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Review

Nutrition and Physical Activity in Musculoskeletal Health

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Abstract: A balanced diet and regular physical activity are essential for maintaining musculoskeletal health. Key nutrients such as calcium, vitamin D, and protein are especially important for preventing falls and fractures. While the benefits of these nutrients are well-established, other dietary components have not been studied as extensively. For instance, vegetables, which are rich in nutrients vital for muscle and bone health, play a crucial role in preventing falls and fractures. Over recent decades, a great emphasis has been given to the combinations of nutrients and foods in dietary patterns that may have synergistic or antagonistic effects. Despite the challenges in researching the impact of nutrition and physical activity on musculoskeletal health due to the extensive heterogeneity of the results, healthcare professionals should continue to promote healthy eating and regular physical activity, and these principles should be emphasized in public health initiatives. Ultimately, a sufficient and balanced diet, abundant in plant-based foods and low in processed or discretionary foods, along with consistent physical activity, remains the most effective strategy for the prevention of musculoskeletal issues. This article aims to review the updated literature of recent years on the links between nutrition and physical activity with bone and skeletal muscle health.

Keywords: bone; muscle; osteoporosis; sarcopenia; osteosarcopenia; nutrition; exercise; physical activity

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1. Introduction

Bone and skeletal muscle, formerly considered separately in their association with pathological conditions, are currently more frequently considered together due to the relevant consequences of the simultaneous presentation of alterations in skeletal muscle and bone tissue, including mortality [1,2], fragility fractures, falls [2,3], and frailty [4,5]. Musculoskeletal system alterations are relevant at all ages, but this is particularly true in old age, in which adverse consequences of these alterations are frequent [6] and tend toward difficulties in mobility [4,5,7], self-sufficiency [5,7], and mortality [1,2]. In recent years there has been a notable increase in interest in osteosarcopenia, a term first coined by Duque et al. [8] to describe the simultaneous presentation in some older adults of both osteoporosis and sarcopenia, defined by the presence of low bone density and fragility fractures together with reduced muscle mass, strength and/or muscle performance [9].

The aging of the global population has emerged as a crucial challenge across all world regions with the confirmation that humans can today expect to live over sixty years in nearly all countries [10]. Due to the high prevalence of osteosarcopenia in old age, this condition is expected to rise in parallel with the aging population, entailing a significant burden on healthcare systems and society [11]. The presence of osteosarcopenia means that a person is affected by both osteoporosis and sarcopenia—well-defined clinical conditions listed by the International Classification of Diseases (ICD)—simultaneously [12]. Osteoporosis, characterized by low bone mass and microarchitectural deterioration of bone tissue, increases the risk of fragility fractures and of loss of independence [13]. Sarcopenia comprises the progressive loss of muscle mass, strength, and function, leading to impaired physical performance, increased risk of falls, and functional decline [14].

The risk factors for fractures and falls are various and include both modifiable and non-modifiable factors. Among the modifiable risk factors, the key role of nutrition in osteoporosis and sarcopenia has become increasingly apparent. Combining healthy lifestyle components, including maintaining a well-balanced diet and regular physical activity, play a crucial role in optimizing musculoskeletal health [15,16]. Compelling evidence supports the notion that protein, calcium, and vitamin D are fundamental to maintain bone and muscle health [15–17]; however, there is growing evidence that several other nutrients, and especially the combinations of nutrients/foods in dietary patterns, may play an important role. There is strong evidence confirming that physical activity, in particular balance and resistance exercise, can decrease the risk of falls and fractures [18,19] and the 2022 World Guidelines for Falls Prevention and Management for Older Adults recommend performing a nutritional assessment, beyond the traditional fall risk evaluation, that comprises the evaluation of vitamin D status and protein consumption [20]. Other fundamental nutrients with antioxidant and anti-inflammatory properties, such as vegetables, fruits, nuts, and legumes and their combination in healthy dietary patterns, have recently become the focus of attention and the evidence to support these as contributing factors to musculoskeletal health is growing [21,22].

This article aims to review updated literature of recent years on the links between nutrition and physical activity with bone and skeletal muscle health. First, we will describe the concept of the bone–muscle unit, as both tissues have a parallel embryological origin and development. We will then describe the definition, prevalence, risk factors, and consequences of osteosarcopenia as the aging of the bone–muscle unit. We will continue by reviewing the updated literature of recent years on the links between nutrition and physical activity with bone and skeletal muscle health. Finally, we will briefly discuss practical clinical recommendations.

2. The Concept of the Bone–Muscle Unit

During embryogenesis, muscle acts as a force generator in early development, exerting a mechanical load that is translated into signals that combine with the genetic program of organogenesis in adjacent tissues as development progresses and lasts throughout life [23]. This is exemplified by studies on limb development, in which the progenitors of the wrist tendon are shown to gradually develop, integrating muscle with the skeleton. This induction is followed by the elongation of the wrist tendon, occurring alongside the growth of both the skeleton and of the muscles [23]. Mechanical load is necessary during the formation of the bone–muscle unit, as it influences the development of the tendon, muscle, and their attachments [24]. Without mechanical load, the mineralized fibrocartilage in the enthesis disappears, and tendon development is halted when muscle is absent. Proper maturation of the myotendinous junction relies on muscle contraction. In the absence of muscle contraction, the number of myotubes decreases, resulting in smaller-than-normal muscles. Additionally, muscle contraction is essential for maintaining a pool of muscle progenitor cells. Muscle contraction is also needed to prevent neuromuscular joint degeneration [24].

The remarkable capacity of tissues to uphold their function and undergo self-restoration following injury can be attributed to the existence of resident adult stem cells. These cells remain in a dormant state within all tissues and, when prompted by suitable circumstances, possess the ability to activate themselves, replenishing depleted cells [25]. Interestingly, the same multipotent cell can give rise to bone, muscle, and fat cells, as well as other types of cells such as neurons and chondrocytes [25].

Growth, in the presence of unloading, results in both a bone that lacks the specific shape that is unique for its function and a muscle that lacks functional capacity. As proposed by Harold Frost over 20 years ago, while the development of muscle and bone during growth is influenced by gravitational forces associated with body weight and physical activity, forces produced by muscle contraction dominate the skeleton's postnatal structural adaptation to loading [26]. Therefore, as muscles become larger and stronger during growth or in response to increased loading (exercise), bones should adapt to increased loads imparted by muscles by adding mass, size, and strength. This biomechanical link between muscle and bone supports the concept of a 'functional muscle–bone unit', in which changes in muscle mass and strength should affect bone mass, size, and strength predictably and correspondingly [26].

Muscle and bone are generated and grow together but they also age together. The decline in muscle size, quality and function induced by aging are assumed to contribute to catabolic bone alterations; however, age-associated changes in bone also profoundly modify its response to muscle-derived stimuli [27]. Overall, as with other age-related parameters that are multifactorial, there is a high variability in how aging affects the muscle-to-bone ratio, illustrated by the results of the systematic review by Novotny et al., which reported that the ratio remained unchanged with aging in 19 of the 39 ratios, 15 ratios decreased with age and 5 ratios increased [27].

3. Osteosarcopenia: Definition, Prevalence, Risk Factors, and Consequences

Osteosarcopenia is a relatively new syndrome describing the coexistence of osteoporosis and sarcopenia, two chronic conditions mostly associated with advancing age [6,9]. Both have an ICD code [12], and there is probably no need for a new code for osteosarcopenia because the combination of these two already coded conditions can be used. For over two decades osteoporosis has been defined as the presence of low bone mass loss, microarchitectural deterioration and the presence of fragility fractures [28]. The term 'sarcopenia' was introduced in 1988 by Rosemberg and refers to the loss of muscle mass, strength and function [29]. However, there is no universal definition of sarcopenia. Numerous definitions proposed by international working groups dedicated to sarcopenia have emerged over the years (Table 1).

Table 1. Some of the international working groups dedicated to the study of sarcopenia and references for their proposed definitions.

Acronym	Sarcopenia Working Group
EWGSOP1	• European Working Group on Sarcopenia in Older People [30]
EWGSOP2	• Revised version of the EWGSOP [31]
AWGS	• Asian Working Group on Sarcopenia [32]
AWGS 2019	• Revised version of the AWGS [33]
IWGS	• International Working Group on Sarcopenia [34]
FNIH	• Foundation of the National Institute of Health-Sarcopenia Project [35]
SDOC	• Sarcopenia Definition and Outcomes Consortium [36]

The lack of a univocal definition means that it is problematic to compare data deriving from different populations and different definitions and which are therefore responsible for the variability of the prevalence of this condition. In a recent meta-analysis among 31 studies the prevalence ranged from 1.5 to 65.7%, with an overall pooled prevalence of 18.5% (CI: 16.7–20.3%) [37]. Despite the variability of prevalence, the importance of osteosarcopenia deserves the highest attention because the combination of osteoporosis and sarcopenia often exist in frail people, mostly older adults, and leads to relevant and disabling health outcomes [14]. A recent study compared the prevalence and consequences of osteosarcopenia using different definitions. As expected, there were some variations in prevalence depending on the definition. Nevertheless, severe osteosarcopenia conferred a significant increased rate of impaired physical performance, falls, and fractures when either the EWGSOP2 or NIH definitions were employed [38].

