



Review Article

Effects of vegetarian diet on bone mineral density

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ABSTRACT

Factors, such as hormonal changes in postmenopausal women, natural aging degeneration, race, gender, body size, lifestyle, physical activity, sunlight, dietary intake, medications, or other environmental issues, can affect the rate of bone formation or reabsorption, cause changes in bone mineral content, and influence the development of osteoporosis. Do vegetarian diets adversely affect bone mineral density (BMD)? Among postmenopausal Buddhists, long-term practitioners of vegan vegetarian were found to have a higher risk exceeding the lumbar fracture threshold and a lower level of hip BMD after controlling for other variables. However, results of several prospective longitudinal studies failed to show a harmful effect of vegetarianism on bone health. In the Taiwanese adult population, researchers also did not find that a vegetarian diet significantly affects age-related BMD decline. Due to the various levels of nutrients in the diet (such as protein, alkali, calcium, Vitamin K, and phytoestrogens) and major lifestyle factors (such as smoking and physical exercise), determining the impact of a vegetarian diet on bone health is very complex. Good-quality vegetarian food can provide a healthy foundation for building and maintaining healthy bones and preventing fractures.

KEYWORDS: *Bone mineral density, Nonvegetarian, Omnivore, Vegetarian*

INTRODUCTION

Remodeling of bones is a continuous and complex process. In assessing the combined effects of physical and nutritional factors on bone health in children and adolescents, physical activity and diet were found to be the most relevant factors affecting bone mineral density (BMD) and fracture risk [1]. Similarly, diet is considered one of the leading causes of bone mineral loss in the elderly [2]. Just as experts recommend following a plant-based diet to improve health, vegetarian diets have become increasingly popular, especially among environmentalists and Buddhists, and are generally accepted by the elderly. Vegetarian diets differ significantly in nutritional components from meat diets, and many of the nutrients may affect bone metabolism, some beneficially and some unfavorably [3]. A plant-based diet has been proven to be harmless to bone development in young adults [3]. We discuss the health issues, nutrients, dietary acid load and calories associated with plant-based and meat-based diets, and the relationship of a vegetarian diet to BMD.

HEALTH ISSUES AND BONE MINERAL DENSITY

The advancement of medical technology and improvements in economic conditions and living standards have greatly prolonged human life [2]. Aside from other diseases, such as cardiovascular disease (CVD), metabolic problems,

and malignancy, osteoporosis and its prevention have become increasingly important [4]. Osteoporosis, characterized by low bone mass and a tendency to experience fractures, is a disease found predominantly in women but also in men. With the increase in age, the BMD of men gradually decreases, while that of women declines sharply after the fifth decade due to menopause [2]. Fractures are associated with increased morbidity and mortality [5], as well as huge economic costs to health care and families [6]. It is critical to identify risk factors associated with poor bone health to reduce fracture rates and mortality, thereby reducing medical-related costs [7].

DIETS, CALORIES, AND HEALTH ISSUES

The different types of vegetarians range from the strict vegan (diet without any animal products), lactovegetarian (diet containing dairy products but not eggs), ovo-lacto vegetarian (diet including dairy products and eggs), or omnivores who only periodically follow a vegan diet [8,9]. Vegetarian foods usually have fewer saturated fats and cholesterol, and the increase in dietary fiber and presence of many phytochemicals

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promote health [10]. The body mass index (BMI) of people following a meat-based diet tends to be higher than that of people adhering to an ovo-lacto vegetarian or vegan diet; however, individuals adhering to a vegan diet had superior diet quality as compared to those in the other diet groups [3]. In addition to lower BMI, vegetarians usually have lower serum total and low-density lipoprotein cholesterol levels and lower blood pressure [10]. Vegetarian foods are health-related and reduce the incidence of obesity, diabetes, hypertension, metabolic syndrome, ischemic heart disease, CVD, and certain cancers, especially in the light of the link of such foods to lower BMI values [11-16]. High fiber intake is associated with significant reductions in pancreatic cancer, CVD mortality, and all-cause mortality [17]. However, the restrictive nature of the diet raises concerns about possible nutritional deficiencies and an increased risk of osteoporosis [18].

Vegetarians consumed fewer total calories than nonvegetarians [19]. Calorie restriction (CR) lowers inflammation, insulin resistance, and CVD, subsequently benefiting bone health by reducing those known risk factors for osteoporosis and fractures [20-24]. However, CR-induced weight loss is also accompanied by decreased regional BMD, and reduction in bone mass and bone size is considered harmful to bone health [25]. The positive effect of CR on osteoporosis risk factors appears to be at least partially offset by the reduced hip/lumbar BMD caused by weight loss [26].

