

## Non-pharmacological management of osteoporosis: a consensus of the Belgian Bone Club

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**Abstract** This consensus article reviews the various aspects of the non-pharmacological management of osteoporosis, including the effects of nutriment, physical exercise, lifestyle, fall prevention, and hip protectors. Vertebroplasty is also briefly reviewed. Non-pharmacological management of osteoporosis is a broad concept. It must be viewed as an essential part of the prevention of fractures from childhood through adulthood and the old age. The topic also includes surgical procedures for the treatment of peripheral and vertebral fractures and the post-fracture rehabilitation. The present document is the result of a consensus, based on a systematic review and a critical

appraisal of the literature. Diets deficient in calcium, proteins or vitamin D impair skeletal integrity. The effect of other nutriment is less clear, although an excessive consumption of sodium, caffeine, or fibres exerts negative effects on calcium balance. The deleterious effects of tobacco, excessive alcohol consumption and a low BMI are well accepted. Physical activity is of primary importance to reach optimal peak bone mass but, if numerous studies have shown the beneficial effects of various types of exercise on bone mass, fracture data as an endpoint are scanty. Fall prevention strategies are especially efficient in the community setting, but

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less evidence is available about their effectiveness in preventing fall-related injuries and fractures. The efficacy of hip protectors remains controversial. This is also true for vertebroplasty and kyphoplasty. Several randomized controlled studies had reported a short-term advantage of vertebroplasty over medical treatment for pain relief, but these findings have been questioned by recent sham-controlled randomized clinical studies.

**Keywords** Lifestyle · Nutrition · Osteoporosis · Physical exercise · Treatment · Vertebroplasty

## Introduction

Osteoporosis is a chronic disease affecting one in three women and one in five men over the age of 50 years [1]. Osteoporotic fractures are associated with high morbidity, increased mortality risk, and major economical impact [2]. In the field of osteoporosis, the medical literature frequently reports data from large randomized controlled trials describing impressive drug-induced reduction of fracture risk [3]. The availability of most of these drugs makes it easy for the clinician to find an appropriate treatment for most patients. Unfortunately, in the daily practice, osteoporosis treatment too often consists of drug prescription, without any other preventive or therapeutic measure. Besides drug prescription, non-pharmacological osteoporosis management is an important and very broad concept. It must be considered as part of the long-term prevention of fractures, for men and for women, not only for postmenopausal women, but from childhood through adolescence, pre- and perimenopause. This topic also includes the surgical or invasive procedures for the treatment of peripheral and vertebral fractures and the post-fracture rehabilitation.

Lifestyle habits including calcium intake, general nutrition and weight-bearing exercise during adolescence and early adulthood contribute up to 20% of the observed variation in the attainment of peak bone mass, as well as to the rate of bone loss later in life [4, 5]. Falls in the elderly are a major health problem, contributing to significant increase in fracture risk, morbidity, and even mortality [6]. Fall prevention is consequently important in the elderly as nearly one out of three adults living in the community falls at least once each year, the risk being from far more important for institutionalized patients or those with neurologic disturbances [7]. In the context of patients with high risk of falls, the use of hip protectors, aimed at reducing the impact of falls onto the hip, has been suggested as an effective strategy for hip fracture in nursing home residents and potentially among other high-risk individuals [8]. Vertebroplasty and kyphoplasty through

percutaneous injection of bone cement into fractured vertebral bodies have been proposed for short- and long-term pain management. For many years, results of these surgical procedures have been evaluated positively in retrospective non-randomized trials but results of recent controlled studies are becoming available [9, 10].

The present document is the result of a national consensus, based on a systematic review and a critical appraisal of the literature. It aims at providing clinicians with an overview of the currently available non-pharmacological measures for the prevention and treatment of osteoporosis in men and women.

## Methods

We included randomized controlled trials (RCTs), meta-analyses, and epidemiologic, retrospective, or prospective studies, evaluating the non-pharmacological interventions or environmental factors associated to an increase or a decrease in the risk of osteoporotic fracture: diet (sodium, potassium, phosphorus, protein, minerals, fibre, caffeine, or vitamins intake); physical exercise or life style measures (soda drinks or alcohol consumption, smoking, or sun exposure) that have an effect on bone health; factors associated to risk of falls and fall prevention strategies. The efficacy of hip protector devices, of vertebroplasty and kyphoplasty procedures, and the orthopaedic aspects of orthopaedic fracture treatment have been similarly evaluated through a systematic search, from 1966 to 2010, in MEDLINE and databases such as the Cochrane Controlled Register, for citations of relevant articles. After this extensive search of the literature, a critical appraisal of the data was obtained through a consensus expert meeting.

## Nutrition and osteoporosis

As many other chronic conditions, osteoporosis (OP) has a multifactorial origin. If it is admitted that at least 46–62% of the variance in bone mineral density (BMD) depend of genetic factors, consequently around 38–54% of the variance of BMD can be modified by environmental factors, in which nutrition plays a large part [11, 12]. Regarding the skeleton, nutrition could theoretically have a direct and indirect role: firstly, to maximize bone strength during growth through the amelioration of the peak bone mass, by improving both the proteic compartment of bone and the mineralization, and by decreasing the rate of bone loss with ageing; secondly, to maintain the muscle strength by restraining sarcopenia in elderly. Physical activity has also a role, either isolated or in combination with nutrition.

Increase in physical activity and calcium intake can indeed maximize bone gain chiefly at loaded sites [13, 14]. The combined effect of nutrition and exercise has been less studied for other nutriment. Moreover, during growth, an interaction between environment, hormonal factors, nutrition, ethnicity, sex, and genetics probably exists. Even complicating more the study of the relationship between nutrition and BMD, studies have shown a positive link between maternal nutrition, body build, and fat stores during pregnancy with whole body bone mineral content in children at the age of 9, and even with adult bone mass [15]. A higher whole body peak bone mass has been associated with breastfeeding, suggesting the presence of other factors than nutritive factors in human milk [16]. These direct and indirect incentives of nutrition on BMD, bone structure, and bone metabolism, as well as the weak correlation between the nutritional intakes and their quantitative evaluation (e.g. food frequency questionnaires;  $r=0.31-0.71$ ) might only partly reflect the long-term influence of feeding on bone. This could explain the difficulty in determining precisely the role of the nutritional intakes [17]. On the top of these difficulties, it should be remembered that the influence on the skeleton of some nutriment such as calcium is not linear, but has a threshold effect probably variable across the age groups [18]: lower than the threshold, there is some risk of bone loss, around the threshold, bone maintenance is observed, and above the threshold, there is no further additive effect [18]. The role of calcium and vitamin D in the treatment of OP has been recently reviewed in the last BBC consensus [3]. Therefore their role will not be further discussed. Suffice here to remember that the antifracture efficacy is better for a daily intake of 1,000–1,200 mg calcium and 800–880 IU vitamin D [19].

Excesses in sodium intake have a negative impact on calcium balance by increasing the urinary calcium excretion. There is, however, an interindividual differences in salt sensitivity. Obligatory urinary calcium losses are correlated with urinary sodium excretion [20]. For every 100 mmol of sodium excreted, approximately 1 mmol loss of urinary calcium is observed [20]. It has been suggested, however, that enough calcium in the diet could overcome the salt deleterious effect. There could be 2-fold differences in sodium-induced calciuria with low and high calcium intakes. In a recent study, as compared with a low salt diet (3.9 g/day), a high salt intake (11.2 g/day), corresponding to upper intakes in postmenopausal women on a Western-style diet provoked a significant increase in urinary calcium excretion (+36%). The negative bone calcium balance was not counteracted by a high calcium diet (1,284 mg/day). Paradoxically, the negative bone calcium balance induced by both high and low salt diets was less marked with a low calcium intake. There was a significant increase in the levels of parathyroid hormone (+11.4%) and of urinary *N*-

telopeptide (+19%) in response to the high sodium diet [21].