In the meta-analysis by Huang et al., subgroup analyses revealed that the groups at highest risk of osteosarcopenia are women, older adults, and persons who have already undergone a fracture [37]. The risk factors for osteoporosis and sarcopenia are common and include aging, vitamin D deficiency, chronic inflammation, metabolic dysfunction, inactivity, corticosteroid use, genetical factors, fat infiltration, and the presence of multimorbidity [9].

Data from a recent and extensive meta-analysis by Chen et al. show that frailty (OR = 4.72, 95% CI: 2.71–8.23), malnutrition (OR = 2.63, 95% CI: 1.47–4.71), female sex (OR = 5.07, 95% CI: 2.96–8.69) and higher age (OR = 1.10, 95% CI: 1.06–1.15) were significantly associated with a higher risk for osteosarcopenia [2]. In the same meta-analysis considering cohort studies, osteosarcopenia was found to significantly increase the risk of developing fractures (HR = 2.13, 95% CI: 1.61–2.81 in 7 studies), falls (HR = 1.54, 95% CI: 1.20–1.97 in 3 studies), and mortality (HR = 1.75, 95% CI: 1.34–2.28 in 5 studies) [2]. The strong association of osteosarcopenia with fractures was also shown by another meta-analysis, including 8 cohort studies, which also reported an increased risk of falls in 3 cohort studies and a significant increased mortality risk in 3 cohort studies [3]. A recent larger meta-analysis, including 9 prospective studies of generally good quality and 14,429 participants, found a significantly higher mortality risk of more than 50% (OR: 1.53; 95%CI: 1.28–1.78) over a mean follow-up of 6.6 years [1]. Data from the Hertfordshire Cohort Study show that participants living with frailty were often osteosarcopenic and that multimorbidity was frequent in participants with either sarcopenia or osteoporosis [39]. Early identification of sarcopenia and osteoporosis may be an opportunity to mitigate frailty risk.

The muscle/bone interaction is complex, unveiling the concept that, in addition to their primordial mechanical interaction, muscles and bones communicate via hormonal and biochemical messengers in a complex cross-talk [40]. In fact, bone and muscle interact through the endocrine system by growth factors and a family of cytokines generated in the muscle or myokines, and osteokines, derived from bone cells. Adipose tissue also intervenes in this cross-talk with the cytokines generated in this tissue, known as adipokines [40,41] (Figure 1).

It is certainly recognized that the development and maintenance of bone mass are largely dependent on muscle-derived mechanical loads, a concept that has been confirmed for a long time as the effects of mechanotransduction [42], which help explain the detrimental effects of physical inactivity on bone fragility [43] and sarcopenia [44]. In addition, the secretion of myokines and osteokines reciprocally modulate tissue homeostasis and remodeling. Another muscle–bone interaction involves the resident mesenchymal stromal cell in the skeletal muscle, i.e., fibro-adipogenic progenitors, which can migrate to the bone injury site and contribute to bone regeneration [41]. All of these novel bone–muscle interactions may affect other organs and systems with potential clinical consequences beyond the musculoskeletal system [45]. Beyond the mechanical roles of muscle and bone, both are also major regulators of whole-body metabolism. For instance, skeletal muscle is a storage site and consumer of amino acids and glucose, and produces various myokines that affect metabolism in other tissues. Bone is a major mineral storage in the body for maintaining serum physiological levels of crucial ions such as calcium and magnesium, and also secretes active endocrine products [46].

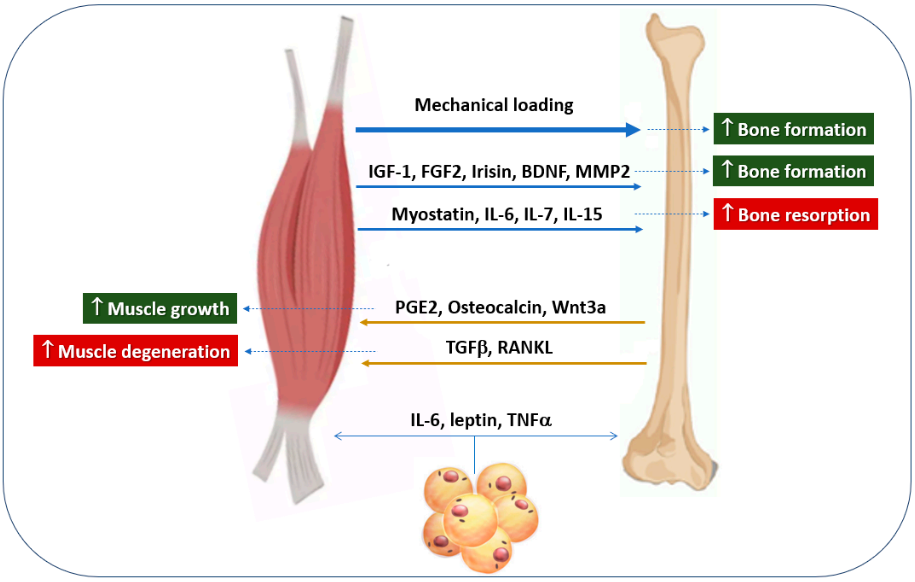

Figure 1. Cross-talk among muscle, bone, and adipose tissue. BDNF: brain-derived neurotrophic factor; FGF2: fibroblast growth factor 2; IGF-1: insulin like growth factor-1; IL: interleukin; MMP2: matrix metalloproteinase 2; PGE2: prostaglandin E2; RANKL: receptor activator of nuclear factor kappa-B ligand; TGFβ: transforming growth factor β; TNFα: tumor necrosis factor α.

4. Adequate Nutrition for Maintaining Bone and Muscle Health

There is currently a growing awareness that nutritional factors and physical activity have major impacts on the risk of age-associated chronic non-communicable diseases [47,48]. Healthy lifestyle behaviors, including a well-balanced diet and regular physical activity play a key role in improving and maintaining musculoskeletal health [15,16,49]. Adequate nutrition is crucial in the maintenance of both bone and skeletal muscle structure and function [49,50], as well as in the prevention and management of osteoporosis and sarcopenia. In fact, nutritional factors can influence modifications in bone mineral density (BMD), bone metabolism, bone matrix mineralization, microstructure, geometry, and material properties, which are crucial bases of bone resistance and fracture risk [16]. There is compelling evidence linking nutritional intake to bone growth and bone loss later in life, both of which influence fracture risk [16,50]. The variety and quality of diets consumed are important and can often undergo alterations in old age [51]. On the other hand, nutritional factors are also fundamental for the maintenance of skeletal muscle structure and performance [49]. Protein intake, calcium, and vitamin D are frequently recommended to support bone and muscle health. However, there are other nutrients, foods, and their combinations that may also play an important role and that can influence both, bone and skeletal muscle, and may be involved in the prevention of osteoporosis and sarcopenia [16,49,52]. In the next subsections, we will review the updated evidence of some of the nutrients, foods, and dietary patterns that are fundamental for bone and muscle.

4.1. Search Methods

We aimed to review the available and updated evidence on the impact of protein intake, vitamin D and calcium supplementations, dietary patterns, and exercise on bone and muscle health. A PubMed search was conducted for English language, peer-reviewed, human RCTs, longitudinal studies, narrative reviews, systematic reviews, meta-analysis, and umbrella reviews published from the database's inception to December 1st, 2024 using terms such as "protein", "vitamin D", "calcium", "dietary pattern", "exercise", combined with "bone", and "muscle". To ensure comprehensive coverage, reference lists of relevant reports and papers were also examined. We also supplemented the search with studies known to the authors and additional forward citation searches. Studies published before 2017 were excluded. Interventions specifically targeting the prevention of sarcopenic obesity (low muscle mass combined with high fat mass) were not considered. Other article types, including case reports, case series, editorials, letters to the editor, comments, short reports, short communications, and perspectives, were also excluded. Emphasis was placed on the largest studies and the most recent publications.

4.2. Proteins

There is general agreement that sufficient protein intake is fundamental for musculoskeletal health [53]. The role of protein in the maintenance of skeletal muscle structure and function is well recognized, even if much of the evidence comes from intervention studies, often in combination with resistance exercise training [52]. There is also evidence for the importance of protein intake for bone health [16]. Dietary guidelines generally recommend a daily protein intake of 0.8–1.0 g/kg of body weight daily for adults. However, it has been recognized that older adults have a higher requirement of protein intake because they are at higher risk of bone fragility and sarcopenia, as well as of malnutrition. The current recommendation, if not contraindicated due to significant kidney function decline, is of 1.0–1.5 g/kg/d [54,55].

Table 2 summarizes the results of recent systematic reviews and meta-analyses on the role of protein intake in bone and muscle health. The association of dietary protein intake with BMD has been evaluated in systematic reviews and meta-analyses [54,56]. Shams-White et al. found that, although there were positive trends for the association of BMD and protein intake at most bone sites, only the lumbar spine showed moderate evidence to support the benefits of higher protein intake. The authors also remark that the studies were heterogeneous, and that confounding could not be excluded. Nevertheless, no adverse effects of higher protein intakes were reported [56]. Another systematic review and meta-analysis by Darling et al. found little benefit from increasing protein intake for bone health in healthy adults across the life-course but also no detrimental effects for the protein intakes reported in the included studies (0.8–1.3 g/Kg/d). After adjustment for confounders, lumbar spine and femoral neck BMD were not associated with protein intake. Likewise, there was no association between total, animal, or vegetable protein intake with the risk of osteoporotic fractures [54]. Conversely, another systematic review and meta-analysis, including 16 RCTs and 13 prospective cohort studies examining the relationships between varying doses of protein intake at or above the U.S. RDA (0.8 g/kg/d) from any source, found that high vs. low protein intakes resulted in a statistically significant 16% decrease in hip fractures with no differences between animal or plant proteins [57]. All of these findings must be interpreted with caution because, as is often the case in nutritional epidemiological research, the included studies are heterogenous in terms of population characteristics, the amount of protein intake, and methods of reporting (e.g., total intake, per body weight, per total percent of energy intake, etc.). This can hinder a univocal recommendation about the optimal protein need for bone health and fracture prevention.