DIETS AND NUTRIENTS

In Asia, most vegetarians are Buddhists, derived from the Buddha's "do not kill" doctrine. Some eat dairy products and eggs in addition to plant-based foods (ovo-lacto vegetarians) [27]. In Taiwanese adults over 45 years, the prevalence of vegetarianism is estimated to be 2.3% among men and 4.4% among women [28]. Most people still believe that foods of animal origin are more nutritious than foods of plant origin. Vegan diets lack calcium-rich food items, and are rich in inhibitors of calcium absorption, including oxalic acid, phytic acid, and fiber [9]. Due to their religious beliefs, the calcium intake of strict Buddhist vegetarians in Taiwan is below 75% of the recommended daily allowance [9]. Many evidences suggest that dietary protein is particularly important for osteogenesis and to reduce the risk of fractures, especially in the elderly [3]. Vegetarian food is related to factors that may not support bone health and may help promote bone loss, such as low body weight, low protein intake, and limited intake of calcium and phosphorus [3,29,30]. Compared to the meat diet, the intake of Vitamin B12 in the vegetarian diet is significantly reduced [3]. Some vegans have been reported to have low Vitamin D intake due to not taking Vitamin D supplements or consuming dairy products, fortified rice milk, soy milk, orange juice, cereals, and margarine [31]. Compared to different types of plant-based diets, egg-milk diets have higher levels of specific nutrients essential for bone health that are found in animal foods, such as calcium, protein, Vitamin D, Vitamin B12, and retinol, which are lower in vegetarian diets [32]. Dairy products and eggs are a good source of Vitamin B12, and vegans must get Vitamin B12 by regularly using Vitamin B12-fortified foods [10].

Compared to pure omnivores, those who stick to vegan diets have significantly more magnesium, folic acid, and Vitamin K [3]. Vegetarians have a higher intake of Vitamin K, which is found in green leafy vegetables and vegetable oils [33,34]. Although zinc is found in beans, nuts, and whole grains, the phytate in these foods makes it less bioavailable than that from animal sources [35]. The vegetarian diet has a higher content of n-6 fatty acids, and the elimination of fish reduces the intake of n-3 fatty acids for many vegetarians, while walnuts, flax seed, and canola oil also contain n-3 fatty acids (specifically α -linoleic acid [ALA]) [35]. Vegetarians' iron intake is usually similar to or slightly better than that of nonvegetarians [10]. In terms of protein, the Taiwanese vegetarian diet contains a large amount of soy products as a major alternative to animal products, instead of the milk and cheese typical of Western countries [36]. Compared to nonvegans, Taiwanese vegetarians consume fewer calories, more carbohydrates, and less fat and protein [36].

DIETS, DIETARY ACID LOAD, AND BONE MINERAL DENSITY

In healthy individuals, buffering of metabolic acids is controlled by the kidneys, lungs, and bones [37]. Bone is sensitive to the environment, and slight changes in nutrient utilization and the acid-base balance can acutely affect bone metabolism [38,39]. Almost all foods contain precursors of acids (oxidation of organic sulfur to sulfates), while fruits and vegetables also contain precursors of bases (metabolizing of citrate or malate to bicarbonate) [40,41]. Vegetarian diets are more alkaline than omnivorous ones, a factor that contributes to the higher BMD of vegetarians [42-44]. Potential renal acid load is often estimated from dietary intake using the equation: $0.49 \times \text{protein (g)} + 0.037 \times \text{phosphorus (mg)} - 0.021 \times \text{potassium (mg)} - 0.026 \times \text{magnesium (mg)} - 0.013 \times \text{calcium (mg)}$ [45]. In Knurick's study, the urine pH of ovo-lacto vegetarian and vegetarian groups was more alkaline than that of omnivores (6.5 ± 0.4 , 6.7 ± 0.4 and 6.2 ± 0.4 , respectively, $P = 0.003$); however, the pH of urine was associated with BMD in omnivores only [3]. Dietary habits can result in the loss of 15% of bone calcium over 10 years when dietary practices cause buffering of mild metabolic acidosis [46].

Higher alkaline states achieved by dietary or pharmacological means can positively affect calcium balance and elevate the blood pH [47]. By adding potassium bicarbonate or bicarbonate-rich mineral water to diet, bone absorption is reduced through balancing of the nutritional alkali load [48,49]. However, a retrospective two-center analysis showed no effect of dietary alkali treatment on changes in BMD or bone resorption [50]. Diet acid load may be a quantitatively smaller factor than age, gender, weight, and level of exercise [40]. In people with normal renal function and normal acid excretion capacity, acid loading in the diet is not easily detectable as a factor in lowered BMD and osteoporosis development [40]. Over decades, some amount of acid in the body, titrated by skeletal bases daily, could cause a large consumption of bone minerals [40].

