 recent systematic reviews and meta-analyses concluded that leucine intake significantly
315 increases the muscle protein fractional synthetic rate and exerts beneficial effects on body
316 weight and LM in older persons and may be of benefit to address sarcopenia [65, 66]. Results
317 from a recent study suggest that provision of a supplement containing vitamin D, leucine-
318 enriched whey protein and a mixture of micronutrients may be important to increase gains in

319 appendicular LM (aLM) and improved functionality in sarcopenic older adults, as compared to
320 a control group [67].

321 More recently, β -hydroxy- β -methyl-butyrate (HMB), an active metabolite of the essential
322 amino acid leucine, has attracted interest, with reported anabolic and anticatabolic effects on
323 muscle. Recent research has been focused on the use of HMB to maintain or rebuild muscle
324 mass in older populations, especially those at risk of LM loss. Some studies have demonstrated
325 the benefits of HMB supplementation, alone or in combination with other amino acids, for
326 preserving and rebuilding LM in older adults [27, 68, 69]. A recent study conducted by Kuriyan
327 et al. [70] revealed an age-related decline in endogenous plasma HMB levels, which was
328 positively correlated with appendicular aLM and muscle grip strength in young and older
329 adults. This indicates that HMB supplementation may be beneficial especially for individuals
330 with or at risk of LM loss, such as older adults or those with disease-related loss of LM.

331 Moreover, a recent meta-analysis of clinical studies conducted using HMB alone, or combined
332 with other amino acids, in older populations demonstrated that HMB supplementation was
333 significantly associated with an increased muscle mass [71]. Even though research on the
334 effects of HMB in muscle health mainly is limited by the small number of studies,
335 heterogeneous methodological approaches, and the interaction of HMB with other nutrients
336 and with exercise, HMB has been documented to prevent muscle mass loss, improve muscle
337 mass, and increase muscle function and physical performance [72, 73]. Moreover, the
338 NOURISH study [74], which is one of the largest clinical studies of its kind, showed that
339 administration of two servings of an ONS containing CaHMB reduced the risk of mortality by
340 50% through 90 days post-hospital discharge in malnourished, cardiopulmonary patients, 65
341 years or older, as compared to standard nutritional care and placebo. This clinical trial,
342 including over 600 patients, also demonstrated improved nutritional status, body weight, and
343 vitamin D levels over standard care within 90 days of hospital discharge in those individuals
344 receiving the ONS containing CaHMB.

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

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

369 In addition to providing adequate levels of macro- and micronutrients, follow-up is essential to
370 ensure continuity of care between healthcare settings. Appropriate monitoring should be

371 instigated to confirm that nutritional needs are being met and ensure patients receive
372 nutritional support for the correct duration of time.

373

374 **8. Conclusions**

375 Skeletal muscle loss is one of the main features of malnutrition in community dwelling and
376 hospitalized patients and dramatically impacts on their need for care and quality of life. Early
377 identification of malnutrition in high risk populations is essential, yet current tools to
378 screen/diagnose malnutrition based on measures of body weight do not reflect skeletal muscle
379 loss. Malnutrition needs to be addressed as a muscle-related disorder across the continuum of
380 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

381

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

385

386 Early intervention is key to prevent or minimise loss of muscle mass and function. Multimodal
387 interventions including nutrition and exercise need to be implemented to counteract
388 malnutrition-related skeletal muscle loss. High protein, vitamin D and other key nutrients,

389 leucine or its active metabolite, HMB, are all valuable approaches to restore muscle anabolism
390 and combat malnutrition in hospital, and in community health and care settings. Monitoring
391 and discharge plans are important to ensure continuity of nutritional care between settings,
392 and to ensure patients receive optimal treatment for the right duration of time to support
393 muscle mass and functional recovery. Therefore, this position paper highlights the importance
394 of addressing skeletal muscle loss in malnourished older adults in a timely manner. Some
395 guidance and recommendations are provided to tailor appropriate intervention, which include
396 early identification using validated tools and early use of multimodal therapies including
397 optimal nutrition and exercise to restore muscle anabolism and combat malnutrition in
398 different care settings.