In previous studies such as the Framingham study, in a 12-year follow-up, the risk of hip fracture over each 2-year period was found significantly increased by the consumption of  $\geq 2.5$  units of caffeine per day (one cup of coffee=one unit of caffeine, and one cup of tea=0.5 unit of caffeine) [22]. There is a theoretical explanation to the fragilization of bone by caffeine intake: caffeine increases urinary and faecal calcium losses and may provoke a negative calcium balance in presence of a low calcium diet [23]. Caffeine at a dose of 330 mg/day (i.e. four cups (600 ml)) possibly might be associated with a modestly increased risk of osteoporotic fractures (Hazards ratio, 1.20 (95% confidence interval (CI), 1.07–1.35)), compared with a low caffeine intake (<200 mg/day) [24]. However, this deleterious effect of caffeine seems to be offset by increasing calcium intake (by 40 mg calcium for every 177.5 ml serving of caffeine-containing coffee, i.e. ~1 cup) [25]. This positive calcium effect greatly minimizes a potential role for caffeine in BMD maintenance and bone strength. No study has been done with decaffeinated coffee.

High phosphorus intakes are associated with lower levels of calcium urinary excretion, but a slightly higher intestinal calcium excretion. These opposite effects neutralize themselves and does not seem to negatively impact on calcium balance [26, 27].

The role of protein intake remains controversial in the development of osteoporosis. Excessive protein intake can be responsible for a metabolic increase of acid production and acid renal excretion, with increased calciuria potentially favouring bone loss and hip fracture [26, 28]. Hypercalciuria is not necessarily due to an increase in bone resorption. Intestinal calcium absorption is indeed positively influenced by protein intakes, probably secondary to insulin-like growth factor-1 (IGF-1) production [29, 30]. On the contrary, in postmenopausal women, but also in men, a positive association between protein intakes and BMD has been rather observed [28, 31]. In men and women, a mean loss of BMD of -4.61% and -3.72% was observed in patients with the lowest quartile of protein intake (17–53 g/day), versus a loss of -2.32% and -1.11% in patients with the highest quartile (84–152 g/day) at the femoral neck and spine, respectively [31]. Munger et al. also observed that the risk of hip fracture was not associated with calcium or vitamin D intake, but was negatively related to total protein intake. Proteins of animal and not vegetable origin apparently accounted for this association. The relative risk for hip fracture seemed to decrease paralleling the intake in animal protein [32]. In another study, elderly women consuming less than 66 g protein/d had lower values (1.3–2.2%) of quantitative ultrasound of the heel (broadband attenuation and stiffness measurements) and lower hip BMD (2.5–3.0%)

than patients eating more than 87 g protein/day [33]. Contrarily to these positive effects of protein intake on BMD, Sellmeyer et al. showed in a prospective cohort study that a high diet ratio of dietary proteins of animal origin over vegetable protein could induce a higher rate of bone loss at the femoral neck and an increased risk for hip fractures (relative risk=3.7) in women aged more than 65 years [34]. This apparent deleterious effect of animal protein intake could be counteracted by dietary or supplemental calcium (500 mg as calcium citrate malate and vitamin D (700 IU) per day) [35]. As far as the relationship between fractures and protein intakes were concerned, some contradictory results have been observed for the forearm fracture and hip fractures [36]. A slightly higher risk for forearm fractures was observed in women consuming more than 95 g per day protein as compared with those consuming less than 68 g per day (relative risk=1.22), whereas no association was found with hip fracture [36]. This discrepancy could find its origin in the fact that people with a higher protein intake have a longer life expectancy possibly accounting for a higher forearm fracture incidence [37]. Calcium intake can also interfere with protein intake, a low dietary calcium potentially blunting the positive effect of high protein intake [31, 35]. However, data from the 1999 to 2002 National Health and Nutrition Examination Survey does not show any association between total calcium intake and risk of fracture in postmenopausal women. An inadequate dietary protein intake in the presence of adequate total calcium intake does not seem to confer any protection against fractures [38]. Once hip fracture has occurred, a 20-g protein supplementation could lead to a lower rate of general complications such as bed-sores, infections, deaths, etc., and allow a shorter stay in the hospital as shown in a study [39]. The observed effect is probably due to a positive influence of dietary proteins on the production of IGF-I [30]. Some studies incriminated vegetarianism for increasing bone remodelling and decreasing BMD [40, 41]. The lower BMD observed might not be clinically relevant, no difference in fracture risk between vegetarians and nonvegetarians having been demonstrated in a large study [42]. Vegetarianism should therefore not be considered as a risk factor for osteoporotic fracture. As this issue is that complicated, it seems reasonable to recommend a balanced diet between vegetable and animal proteins until further studies determine the most appropriate regime. Indeed, it is not yet clearly demonstrated that bone resorption induced by vegetables is dependent of acid–base changes in protein intake [43]. Finally, protein might play a role in maintenance of BMD by different mechanisms, e.g. by increasing IGF-1, calcium absorption, and muscle strength and mass, which all could benefit the skeleton [44].

Potassium content, high in fruits and vegetables has a protective effect against urinary calcium loss. However, this

positive effect can be completely offset by a low calcium intake or a reduction in intestinal absorption. The best way to preserve the body calcium economy is to encourage the consumption of foods such as dairy products, which are rich in calcium, proteins, phosphorus, and potassium [45].

In postmenopausal women, an increased intake of some minerals and vitamins could prove to be able to decrease bone loss [46]. This favourable effect has been suggested for magnesium, boron (contained in dried-plums), vitamin C, vitamin K, and fluor, but it is not commensurate to the effect of calcium and vitamin D. Mononutritional supplements will frequently be inadequate and preference should go to the use of complete supplements or foods (e.g. dairy products) [45]. These supplements should be potentially useful mostly in late postmenopause and in elderly people [46]. However, their exact role in bone metabolism as compared with calcium/vitamin D supplementation remains to be demonstrated [47, 48].

High-fibre diets ( $\geq 30$  g/day) could provoke a 20–30% decrease in intestinal calcium absorption [49]. A lowered plasma estradiol level has also been attributed to fibre excess, but the effect on the skeletal integrity has not been clearly settled [50].

Soy isoflavones are natural products structurally and functionally related to 17 beta-estradiol. In vitro and animal studies have suggested that phytoestrogens act on both osteoblasts and osteoclasts through genomic and nongenomic pathways [51]. In a recent meta-analysis including data from 1,240 postmenopausal women, daily ingestion of on average 82 mg soy isoflavones for 6 to 12 months was accompanied by a significant increase in spine BMD (+2.38% (95% CI, 0.93–3.83;  $p=0.001$ )), compared with controls [52]. In a large randomized, placebo-controlled trial, ipriflavone, another soy isoflavone did not prevent bone loss nor affected biochemical markers of bone remodelling in Western Caucasian postmenopausal women. Moreover, lymphocytopenia was observed in a significant number of women [53]. However, several epidemiological studies and clinical trials suggest that some soy isoflavones have beneficial effects on bone turnover markers and bone mechanical strength in postmenopausal women [54]. It is possible that the varying effects of isoflavones on spine BMD across trials might depend on study characteristics, duration of therapeutic intervention (6 versus 12 months), origins of the patients (Asia versus Western countries), race, and baseline BMD (normal BMD, versus osteopenia, or osteoporosis). No significant effect has ever been observed on femoral neck, total hip and trochanter BMD. Further longer studies are necessary, because the role of soy isoflavones in bone economy remains unclear. Their long-term safety is still to be precisely stated. Use of calcium-reinforced soy isoflavones could be considered.

Bone quality in adults mostly depends on the equilibrium in bone remodelling. The latter is influenced by hormonal



factors, in connexion with adequate mechanical loading and sufficient intake of macro- and micronutrients. The well known, because better and more extensively studied, elements are calcium, proteins and vitamin D. Diets deficient in one of the above-mentioned nutrients will certainly be at risk of impairing skeleton integrity. However, it is possible that the optimal health of the skeleton requires a good equilibrium between all nutrients. As already mentioned above, it is probable that mononutrient supplementation, as frequently recommended in several diets will not necessarily lead to an adequate bone quality [53].