High protein intake can have a detrimental effect on bone health, as it increases the amount of dietary acid, which is the result of hydrogen ions produced during oxidation of the sulfur-containing amino acids cysteine and methionine [51]. As the dietary acid load stimulates osteoclast activity and bone resorption, the neutralized carbonate and hydroxyapatite salts are released from the bone, thus preventing bone mineralization [47,48]. Fruits and vegetables are associated with a low dietary acid load and are known to be associated with lower bone absorption and therefore with higher BMD [52]. Fruits and vegetables are also principal sources of potassium and provide a buffer through the production of bicarbonate [53]. Regardless of the source, high potassium intake is positively correlated with bone metabolism [54]. Although protein intake is considered a net acid-producing substance and therefore a net negative risk factor for osteolysis, eating protein with enough calcium, potassium, and other minerals can have an overall beneficial effect on skeletal metabolism [55,56].

VEGETARIAN AND BONE MINERAL DENSITY

Reports on the effect of a vegetarian diet on BMD are conflicting. Lloyd *et al.* reported no significant difference in spine bone density between premenopausal vegetarian and nonvegetarian women [57]. The results of a 2009 meta-analysis of 9 studies and 2,749 subjects suggested that BMD at the femoral neck and lumbar spine was about 4% lower and fracture risk was about 10% higher in vegetarians than in omnivores, but the magnitude of the association was clinically insignificant [58]. Similarly, in a 2015 study, compared to those who ate an omnivorous diet, people who adhered to a meat-free diet had a 4%–5% reduction in BMD with unobvious difference [3]. This study of young, nonobese adults showed no significant difference in BMD over a 1-year period between omnivores, ovo-lacto vegetarians, and vegans [3].

Compared with nonvegetarian postmenopausal women, women of the same age who were ovo-lacto vegetarians had no differences in cortical and trabecular BMD according to Tesar *et al.* [59]. In a study of 1,600 women in Southwestern Michigan by Marsh *et al.*, by age 80, women who maintained an ovo-lacto vegetarian diet for at least 20 years had a reduction of only 18% in bone mineralization [60]. In comparison, Marsh's data showed a 35% reduction in bone mineralization in the nonvegetarian women [60].

Comparisons between Taiwanese vegetarians and non-vegetarians, either men or women, revealed no statistically significant difference in BMD, with comparable proportions of subjects with osteopenia or osteoporosis between groups [2]. The BMD showed age-related declines in men and women in Taiwan, but a vegetarian diet did not seem to affect this decline [2]. However, Chiu *et al.* reported that long-term vegetarian diets have been linked to a higher incidence of osteopenia of the femoral neck in postmenopausal Buddhist women in Taiwan [8]. Compared with other non-long-term or nonstrict vegans, long-term practitioners of veganism had statistically significantly greater age, lower height, lower lumbar spine BMD, and lower total hip BMD in subgroup analysis [8]. The total number of years of following

a vegetarian diet was also significantly negatively correlated with BMD [8]. Lau *et al.* reported that, among older Chinese women, the BMD of the hips of vegetarians was lower than that of nonvegetarians [19]. A 2019 meta-analysis of 20 studies and 37,134 participants showed that vegetarian and vegan diets were associated with lower BMD at the femoral neck and lumbar vertebrae compared to an omnivore diet [7]. Vegans, unlike other vegetarians, were more prone to fractures than omnivores, in subgroup analysis in a study by Iguacel *et al.* [7]. This result suggests that the lower BMD of vegetarians and vegans may be clinically relevant, as vegans are at a higher risk of fractures than omnivores [7].

The different results of various studies may be partly attributed to the differences in the studied populations (different races, genders, age, or menstrual status), different intervals of following a vegetarian diet (long-term or short-term), different degree of strictness in adhering to a vegetarian diet (vegan, lactovegetarian, or ovo-lacto vegetarian), different quality between studies, and different substitutes for meat products [2,3,7]. Lifestyle factors may also influence the association between diet and BMD. Vegans and vegetarians are more likely to exhibit healthier behaviors than omnivores, such as higher levels of physical exercise, lower smoking rates, and lower intake of alcohol and caffeine [61].

NUTRIENTS AND BONE MINERAL DENSITY

Bone is a dynamic, metabolically active tissue that requires sufficient nutrients throughout its life cycle for bone modeling and mineralization [3]. Dietary intake of Vitamin D, protein, calcium, caffeine, and alcohol all influence the regulation of the rate of bone remodeling [62]. Vegetarian foods are linked to factors that are bad for bone health, such as low BMI and low intake of calcium, Vitamin D, Vitamin B12, and protein, but these diets are also rich in nutrients that are good for bone health, including potassium, magnesium, Vitamins C and K, and n-3 fatty acids [10,35]. A high-quality vegetarian diet may include consumption of more of the nutrients which protect bones. These nutrients include potassium, magnesium, Vitamin K, antioxidants (including Vitamins E and C and carotenoids), as well as the anti-inflammatory phytonutrients found in fruits, vegetables, nuts, legumes, herbs, and tea [35]. Increased consumption of fruits and vegetables with high magnesium and potassium content has a positive impact on calcium and bone metabolism [63]. Magnesium enhances bone strength and regulates calcium transport in the intestine [64]. Vitamin K has been associated with protection against fracture risk [33,34].