399 **Conflict of interest**

400 FL has received speaker fees and funds for educational activities from Abbott Nutrition. MCR is
401 employed by Abbott Nutrition. DEB has received speaker fees, conference attendance support
402 or consulting fees from Nutricia, Baxter, BBraun, Fresenius Kabi, Abbott Nutrition, Nestle
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404 MedSystems UK. TC has received unconditional research grants from Nutricia, Nestle and
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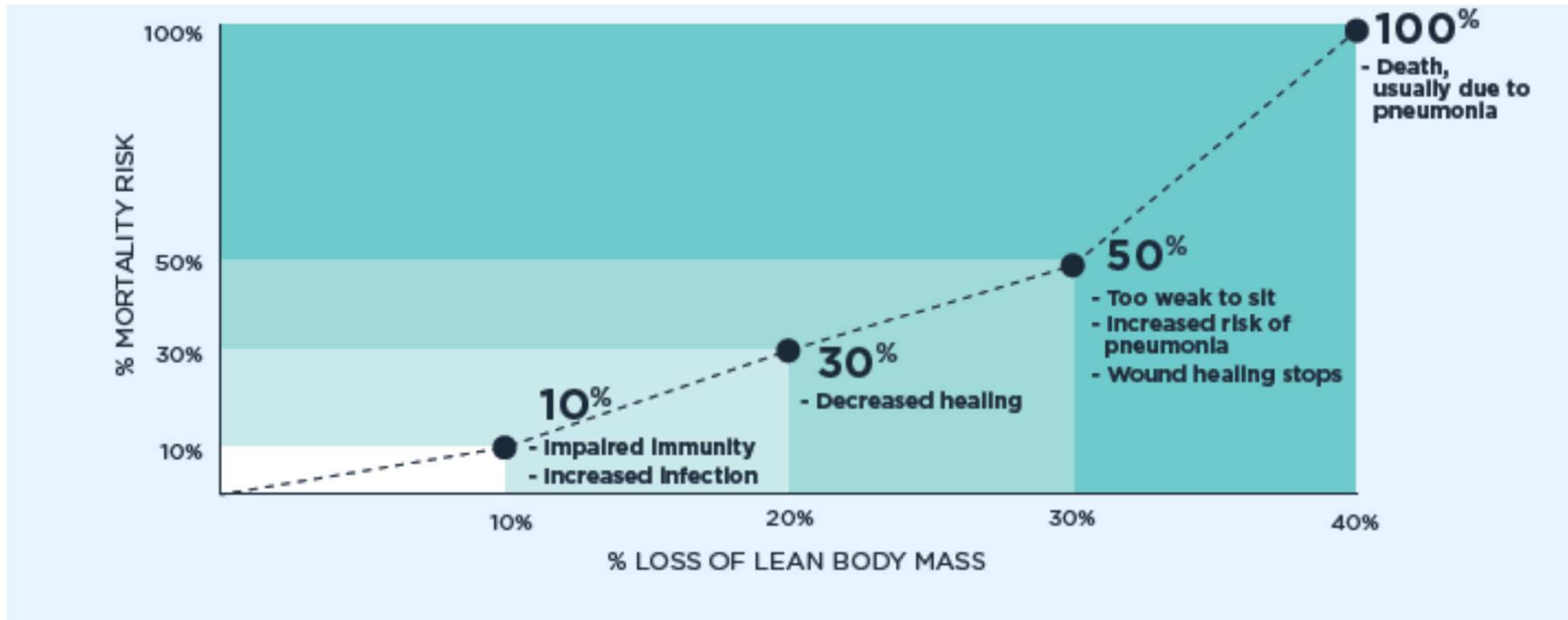
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Figure 1. Complications increase with greater lean mass loss*. Adapted from Demling et al 2009 [10].