### Physical exercises

The main objective of physical exercise in the prevention or treatment of osteoporosis is to reduce fracture incidence. Unfortunately, no large, well-designed controlled trial assessed, so far, the effect of exercise therapy with fracture as an outcome. As a result, exercise interventions for patients with osteoporosis mainly reported the reduction of risk factor for fracture, i.e. a decrease in the propensity to fall and/or an increase in BMD. Because mobility impairments, such as reduced balance and muscle strength, are risk factors for falls and fractures, they have also been used as outcomes in clinical trials [55].

#### 1. Target bone mineral density

In young, healthy subjects, it was shown that the type (e.g. with land impact or not) and intensity (e.g. endurance or not) of exercise have independent and additive effects on bone density [56] suggesting that any physical activity could be of primary importance to reach optimal peak bone mass, bone strength and bone geometry. This is of primary importance from a prevention point of view as an optimal BMD (as best clinical surrogate for bone strength) before menopause is of major importance to reduce the risk of fracture. It has been suggested that pre and postmenopausal women could have different responses (e.g. on BMD) to exercise therapy [57].

From a primary prevention point of view, the convergence of two factors greatly promotes bone health: the critical period of bone accrual during childhood and the importance of bone loading through specific physical activity [58]. As a matter of fact, a lot of clinical trials show that well-designed childhood physical activity programmes (not to vigorous activities [59]) improve BMD in children [58, 60], with different responses between boys and girls [61, 62]. However, it should be pointed out that there is little information if the benefits are sustained into young adulthood.

A recent meta-analysis, performed among premenopausal women, showed that combined protocols inte-

grating odd- or high-impact exercise with high-magnitude loading (resistance exercises such as vertical jumps or rope jumping, running, aerobic or step classes, bounding exercises, agility exercises, and games where movements included directional elements to which the body is not normally accustomed), were effective in increasing BMD at both lumbar spine and femoral neck (weighted mean difference (WMD) 0.009 g/cm<sup>2</sup> 95% CI (0.002–0.015) and 0.007 g/cm<sup>2</sup> 95% CI (0.001–0.013);  $P=0.011$  and 0.017, respectively). High-impact only protocols were effective on femoral neck BMD (WMD (fixed effect) 0.024 g/cm<sup>2</sup> 95% CI (0.002–0.027);  $P<0.00001$ ) [63]. In an individual patient data (IPD) meta-analysis in premenopausal women showed that resistance exercise was not significantly effective for increasing or maintaining lumbar spine and femoral neck BMD [64]. However, this IPD meta-analysis only include 143 subject in the analysis.

Several high-quality studies showed that exercise interventions can successfully maintain or increase BMD in postmenopausal women, as shown in several meta-analyses [65, 66]. In such population, the last Cochrane review, updated in 2002, including 18 RCTs meeting the inclusion criteria, shows that aerobics, weight-bearing and resistance exercises were all effective on the spine BMD. The weighted mean differences of the percentage change from baseline for the combined aerobics and weight-bearing programme on the spine was 1.79 (95% CI (0.58, 3.01)). Interestingly, the analysed results showed walking not to be effective on BMD of the spine but effective at the hip 0.92 (95% CI (0.21, 1.64)). Aerobic exercise was effective in increasing BMD of the wrist 1.22 (95% CI (0.71, 1.74)). More recently, another meta-analysis aimed to assess the effects of prescribed walking programmes on BMD at the hip and spine in postmenopausal women [67]. It was showed no significant change in spine BMD (WMD 0.007 g/cm<sup>2</sup> 95% CI (–0.001 to 0.016);  $P=0.09$ ). At the femoral neck, results were inconsistent, because of heterogeneity, in showing a positive effect of walking on BMD (WMD (random effects) 0.014 g/cm<sup>2</sup> 95% CI (0.000 to 0.028);  $P=0.05$ ). Insufficient data were available for meta-analysis of the total hip site. At least, in a IPD meta-analysis in postmenopausal women, no effect of exercise on femoral neck BMD was observed [68].

In subject with an increased risk of fracture (i.e. low bone mineral density (osteoporosis and osteopenia) a very recent systematic review concluded that bone strength was improved by weight-bearing aerobic exercise with or without muscle strengthening exercise when the duration of the intervention was at least a year [69].

2. Target risk factors for falls (i.e. muscular strength, power, and balance)

Muscle weakness, lower power as well as balance impairment, in elderly people, are associated with physical function decline [65–67]. Osteoporotic women also have a reduced muscular power and body balance compared with women with normal bone mass [70]. These limitations represent major contributors to falls and social, health and economic consequences are well reported [68–71].

The large majority of the published studies investigated the effectiveness of a progressive resistance strength training (PRT) to reduce physical disability or to improve balance, in a large variety of patients. Few studies on PRT have been performed specifically in osteoporotic subjects. PRT is widely accepted as an appropriate modality for rehabilitation in elderly people. PRT appears to be an effective intervention to increase strength and has a positive effect on some functional limitations [71, 72]. However, the effect of PRT on physical disability, health related quality of life and balance remains unclear. In a systematic review of 62 trials ( $n=3,674$  subjects), Latham et al. showed that PRT induces a strong positive effect on strength in older subject (SMD 0.68; 95% confidence interval, 0.52–0.84) [71]. A modest effect was found on some measures of functional limitations such as gait speed (WMD 0.07 m/s; 95% CI 0.04, 0.09). No evidence of an effect was found for physical disability (SMD 0.01; 95% CI, –0.14, 0.16). In another systematic review evaluating PRT as a single intervention on balance performance in older adults aged over 60 years, 29 studies were eligible for review [72]. Participants ( $n=2,174$  subjects) included healthy, community-dwelling, mobility-limited, frail cohorts, and those with chronic co-morbidities. Fourteen studies (15 tests representing 22% of all balance tests) reported significantly greater improvements in balance performance following PRT than in controls. Furthermore, some studies have investigated the effectiveness of high-velocity and high-power training (POW) to improve lower extremity muscle power in community-dwelling older adults aged over 65 years [73]. In contrast to traditional PRT, POW specifically focuses on maximizing contraction velocity and power development [73]. Fielding et al. [74] compared the outcomes of POW and traditional slow velocity progressive resistance training over 16 weeks in women aged mean  $73\pm 1$  years, and reported that power training resulted in large improvements of leg extensor power. Inconsistent effects of PRT on various outcomes can partly be explained by heterogeneity of cohort and balance tests, variability in methodology of the balance test and sample size, inadequate dose of

PRT and/or compliance to training, or lack of statistical power. Future studies are requested to investigate the optimal training modalities (volume, duration, etc.) required to elicit significant improvements of muscle power, strength and functional performance in elderly subjects who are at increased risk for subsequent disability and fracture [73].

Besides PRT, other intervention has been assessed in osteoporotic subject. The efficacy of home-based daily exercise on muscle strength of the upper and lower extremities was examined in elderly osteoporotic women [75]. Grip strength and maximum walking speed increased significantly in the intervention group compared with the control group. Another study evaluated the effect of 18-week progressive muscular strength and proprioception training programme on the muscle strength of the quadriceps, in prevention of falls in postmenopausal women with osteoporosis [76]. The intervention promoted a significant difference compared with the control group for various outcomes including muscular power (e.g. SF-36, Timed Up and Go Test, maximum load [1-RM]) and the number of fall.

At least, it is important to note that the positive effect of exercise on muscle power, muscle strength, body balance, gait, BMD, or fall number observed in the majority of clinical trials does not automatically translate into a reduction of fracture incidence. As a matter of fact, these outcomes are only potential surrogates for fracture reduction and an improvement in these outcomes does not automatically translate into fracture reduction. While a BMD loss over time, at the level of the hip, was shown to be associated with an increased fracture risk [77], an increase in BMD after intervention is not systematically associated with a reduction in fracture incidence. Improvement in BMD observed with anti-osteoporotic drugs only explains part of the reduction of fracture incidence [78].

In conclusion, some indirect evidence supports the use exercise and training to reduce the risk of fracture. Even if the optimal type, duration, and intensity remain unclear and deserve researches, some practical recommendations can be made based on the current knowledge. General recommendation is that exercises should be performed two to three times per week and must include 15–60 min of aerobic exercises and a set of strength training. The exercise intensity should be at 70–80% of functional capacity or maximum strength. In the prevention of osteoporosis, high-impact exercise (e.g. skipping and jogging) is important as it has the greatest potential to improve BMD but low to medium impact exercise (e.g. step aerobics and intermittent jogging) is more appropriate for those not used to

exercising and those over 50 years of age. In patients with osteoporosis, it is advised that any form of strength training should be site specific (i.e. targeting areas such as the muscle groups around the hip, quadriceps, dorsi/plantar flexors, wrist extensors and back extensors). Weight-bearing exercises should be targeted to loading bone sites predominantly affected by osteoporotic fracture. In all patients, these exercise programmes should start at an easy level and be progressive in terms of intensity and impact. Obviously, the persistence to regular exercise and physical activity is of primary importance.

## Lifestyle

Epidemiological studies have identified a large number of risk factors for osteoporotic fracture. These can be risk factors related to bone strength, i.e. bone density, geometry and/or quality, or factors independent of bone strength, essentially related to risk for falls (one for review). Amongst the identified risk factors only some are potentially modifiable. Such risk factors that can be considered as somehow related to lifestyle are listed in Table 1.

Low body weight or low BMI is a well-recognized risk factor for fracture, whereas overweight and obesity have generally been considered as protective [79, 80]. However, recent evidence tends to challenge this view and suggests that increased adiposity and obesity, which has been associated with higher prevalence of vitamin D insufficiency and in some studies also of secondary hyperparathyroidism [81, 82], can have a negative impact on indices of bone strength and possibly on fracture risk [83–87]. Albeit the available evidence thus suggests that a lifestyle that helps maintaining a more ideal body weight is beneficial for

bone health, presently there is no evidence that interventions aimed at gaining or losing weight in thin and obese persons, respectively, can reduce fracture risk. In fact, weight loss in obese subjects has been associated with increased bone loss [88]. In this context, weight loss following bariatric intestinal bypass surgery, but probably not following gastric banding, has been associated with prolonged elevations of the levels of biochemical markers of bone turnover and with bone loss, also in absence of vitamin D insufficiency or increase of serum PTH [82, 89, 90].

As to more specific lifestyle factors related to diet, the potential adverse skeletal effects of low calcium intake, high sodium intake and excessive caffeine consumption have been addressed in the section on nutrition. The use of carbonated soda drinks and more in particular of colas has been associated with lower bone mass. Besides displacement of more nutrient- and calcium-rich beverages, caffeine, and phosphoric acid content in colas have also been implicated as contributing to the adverse skeletal effects [13, 91].

Excessive alcohol consumption is generally recognized as a secondary cause of osteoporosis and as a risk factor for fracture [79]. Alcohol may interfere with bone metabolism through direct toxic effects on osteoblasts and indirectly through adverse skeletal effects of nutritional deficiencies in calcium, vitamin D, and proteins that are prevalent in heavy drinkers. However, increased fracture risk is explained only for a minor part by increased bone fragility and other factors, perhaps resulting in an increased risk for falls, are involved. In a meta-analysis of three prospective studies in a total of 5,939 men and 11,032 women, followed for 75,433 person-years [92], alcohol consumption was non-linearly associated with an increased fracture risk. Consumption of 2 units or less (1 unit=10 g ethanol) per

**Table 1** Risk factors for osteoporotic fractures related to lifestyle

Risk factor	Related to bone strength, falls, other?
Dietary	
Low body weight	Bone strength
Overweight, obesity (?)	Bone strength, (other?)
Low calcium intake	Bone strength, (falls?)
High sodium intake	Bone strength
Excess caffeine intake	Bone strength
Excessive use of cola drinks	Bone strength
Others	
Excessive alcohol intake	Bone strength, falls
Smoking	Bone strength, other (?)
Low sun exposure	Bone strength, falls
Use of hypnotic and sedative drugs	Falls
Inappropriate housing conditions	Falls
Physical inactivity	Bone strength, falls

day was not associated with an increased fracture rate, whereas higher alcohol intake was associated both in men and women with an increased risk of any fracture (risk ratio (RR)=1.23; 95% CI, 1.06–1.43), any osteoporotic fracture (RR=1.38; 95% CI, 1.16–1.65), or hip fracture (RR=1.68; 95% CI, 1.19–2.36). A similar threshold of around 2 units per day for the association of alcohol intake and fracture risk was reported in earlier studies [93, 94]. At variance with the findings in some other studies, there were no significant difference between gender for either the risk ratios or threshold; above the threshold, there was a dose–effect. Also at variance with some other studies reporting a J-shaped association between alcohol consumption and fracture risk, fracture risk was not higher in subjects abstaining from alcohol use as compared with those consuming 1 or 2 units per day [79, 92]. However, it should be noted that a number of both cross-sectional and prospective studies failed to detect an increased fracture risk associated with alcohol intake (see reference [1] for review).

Smoking has adverse skeletal effects and current smoking is associated with an increased fracture risk [79]. Albeit it has been reported that the adverse effects on BMD are apparent after the age of 50 and increase with age [95], smoking has been shown to also adversely affect bone health in young individuals during bone maturation [96]. In a meta-analysis of prospective studies involving 59,232 subjects (74% women) [97], current smoking was associated with increased risk of any fracture compared with non-smokers (RR=1.25; 95% CI, 1.15–1.36) with the highest risk observed for hip fracture (RR=1.84; 95% CI, 1.52–2.22). The risk ratio was adjusted downward when account was taken of BMD, but remained significant (RR=1.15 and 1.60 for any fracture and hip fracture, respectively); low BMD accounted for only 23% of the increased risk for hip fracture associated with current smoking. The fracture risk was also adjusted downward when accounting for a lower BMI in smokers, but risk ratios for any fracture and hip fracture remained above unity and significant when adjusting for either BMI or both BMI and BMD. Risk ratios associated with smoking were higher in men compared with women for any fracture and osteoporotic fracture, but not for hip fracture. Risk ratio increased with age for any fracture and osteoporotic fracture, but decreased with advancing age for hip fracture. Subjects with a history of smoking had a significantly higher fracture risk than never smokers, but a lower risk than current smokers [97].

The mechanisms of the BMD-independent increased fracture risk associated with smoking are unknown, but might hypothetically involve altered bone geometry or material property not captured by DXA evaluation [96], relative physical inactivity and co-morbidity such as chronic lung disease resulting in frailty and increased risk for falls.

In most countries, in particular in mid- and southern Europe, the diet provides only a minor part of the vitamin D requirement. A major source of vitamin D<sub>3</sub> is synthesis in the skin under influence of UV light, as is illustrated by the marked seasonal variations in serum 25-hydroxyvitamin D levels [98]. The reported very high prevalence of vitamin D inadequacy in particular, but not exclusively, in elderly subjects [98–100] indicates that a low dietary intake of vitamin D is not compensated by sufficient synthesis in the skin. This might in turn result from insufficient skin exposure to the sunlight and a lesser efficacy of vitamin D synthesis in the skin of elderly persons [98]. In urban areas, pollution may contribute to the limitation of effective exposure to UV from sunlight [101].

The fact that sun exposure tend to be generally low in elderly subject is illustrated by the paradoxical finding in a multi-country study in European elderly subjects of a positive association between mean serum 25-hydroxyvitamin D levels and degree of northern latitude [94]. This is most likely explained by a generally low sun exposure, also in southern European countries, and higher vitamin D availability in the diet and/or as supplements in Northern European countries. The low sun exposure in elderly persons is related to an indoor style of living and/or clothing leaving little skin exposed. In this regard, there are groups that are at higher risk of vitamin D deficiency, already at younger age, as a consequence of their habit to wear clothing that (nearly) completely covers the skin for traditional cultural and/or religious reasons [102, 103]; in these high-risk groups, high prevalence of vitamin D deficiency during pregnancy is of particular concern in view of the potential adverse skeletal consequences for mother and child.