Vitamin B12, found only in animals, is involved in regulating growth and bone mass [65]. Inadequate Vitamin B12 status is associated with low BMD, increased fracture risk, and osteoporosis [66,67]. Phytic acid and oxalic acid may interfere with the absorption and retention of calcium, thereby negatively affecting BMD [68]. Lower levels of serum and bone zinc have been noted in patients with osteoporosis [69]. A higher ratio of n-6 to n-3 fatty acid intake is also associated with lower hip BMD [70], and dietary ALA is associated with a lower risk of hip fracture [71].

Vitamin D plays a key role in bone health by promoting calcium absorption and normal bone mineralization [68]. Identifying good sources of Vitamin D is a priority for improving bone health in vegetarians and vegans, such as Vitamin D2 in ultraviolet-treated mushrooms, shown to benefit those at risk for Vitamin D deficiency [72]. In Lau's study, Chinese vegetarians consumed fewer total calories; less fat and protein; and more calcium, potassium, and sodium than Chinese non-vegetarians. However, none of these dietary differences were found to be significantly associated with BMD [19]. Appleby's study suggests that vegans are at a higher risk of fractures only when their calcium intake is < 525 mg/day [73]. These studies suggest that insufficient protein and calcium intake of the subjects may explain the unfavorable results of vegetarian diets on bone health [10].

A relatively large amount of protein, one of the main components of the bone matrix, is required during bone formation during normal bone remodeling and overall bone tissue maintenance in older women [74]. The anabolic effect of proteins on bones is mediated by insulin-like growth factor 1, which can increase plasma osteocalcin and promote the recruitment and the activity of osteoblasts [75]. Dietary protein is significantly correlated with BMD in all dietary types (omnivore, ovo-lacto vegetarian, and vegan) [3]. Higher BMI and increased protein intake have been associated with a significantly lower risk of lumbar spine osteopenia [9]. In one study, when vegetarians increased their intake of plant protein from < 3 times a week to more than once a day, wrist fractures were reduced by 68% [76]. However, another study of postmenopausal Asian females found no difference in the risk of vertebral fractures between vegetarians (who consumed 40% less protein daily) and omnivores [77].

The benefit to BMD of greater protein intake may be compromised by the unfavorable effect on BMD of the higher dietary acid load of protein sulfur [3,78]. High intake of fruits and vegetables reduces the acid load in the diet by providing neutralizing anions [79]. For those on plant-based diets, it is still important to have sufficient dietary protein intake to maintain bone health in an alkaline environment [3]. Consumption of soy, a common Asian substitute for meat protein, seems to be good for bone health [10]. Compared with placebo, soy isoflavones have significant benefits in terms of spinal BMD by inhibiting bone resorption and stimulating bone formation [80]. Soy isoflavones and soy phytoestrogens have been shown to positively affect BMD in postmenopausal women [81,82]. Some diets for vegetarian may contain lot of proteins, such soybean, tofu, and soy milk, which might be benefit for bone health in these people.

GENDER, HORMONE, AND CULTURE

Estrogen, a key regulator of bone metabolism in men and women, has inhibitory effects blocking the activation of osteoclasts either directly or via osteoblasts and T-cells, ultimately decreasing bone resorption and maintaining bone formation [83]. Menopause and loss of ovarian estrogens are associated with declines in BMD [84]. A study showed an association between low protein intake and greater

bone loss and hip fractures in the younger Framingham Offspring women but not in men [85]. Isoflavones are natural phytochemicals belonging to the category of "phytoestrogens" [86]. Phytoestrogens have the potential to reduce bone loss during menopause, as evidenced by the clinical use of synthetic isoflavone-*ipriflavone* [87]. Soy protein also has the potential to prevent bone loss associated with ovarian estrogen deficiency [88]. For postmenopausal women, ingesting soy protein at a high isoflavone concentration for 6 months can prevent bone loss in the spine [89]. Taiwanese vegetarian diet often uses soy products such as tofu, fake meat, and fake fish as a major alternative to animal products of protein. However, in Western countries, vegetarians often eat milk, yogurt, and cheese as substitutes of protein sources [36]. In Western countries, the transition from a meat diet to a plant-based diet, including the consumption of large amounts of soy products and intake of sufficient calcium, may be beneficial to bone health, but it is impossible to offset limited physical activity and low estrogen exposure [90]. In Asia, the incidence of osteoporosis-related fractures is lower than in most Western communities, but it is difficult to discern whether the intake of isoflavones in soy foods can explain this difference, especially because there are many other factors that can explain these epidemiological findings [91,92]. There are few studies focusing on the other nutrients between different gender and culture. For women living in Western-style environments, the effect on BMD and bone loss was limited to postmenopause women with a calcium intake below 400 mg per day [93].