Sufficient protein intake is widely recommended for adequate growth during childhood and adolescence [58]. However, there are some data pointing to the potential hazards of high protein intake on linear growth in children and adolescents, which suggests that caution is needed when promoting increased protein consumption in children and adolescents who already have a high intake of protein [59]. However, a lack of dietary protein may lead to more severe consequences than consuming an excess of protein [16].

Regarding muscle, despite the widely accepted perceptions that older adults need to increase protein intakes to overcome their greater requirements, there is currently little evidence of the association of low habitual intakes of protein in mid-adulthood or young-older age with higher age-related declines in muscle function and no RCTs that report any positive effects of consuming additional protein according to the narrative review by Robinson et al. [52]. There is concern that recommendations to increase protein intakes are extrapolated from results of acute feeding studies, which are not directly applicable to set whole-body protein requirements [60]. A systematic review looking specifically at the health effects of increasing habitual protein intakes above the population reference intake of 0.8 g/kg/d found insufficiently convincing data that increasing protein intake in older adults above the reference intake affects health outcomes [61]. Recent systematic reviews and meta-analyses found that whey protein combined with resistance training improved muscle mass, strength, and physical performance [62–64], although it is difficult to determine the role of protein alone in the benefit. Other recent meta-analysis showed that protein supplementation was able to increase muscle mass [65] and that a low protein intake (below 0.8 g/kg/day) was associated with an increased risk of sarcopenia or low handgrip strength [66].

In summary, there is no conclusive data that protein supplementation may have a benefit in terms of increased BMD or reduced risk of fractures. Protein supplementation has been variably associated with indices of muscle mass, strength and muscle performance when given alone. When combined with resistance exercise, it appears that whey protein may be associated with benefit. Perhaps increasing protein intake above the recommended amount does not help improve muscle function, but malnutrition involving low protein-calorie intake is certainly an important risk factor for osteosarcopenia [2].

Table 2. Summary of characteristics and results from some recent systematic reviews and meta-analyses on the effects of protein intake on bone and muscle outcomes.

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Shams-White et al., 2017 [56]	SR and MA	16 RCTs and 20 cohort	Mixed	BMD and fractures	Positive trends on BMD at most bone sites, but only LS showed moderate evidence of benefits at higher protein intake. No benefit on fractures. No adverse effects of higher protein intakes. Studies were heterogeneous, and confounding could not be excluded.
Wallance et al., 2017 [57]	SR and MA	29 (16 RCTs, 13 cohort)	Healthy adults aged 18 and older	BMD, fractures, turnover markers	MA of prospective studies showed high vs. low protein intakes that were associated with a 16% decrease in HF. Protein intake above the current RDA is beneficial to BMD. No differences between animal or plant proteins, although data were scarce.
Darling et al., 2019 [54]	SR and MA	127 (74 correlational, 23 observational, 30 trials)	Mixed	BMD and fractures	Little benefit of increasing protein intake for bone health in healthy adults but no indication of detrimental effects, at least for protein intakes around 0.8–1.3 g/Kg/day.
Hengeveld et al., 2023 [61]	SR	18 RCTs	Older adults	MM, strength, physical performance, bone health	In 7 of 18 RCTs, increased protein intake beneficially affected lean body mass. For muscle strength, this applied to 3 of 8 RCTs in the context of physical exercise and in 1 of 7 RCTs without physical exercise. Insufficiently convincing data that increasing protein in older adults $\geq$ 0.8 g/kg/d elicits health benefits.

Table 2. *Cont.*

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Al-Rawhani et al., 2023 [62]	SR and MA	SR 30 MA 26 RCTs	Age 60 and older	MM, strength, physical performance	WPS, when combined with resistance training, can enhance lower body strength but not handgrip strength, physical performance, or body composition.
Han et al., 2024 [66]	SR and MA	SR 23 (16 cross-sectional, 5 RCTs, 2 non-RCTs), MA 9	Korean older adults	Sarcopenia, muscle strength	Increased risk of sarcopenia and low HGS for protein intake < 0.8 g/kg/day vs. higher. No significant associations with other sarcopenia indicators (MM, SPPB, BT, GS, TUG).
Hettiarachchi et al., 2024 [65]	SR and MA	38 RCTs (28 community dwelling, 8 institutionalized	Age 65 and older	MM	Protein supplementation improved MM in community-dwelling older adults but its dose, frequency or timing does not significantly influence the effect. Data including hospitalized and institutionalised populations were limited.
Liao et al., 2024 [64]	NMA	78 RCTs	Older adults	MM, HGS, GS	WPS increased MM, HGS, and GS in older adults undergoing resistance training.
Li et al., 2024 [63]	SR and MA	10 RCTs	Older adults with sarcopenia	MM, strength, and physical performance	WPS improved MM and GS in the group without resistance training. In the WP with resistance training group there was a significant increase in HGS.

BMD: bone mineral density; BT: balance test; GS: gait speed; HF: hip fracture; HGS: handgrip strength; LS: lumbar spine; MA: meta-analysis; MM: muscle mass; NMA: network meta-analysis; RCTs: randomized controlled trials; RDA: recommended daily allowance; SPPB: short physical performance battery; SR: systematic review; TUG: time up and go; WPS: whey protein supplement.

4.3. Calcium and Vitamin D

It is well accepted that calcium and vitamin D act synergistically to promote musculoskeletal health. Vitamin D is fundamental for calcium and phosphorus intestinal absorption, renal calcium reabsorption, and mobilization from the bone through the active metabolite 1,25[OH]2D (or calcitriol) and its binding to the vitamin D receptor in diverse organs. Vitamin D, together with the parathyroid hormone and fibroblast growth factor 23, conform an endocrine network, which plays a crucial role in maintaining calcium and phosphate homeostasis, normal bone mineralization and growth [67]. Vitamin D is mainly produced (80–90%) through the body's natural synthesis in the skin when exposed to sunlight, with dietary vitamin D contributing only around 10–20% [67,68]. Thus, the amount of dietary vitamin D needed can vary based on factors such as sun exposure, geographic location, seasonal changes, and skin pigmentation.

Sufficient levels of circulating 25OHD and calcium are fundamental not only for bone health but also for muscle physiology and function [69,70]. Vitamin D supplementation is commonly used to address 25OHD deficiency. However, the most significant improvements in muscle function are seen in people with vitamin D deficiency, while those with adequate levels of 25OHD do not experience similar benefits. This is an important concept when considering nutritional interventions, as the most significant benefits are likely to occur when intake is insufficient or when a deficiency is present. Once the recommended levels are achieved and maintained, additional nutritional supplementation is unlikely to lead to further improvements. For example, vitamin D alone reduced the risk of falls in participants with baseline 25(OH)D levels < 50 nmol/L, but not in those with levels > 50 nmol/L, compared with placebo or no treatment. Additionally, vitamin D combined with calcium reduced the risk of falls compared with placebo or no treatment [71]. Likewise, a notable prospective study by Leboff et al. [72] showed no effect of vitamin D supplementation on fractures risk but most of participants enrolled were not vitamin D deficient. Another important factor is the promotion of a whole foods approach, as it offers a broader range of nutrients, including protein, which is found in many foods rich in vitamin D and calcium (e.g., eggs, oily fish, dairy) [73]. As such, there is evidence that the consumption of milk and dairy products not only provide calcium but also protein, phosphorus, vitamins, and calories. Table 3 summarizes the results of some recent systematic reviews and meta-analyses on the role of vitamin D and calcium intake in bone and muscle health. A recent meta-analysis of RCTs involving children and adolescents [74] found a modest but statistically significant increase in BMD among participants who received supplementation with dairy products. Additionally, another meta-analysis of 20 RCTs in adults showed that milk supplementation led to a small but significant increase in lumbar spine and total hip BMD, along with lower levels of bone resorption markers [75]. There is also evidence from meta-analyses showing a lesser rate of hip fracture risk in people consuming dairy products, including milk, yoghurts, and cheese [16,76]. However, the results for dairy products are not homogeneous. Two out of three meta-analyses examining the impact of milk and dairy products consumption on osteoporosis and fracture risk found that protein-rich products, such as milk and milk-based beverages, positively affected BMD [77,78], with one study also reporting a reduced fracture risk [77]. Another meta-analysis reported that the intake of dairy products did not reduce the risk of osteoporosis and hip fracture [79].

The potential association between hypovitaminosis D and sarcopenia has been reported by several epidemiological studies [80–83]. Nevertheless, whether administration of vitamin D metabolites are able to prevent physical performance and muscle strength decline is still unclear [84]. A recent systematic review and meta-analysis by Prokopidis et al. [85], comprising data from ten RCTs investigating the impact of vitamin D supplementation monotherapy on indices of sarcopenia in community-dwelling older adults, found a significant decrease in short physical performance battery (SPPB) scores with vitamin D supplementation compared with placebo, and no effect on handgrip strength, time up and go, appendicular lean mass, general muscle strength, or general physical performance [85]. The various forms of vitamin D supplementation, including plant-based vitamin D (D2, ergocalciferol), animal-based vitamin D (D3, cholecalciferol), and calcifediol (25OHD or calcidiol), differ in their potency and pharmacokinetic properties [67]. Nearly all of the studies included in the meta-analysis mentioned above [85] used cholecalciferol or ergocalciferol for vitamin D supplementation, with only one study utilizing the active form calcitriol (1,25(OH)2D). None of the studies used calcifediol. Evidence suggests that calcifediol is more effective in correcting vitamin D deficiency, achieving results in a shorter period compared with cholecalciferol [67,86]. A recent systematic review and meta-analysis regarding the effects of calcifediol on physical performance and muscle strength found that calcifediol significantly enhanced several muscle strength parameters and certain physical performance tests, regardless of the dose administered, over a median supplementation period of 24 weeks [70]. These findings indicate that calcifediol could play a role in preventing and treating sarcopenia, a disabling disorder in older people. Another recent meta-analysis found that daily oral administration of 800 IU of vitamin D3 along with 1200 mg of calcium helped reduce hip fractures and non-vertebral fractures in older adults, though it had no effect on femoral neck BMD [87]. However, the results are not homogeneous with two other meta-analyses [88,89] showing negative results. De Souza et al. found that vitamin D supplementation did not lower the total number of fractures, non-vertebral fractures, or falls compared with placebo. Moreover, women experienced an increased risk of hip fractures [88]. Likewise, Jiao et al. reported no significant difference in mortality rates or reduction in incident fractures between the vitamin D plus calcium group and controls, although gastrointestinal adverse reactions were more common in the treatment group [89].

In summary, there are no unequivocal or definitive results showing a benefit of vitamin D or calcium supplementation. However, it is interesting that the only meta-analysis that took into account the difference between older adults with low 25OHD values compared with high values found significant protective effects against falls with vitamin D supplementation [71]. Hence, further large, well-designed studies taking into account vitamin D-deficient populations are warranted, as supplementation in people who are not vitamin D deficient may not demonstrate any effect on musculoskeletal health.

Table 3. Summary of characteristics and results from some recent systematic reviews and meta-analyses on the effects of vitamin D and calcium supplementation on bone and muscle outcomes.

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Fabiani et al., 2019 [77]	SR and MA	20 RTCs	Mixed	BMD and fractures	The "Milk/dairy" pattern result in stronger reduction in low BMD risk and fractures vs. the "Western" pattern.
Malmir et al., 2020 [79]	SR and MA	15 (8 cross-sectional, 3 case-control, 4 cohort)	Mixed	BMD and fractures	Inverse association between milk and dairy intake with osteoporosis or HF in cross-sectional and case-control studies, but no association in cohort studies.
Ling et al., 2021 [71]	MA	31 RTCs (21 with vitamin D alone, 10 vitamin D plus calcium)	Older adults with vitamin D deficiency	Fall risk	Reduced fall risk with VD alone in participants with baseline 25(OH)D < 50 nmol/L but not in those > 50 nmol/L vs. placebo or no treatment. Reduced fall risk with VD plus calcium vs. placebo or no treatment.
Prokopidis et al., 2022 [85]	SR and MA	10 RTCs	Community-dwelling older adults	Indices of sarcopenia	VD supplementation did not improve any sarcopenia indices and may compromise some aspects of physical performance.
Barbagallo et al., 2022 [70]	SR and MA	7 RTCs	Mixed	Physical performance and muscle strength	Calcifediol significantly improved GS, HGS, and leg extension vs. baseline values.
Hidayat et al., 2023 [75]	SR and MA	21 RTCs	Age 3 to 18	BMD and bone biochemical markers	Dairy supplementation led to a small but significant increase in BMD parameters and changes in biochemical markers of bone health.
Manoj et al., 2023 [87]	SR and MA	7 RCTs	Older adults	BMD and HF	Daily oral 800 IU of VD3 plus 1200 mg of calcium reduced HF and non-vertebral fracture in older people without any effect on femoral neck BMD. Other lifelong preventive measures are also recommended.
de Souza et al., 2024 [88]	MA	7 RTCs	Healthy older adults aged over 60	Fractures	VD supplementation did not reduce total fracture, non-vertebral fractures, or falls vs. placebo; however, women had an increased risk for HF.
Jiao et al., 2024 [89]	MA	19 RTCs	Older adults	Fractures	No difference in mortality rate. Reduction of incident fractures for VD plus calcium vs. controls, but higher GI adverse reactions.

BMD: bone mineral density; GI: gastrointestinal; GS: gait speed; HF: hip fracture; HGS: handgrip strength; MA: meta-analysis; RCTs: randomized controlled trials; SR: systematic review; 25(OH)D: 25 hydroxy vitamin D; VD: vitamin D.

4.4. Dietary Patterns

In recent decades, nutritional research has shifted from a focus on individual healthy foods or nutrients to examining the interactions between nutrients and foods within dietary patterns, including their potential synergistic and antagonistic effects. This approach could also make health messages and recommendations clearer to the public, who may struggle to understand advice about isolated nutrients and foods, as they ultimately consume them in combinations [90]. Indeed, healthy diets full of nutrient-dense foods can help reduce age-related changes in bone and muscle. Analysis of data from an extensive prospective study, the Swedish Mammography Cohort, found that during a median follow-up time of 25.5 years, hip fracture rate was 31% lower in the highest compared with the lowest quartile of participants adhering to the healthy dietary pattern. Conversely, women in the highest compared with the lowest quartile of the Western/convenience dietary pattern had a 50% higher hip fracture rate [91]. The study of dietary patterns is fundamental because they encompass the impact of various foods and nutrients, not just protein, calcium, and vitamin D, but also other minerals, vitamins, and bioactive antioxidant compounds, which may affect musculoskeletal health both independently and in combination. As confirmation of the importance of the combination of foods/nutrients, it is relevant to remember that a severe eating disorder such as anorexia nervosa is associated with falls and fragility fractures [92].

Plant-based diets are gaining popularity because of their potential health benefits, as well as ethical and environmental considerations [93]. These diets may offer improved health outcomes compared with those based on animal products, thanks to their high content of nutrients that support bone and muscle health, such as various minerals, vitamins (other than vitamin D), and bioactive antioxidant/anti-inflammatory compounds. On the other hand, the absence of these nutrients could negatively affect musculoskeletal health [94]. However, vegetarian diets can vary significantly in their nutritional content, and they can be either nutrient-rich or deficient, similar to animal-based diets [95].

Recently, three extensive epidemiological studies [96–98] have reported that vegetarians (those following meat- and fish-free diets) and vegans (those avoiding all animal-derived foods) experience poorer musculoskeletal health, with consistent longitudinal evidence linking adherence to these diets to an increased risk of fractures. A meta-analysis of 20 studies and 37,134 participants found that adherence to vegetarian and vegan dietary patterns was associated with lower BMD and increased fracture risk [99], although important methodological concerns have been found in this meta-analysis [100]. One of the large recent epidemiological studies evaluated data from the UK Women's Cohort and found a 33% increased risk of hip fracture in vegetarians as compared with regular or occasional meat or pescatarians eaters [97]. In a larger UK cohort including men and women the risk of hip fracture was 50% higher for vegetarians vs. regular meat eaters [101]. The findings from the three studies were consistent, showing that strict vegetarians had a 17 to 33% higher risk of hip fracture compared with meat-eaters, with follow-up periods ranging from 8.4 to 22.1 years [96–98]. Vegetarians, especially vegans, may face a higher risk of deficiencies in essential nutrients for bone and muscle health, such as protein, calcium, vitamin D, and vitamin B12, which are commonly found in animal products [102,103]. Additionally, vegetarians and vegans may be more susceptible to chronic iron deficiency, a condition associated with an increased risk of disrupted bone homeostasis [104], and a higher likelihood of falls [105].

In contrast, plant-based diets seem to have favorable effects on diverse parameters of bone and muscle health, particularly when compared with western diets. A systematic review and meta-analysis by Denova et al. [106] among 31 studies found that a "Prudent/Healthy" diet was linked to a lower risk of low BMD in all age groups, while a "Western/Unhealthy" diet was associated with a higher risk of low BMD in older adults. The "Prudent/Healthy" diet pattern provided protection against fracture risk in men, whereas the "Western/Unhealthy" diet was associated with an increased incidence of fractures. Zeng et al. [107] conducted a meta-analysis among 10 studies showing that the consumption of a vegetable-based diet was linked to a reduced risk of osteoporosis in postmenopausal women. Likewise, Panahande et al. [108] found that following the alternative healthy eating index, a predominantly plant-based diet and indicative of high diet quality, was linked to a lower risk of hip fractures. Nguyen et al. [109] in a further meta-analysis of 21 studies reported a protective link between a 'healthy' diet pattern and hip fracture even if there was contradictory evidence regarding the relationship between 'healthy' and 'Western' diets and BMD.

The Mediterranean diet, a high-quality eating plan primarily focused on plant-based foods, such as vegetables, fruits, olive oil, whole grains, legumes, and nuts and which does not totally exclude animal products but rather recommends them in smaller quantities and frequency, appears to be beneficial for many age-related conditions and also for musculoskeletal health [110]. A meta-analysis of observational studies involving over thirteen thousand participants found a positive linear relationship between greater adherence to a Mediterranean diet and higher total hip and trochanter BMD [111]. Similarly, a previous meta-analysis showed that individuals with higher adherence to the Mediterranean diet had a lower risk of hip fractures [112]. A recent narrative review of the Mediterranean diet's impact on osteoporosis and sarcopenia highlighted evidence linking greater adherence to the diet with improvements in BMD, muscle mass, physical function, and a reduced risk of osteoporosis and sarcopenia [113]. However, most of the available data come from cross-sectional and prospective studies, which cannot establish causality, so clinical trials are still needed to confirm cause-and-effect relationships. There is some recent evidence suggesting that a modified or alternative Mediterranean diet may lower the risk of hip fracture, while the dietary approaches to stop hypertension (DASH) could enhance lumbar spine BMD [114].

A recent systematic review found that, in general, adherence to the Mediterranean diet had a positive impact on muscle mass and function, with less consistent effects on strength. However, there was no evidence supporting the Mediterranean diet's influence on sarcopenia [115]. Another recent comprehensive review [49] highlighted that, while emerging evidence suggests that higher adherence to the Mediterranean diet may benefit sarcopenia and its components in prospective studies of older adults, most of the positive associations observed in recent years stem from cross-sectional studies, which are prone to reverse causality. Greater adherence to the Mediterranean diet was linked to better lower extremity function, mobility, and walking speed, although associations with sarcopenia were mostly non-significant, albeit based on limited data. The studies show considerable heterogeneity, and no clinical trials have yet been conducted [49].

Other dietary patterns with some studies available in the medical literature are the Nordic diet [116] and the ketogenic diet [117]. A systematic review in six studies found that greater adherence to the Nordic diet was linked to improved handgrip/leg strength (1 study) and physical performance (2 studies) specifically in women, as well as a reduced risk of mobility limitations. A meta-analysis was not conducted due to the variation in outcomes. Regarding the ketogenic diet, Garofalo et al. [117] conducted a systematic review aiming to evaluate the relationship between different types of ketogenic diet and bone health, as supported by the scientific literature. They found no significant changes in BMD or bone turnover markers following the ketogenic diet and concluded that there is a lack of sufficient well-designed human studies to definitively assess the impact of ketogenic diet on bone health.

Contrary to a healthy diet, the western or pro-inflammatory dietary pattern, rich in excess meat, processed products, soft drinks, fried foods, sweets and refined grains, has been associated with a higher risk of osteoporosis [118]. In a scoping review on 31 selected studies a lower risk of fracture was found when the highest categories were compared with the lowest categories of a prudent/healthy dietary pattern. Conversely, when the highest categories were compared with the lowest categories of adherence to a western/unhealthy dietary pattern, a greater risk of fracture was observed among men [118].

Unlike a healthy diet, the western or pro-inflammatory dietary pattern, which is high in excessive meat, processed foods, sugary drinks, fried items, sweets, and refined grains, has been linked to an increased risk of low BMD and fractures [77].

In summary, as shown in Table 4, despite the variability that is always observed in studies evaluating the effects of different dietary patterns on bone and muscle health, it can be said that a healthy diet predominantly based on plant-based foods is more favorable in terms of bone outcomes such as BMD and fractures when compared with a western diet pattern, as well as in indices of muscle function. For other dietary patterns such as the Nordic and ketogenic diets, there are not enough data to make definitive conclusions.

Table 4. Summary of characteristics and results from some recent reviews and meta-analysis on the effects of dietary patterns on bone and muscle outcomes.

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Movassagh et al., 2017 [118]	Scoping review	49 (26 cross-sectional, 2 case-control, 20 longitudinal, 1 clinical trial)	Mixed	BMD, bone biomarkers, osteoporosis, and fractures	Dietary patterns emphasizing fruit, vegetables, whole grains, poultry and fish, nuts and legumes, and low-fat dairy products and which de-emphasized soft drinks, fried foods, meat and processed products, sweets and desserts, and refined grains showed a beneficial impact on BMD and decreased osteoporosis and fracture risk.
Denova et al., 2018 [106]	SR and MA	31 (18 cohorts, 1 case-control, and 12 cross-sectional)	Mixed	BMD and fractures	"Prudent/Healthy" diet was associated with lower risk of low BMD across all age groups; "Western/Unhealthy" diet was associated with higher risk of low BMD in older adults. "Prudent/Healthy" diet pattern was protective against fracture risk among men, while "Western/Unhealthy" diet was associated with greater fracture incidence.
Fabiani et al., 2019 [77]	SR and MA	20 RTCs	Mixed	BMD and fractures	The "Healthy" and "Milk/dairy" patterns were associated with a reduced risk of low BMD and fracture. In contrast, the "Western" pattern was inversely associated.
Iguacel et al., 2019 [99]	SR and MA	20 (18 longitudinal, 2 cross-sectional)	Mixed	BMD and fractures	Vegetarians and vegans had lower BMD at the FN and LS vs. omnivores and vegans also had higher fracture rates.
Chan et al., 2021 [94]	SR	17 (9 cross-sectional, 6 RCTs)	Middle-aged and older adults	body composition, muscle strength and function	Possible relationship between plant-based diets and better body composition in older adults, different for men and women. Inconclusive association with muscle function. Large heterogeneity across the studies.
Noori et al., 2022 [111]	SR and MA	8 (7 cross-sectional, 1 cohort)	Mixed	BMD	Greater MedDiet adherence was associated with a small but significant increase in BMD at the LS, FN, hip, trochanter, and whole body.
Malmir et al., 2018 [112]	SR and MA	13 (6 cohort, 6 cross-sectional, 1 case–control)	Mixed	BMD and fractures	Adherence to MedDiet was associated with a reduced risk of fractures as well as with a higher mean BMD.
Zeng et al., 2019 [107]	SR and MA	10 (4 case-control, 6 cross-sectional)	Postmenopausal women	BMD	Higher consumption of VDI was associated with a lower risk of OPS.
Panahande et al., 2019 [108]	SR and MA	5 (4 cohort, 1 case-control)	General population	HF	Adherence to the AHEI (as an indicator of diet quality) was associated with a reduced risk of HF.
Nguyen et al., 2021 [109]	SR and MA	23 (12 cross-sectional, 10 cohort, 1 case-control)	Healthy adults	BMD and fractures	Protective association of 'healthy' pattern for HF. Conflicting evidence for associations of 'healthy' and 'Western' diets with BMD.
Chen et al., 2023 [114]	Scoping review	6 (4 cohort, 2 cross-sectional)	Older adults	BMD and fractures	There is some evidence that a modified and alternative MedDiet may reduce the risk of HF, and DASH may improve LS BMD.

Table 4. *Cont.*

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Garofalo et al., 2023 [117]	SR	7 (5 RCTs, 2 CCTs)	Mixed	BMD	No significant changes in BMD or bone turnover markers after KD. No sufficient human studies with adequate designs to definitively understand the impact of KD on bone health.
Papadopoulou et al., 2023 [115]	SR	10 (4 cross-sectional studies, 6 prospective)	Healthy over 65 adults	Sarcopenia, MM	MedDiet adherence had, in general, a positive role in MM and function, with less clear results for strength. No evidence of MedDiet effect on sarcopenia.
Hanbali et al., 2024 [116]	SR	6 (5 cohort, 1 cross-sectional)	Older adults	Muscle strength, physical performance	Greater adherence to the ND was associated with improved HG/leg strength (1 study) and physical performance (2 studies) only in women, and with a lower risk of mobility limitations. A meta-analysis was not performed due to heterogenous outcomes.

AHEI: alternative healthy eating index; BMD: bone mineral density; CCTs: controlled clinical trials; FN: femoral neck; DASH: dietary approaches to stop hypertension; HF: hip fracture; KD: ketogenic diet; LS: lumbar spine; MA: meta-analysis; MedDiet: Mediterranean diet; MM: muscle mass; ND: Nordic diet; OPS: osteoporosis in postmenopausal subjects; RCTs: randomized controlled trials; SR: systematic review; VDI: vegetable-based diet intake.

5. Physical Activity for Bone and Skeletal Muscle Health

5.1. Bone

It is well-established that physical inactivity (i.e., failing to meet the recommended physical activity guidelines for the population) is a modifiable risk factor for osteoporosis. Increasing physical activity throughout life has a positive impact on bone health, whereas inactivity and reductions in physical activity can lead to bone loss [119]. A confirmation of these effects is what happens to the musculoskeletal system under microgravity conditions during space-flight travels. The lack of gravitational forces means less weight-bearing activity, which may lead to a reduction in BMD, resulting in site-dependent altered biomechanical and endocrine functions, deterioration of bone integrity and bone strength similar to conditions like osteoporosis on Earth [120]. An extensive study comprising 37,238 women (born 1914–1948) from the Swedish Mammography Cohort and 45,906 men (born 1918–1952) from the Cohort of Swedish Men, followed for a maximum of 17 years, showed that both moderate and high self-reported frequency of physical activity was associated with reduced future risk of fracture [121]. Although there are various studies evaluating the impact of physical activity on the prevention and treatment of osteoporosis, there is extensive heterogeneity among the results. Some of them have indicated that weight-bearing and resistance exercises may be most effective [122,123]. A recent systematic review [124] explored the effects of high velocity resistance training (HVRT) on BMD in older adults among 25 studies (12 trials and 13 follow up studies of these original interventions). The heterogeneity of studies precluded the possibility of performing a meta-analysis. Moderate evidence has suggested a small statistically significant effect of HVRT on BMD in older adults at the lumbar spine, total hip, and femoral neck ranging from 0.9% to 5.4%. BMD measurements significantly decreased post-intervention in follow-up studies where the interventions had ceased for over six months. Dose response of HVRT showed a positive impact on BMD when more than two sessions per week were completed [124]. Another recent systematic review and meta-analysis [125] examined the effects of over ten weeks of resistance training on BMD, as well as on muscle structure and function, in older people with sarcopenia. Among thirteen trials with 2080 sarcopenic older adults the authors found no favorable results for BMD, while handgrip strength, isometric muscle strength, chair stand test, and skeletal muscle mass index improved with resistance training [125].

In any case, the available data are still very limited and more quality studies are still needed to be able to draw definitive conclusions. In addition, comparing studies on physical activity and osteoporosis can be challenging due to several key difficulties: first, study designs can vary from observational cohort studies to RCTs, which generally provide stronger evidence but are scarce because they are more resource-intensive, while cohort studies are easier to conduct but subject to confounding variables. Second, the length of the study varies significantly. Short-term studies may not capture the long-term effects of physical activity on osteoporosis risk, while longer studies may face challenges such as participant dropout or changes in lifestyle over time. Third, the studies can include diverse physical activity programs regarding intensity, frequency, and duration, as well as diverse types of exercise (one domain of physical activity). The outcomes for each type of exercise might differ, making it hard to generalize the results. Another important source of variability lays in the characteristics of the populations involved with variable age and gender distribution, as well as the presence of comorbidities, all of which are risk factors that can significantly affect the outcomes. These difficulties highlight the complexity of comparing studies on physical activity and osteoporosis, which are similar to those occurring with muscle outcomes.

Guidelines typically recommend high- or low-impact weight-bearing and muscle-strengthening exercises to help prevent osteoporosis [126–128]. High-impact exercises include jogging, jumping, and aerobics, while lower-impact options involve walking and step aerobics. Muscle-strengthening exercises encompass weightlifting, the use of elastic exercise bands, and activities that involve resistance against gravity. The 'Lifting Intervention For Training Muscle and Osteoporosis Rehabilitation' study found that a combination of high-intensity progressive resistance and impact weight-bearing training was more effective in improving BMD at the lumbar spine compared with a home-based, low-intensity program in postmenopausal women [129]. A long-term regimen that incorporates weight-bearing and resistance exercises has been linked to higher markers of bone formation, with only slight or no increase in markers of bone resorption [130]. Nevertheless, a multicomponent strength training program seems to be associated with the most significant improvements. A systematic review [131] explored the effects of multicomponent exercise training in older women with osteoporosis among fourteen RCTs (544 participants in the experimental group and 495 in the control group) combining two to four different exercise types, including strength, aerobic, balance, flexibility, and/or functional fitness training. The multicomponent training, undertaken for an average of 27.2 weeks, 2.6 sessions per week, and 45 min per session, showed improvements in strength, flexibility, quality of life, BMD, balance, and functional fitness and reduced the risk of falls in older women with osteoporosis [131].

5.2. Skeletal Muscle

For most adults and older adults, participating in activities that promote muscle and bone strength is safe if adapted to personal conditions and will help to maintain or improve musculoskeletal and general function, irrespective of age or health [132,133]. Providing effective guidance may help increase physical activity and exercise, which have wider positive effects on physical, social and psychological health [134].

Growing evidence suggests that sarcopenia may be partially reversible, emphasizing the importance of early interventions for managing the condition [135]. Some exercise interventions have been shown to improve physical fitness in older adults, including increases in muscle mass, strength, endurance, and cardiovascular capacity [136,137]. This underscores the potential benefits of exercise for both preventing and treating sarcopenia. However, there is considerable variability in the results. Additionally, most exercise studies have focused on healthy older adults or those at risk of sarcopenia [138,139], with fewer studies targeting individuals already diagnosed with the condition. Those with sarcopenia typically have lower physical function and may respond differently to exercise interventions compared with individuals in the early stages of the disease.

The varying characteristics of participants are a key factor contributing to the frequent inconsistency in the effectiveness of exercise for sarcopenia. For example, some studies report significant improvements, such as enhanced walking speed after a 6-month exercise program in older adults with sarcopenia [140], while others [141] show only limited gains. Similarly, systematic reviews and meta-analyses on the topic have produced heterogeneous results. Vlietstra et al. [142] found that exercise led to significant improvements in strength, balance, and muscle mass in older adults with sarcopenia across six trials, whereas Bao et al. [143] reported some modest improvements in muscle strength and performance from 22 studies, with no changes in muscle mass.

A recent study systematically evaluated the impact of exercise interventions on muscle strength, muscle mass, and physical performance in older adults with sarcopenia [144]. The findings indicate that exercise interventions notably enhanced grip strength, knee extension strength, lower extremity muscle mass, walking speed, and functional mobility in this population. However, exercise had no effect on fat-free muscle mass, appendicular muscle mass, skeletal muscle mass, or upper extremity muscle mass. Subgroup analyses showed that both resistance training and multicomponent exercises significantly improved muscle strength, while aerobic exercise did not [144]. A cross-sectional analysis of data from the PREDIMED-Plus trial reported an inverse association between sarcopenia and each hourly increment in total, moderate, vigorous, and moderate–vigorous physical activity. Incrementing 1 h/day total and moderate vigorous physical activity was inversely associated with BMI, waist circumference (WC), and fat mass, while it was positively associated with bone mass and lower-limb muscle strength. One hour/day increase in total sedentary behavior was positively associated with BMI, WC and fat mass. Conversely, light physical activity was not significantly associated with any outcome [145].

A comprehensive method to measure sarcopenia is the evaluation of physical performance. The effects of a multicomponent exercise intervention on physical performance assessed with the SPPB and functional status were evaluated in an RCT including 370 hospitalized patients. The intervention group underwent individualized moderate-intensity resistance, balance, and walking exercises (2 daily sessions; the median duration of the intervention was five days) compared with a control group receiving usual hospital care, which included physical rehabilitation when needed. The intervention group showed a mean increase of 2.2 points (95% CI, 1.7–2.6 points) on the SPPB scale (indicative of physical performance) and 6.9 points (95% CI, 4.4–9.5 points) on the Barthel Index (indicative of self-sufficiency) over the usual-care group. Of importance, no adverse effects were observed with the intervention [146]. The possibility that initiating a structured, adapted, and monitored exercise program may be useful in preventing motor disability in sedentary older adults was verified in The Lifestyle Interventions and Independence for Elders (LIFE) studies [147]. This multicenter RCT enrolled 1635 sedentary men and women aged 70 to 89 years who had physical limitations (SPPB $\leq$ 9) but were able to walk 400 m. Participants were randomized to a structured, moderate-intensity physical activity program (n = 818) conducted in a center (twice/week) and at home (3–4 times/week) that included aerobic, resistance, and flexibility training activities or to a health education program as control (n = 817) consisting of workshops on topics relevant to older adults and upper extremity stretching exercises. The results of this RCT showed that participants in the intervention group compared with the health education program had a significantly reduced major mobility disability over a mean follow-up of 2.6 years [147].

Several systematic reviews and meta-analyses of RCTs on different modalities of exercise interventions have been published recently with generally positive results (Table 5). For example, a meta-analysis of 12 RCTs of Tai Chi exercise involving postmenopausal women reported an improvement in BMD, without changes in balance or falls [148]. Another meta-analysis of 13 RCTs in older adults showed an improvement in physical function including balance, lower body strength, and mobility with Otago exercise programs [149]. Hu et al. [150] found that a high-intensity resistance circuit training in older adults was effective for improving body composition and muscle strength, while moderate-to-low intensity training was more effective for lowering blood pressure. A meta-analysis of 31 RCTs among older adults reported that high-volume resistance training enhanced muscle strength, particularly in longer interventions [151]. Guirguis-Blake et al. [152] found that multifactorial and exercise interventions were associated with reduced falls in eighty-three good-quality RCTs in community-dwelling older adults. Older adults in residential care or living in the community experienced beneficial effects with a multi-component exercise on functional and psychosocial health in a meta-analysis of 14 RCTs [153]. Furthermore, even frail older adults can benefit from these programs. A meta-analysis by Yang et al. [154] comprising 28 RCTs involving frail older adults showed that a multicomponent exercise intervention can improve frailty status and promote enhancement of physical functional abilities. Another meta-analysis of 19 RCTs among community-dwelling frail older adults reported that multicomponent exercises significantly helped improve muscle strength, balance, and endurance, even if there was no conclusive evidence of the effects on enhancing quality of life or long-term health outcomes [155]. Cheng et al. [156] conducted a meta-analysis in 12 RCTs involving patients with secondary sarcopenia due to diverse chronic pathologies (type 2 diabetes, Alzheimer's disease, hemodialysis, and pancreatic cancer). The authors found that resistance training can effectively enhance muscle mass and strength; however, it did not significantly improve physical function. As expected, the different pathologies and complications associated with them resulted in variable effectiveness of the intervention. In addition, different resistance training methods had different effects on these types of patients [156]. Finally, an umbrella review including 106 systematic reviews found that exercise may be the most appropriate falls prevention intervention for older adults in residential aged care as well as among community-dwelling older adults [157].

Table 5. Summary of characteristics and results from some recent reviews and meta-analyses on the effects of exercise on bone and muscle outcomes.

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Vlietstra et al., 2018 [142]	SR and MA	6 (5 RCTs, 1 quasi-experimental intervention study)	Sarcopenic older adults	KES, TUG, MM,	Exercise interventions improved strength, balance and MM. However, the number of trials was small and the training effect was inconsistent due to heterogeneity in exercise mode, duration and intensity.
Bao et al., 2020 [143]	SR and MA	22 (19 RCTs, 3 CCT)	Sarcopenic older adults	MM, HGS, CST, GS, TUG	Exercise programs showed overall significant positive effects on muscle strength and physical performance but not on MM in sarcopenic older adults.
Linhares et al., 2022 [131]	SR and MA	14 RCTs	Older women with osteoporosis	Strength, flexibility, QoL, BMD, balance, functional fitness, falls	Multicomponent training for an average of 27.2 weeks improved strength, flexibility, QoL, BMD, balance, and functional fitness and reduced the risk of falls.
Wang et al., 2022 [144]	SR and MA	23 RCTs	Sarcopenic older adults	HGS, KES, MM, GS, functional mobility	Exercise intervention can effectively improve muscle function and physical performance in older adults with sarcopenia, but has limited effects on the muscle mass of the upper extremities.

Table 5. *Cont.*

Authors Country Year	Type of Review	n. and Type of Studies	Population	Outcome	Summary of Results
Haque et al., 2024 [124]	SR	25 (8 RCTs, 13 follow-up studies of these original interventions)	Older adults	BMD	HVRT increased LS, FN, and TH BMD. Higher intensity exercise performed $\geq$ 2 sessions/week had the greatest skeletal benefits. If exercise is stopped for >6 months, benefits achieved may be lost.
Peng et al., 2024 [125]	SR and MA	13 RCTs	Sarcopenic older adults	BMD, HGS, IMS, CST, MM	Over 10 weeks of RT has beneficial effects on muscle but no favorable effect on BMD
Zhang et al., 2024 [148]	MA	12 RCTs	Postmenopausal women	BMD, HSS, balance, falls	Tai Chi exercise improved BMD but not balance or number of falls.
Guirguis-Blake et al., 2024 [152]	SR	83 RCTs	Community-dwelling older adults	Falls	Multifactorial and exercise interventions were associated with reduced falls in multiple good-quality trials.
Cheng et al., 2024 [156]	SR and MA	12 RCTs	Sarcopenic patients due to obesity, T2D, AD, HD, PC	HGS, SMI, GS	For patients with secondary sarcopenia, RT can effectively enhance muscle strength and MM; however, it does not significantly improve physical function. Different RT intervention methods have different effects on patients. Different complications may influence the effectiveness of RT intervention.
Yang et al., 2024 [154]	SR and MA	28 RCTs	Frail older adults	Muscle strength, GS, balance, SPPB, TUG	Multicomponent exercise intervention can improve frailty status in older adults and promote enhancement of physical functional abilities.
Shoukat et al., 2024 [153]	SR	14 RCTs	Older adults in RAC or community	Falls, mobility, balance, muscle strength	Multi-component exercises were found to have a positive impact on the functional and psychosocial health of the geriatric population.
Wang et al., 2024 [155]	SR and MA	19 RCTs	Community-dwelling frail adults	SPPB, TUG, HGS, KES, GS, QoL	Although multicomponent exercises significantly improve muscle strength, balance, and endurance in frail older adults, there is no conclusive evidence of their effect on enhancing QoL or long-term health outcomes.
Wu et al., 2024 [149]	SR and MA	13 RCTs	Older adults	Balance, lower and upper body strength, mobility	The OEP could improve physical function including balance, lower body strength, and mobility.
Hu et al., 2024 [150]	SR and MA	15 RCTs	Older adults	LBM, upper and lower limb strength	High-intensity RCT improved body composition, and muscle strength.
Rocha et al., 2024 [151]	SR and MA	31 RCTs	Older adults	Muscular strength, functional fitness, and body composition	HV-RT enhanced muscle strength, particularly in longer interventions.
Meulenbroeks et al., 2024 [157]	Umbrella	106 SR	Older adults in RAC or community	Falls	Exercise interventions may be the most appropriate fall prevention intervention for older adults in RAC and community settings.

AD: Alzheimer's disease; BMD: bone mineral density; FN: femoral neck; GS: gait speed; CST: chair stand test; HD: hemodialysis; HGS: handgrip strength; HSS: health status score; HVRT: high velocity resistance training; IMS: isometric muscle strength; LBM: lean body mass; KES: knee extension strength; LS: lumbar spine; MA: meta-analysis; MM: muscle mass; OEP: Otago exercise program; PC: pancreatic cancer; QoL: quality of life; RAC: residential aged care; RCTs: randomized controlled trials; RCT: resistance circuit training; RT: resistance training; SMI: skeletal muscle mass index; SPPB: short physical performance battery; SR: systematic review; T2D: type 2 diabetes; TH: total hip; TUG: time up and go.

As mentioned with regard to studies on bone health, testing physical activity and exercise programs on muscle function and sarcopenia in research studies can be challenging for several reasons, spanning both the design of the studies and the factors that influence outcomes. Some of the main difficulties include the heterogeneity of the populations, which include those with age-related comorbidities and related polypharmacy and with baseline fitness level variability, making it harder to generalize results across the population. Another challenge lies in the methods of measurement, which may include muscle mass and function assessment with different techniques (e.g., dual-energy X-ray absorptiometry, and magnetic resonance imaging) and diverse muscle function tests (e.g., grip strength, walking speed, chair rises, and physical performance), all of which can be influenced by factors other than muscle mass, such as joint health, pain, and cognitive function. Additionally, as discussed above, there is no universal consensus on the best outcome measures for sarcopenia or muscle function. The physical activity and exercise programs vary widely in terms of type, intensity, frequency, and duration. Sarcopenia develops over a long period, and changes in muscle mass and function may take months or even years to detect. Many studies are of limited duration, which may not capture the long-term effects of exercise interventions on sarcopenia. Furthermore, nutritional factors are essential for muscle mass maintenance and growth depends not only on exercise but also on adequate nutrition, particularly protein intake. In older adults, issues like poor diet, malabsorption, or reduced appetite can confound the effects of exercise. Nutrition is often not tightly controlled or monitored in exercise studies, making it hard to determine whether changes in muscle function are due to exercise alone, to a combination of exercise and dietary factors, or to the use of supplements like vitamin D or protein, which could influence outcomes. These challenges make it difficult to draw clear, generalized conclusions from studies testing exercise programs on muscle function and sarcopenia.

In summary, there is accumulated evidence, which, despite the difficulties caused by the heterogeneity of exercise programs and the various conditions of the participants in the different studies, shows that structured, regular physical exercise, particularly with a program that includes resistance training, can be considered very useful for musculoskeletal health. Nevertheless, to improve the reliability of findings, researchers need to consider a variety of factors, including better standardization of measures, more homogeneous populations, and control for confounding variables like nutrition and comorbidities.

6. Clinical Implications

The management of osteosarcopenia currently involves treatments targeting the individual aspects of the condition, namely bone and muscle loss, alongside nutritional adequacy, eventual supplementation, and exercise. As discussed above, intervention studies typically focus on specific exercises of varying intensity and duration, often combined with ensuring an adequate balanced diet, sufficient intake of protein, calcium, and vitamin D through diet or supplements, as well as the use of pharmacological treatments for osteoporosis when indicated. There are no specific guidelines for the management of osteosarcopenia but, in the presence of these two entities, the existing national and international guidelines for the individual clinical conditions, osteoporosis [119,127,158,159] and sarcopenia [31,33,160], must be followed. Figure 2 presents an approach that clinicians can use to assess and manage older adults at risk for sarcopenia, osteoporosis or the contemporary presence of both conditions, that is, osteosarcopenia.

Strong recommendations exist for actively screening and prevention of both osteoporosis and sarcopenia. The presence of either condition should trigger an investigation into osteosarcopenia, as both conditions commonly occur together in older adults. The evaluation for osteosarcopenia involves a detailed history (including medical, social, falls, fractures, and medication histories), identification of risk factors, physical examinations, and specific investigations according to the national and international guidelines [31,33,119,127,158–160].

Preventing and treating muscle and bone mass loss, particularly in older adults who are more vulnerable, could help prevent sarcopenia, osteoporosis, and osteosarcopenia. Achieving this would reduce the risk of falls and fractures, making older adults less prone to mobility limitations or severe disabilities that could compromise their independence [20,161,162]. Figure 3 briefly illustrates the components of screening and of primary, secondary, and tertiary prevention of osteoporosis and sarcopenia, including key measures from a nutritional and exercise point of view.

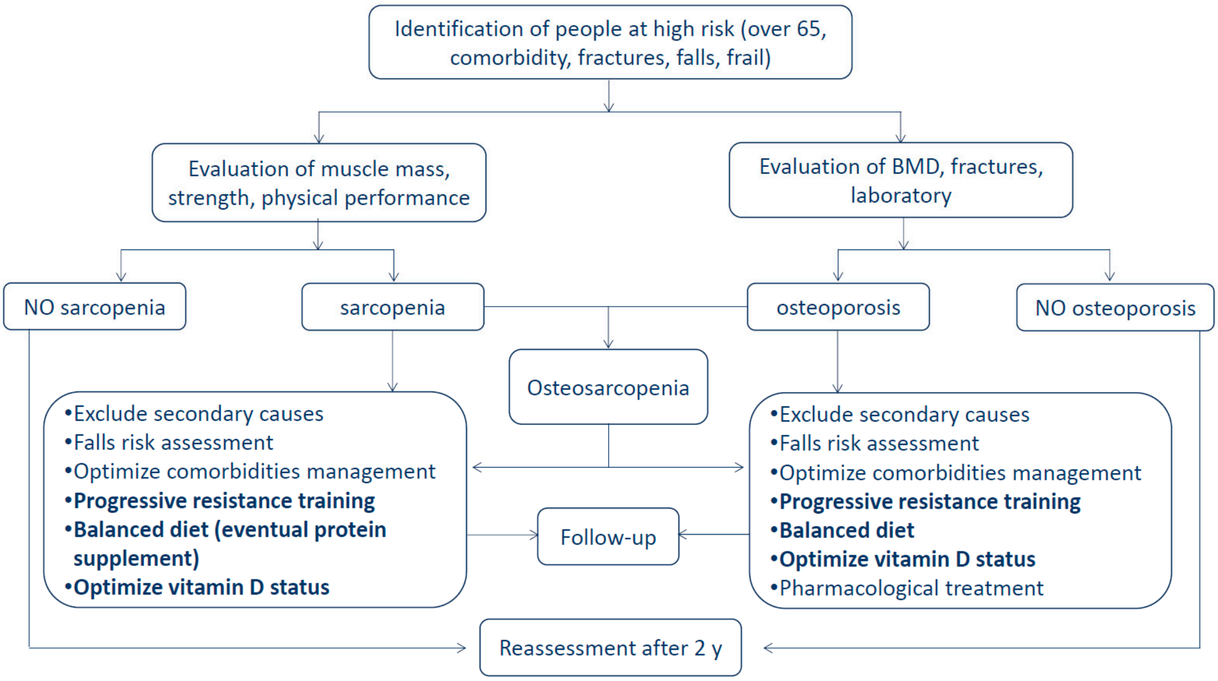

Figure 2. Proposed algorithm for the diagnosis and therapeutic approach to osteoporosis, sarcopenia, and osteosarcopenia. BMD: bone mineral density.

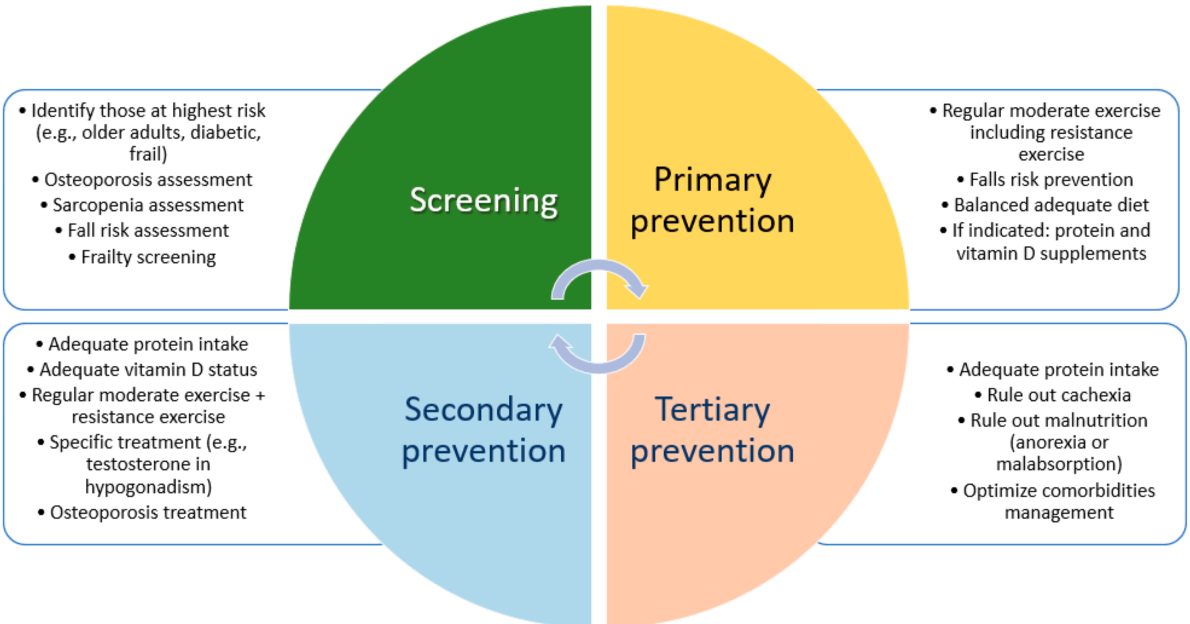

Figure 3. Proposed measures for prevention in bone and muscle health.

Despite its significant impact on older adults, sarcopenia has not been fully integrated into the knowledge and practices of physicians. A recent online survey [163] of 253 practicing U.S. physicians evaluated their knowledge of sarcopenia, use of the term in clinical practice, motivations for screening patients, and approaches to diagnosis and treatment. Fewer than 20% of internists and family medicine physicians reported being very familiar with the term sarcopenia, while geriatricians (70%) and physical medicine and rehabilitation specialists (41%) showed significantly higher levels of familiarity. Participants substantially overestimated sarcopenia prevalence in older adults, and over 75% reported not using specific diagnostic criteria. Only 8% indicated "sarcopenia" in medical charts for patients with significant muscle mass and strength loss [163]. This lack of familiarity may be due, at least in part, to the perception that sarcopenia screening is difficult or time consuming. In reality, the initial screening evaluation can be quite simple. Figure 4 presents two of the physical performance tests, the '30 s sit to stand test' and 'the time up and go' (TUG) test, as an example of how simple and quick they are and, in a similar manner to other tests, such as walking speed or handgrip strength assessments, without the need for sophisticated instruments.

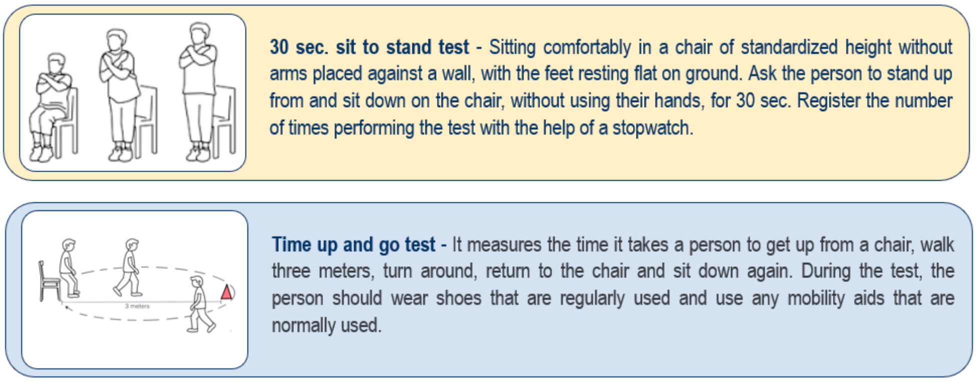

Figure 4. Example of tests to evaluate physical performance with little time consumption.

Although a perfect screening tool for sarcopenia is not yet available, the Strength, Assistance with Walking, Rising from a Chair, Climbing Stairs, and Falls (SARC-F) questionnaire, a five-item assessment, could also serve as a useful starting point. While this tool has low sensitivity, it does demonstrate high specificity. In fact, the 2018 meeting of the EWGSOP recommended a diagnostic approach that begins with the SARC-F, followed by functional and strength evaluations, and measurement of muscle mass [163].

There is also little awareness of the importance of assessing nutritional status in older adults at risk of loss of appetite and/or reduced food intake, which can be associated with undernutrition, sarcopenia, functional decline, loss of independence and other adverse health outcomes. These conditions are often overlooked by physicians or perceived as an inevitable part of 'normal' aging. The results of a recent quantitative survey completed by physicians, dietitians and other health care providers highlight the challenges in the care of older adults with or at risk for anorexia of aging [164].

7. Conclusions

This review underscores the crucial role of nutrition and physical activity/exercise in optimizing musculoskeletal health, including and extending beyond vitamin D, calcium, and protein intake, with combinations of healthy foods and behaviors, such as those proposed by plant-based healthy dietary patterns, including the Mediterranean dietary and lifestyle model. This review also highlights the increasing interest in recent years on sarcopenia and osteoporosis and in their simultaneous presentation as osteosarcopenia. These conditions have been associated, individually or in combination, with relevant health consequences including mortality, fragility fractures, falls, and frailty. Despite the relevant challenges faced by the research discussed in this review regarding the demonstration of the effects of nutritional factors and exercise on musculoskeletal health, a predominantly plant-based balanced diet and regular physical activity should be encouraged by healthcare professionals and emphasized in public health campaigns. Ultimately, a diet rich in vegetables and low in processed and discretionary foods, combined with regular exercise, remains the most effective prevention strategy for optimizing musculoskeletal health. Professional societies should take the initiative in increasing public and medical awareness that sarcopenia and osteoporosis are not unavoidable aspects of aging and can be prevented and treated.

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