*Assuming no preexisting loss

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

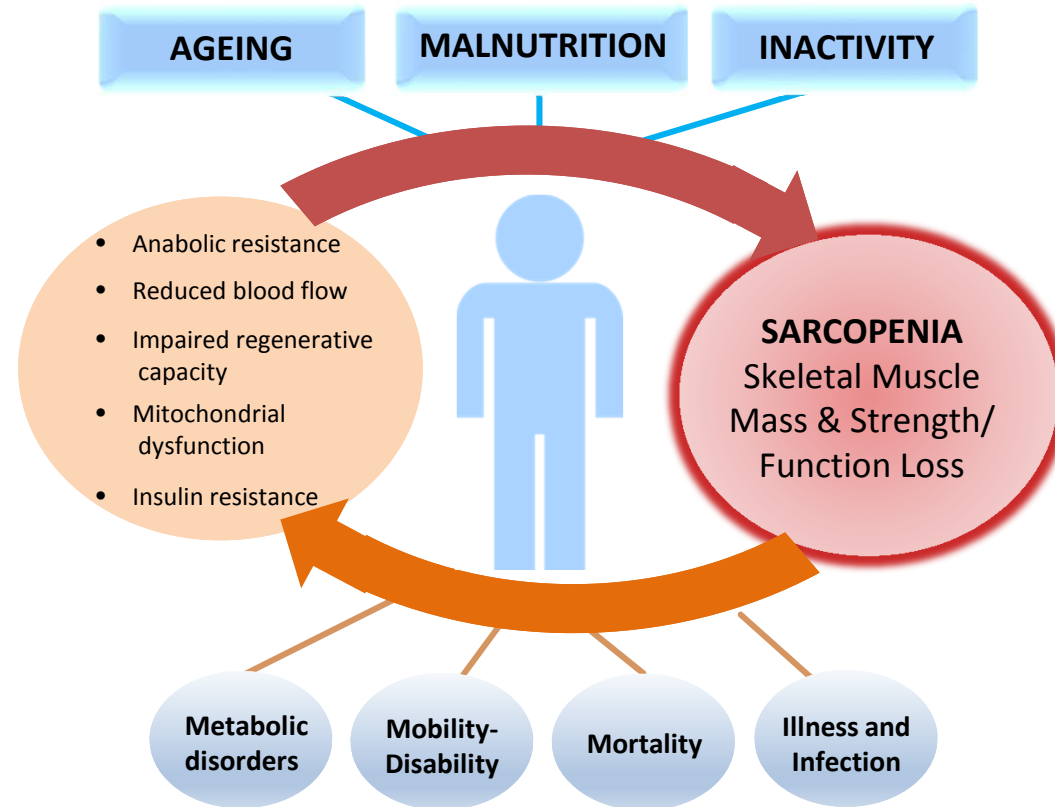


Figure 3. Skeletal muscle loss as a consequence of malnutrition is observed across the continuum of care and should be appropriately addressed in clinical practice.

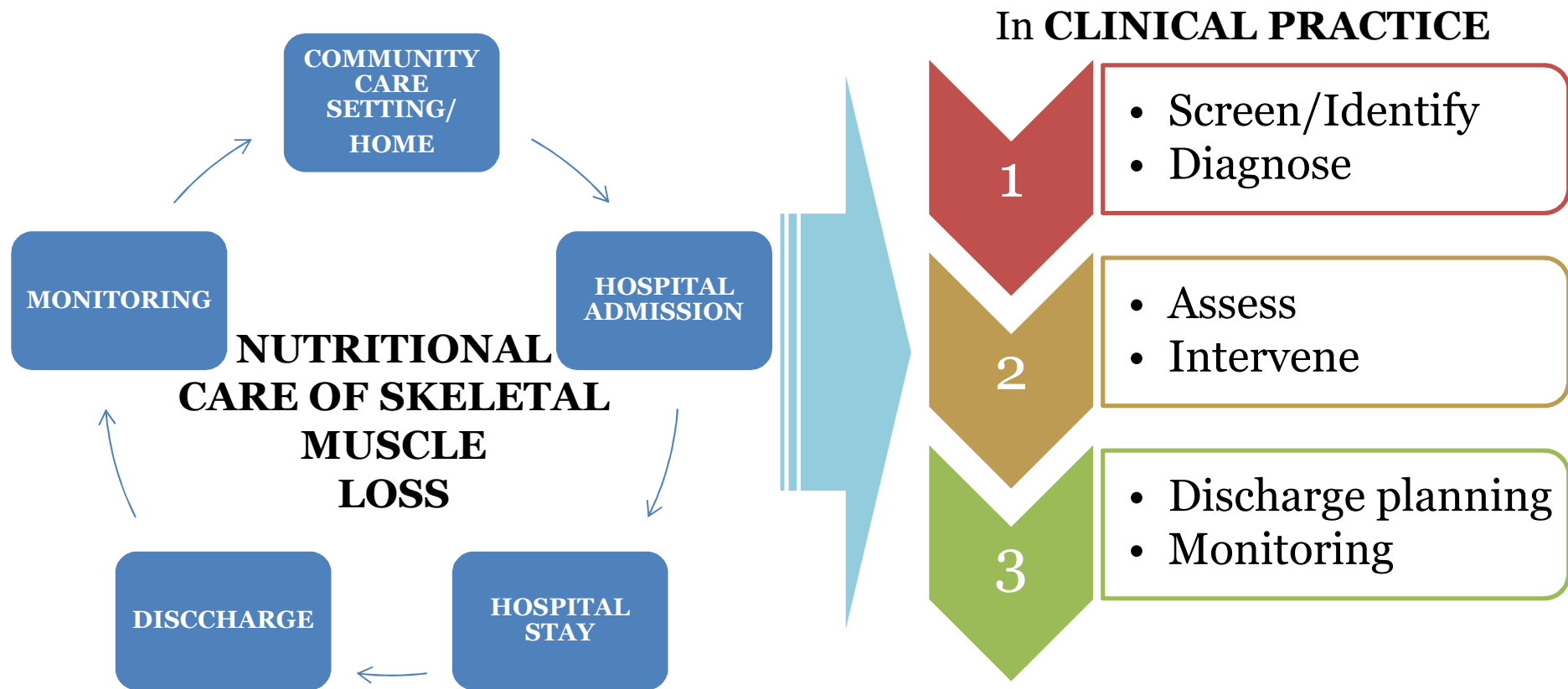


Table 1. Methods routinely available to assess muscle-related outcomes in research and clinical practice. Adapted from Cruz-Jentoft et al 2010 [24] and 2018 [53].

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