FOODS AND DIETETICS

Information related to the nutriology and dietetics, as well as diet suggestions for vegetarian to avoid the osteoporosis, is listed in Table 1 [94]. Discussing the condiments, high salt intake is one of the major risk factors for osteoporosis due to increased calciuria [95]. Sugar, by reducing calcium intake and increasing urinary calcium excretion, is a higher risk factor than salt for osteoporosis when overconsumed [96]. Avoiding too much intake of sweet beverages or dessert can reduce the risk of fractures [96]. Hence, vegetarians need to take care of not consuming too much salt or sugar.

Table 1: Nutrients and food suggestions for vegetarians

Nutrient	Food suggestions for vegetarians
Protein	Eggs, soybean, tofu, soy products, and soy milk
Calcium	Broccoli, cabbage, okra, mustard greens, legumes, milk, yogurt, and cheese
Magnesium	Legumes, spinach, beet, tomatoes, potatoes, sweet potatoes, and raisins
Potassium	Tomatoes, raisins, spinach, potatoes, papaya, oranges, and bananas
Vitamin B12	Nori, shiitake mushroom, yogurt, milk, cheese, and eggs
Vitamin C	Broccoli, grapefruits, oranges, papaya pineapple, and strawberries
Vitamin K	Collard greens, mustard greens, and spinach
Zinc	Beans, nuts, and whole grains
n-3 fatty acids	Walnuts, flax seed, and canola oil

CONCLUSION

In the relation between vegetarian/vegan diet and bone health, it is imperative to consider the possible impact of overall diet quality. A healthy bone diet prescription may increase plant protein intake in people who follow a vegetarian diet plan. The nutritional deficiencies associated with poor bone health can be avoided when a vegetarian or vegan diet is properly planned with high biological value proteins, a variety of fruits and vegetables, legumes, whole grains, nuts, and various soy products. Long-term female vegetarians may need effective nutritional supplements (particularly calcium and Vitamin D) to increase BMD levels and reduce the risk of osteoporosis. Maintaining a healthy lifestyle, by increasing physical activity, reducing caffeine intake, limiting drinking, and quitting smoking, is also crucial for good bone health [61,62].

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Conflicts of interest

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REFERENCES

- Julián-Almárcegui C, Gómez-Cabello A, Huybrechts I, González-Agüero A, Kaufman JM, Casajús JA, et al. Combined effects of interaction between physical activity and nutrition on bone health in children and adolescents: A systematic review. *Nutr Rev* 2015;73:127-39.
- Wang YF, Chiu JS, Chuang MH, Chiu JE, Lin CL. Bone mineral density of vegetarian and non-vegetarian adults in Taiwan. *Asia Pac J Clin Nutr* 2008;17:101-6.
- Knurick JR, Johnston CS, Wherry SJ, Aguayo I. Comparison of correlates of bone mineral density in individuals adhering to lacto-ovo, vegan, or omnivore diets: A cross-sectional investigation. *Nutrients* 2015;7:3416-26.
- Woo J, Ho SC, Yu LM, Lau J, Yuen YK. Impact of chronic diseases on functional limitations in elderly Chinese aged 70 years and over: A cross-sectional and longitudinal survey. *J Gerontol A Biol Sci Med Sci* 1998;53:M102-6.
- Abrahamsen B, van Staa T, Ariely R, Olson M, Cooper C. Excess mortality following hip fracture: A systematic epidemiological review. *Osteoporos Int* 2009;20:1633-50.
- Becker DJ, Kilgore ML, Morrisey MA. The societal burden of osteoporosis. *Curr Rheumatol Rep* 2010;12:186-91.
- Iguacel I, Miguel-Berges ML, Gómez-Bruton A, Moreno LA, Julián C. Veganism, vegetarianism, bone mineral density, and fracture risk: A systematic review and meta-analysis. *Nutr Rev* 2019;77:1-8.
- Chiu JF, Lan SJ, Yang CY, Wang PW, Yao WJ, Su LH, et al. Long-term vegetarian diet and bone mineral density in postmenopausal Taiwanese women. *Calcif Tissue Int* 1997;60:245-9.
- Pilis W, Stec K, Zych M, Pilis A. Health benefits and risk associated with adopting a vegetarian diet. *Rocz Panstw Zakl Hig* 2014;65:9-14.
- Craig WJ. Nutrition concerns and health effects of vegetarian diets. *Nutr Clin Pract* 2010;25:613-20.
- Dewell A, Weidner G, Sumner MD, Chi CS, Ornish D. A very-low-fat vegan diet increases intake of protective dietary factors and decreases intake of pathogenic dietary factors. *J Am Diet Assoc* 2008;108:347-56.
- Key TJ, Appleby PN, Spencer EA, Travis RC, Allen NE, Thorogood M, et al. Cancer incidence in British vegetarians. *Br J Cancer* 2009;101:192-7.
- Rizzo NS, Sabaté J, Jaceldo-Siegl K, Fraser GE. Vegetarian dietary patterns are associated with a lower risk of metabolic syndrome: The adventist health study 2. *Diabetes Care* 2011;34:1225-7.
- Snowdon DA, Phillips RL. Does a vegetarian diet reduce the occurrence of diabetes? *Am J Public Health* 1985;75:507-12.
- Kwok CS, Umar S, Myint PK, Mamas MA, Loke YK. Vegetarian diet, Seventh Day Adventists and risk of cardiovascular mortality: A systematic review and meta-analysis. *Int J Cardiol* 2014;176:680-6.
- Fraser GE. Associations between diet and cancer, ischemic heart disease, and all-cause mortality in non-Hispanic white California Seventh-day Adventists. *Am J Clin Nutr* 1999;70:532S-538S.
- Veronese N, Solmi M, Caruso MG, Giannelli G, Osella AR, Evangelou E, et al. Dietary fiber and health outcomes: An umbrella review of systematic reviews and meta-analyses. *Am J Clin Nutr* 2018;107:436-44.
- New SA. Do vegetarians have a normal bone mass? *Osteoporos Int* 2004;15:679-88.
- Lau EM, Kwok T, Woo J, Ho SC. Bone mineral density in Chinese elderly female vegetarians, vegans, lacto-vegetarians and omnivores. *Eur J Clin Nutr* 1998;52:60-4.
- Rizza W, Veronese N, Fontana L. What are the roles of calorie restriction and diet quality in promoting healthy longevity? *Ageing Res Rev* 2014;13:38-45.
- Fontana L, Meyer TE, Klein S, Holloszy JO. Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. *Proc Natl Acad Sci U S A* 2004;101:6659-63.
- Ding C, Parameswaran V, Udayan R, Burgess J, Jones G. Circulating levels of inflammatory markers predict change in bone mineral density and resorption in older adults: A longitudinal study. *J Clin Endocrinol Metab* 2008;93:1952-8.
- Dennison EM, Syddall HE, Aihie Sayer A, Craighead S, Phillips DI, Cooper C. Type 2 diabetes mellitus is associated with increased axial bone density in men and women from the Hertfordshire Cohort Study: Evidence for an indirect effect of insulin resistance? *Diabetologia* 2004;47:1963-8.
- Veronese N, Stubbs B, Crepaldi G, Solmi M, Cooper C, Harvey NC, et al. Relationship Between Low Bone Mineral Density and Fractures With Incident Cardiovascular Disease: A Systematic Review and Meta-Analysis. *J Bone Miner Res* 2017;32:1126-35.
- Huang TH, Ables GP. Dietary restrictions, bone density, and bone quality. *Ann N Y Acad Sci* 2016;1363:26-39.
- Veronese N, Reginster JY. The effects of calorie restriction, intermittent fasting and vegetarian diets on bone health. *Ageing Clin Exp Res* 2019;31:753-8.
- Lin CL, Huang JF, Lin YC, Huang CY, Lin PY. Acceptability of lacto-ovo-vegetarian diet by patients at tzu chi general hospital. *Tzu Chi J* 1997;9:199-206.
- Pan WH, Kao MD, Tzeng MS, Yen LL, Hung YT, Lee LA, et al. Nutrition and health survey in Taiwan (NAHSIT) 1993-1996: Design, contents, and operations. *J Chin Nutr Soc* 1999;24:1-10.
- Marsh AG, Sanchez TV, Midkelsen O, Keiser J, Mayor G. Cortical bone density of adult lacto-ovo-vegetarian and omnivorous women. *J Am Diet Assoc* 1980;76:148-51.
- Ellis FR, Holesh S, Ellis JW. Incidence of osteoporosis in vegetarians and omnivores. *Am J Clin Nutr* 1972;25:555-8.
- Dunn-Emke SR, Weidner G, Pettengill EB, Marlin RO, Chi C, Ornish DM. Nutrient adequacy of a very low-fat vegan diet. *J Am Diet Assoc* 2005;105:1442-6.
- Melina V, Craig W, Levin S. Position of the academy of nutrition and dietetics: Vegetarian diets. *J Acad Nutr Diet* 2016;116:1970-80.
- Booth SL, Tucker KL, Chen H, Hannan MT, Gagnon DR, Cupples LA, et al. Dietary Vitamin K intakes are associated with hip fracture but not with bone mineral density in elderly men and women. *Am J Clin Nutr* 2000;71:1201-8.
- Feskanich D, Weber P, Willett WC, Rockett H, Booth SL, Colditz GA. Vitamin K intake and hip fractures in women: A prospective study. *Am J Clin Nutr* 1999;69:74-9.

35. Tucker KL. Vegetarian diets and bone status. *Am J Clin Nutr* 2014;100 (Suppl 1):329S-35S.
36. Lu SC, Wu WH, Lee CA, Chou HF, Lee HR, Huang PC. LDL of Taiwanese vegetarians are less oxidizable than those of omnivores. *J Nutr* 2000;130:1591-6.
37. Tylavsky FA, Spence LA, Harkness L. The importance of calcium, potassium, and acid-base homeostasis in bone health and osteoporosis prevention. *J Nutr* 2008;138:164S-5S.
38. Arnett TR, Dempster DW. Effect of pH on bone resorption by rat osteoclasts *in vitro*. *Endocrinology* 1986;119:119-24.
39. Ahn H, Kim JM, Lee K, Kim H, Jeong D. Extracellular acidosis accelerates bone resorption by enhancing osteoclast survival, adhesion, and migration. *Biochem Biophys Res Commun* 2012;418:144-8.
40. Frassetto L, Banerjee T, Powe N, Sebastian A. Acid balance, dietary acid load, and bone effects—a controversial subject. *Nutrients* 2018;10:517.
41. Lennon EJ, Lemann J Jr. Influence of diet composition on endogenous fixed acid production. *Am J Clin Nutr* 1968;21:451-6.
42. Deriemaeker P, Aerenhouts D, Hebbelinck M, Clarys P. Nutrient based estimation of acid-base balance in vegetarians and non-vegetarians. *Plant Foods Hum Nutr* 2010;65:77-82.
43. Burckhardt P. The effect of the alkali load of mineral water on bone metabolism: Interventional studies. *J Nutr* 2008;138:435S-7S.
44. Wynn E, Krieg MA, Lanham-New SA, Burckhardt P. Postgraduate Symposium: Positive influence of nutritional alkalinity on bone health. *Proc Nutr Soc* 2010;69:166-73.
45. Remer T, Dimitriou T, Manz F. Dietary potential renal acid load and renal net acid excretion in healthy, free-living children and adolescents. *Am J Clin Nutr* 2003;77:1255-60.
46. Wachman A, Bernstein DS. Diet and osteoporosis. *Lancet* 1968;1:958-9.
47. Lemann J Jr., Bushinsky DA, Hamm LL. Bone buffering of acid and base in humans. *Am J Physiol Renal Physiol* 2003;285:F811-32.
48. Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 1994;330:1776-81.
49. Buclin T, Cosma M, Appenzeller M, Jacquet AF, Décosterd LA, Biollaz J, et al. Diet acids and alkalis influence calcium retention in bone. *Osteoporos Int* 2001;12:493-9.
50. Frassetto LA, Hardcastle AC, Sebastian A, Aucutt L, Fraser WD, Reid DM, et al. No evidence that the skeletal non-response to potassium alkali supplements in healthy postmenopausal women depends on blood pressure or sodium chloride intake. *Eur J Clin Nutr* 2012;66:1315-22.
51. Remer T. Influence of diet on acid-base balance. *Semin Dial* 2000;13:221-6.
52. Burckhardt P. The role of low acid load in vegetarian diet on bone health: A narrative review. *Swiss Med Wkly* 2016;146:w14277.
53. Frassetto L, Morris RC Jr, Sebastian A. Long-term persistence of the urine calcium-lowering effect of potassium bicarbonate in postmenopausal women. *J Clin Endocrinol Metab* 2005;90:831-4.
54. Macdonald HM, New SA, Fraser WD, Campbell MK, Reid DM. Low dietary potassium intakes and high dietary estimates of net endogenous acid production are associated with low bone mineral density in premenopausal women and increased markers of bone resorption in postmenopausal women. *Am J Clin Nutr* 2005;81:923-33.
55. Dawson-Hughes B. Interaction of dietary calcium and protein in bone health in humans. *J Nutr* 2003;133:852S-4S.
56. Bonjour JP. Dietary protein: An essential nutrient for bone health. *J Am Coll Nutr* 2005;24:526S-36S.
57. Lloyd T, Schaeffer JM, Walker MA, Demers LM. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. *Am J Clin Nutr* 1991;54:1005-10.
58. Ho-Pham LT, Nguyen ND, Nguyen TV. Effect of vegetarian diets on bone mineral density: A Bayesian meta-analysis. *Am J Clin Nutr* 2009;90:943-50.
59. Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. *Am J Clin Nutr* 1992;56:699-704.
60. Marsh AG, Sanchez TV, Michelsen O, Chaffee FL, Fagal SM. Vegetarian lifestyle and bone mineral density. *Am J Clin Nutr* 1988;48:837-41.
61. Davey GK, Spencer EA, Appleby PN, Allen NE, Knox KH, Key TJ. EPIC-Oxford: Lifestyle characteristics and nutrient intakes in a cohort of 33 883 meat-eaters and 31 546 non meat-eaters in the UK. *Public Health Nutr* 2003;6:259-69.
62. Reed JA, Anderson JJ, Tylavsky FA, Gallagher PN Jr. Comparative changes in radial-bone density of elderly female lacto-ovo vegetarians and omnivores. *Am J Clin Nutr* 1994;59:1197S-202S.
63. New SA. Intake of fruit and vegetables: Implications for bone health. *Proc Nutr Soc* 2003;62:889-99.
64. Li M, Hasegawa T, Masuki H, Liu Z, Guo Y, Suzuki R, et al. Ultrastructural assessment of mineral crystallization and collagen mineralization in bone. *J Oral Biosci* 2010;52:94-9.
65. Roman-Garcia P, Quiros-Gonzalez I, Mottram L, Lieben L, Sharan K, Wangwitsin A, et al. Vitamin B (1)(2)-dependent taurine synthesis regulates growth and bone mass. *J Clin Invest* 2014;124:2988-3002.
66. Dhonukshe-Rutten RA, Pluijm SM, de Groot LC, Lips P, Smit JH, van Staveren WA. Homocysteine and Vitamin B12 status relate to bone turnover markers, broadband ultrasound attenuation, and fractures in healthy elderly people. *J Bone Miner Res* 2005;20:921-9.
67. McLean RR, Jacques PF, Selhub J, Fredman L, Tucker KL, Samelson EJ, et al. Plasma B vitamins, homocysteine, and their relation with bone loss and hip fracture in elderly men and women. *J Clin Endocrinol Metab* 2008;93:2206-12.
68. Mangels AR. Bone nutrients for vegetarians. *Am J Clin Nutr* 2014;100 Suppl 1:469S-75S.
69. Atik OS. Zinc and senile osteoporosis. *J Am Geriatr Soc* 1983;31:790-1.
70. Weiss LA, Barrett-Connor E, von Mühlen D. Ratio of n-6 to n-3 fatty acids and bone mineral density in older adults: The Rancho Bernardo Study. *Am J Clin Nutr* 2005;81:934-8.
71. Farina EK, Kiel DP, Roubenoff R, Schaefer EJ, Cupples LA, Tucker KL. Dietary intakes of arachidonic acid and α -linolenic acid are associated with reduced risk of hip fracture in older adults. *J Nutr* 2011;141:1146-53.
72. Stephensen CB, Zerofsky M, Burnett DJ, Lin YP, Hammock BD, Hall LM, et al. Ergocalciferol from mushrooms or supplements consumed with a standard meal increases 25-hydroxyergocalciferol but decreases 25-hydroxycholecalciferol in the serum of healthy adults. *J Nutr* 2012;142:1246-52.
73. Appleby P, Roddam A, Allen N, Key T. Comparative fracture risk in vegetarians and nonvegetarians in EPIC-Oxford. *Eur J Clin Nutr* 2007;61:1400-6.
74. Tylavsky FA, Anderson JJ. Dietary factors in bone health of elderly lactoovo vegetarian and omnivorous women. *Am J Clin Nutr* 1988;48:842-9.
75. Schürch MA, Rizzoli R, Slosman D, Vadas L, Vergnaud P, Bonjour JP. Protein supplements increase serum insulin-like growth factor-I levels and attenuate proximal femur bone loss in patients with recent hip fracture. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1998;128:801-9.
76. Thorpe DL, Knutsen SF, Beeson WL, Rajaram S, Fraser GE. Effects of meat consumption and vegetarian diet on risk of wrist fracture over 25 years in a cohort of peri- and postmenopausal women. *Public Health Nutr* 2008;11:564-72.
77. Ho-Pham LT, Vu BQ, Lai TQ, Nguyen ND, Nguyen TV. Vegetarianism, bone loss, fracture and Vitamin D: A longitudinal study in Asian vegans and non-vegans. *Eur J Clin Nutr* 2012;66:75-82.
78. Thorpe M, Mojtahedi MC, Chapman-Novakofski K, McAuley E,

- Evans EM. A positive association of lumbar spine bone mineral density with dietary protein is suppressed by a negative association with protein sulfur. *J Nutr* 2008;138:80-5.
79. Adeva MM, Souto G. Diet-induced metabolic acidosis. *Clin Nutr* 2011;30:416-21.
80. Ma DF, Qin LQ, Wang PY, Katoh R. Soy isoflavone intake inhibits bone resorption and stimulates bone formation in menopausal women: Meta-analysis of randomized controlled trials. *Eur J Clin Nutr* 2008;62:155-61.
81. Chen YM, Ho SC, Lam SS, Ho SS, Woo JL. Soy isoflavones have a favorable effect on bone loss in Chinese postmenopausal women with lower bone mass: A double-blind, randomized, controlled trial. *J Clin Endocrinol Metab* 2003;88:4740-7.
82. Mei J, Yeung SS, Kung AW. High dietary phytoestrogen intake is associated with higher bone mineral density in postmenopausal but not premenopausal women. *J Clin Endocrinol Metab* 2001;86:5217-21.
83. Khosla S, Oursler MJ, