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Exercise and nutritional approaches to prevent frail bones, falls and fractures: an update

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ABSTRACT
Osteoporosis (low bone strength) and sarcopenia (low muscle mass, strength and/or impaired function) often co-exist (hence the term ‘sarc-o-osteoporosis’) and have similar health consequences with regard to disability, falls, frailty and fractures. Exercise and adequate nutrition, particularly with regard to vitamin D, calcium and protein, are key lifestyle approaches that can simultaneously optimize bone, muscle and functional outcomes in older people, if they are individually tailored and appropriately prescribed in terms of the type and dose. Not all forms of exercise are equally effective for optimizing musculoskeletal health. Regular walking alone has little or no effect on bone or muscle. Traditional progressive resistance training (PRT) is effective for improving muscle mass, size and strength, but it has mixed effects on muscle function and falls which may be due to the common prescription of slow and controlled movement patterns. At present, targeted multi-modal programs incorporating traditional and high-velocity PRT, weight-bearing impact exercises and challenging balance/mobility activities appear to be most effective for optimizing musculoskeletal health and function. Reducing and breaking up sitting time may also help attenuate muscle loss. There is also evidence to support an interaction between exercise and various nutritional factors, particularly protein and some multi-nutrient supplements, on muscle and bone health in the elderly. This review summary provides an overview of the latest evidence with regard to the optimal type and dose of exercise and the role of various nutritional factors for preventing bone and muscle loss and improving functional capacity in older people.

Introduction
Age-related losses in muscle mass, strength and function (termed sarcopenia) which are often accompanied by concomitant reductions in the mass, structure and strength of bone (termed osteoporosis) contribute to multiple adverse health consequences, including an increased risk of falls, fractures and frailty, which can lead to a loss of independence, disability, increased morbidity and mortality and reduced quality of life. Importantly, there are several similarities in the pathophysiological pathways to both sarcopenia and osteoporosis. Both are multifactorial in origin, and their onset and progression share many of the same risk factors, including inadequate nutrition, physical inactivity, changes in various hormones (gonadal sex hormones, growth hormone/insulin-like growth factor-1 and calcitropic hormones) and inflammatory markers. Given this close link between muscle and bone, the term ‘osteosarcopenia’ or ‘sarc-o-osteoporosis’ has been coined to describe a subset of individuals presenting with the concurrent clinical criteria for sarcopenia and osteopenia/osteoporosis. While such individuals tend to be frailer and at greater risk for falls, fractures and hospitalization, most current diagnostic and therapeutic interventions target these conditions separately. Therefore, identifying safe and effective strategies that can simultaneously optimize muscle and bone health and functional capacity are likely to provide the greatest protection against falls and subsequent fractures.

Currently, pharmaceutical agents targeting bone mineral density (BMD) are the first line of treatment for osteoporosis because they reduce fracture risk by approximately 20–60%. However, up to 50% of patients discontinue treatment after 12 months, side-effects can occur and some people are not willing to take these drugs. Moreover, these agents have no effect on other key fracture risk factors, such as muscle strength, power or gait speed, which are associated with an increased risk of falls and fracture, independent of BMD. Exercise and nutrition are key lifestyle strategies that have the potential to improve multiple fall and fracture risk parameters, if they are tailored to each individual’s needs and appropriately prescribed in terms of the type and dose. In terms of exercise, it is well established that different modes and dosages can influence entirely different body systems and lead to different physiological responses and adaptations. Globally, authorities such as the American College of Sports Medicine are using the term ‘exercise medicine’ to refer to targeted exercise that is specifically prescribed to prevent and treat diagnosed diseases. This review summary provides an overview of the latest evidence with regard to the optimal type and dose of exercise and the role of various
nutritional factors for preventing bone and muscle loss and improving functional capacity in older adults and the elderly.

Exercise for falls and fracture prevention

Whether exercise can prevent fragility fractures remains uncertain because there have been no long-term and adequately powered, randomized, controlled trials (RCTs). An exercise trial with fracture as the endpoint is never likely to be conducted since a sample size of approximately 7000 high-risk persons would be needed. Nevertheless, a systematic review and meta-analysis of controlled trials that reported fracture number as the endpoint or observation in adults aged 45 years and older found that exercise reduced overall fracture number by 51% (relative risk (RR) 0.49; 95% confidence interval (CI) 0.31–0.76) and vertebral fracture number by 44% (RR 0.56; 95% CI 0.30–1.04). Although there was evidence of publication bias which weakens the findings from this study, another meta-analysis of 15 RCTs including 3136 participants reported that exercise reduced fall-related fractures by 40% (RR 0.60; 95% CI 0.45–0.84). While there is evidence that high-challenging balance training performed for at least 3 h per week may be most effective for falls prevention in community-dwelling older adults, such training has been shown to have no effect on bone. At present, questions still remain as to the optimal type and dose (frequency, intensity, duration) of exercise that is most effective for improving multiple fracture risk parameters (fall risk, fall impact, bone strength), but it is clear that not all forms of exercise are equally effective in terms of improving musculoskeletal health and function.

Regular walking is frequently prescribed to prevent osteoporosis, but it has little or no effect on preventing bone loss. This can be explained by the low-impact loading forces (strains) imparted to bones by walking together with the fact that it is a customary activity for most people, and thus bones do not experience loads of a sufficient magnitude, rate or distribution to stimulate cells (osteocytes) to cause an adaptive skeletal response. While there is some evidence that brisk walking, hill walking or walking in combination with weighted vests or other weight-bearing impact exercises may provide some protection against bone loss, others have reported that frequent walking is associated with an increased risk of falls and fracture. On this basis, the prescription of walking as a single intervention to optimize musculoskeletal health and function during aging is not recommended.

Programs that include moderate- to high-impact and novel or diverse multi-directional weight-bearing activities have been shown to maintain or improve (1–3%) hip and spine BMD in healthy older adults. Importantly, relatively few impact loads (~50 multidirectional jumps per day, 3–7 times per week) appear necessary to stimulate an osteogenic response. In addition, such targeted loading can improve skeletal integrity at specific sites of focal bone weakness within the hip, including the superior region of the femoral neck which is prone to spontaneous ‘tensile’ fractures, and is a site of crack initiation when falling sideways. Furthermore, such programs appear to have no adverse effects on cartilage or joint health, including in people with mild knee osteoarthritis. However, this mode of exercise may be contraindicated in individuals with severe osteoporosis or a recent history of fracture, although no trials have evaluated the feasibility and efficacy of weight-bearing exercise in ‘high-risk’ patients.

Progressive resistance training (PRT) is another mode of exercise frequently prescribed because it has been consistently shown to be safe and effective for improving muscle mass, size and strength in middle-aged and older adults, frail elderly and even those with a history of fracture. However, there are mixed findings with regard to the effects of PRT alone on hip and spine BMD in postmenopausal women and older men. The most effective programs were those that incorporated the principle of progressive overload, and applied moderate to high loads (70–85% of maximal strength), performed at least twice per week, and which specifically targeted muscles attached to or near the hip and spine. In term of functional outcomes (e.g. balance, gait, mobility) and falls prevention, PRT alone has also been shown to have mixed effects, which is likely due to the fact that most programs focus on maximizing muscle strength through slow and controlled movements. In recent years, it has been recognized that muscle power, or the ability to produce force quickly, is more important than maximal muscle strength for improving functional performance. Furthermore, lower limb muscle power has been shown to decline earlier and more rapidly with increasing age compared to muscle strength. To counter this decline, high-velocity (HV)-PRT (or power training), which involves rapid concentric muscle contractions, has been shown to be safe and more effective for improving muscle power and functional performance than traditional PRT in older adults, even if a low external resistance (weight) is used. There is also some evidence that power training may have a positive effect on bone health, due to the high rate of loading, but the evidence is currently limited.

Multi-modal exercise programs that incorporate moderate- to high-intensity PRT and/or power training combined with a diverse range of weight-bearing impact activities and functional balance/mobility training appear to be most effective for improving multiple musculoskeletal outcomes. For instance, in a 12-month community-based RCT in 162 older adults (mean age 67 years) with risk factors for falls and/or low BMD, Gianoudis and colleagues found that traditional and HV-PRT combined with weight-bearing impact exercises and challenging balance/mobility training performed three times per week led to significant net gains in femoral neck and lumbar spine BMD, muscle strength, functional muscle power (timed stair climb) and dynamic balance (four square step test, sit-to-stand) relative to usual care controls. In the elderly residing in long-term care facilities, the findings from a meta-analysis of 12 RCTs also revealed that combined resistance and balance training programs were effective at preventing falls (RR 0.71; 95% CI 0.55–0.90), with the strongest effects observed with long-term (>6 months) programs with a frequency of at least two to three sessions per week. For many older adults, the risk of falling increases...
when they are required to undertake a concurrent motor or cognitive task (referred to as the ‘dual-task paradigm’), such as walking while carrying objects. Intervention trials have shown that dual-task training, which involves exercise whilst performing a secondary cognitive or motor task (e.g. dancing in time to music), can improve dual-task performance and reduce falls, including in those with impaired cognition. Collectively, these findings highlight that multi-component programs targeted to each individual’s needs and functional ability are likely to provide the greatest musculoskeletal health and functional benefits. However, the challenge is that many older people are not willing to partake in regular structured and supervised exercise programs. Thus, there is a need to identify whether other less structured (and strenuous) approaches can offer any musculoskeletal and/or functional benefits.

In the last decade, sedentary behavior, or too much sitting, has emerged as a new health risk because it has been shown to be adversely associated with multiple cardiometabolicism-related biomarkers and diseases as well as premature mortality, independent of physical activity levels. Although few studies have examined the effects of sedentary behavior on musculoskeletal health and function in older people, there is some evidence that prolonged sitting is independently associated with reduced muscle mass, strength, power, mobility and an increased risk disability. Emerging data also indicate that breaking up prolonged sedentary bouts is associated with better physical function and a lower risk of disability, independent of physical activity. This is consistent with earlier research showing that more frequent breaks in sitting are associated with better cardiometabolic health outcomes. However, at present the strength of the evidence is limited due to the cross-sectional or prospective observational nature of most studies, which limits causality. Nevertheless, given that many older people spend up to 80% of waking hours sedentary, further research is warranted to examine the feasibility and efficacy of breaking up and reducing sedentary time as a strategy to maintain musculoskeletal health and function (and evaluate whether there is a given dose that is optimal). In the meantime, however, it is advisable that all older adults are encouraged to sit less and move more.

Nutritional factors for falls and fracture prevention

Nutritional strategies focusing on calcium, vitamin D and protein are widely recommended for the prevention and management of osteoporosis and/or sarcopenia. However, recent controversies around the potential adverse effects of calcium supplements on myocardial infarction risk and high-dose vitamin D treatment on falls risk have led to some questioning about the clinical benefits of such treatment. Nevertheless, meta-analyses of RCTs have generally shown that combined calcium and vitamin D supplementation is safe and effective for reducing the risk of fractures in older people. Indeed, supplementation with vitamin D at doses of 800–2000 IU/day (median 800 IU/day) or to a target serum 25-hydroxyvitamin D (25(OH)D) concentration >60 nmol/l, particularly when combined with adequate dietary calcium (at least 1000 mg/day), can slow bone loss and reduce hip and vertebral fracture risk. Meta-analyses of intervention studies have also reported that vitamin D treatment can improve muscle strength, particularly in those with low vitamin D status, and reduce the risk of falling by 14–19%. With reports that daily doses of >700–800 IU and/or when serum 25(OH)D exceeds 60 nmol/l, are most effective. However, others have concluded that vitamin D treatment has no benefit on the risk of falls, with some reports that high-dose or bolus administration of vitamin D may increase falls risk, particularly when serum 25(OH)D concentrations exceed 100–112 nmol/l. At present, the mechanism(s) underlying this increased falls risk is not known and, until further safety data are available, some have suggested that daily or bolus dosing should not exceed 3000 IU. However, for most older adults, current clinical guidelines recommend 800–1000 IU/day of vitamin D with the aim to maintain serum 25(OH)D concentrations >50 nmol/l year-round in combination with a total calcium intake of at least 1000 mg/day.

For dietary protein, there has been a long-standing debate as to whether high intakes are beneficial or detrimental to bone health because of its potential calcific effect. However, higher protein intakes can increase circulating insulin-like growth factor-1 (IGF-1), which has stimulatory effects on osteoblastic function and muscle, promotes intestinal calcium absorption, suppresses parathyroid hormone levels, and improves muscle mass and strength, all of which can have a favorable effect on bone. Epidemiologic studies have shown that higher protein intakes are associated with favorable effects on bone and a lower fracture risk, particularly when calcium intakes are adequate. However, questions still remain as to the optimal dose and type of protein required. There have been mixed findings with regard to the effects of milk, meat, soy and vegetable (plant) based sources of protein on bone and fracture risk, and the findings from two long-term (18–24 months) RCTs failed to observe any favorable effects of whey protein supplementation on BMD in older adults. The lack of an effect in these studies may relate to the relatively high baseline protein intake of the participants (~1.1 g/kg/day), as it has been suggested that the greatest benefits of dietary protein may be observed in those who are malnourished or have habitually low intakes. For instance, in elderly patients post-hip fracture, protein supplementation (all patients in this study received calcium and vitamin D) increased serum IGF-1 and proximal femur BMD and reduced the length of hospital stays.

Another mechanism by which protein might have a positive effect on bone is via an increase in muscle mass and strength. Protein is a well-known anabolic stimuli for muscle protein synthesis (MPS), but there is evidence that older adults experience a blunted response to protein (termed ‘anabolic resistance’ to aging). As a result, protein intakes above the current recommended dietary allowance (RDA) (~0.8–1.0 g/kg/day) are recommended to maintain (or prevent) age-related muscle loss. Although acute studies have consistently reported that the provision of high-quality, rapidly digested, leucine-rich protein sources can stimulate an
increase in MPS in older adults\textsuperscript{74}, there are mixed findings with regard to the long-term effects (>12 weeks) of protein supplementation alone as a strategy to preserve muscle mass, strength or function in the elderly\textsuperscript{71,72}. PRT has also been shown to be a potent stimulus for MPS, but there are mixed findings as to whether protein supplementation can augment the effects of PRT on muscle mass, strength and function in the elderly\textsuperscript{75}. A range of factors including differences in the type of protein (animal, plant, whey, casein, soy) or amino acids (leucine) used, the dose, pattern/distribution and timing of intake, the spread and/or change in intake, as well as habitual (baseline) levels and co-ingestion with other nutrients, may all contribute to the heterogeneity in the findings from the available long-term human intervention trials\textsuperscript{75}. Nevertheless, a recent consensus statement recommended a daily protein intake of 1.0–1.2 g/kg, with at least 20–25 g of high-quality protein at each meal (and post-exercise) for older people\textsuperscript{35}.

There has also been considerable interest into whether co-ingestion of multiple nutrients (e.g. vitamin D, calcium, magnesium, omega-3 fatty acids) can produce additive or synergistic benefits in combination with protein and/or exercise on muscle (and to a lesser extent bone) health. While the vast majority of the research to date has been conducted in the elderly, institutionalized or sarcopenic older adults, these trials have shown that supplementation with protein-energy, vitamin D and/or calcium (some have also included prebiotics (short-chain fructo-oligosaccharides) which have been shown to promote calcium absorption, and omega 3 fatty acids which may reduce inflammation) can improve muscle mass and reduce falls, although the effects on functional outcomes (gait, balance, strength) remain mixed\textsuperscript{76–78}. The addition of a multi-nutrient supplement (protein, vitamin D and/or calcium) to exercise as a part of a weight loss program or bariatric surgery has also been shown to improve or preserve muscle mass and BMD\textsuperscript{79,80}. Whether similar benefits would be detected in healthy middle-aged and older adults (who are less likely to be deficient or have insufficient intakes) is not known, and what combination is optimal remains uncertain (and difficult to determine) but warrants further investigation.

**Conclusion and recommendations**

There is considerable evidence to support the role of exercise and nutrition, particularly vitamin D, calcium and protein, as strategies to prevent and/or manage osteoporosis, sarcopenia and falls. However, such approaches must be individually tailored and appropriately prescribed in terms of the type and dose to elicit the greatest benefits. Not all forms of exercise are equally effective. Regular walking alone has little or no effect on preventing bone or muscle loss. Traditional progressive resistance training (PRT), which focuses on slow and controlled muscle contractions, is safe and effective for improving muscle mass and strength in older people and the frail elderly, but has mixed effects on muscle function and falls. In contrast, high-velocity PRT (or power training), which involves rapid muscle contractions, can concurrently improve muscle mass, function and power (ability to produce force quickly) in older adults. Currently, however, targeted multi-modal programs incorporating traditional and high-velocity PRT in combination with a diverse range of moderate and odd-impact weight-bearing exercises and challenging balance/mobility activities appear to be most effective for optimizing multiple musculoskeletal and functional outcomes in older people. There is also emerging data that reducing and breaking up prolonged periods of sitting may help offset muscle loss, but this requires further investigation. Finally, there is evidence to support an interaction between exercise and various nutritional factors, particularly protein and some multi-nutrient supplements, on muscle and bone health in the elderly, but whether this translates into meaningful improvements in physical function still remains uncertain.

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