A Single randomized controlled trial in a psychogeriatric institution in the Netherlands showed that UV irradiation of 1,000 cm<sup>2</sup> skin of the back of elderly subjects three times per week with half the minimal erythematous dose was as effective as a daily oral dose of 400 IU vitamin D<sub>3</sub> to raise serum levels of 25-hydroxyvitamin D and suppress secondary hyperparathyroidism [104]. Although, this proof of concept with UV irradiation approach is conceptually interesting, oral supplementation remains a more practical solution to prevent or treat vitamin D insufficiency. Moreover, present recommendations suggest higher dosing of vitamin D supplements and besides feasibility, the skin safety of the required equivalent, more extensive UV irradiation might become an issue. Along the same line, although more time spent outdoor and moderate sun exposure should be encouraged in elderly subjects in reasonably good general health, advising a marked increase of exposure to sunlight might be a somewhat confusing message, at odds with advices concerning the prevention of skin cancer. Anyhow, it is unlikely that to encourage increased exposure to sunlight could alleviate the need for oral vitamin D supplementation.



As to physical inactivity, the use of hypnotic and sedative drugs, and inappropriate housing conditions, four important risk factors for fracture related to lifestyle, these are discussed in the sections on exercise and prevention of falls.

Although there undoubtedly exist interactions between different lifestyle-related influences on bone health and fracture risk, available information on such interactions is rather limited. Nevertheless, it has been shown for several of these that they contribute at least to some extent independently to fracture risk, also independently from the effect of low BMD and high age: i.e. low BMI, excess alcohol consumption, and actual smoking [79].

### Fall prevention

Between 28% and 35% of adults aged 65 years and older and living in the community experience at least one fall each year, and the annual fall prevalence increases with ageing [105, 106]. Between 10% and 31% are recurrent fallers [107, 108]. More importantly, community-dwelling persons with dementia have the highest risk for falls with prevalence rates up to 66%, with clear differences depending on the subtype of dementia (e.g. prevalence of falls in Alzheimer's disease 47%, vascular dementia 47%, Lewy body dementia 77%, and Parkinson's disease dementia 90%, respectively) [109].

For those living in nursing care facilities, the annual risk of falls has been estimated to be also three times higher (i.e. up to 70%), and 15% to 40% are recurrent with rates between 1.1 and 1.4 per person per year for non-psychogeriatric residents and between 2.1 and 2.4 per person per year for psychogeriatric residents [107, 110].

But falls represent a frequent and serious problem in hospitals as well, with a variability in the incidence of falls depending on ward type and hospital population (between 2.2 and 17.1 falls per 1,000 patient days). Patients most likely to fall are older inpatients: approximately 2% to 12% of all patients experience at least one fall during their hospital stay, but this proportion may increase to 11.9% and 24.8% in geriatric wards and to even 46% in stroke rehabilitation units, respectively [111–115].

Falls in older persons are associated with considerable mortality and morbidity. Unintentional injuries are the fifth most important cause of death in people aged 75 and over [106, 116]. Falls are the commonest cause of these unintentional injuries in this age group: 30–50% of falls result in minor trauma, 10–15% lead to serious injuries with around 5–10% resulting in fracture, and 1–2% of these being hip fractures [106]. The risk for (additional) injuries increases when fallers are unable to rise without help and when lying on the floor for a long time. Between 50% and

80% of older persons are unable to get up after at least one fall, with the higher percentages reported in the very old population (age 90 years and over). Up to 30% are lying on the floor for an hour or more, leading to serious complications such as pressure sores, dehydration, hypothermia, rhabdomyolysis, admission to hospital and long-term care, and death [117, 118].

When hospitalized, other consequences are impaired rehabilitation and functional decline, and increased need of being institutionalised, e.g. a 3-fold risk for falling without a serious injury and a 10-fold risk for a serious fall injury [119]. Although not all falls lead to injuries, psychological consequences such as fear of falling are substantial and may lead to loss of confidence, fear of dependence, social isolation, depression, and increased risk of falling [120]. In community-dwelling older persons (fallers and also non-fallers), fear of falling ranges from 20% to 85% and from 15% to 55% for associated avoidance of activity, respectively, with higher rates associated with higher age, female gender, fair and poor perceived general health, and multiple falls [121].

As in all major geriatric syndromes, multiple risk factors are involved in falls with chronic predisposing and acute precipitating factors and interactions playing a crucial role. Older persons with a precarious physiological and physical balance have the potential to fall from seemingly minor physiologic, intrinsic, and/or extrinsic risk factors; and the greater the number of risk factors the greater the risk for falls [122]. The most important intrinsic risk factors are: previous falls, decreased muscle strength (upper or lower extremity), gait and balance deficits, dizziness and orthostasis, visual impairment, depression, functional and cognitive impairment, low body mass index, urinary incontinence, chronic musculoskeletal pain, female sex, and being 80 years and older. Interactions between medications (e.g. polypharmacy), psychotropic medications, and environmental risks (e.g. loose rugs, insufficient lighting) have been identified as major extrinsic risk factors [122–125]. Importantly, fear of falling is not only a consequence of falling as noted above, but also an important psychological risk factor for falls. Fear of falling may lead to restriction of physical activities and social participation and, as a consequence, increase the risk for physical frailty and falls [126].

All these risk factors have been identified in a variety of settings and almost always in the general older population. Until recently, no high-quality studies have examined risk factors for falling specific to dementia. In the largest prospective study to date, Allan and colleagues identified non-modifiable risk factors such as a diagnosis of Lewy body disorder, longer duration of dementia and previous history of falls or recurrent falls. More importantly, they also identified potentially modifiable risk factors such as use of cardioactive medications, autonomic symptoms,

symptomatic orthostatic hypotension, depression, and limitation of physical activity [109].

Although there is substantial evidence that fall prevention strategies reduce the number of falls and risk of falling in the community setting, and preliminary evidence for the residential and acute hospital setting, less evidence is available about their effectiveness in preventing fall-related injuries (e.g. sprains, bruises, and head-injuries) and fractures (e.g. arm and hip fractures) [110, 122, 127, 128]. Despite this, clinicians should use an integrated approach for fall and fracture prevention since many of the previous mentioned risk factors for falls have been shown to increase fracture risk as well [105, 122].

For community-dwelling older adults, single as well as multifactorial fall prevention strategies have been shown to effectively reduce falls in older adults.

### Single-fall prevention strategies

In single-fall prevention strategies, physical therapy, and exercise have been the most investigated interventions, and various reviews and meta-analyses support the use of Tai Chi, progressive balance, and gait and strength training; however, evidence about endurance and flexibility training is inconclusive [122, 127–129]. A meta-analysis of muscle strengthening and balance retraining exercises individually prescribed and delivered at home to older women and men (age 65 to 97 years) showed a reduction in the number of falls and fall-related injuries by 35% (RR=0.65; 95% CI, 0.57–0.75 and RR=0.65; 95% CI, 0.53–0.81, respectively) and these exercises were of most benefit to those individuals aged over 80 years and showed a higher absolute reduction in injurious falls in those with a history of a previous fall [130]. Similarly, the most recent Cochrane meta-analyses showed that programmes delivered at home and containing at least two exercise components are effective: group exercise (RR=0.78; 95% CI, 0.71–0.86; RR=0.83; 95% CI, 0.72–0.97), Tai Chi (RR=0.63; 95% CI, 0.52–0.78; RR=0.65; 95% CI, 0.51–0.82), and individually prescribed exercise (RR=0.66; 95% CI, 0.53–0.82; RR=0.77; 95% CI, 0.61–0.97) have all been shown to reduce the rate of falls and the risk of falling, respectively [128]. However, in contrast to the meta-analysis of Robertson et al. [130], subgroup analyses in the Cochrane meta-analyses [128] could not find any difference between studies targeting people with known falls risk, or people who had not been enrolled on the basis of risk factors; exercises were effective in both subgroups. Finally, physical therapy and exercise seem to be even more effective when embedded in a multifactorial fall prevention strategy (see below), but optimum type, frequency, duration, and intensity of exercise as well as strategies to ameliorate adherence remain to be clarified [105, 122, 128, 129].

Home safety assessment and modification has been tested in a substantial number of studies and the most recent Cochrane meta-analysis found this kind of single strategy not effective when used in older adults at low fall risk (RR=0.90; 95% CI, 0.79–1.03), however it reduced significantly the rate of falling (RR=0.56; 95% CI, 0.42–0.76) and fall risk (RR=0.78; 95% CI, 0.64–0.95) among older adults with previous falls or fall risk factors such as severe visual impairment, respectively [128].

One particular single-fall preventive strategy tested in a number of large studies is vitamin D supplementation, with or without calcium. A thorough discussion of the effects of vitamin D is beyond the scope of this paper. However, a recent meta-analysis by Bischoff-Ferrari [131] concluded that doses of 700 to 1,000 IU supplemental vitamin D a day could reduce falls by 19% or by up to 26% with vitamin D3. This benefit may not depend on additional calcium supplementation, was significant within 2–5 months of treatment, and extended beyond 12 months of treatment.

Reducing the number of medications seems to be another important single strategy to reduce falls given the clear association between falls in older adults and the use of sedatives and hypnotics, antidepressants, and benzodiazepines [125]. A randomized controlled study evaluating the effect of gradual psychotropic medication withdrawal showed a 66% (RR=0.34; 95% CI, 0.16–0.74) reduction for falls [132] and another cluster-randomized controlled trial evaluating an educational and medication review and feedback programme for general practitioners on use of medicines showed a reduction of 39% (OR=0.61, 95% CI, 0.41–0.91) and 44% (OR=0.56; 95% CI, 0.32–0.96) in the number of falls and the number of any kind of injurious falls, respectively [133]. Medication review and removal or adaptation of the regimen seems to be effective; however more studies are needed and special attention will have to go to individuals resuming their psychoactive medication after withdrawal [122, 128].

Other promising single-fall prevention strategies have been successfully tested in a limited number of studies: cardiac pacing in older fallers with carotid sinus hypersensitivity [134] and expedited surgery for first eye cataract older adults [135]. However, older adults receiving second eye cataract surgery did not benefit [136].

### Multifactorial fall prevention strategies

Various multifactorial intervention strategies have been tested in community-dwelling older adults. These prevention programmes consist of an in-depth risk assessment of several known fall risk factors and interventions based on this risk assessment [127, 128, 137]. One typical example of a multifactorial intervention programme can be found in the Table 2. Chang and colleagues showed in their meta-

**Table 2** Example of a multidisciplinary multifactorial intervention program: in-depth multifactorial assessment of known fall risk factors followed by linked interventions (Adapted from Milisen et al. 2009)

Risk factor	Assessment	Evaluation criteria	Interventions
Mobility impairment (muscle weakness and balance deficits)	Four-Test Balance Scale <sup>a</sup>	Inability to hold one of four positions for 10 s	Referral to physiotherapist (GPs)
	Timed Chair Stand <sup>b</sup>	Inability to perform test within 14 s	Education on importance of exercising (nurses)
	Functional reach <sup>c</sup>	Inability to reach further than 25 cm	Individualized exercise program (PhysT) Advise to use assistive devices (OccT)
Medication	Medication count	Polypharmacy ( $\geq 4$ medications)	Review and/or reduce medications (GPs)
	Kind of medication	Use of benzodiazepines, sedatives, neuroleptics, antidepressants, digitalis, diuretics, class IA antiarrhythmics	Education on the effect of medications on falls (Nurses) Referral to GP (PhysT) Referral to GP (OccT)
Postural hypotension	“Do you feel dizzy or lightheaded when getting up from a chair, couch, out of bed, or when bending?”	Reporting dizziness when getting up or bending	Etiology and causal treatment (GPs) Advise to prevent postural hypotension (nurses)
	Evaluation of fall in blood pressure (BP fall) <sup>d</sup>	Systolic BP fall $>20$ mmHg or diastolic BP fall $>10$ mmHg on standing; systolic BP $\leq 90$ mmHg on standing	Advise to prevent postural hypotension (PhysT) Advise to prevent postural hypotension (OccT)
Vision		Reporting difficulty with reading, driving, watching TV	
	“Do you have difficulty with reading, driving, or watching TV?”	Last checkup $>1$ year ago	Referral to ophthalmologist (GPs)
	Date of last checkup	Difficulty using bifocal glasses	Discussion of problem with family (Nurses)
	Evaluation of bifocal glasses	Score $\leq 4/10$	Education on dangers of bifocal glasses (PhysT) Advise to consult ophthalmologist once a year (OccT)
Feet and footwear	Clinical evaluation of feet	Foot disorders (e.g. in-grown nails, calluses, presence of pressure points)	Treatment or referral to orthopaedic surgeon (GPs) Advise decent footwear (Nurses)
	Clinical evaluation of footwear	Unsteady shoes, open-back shoes, high heels, slippery soles	Advise decent footwear (PhysT) Advise decent footwear (OccT)
Environment and behaviour	“Are there any factors in your house that raises the risk for falls?”	Environmental risks (e.g. loose rugs, insufficient lighting)	Referral to occupational therapist (GPs) Checklist for home safety (nurses)
	“Do you turn the light on when you go to the bathroom at night?” <sup>f</sup>	Inappropriate behaviour (e.g. standing on chair or stepladder to get something)	Advise safe environment and behaviour (PhysT) Assessment of environment (OccT)
Fear of falling	“Are you afraid of falling?”	Reporting fear of falling	
	“Do you limit your activity due to fear of falling?”	Reporting restriction of activity as a result of fear of falling	Education on risk factors for falls (GPs) Information about personal alarm system (nurses) Education on getting up after a fall (PhysT) Assess with Falls Efficacy Scale-International (OccT)

GPs general practitioners, *PhysT* physiotherapist, *OccT* occupational therapist

<sup>a</sup> The patient is asked to take the following four positions consecutively: stand with feet together, semi-tandem stand, tandem stand, and one-leg stand

<sup>b</sup> The patient is asked to repeat the following action five times: stand up from a chair without using arms and sit back down again

<sup>c</sup> A metre stick is positioned horizontally on a wall, and the patient is asked to reach as far as possible in standing position and after bending forward (physiotherapists only)

<sup>d</sup> Patient's blood pressure is measured after more than 5 min in a supine position, immediately after standing, and 2 min after standing

<sup>e</sup> The test is performed with the patient positioned 5 m from the chart; both eyes are tested together and the patient wears his/her glasses

<sup>f</sup> The behavioural assessment consisted of three other questions regarding risky behaviour: “Do you perform unsafe activities such as hurrying to the door or to the phone when it rings or using a chair or ladder to reach for things located above your head?”; “Do you wear unsteady shoes (e.g. slippers)?”; “Do you perform other unsafe activities?”

analysis multifactorial intervention strategies to be effective on both risk of falling (RR=0.82; 95% CI, 0.72 to 0.94) and monthly rate of falling (RR=0.63; 95% CI, 0.49 to 0.83) [127]. In line with these findings, the most recent Cochrane meta-analysis showed a significant reduction in the rate of falls (RR=0.75; 95% CI, 0.65–0.86); even when excluding two outliers the results remained significant (RR=0.82; 95% CI, 0.76–0.90). However, the Cochrane meta-analysis could not confirm a significant reduction in risk of falling (RR=0.95; 95% CI, 0.88–1.02). Also, there was no effect on the risk of fracture (RR=0.70; 95% CI, 0.47–1.04) [128]. Although there was no evidence in the Cochrane meta-analysis that assessment and monitoring and follow-up of interventions was more effective than assessment and unmonitored referral or only advice, another recent meta-analysis found only an effect on the number of fallers in trials with higher intensity interventions (RR=0.84; 95% CI, 0.74 to 0.96) [137]. This indicates the need for a more careful monitoring and follow-up to enhance compliance with recommendations and provide more insight in the feasibility of integrating fall prevention strategies into daily practice of primary healthcare disciplines [123, 138, 139]. Gates et al. were unable to assess fall rates, but again showed no effect on fall-related injuries (RR=0.90; 95% CI, 0.68 to 1.20) [137].

With regard to nursing care facilities, a narrative review concluded that multifactorial intervention programmes have the potential to prevent falls [140]. Unfortunately, the two most recent meta-analyses could not confirm this assumption. Overall, both meta-analyses could not find a significant reduction in the rate of falls or risk of falling [110, 141]. However, post hoc subgroup analyses in the Cochrane review showed a significant decrease in the rate of falls (RR=0.60; 95% CI, 0.51–0.72) and risk of falling (RR=0.85; 95% CI, 0.77–0.95) when multifactorial interventions (that included exercises) were provided by a multidisciplinary team; and this in contrast with multifactorial interventions initiated by single health professionals which did not reduce the rate of falls (RR=1.11; 95% CI, 0.90–1.37) or risk of falling (RR=1.07; 95% CI, 0.94–1.23) [110]. Importantly, a subgroup analysis of a limited number of multifactorial interventions provided by a multidisciplinary team and reporting data on proximal femoral fractures, showed a significant reduction in the risk of these fractures (RR=0.48; 95% CI, 0.24–0.98).

In contrast with the established evidence for effective exercise programmes in the community setting, results of the meta-analyses relating to exercise prevention programmes as a single intervention in nursing care facilities are inconsistent [110]. In fact, attention should be paid when applying exercises to frail nursing home residents, as frail residents might be less likely to benefit from exercises, and exercises may paradoxically increase the risk of falls and injuries in this vulnerable population [110, 142].

In a hospital setting, there is preliminary evidence for effective falls prevention programmes, in general, with no evidence however in the “acute” hospital setting. For instance, in our own meta-analyses, including only high-quality studies, we could not show an effect on number of falls (RR=0.82; 95% CI, 0.65–1.03) or number of fallers (RR=0.87; 95% CI, 0.70–1.08) [111]. Another meta-analysis, with broader inclusion criteria than ours, showed only a minor effect on the number of falls (RR=0.82; 95% CI, 0.68–0.99), but again not on the number of fallers (RR=0.95; 95% CI, 0.71–1.27) [37]. The most recent Cochrane meta-analysis showed that multifactorial interventions (RR=0.73; 95% CI, 0.56–0.96) and single supervised exercise interventions (RR=0.44; 95% CI: 0.20–0.97) can both reduce the risk of falling, with multifactorial interventions also reducing the rate of falls (RR=0.69; 95% CI, 0.49–0.96). However, the total number of participants in the single supervised exercise analysis was small and, for all types of interventions, the results were only positive in patients with prolonged hospital stay (at least 3 weeks) or in subacute settings (6). More importantly from the perspective of this paper, all meta-analyses were inconclusive about effects on injuries [110, 111, 141].

## Devices

### Hip protectors

Because of the associated burden in terms of morbidity and mortality, hip fractures are generally considered the most dramatic complication of osteoporosis. In older individuals, falls and other indicators of frailty become the dominant determinant of hip fracture [143]. Reducing the impact of falls onto the hip with the use of hip protectors may therefore be an effective strategy for preventing fractures, particularly in nursing home residents. An external hip protector is a (polypropylene or polyethylene) shell that fits around the hip. It is designed to absorb the energy from a fall and especially to shunt the energy to the soft tissues around the hip and keep the force on the trochanter below the fracture threshold.

Numerous randomized controlled trials have examined the effect of external hip protectors on the incidence of hip fractures, but findings have been conflicting [144–154]. In a number of studies, hip protectors did significantly reduce the incidence of hip fractures [144, 145, 147, 148, 150] some were borderline statistically significant (4, 11), and other did not show statistical significance [149, 151, 153–155]. In addition, several trials were small-sized, including <200 participants [145, 147, 149, 150], and most positive studies did not use individual randomization to assign persons to the hip protector or control group [144, 146,



148, 150, 152]. In several relatively large studies that did use individual randomization, hip protectors were not effective in preventing hip fractures [151, 153, 155]. The different conclusions drawn from clustered and nonclustered randomized trials of hip protectors underscore the methodologic biases in the design and execution of cluster-randomized trials [156].

One example of a well-designed trial was the Amsterdam Hip Protector Study, a randomized controlled trial in which 561 institutionalized elderly persons at high risk for hip fracture were randomized to the hip protector group or to the control group in a 1:1 ratio with a mean follow-up of 70 weeks [153]. Compliance at unannounced visits declined from 61% to 37% during follow-up. In the intervention group, 18 hip fractures occurred versus 20 in the control group. At least four hip fractures in the intervention group occurred while an individual was wearing a hip protector. Both in univariate and multivariate analyses, no statistically significant difference between the intervention group and control group was found with regard to time to first hip fracture (hazard ratio (HR), 1.05; 95% confidence interval [CI], 0.55–2.03). Even the per protocol analysis in compliant participants did not show a statistically significant difference between the groups (HR, 0.77; 95% CI, 0.25–2.38). One of the strengths of the Amsterdam Hip Protector Study—in addition to its use of individual randomization—was its setting: 45 different homes for the elderly and nursing homes in which nurses had to supervise the wearing of the hip protectors, suggesting that the results of this trial can be generalized to most institutionalized elderly persons.

One of the more recent studies that further ignited controversy about this type of intervention was the Hip Impact Protection Project, published by Kiel and colleagues [154]. In this multi-center, randomized controlled clinical trial, 37 nursing homes were randomly assigned to having residents wear a 1-sided hip protector on the left or right hip, allowing each participant to serve as his or her own control. The energy-absorbing/shunting hip protector was selected based on its performance in a pilot study and biomechanical testing that demonstrated superior capacity to reduce peak impact force in simulated drop-weight experiments. The hip protector was made of an outer layer of polyethylene vinyl acetate foam, backed by a hard high-density polyethylene shield, which in turn was backed by a layer of polyethylene vinyl acetate foam. Garments with pad pockets on 1 side were available in various sizes. Each resident was provided as many garments as needed for use around-the-clock, allowing for soilage, laundry turnaround time, losses, and deterioration over time. Participants were 1,042 nursing home residents with a mean age of 85 years; 79% were women. After a 20-month follow-up (676 person-years of observation), the study was terminated due to a lack of efficacy. The incidence rate of hip fracture

on protected versus unprotected hips did not differ (3.1%; 95% CI, 1.8–4.4% vs 2.5%; 95% CI, 1.3%–3.7%;  $P=.70$ ). For the 334 nursing home residents with greater than 80% adherence to hip protector use, the incidence rate of hip fracture on protected vs unprotected hips did not differ (5.3%; 95% CI, 2.6%–8.8% vs 3.5%; 95% CI, 1.3%–5.7%;  $P=.42$ ), adding to the increasing body of evidence that hip protectors, as currently designed, may not be effective for preventing hip fracture [151, 153, 155].

In addition to the inconsistency of the results [144–154, 157] and the lack of documented cost-effectiveness [158], one of the main concerns with external hip protectors is poor compliance [159]. Most of the residents who experienced a hip fracture in negative studies were not wearing the protector at the time of the fall [149, 151, 153, 154]. Thus, adherence is a factor that could potentially be improved with good results. In a systematic review by van Schoor and colleagues [160], primary acceptance with hip protectors varied around a median of 68% and, in those accepting the device, compliance varied around 56%. However, in most studies it was not very clear how compliance was defined (e.g. average wearing time on active days and during waking hours, number of user-days per all available follow-up days, percentage falls with hip protector) and how it was measured. The reasons most frequently mentioned for not wearing hip protectors, were: not being comfortable (too tight/poor fit); the extra effort (and time) needed to wear the device; urinary incontinence; and physical difficulties/illnesses. The authors concluded that compliance is a complex issue in hip protector implementation and that methods to improve compliance should be developed, and their effectiveness tested [160].

Based on the studies that have been published, there is likely to be continued debate and uncertainty about the efficacy of hip protectors because of the heterogeneity of findings, well-documented compliance issues, and potential biases from clustered randomization designs. Nevertheless, recent pooled analyses have suggested that two-sided devices may potentially reduce the risk of hip fracture, at least in institutionalized elderly [161]. And so it would seem that, although available evidence does not allow firm and final conclusions or recommendations, it may not be appropriate to discount the potential benefit of this intervention in a long-term care setting. Larger and more costly clinical trials are required to definitively investigate effectiveness of hip protectors. Consensus recommendations for future research include the following: the use of a hip protector that has undergone adequate biomechanical testing, the use of sham hip protectors, the conduct of clinical trials in populations with annual hip fracture incidence of at least 3%, a run-in period with demonstration of adequate adherence, surveillance of falls and adherence, and the inclusion of economic analyses [162].

## Vertebroplasty and kyphoplasty

Vertebral compression fractures (VCFs) can lead to severe vertebral deformity or hyperkyphosis, which in turn is associated with significant back pain and back dysfunction [163], functional impairment [164], loss of quality of life [165] and even mortality [166]. Standard treatment of painful VCFs is conservative non-surgical management (NSM), consisting of bed rest, analgesics, and bracing. However, in some patients, NSM fails to improve pain and mobility, particularly in cases of chronic pain related to kyphotic deformity [167]. Patients refractory to medical therapy can be considered for vertebroplasty or balloon kyphoplasty, two minimally invasive surgical approaches developed for the management of symptomatic VCFs [168] which are increasingly being proposed as effective and safe [169, 170]. The insertion of bone cement (polymethylmethacrylate-based, PMMA, or calcium phosphate-based, CaP) into the vertebra is thought to stabilize and reduce the fracture and relieve pain.

Vertebroplasty includes the percutaneous insertion of a needle through the pedicles into the vertebral body and the injection of a bone cement (PMMA or CaP) into the cancellous bone [171]. The cement will follow the path of least resistance and the procedure is monitored directly under fluoroscopic control. For balloon kyphoplasty, cannulae placed percutaneously into the vertebral body permit the insertion of two inflatable bone tamps (IBTs) [172]. After removal of the IBTs, the pre-defined cavity is filled with PMMA- or CaP [173] under low manual pressure [174]. Like during vertebroplasty, the procedure is monitored directly under fluoroscopy. Besides stabilizing the fracture, balloon kyphoplasty also aims at restoring vertebral body anatomy with height recovery and angular deformity correction [175]. A thorough discussion of both techniques is beyond the scope of this article, as a systematic in-depth review on the topic by a dedicated IOF Working Group has been submitted for publication (S. Boonen, personal communication).

While a number of randomized controlled studies have demonstrated acute advantage of vertebroplasty over medical treatment in pain relief of VCFs [176, 177], these findings have been questioned by recent sham-controlled randomized clinical studies that could not confirm these conclusions [178, 179], with no significant between-group differences regarding pain reduction, quality of life or physical functioning. In the first of these trials, 78 patients with one or two painful osteoporotic fractures were randomized to undergo VP or a simulated sham procedure [178]. The primary outcome was overall pain score at 3 months, which decreased in both groups significantly compared with baseline. Pain reduction was sustained in both groups for 6 months. Similar improvements were seen

in both groups with respect to physical function, quality of life, and perceived improvement in pain, even after adjustment for baseline levels of previous vertebral fractures and duration of symptoms. In the second single-blind trial, 131 patients were randomly assigned to VP or a simulated sham procedure [179]. The primary endpoints of the study were scores in the modified Roland Morris Disability Questionnaire and perceived back pain intensity after 1 month. Both procedures had an immediate and sustained improvement up to 1 month after the intervention, although not statistically different between the two arms. The improvements of other measures of pain, physical function and quality of life (EQ-5D, SF-36 MCS, and PCS) did not also differ between groups at 1 month. Unfortunately, cross-over of patients in this study precluded longer term randomized comparisons between groups. Nevertheless, both studies have questioned the value of vertebroplasty. In addition, hardly any data exist on the cost-effectiveness of vertebroplasty [180] and the procedure appears to have a high rate of cement extravasations with an associated increased risk of pulmonary emboli and compression of neural foramen [181].

The largest prospective controlled study performed so far comparing minimally invasive surgery in VCFs and non-surgical management was the Fracture Reduction Evaluation Study, a multi-center randomized control trial in 300 patients with 5–6 weeks old VCFs comparing balloon kyphoplasty with non-surgical management [182]. In this trial, the primary outcome was the difference in change from baseline to 1 month in the SF-36 physical component summary in kyphoplasty-treated and control groups. At 1 month, patients quality of life was significantly improved after balloon kyphoplasty compared with non-surgical management ( $p < 0.0001$ ) and this difference was maintained up to 1 year. Back pain score (VAS score) decreased more after kyphoplasty at 1 week ( $p < 0.0001$ ) and after 12 months ( $p < 0.0034$ ) compared with control; this improved pain was concomitant with significantly fewer kyphoplasty patients requiring opioid medications in the first 6 months. Cases of cement extravasation were asymptomatic. At 12 months, no between-group differences were observed in the proportion of patients with new or worsening radiographic vertebral fractures. Literature reviews report a cement leakage rate of about 10% with balloon kyphoplasty [183, 184]. Recent cost-effectiveness analyses using quality-adjusted life years suggest that balloon kyphoplasty may be a cost-effective treatment in osteoporotic patients hospitalized with painful VCFs [185, 186].

In a number of prospective non-randomized studies and one prospective randomized trial comparing VP with BKP for treatment of osteoporotic VCFs [187–189], no significant differences could be documented for pain relief up to

6 months. However, a blinded, randomized clinical trial comparing vertebroplasty, balloon kyphoplasty and a sham procedure is lacking to state definitely of the advantage of one or the other procedure over conservative management. To conclusively determine whether rates of subsequent VCFs are higher among subjects undergoing balloon kyphoplasty compared with those treated non-surgically or with vertebroplasty would require a concurrently controlled study in which risk factors for fracture are evenly distributed across treatment groups.

## Conclusions

It is likely that the optimal health of the skeleton requires an adequate equilibrium between all nutrients. Interactions between various nutrients, e.g. calcium and protein, and between some nutrients and exercise or other lifestyle habits much complicate the interpretation of studies aiming at defining the importance of a particular nutrient. Numerous studies have shown the beneficial effects of various types of exercise on bone mass but data with fracture as an endpoint are scanty. Physical activity is of primary importance to reach optimal peak bone mass and high-impact exercises combined with resistance exercises can increase BMD in premenopausal women. Exercise interventions can successfully maintain or increase BMD also in postmenopausal women. The major benefit of exercise in patients with osteoporosis may be in improving muscle strength and coordination, which, in turn, decreases the frequency of falls.

A low BMI is a well-recognized risk factor for fracture but obesity can also have a negative impact on indices of bone strength and possibly on fracture risk. Current smoking and excessive alcohol consumption are associated with an increased risk for fracture.

Muscle strengthening and balance retraining exercises individually prescribed can reduce the number of falls and fall-related injuries by 35%. Multifactorial fall prevention programs are effective on both risk of falling and monthly rate of falling. Results are less consistent in nursing care facilities than in the community setting. Hip protectors are designed to reduce the impact of falls onto the hip and to prevent hip fracture. Numerous randomized controlled trials have led to conflicting results. One of the main concerns with external hip protectors is poor compliance and recent pooled analyses have suggested that the regular use of two-sided devices might reduce the risk of hip fracture in institutionalized elderly.

Vertebroplasty and balloon kyphoplasty are used to control back pain and to stabilize the vertebral fracture; kyphoplasty also aims at restoring vertebral body anatomy. These procedures are not without risks due to possible

cement extravasation. Limitations of both vertebroplasty and kyphoplasty are the lack of long-term data and the absence of conclusive comparative trials.

**Conflicts of interest** None.

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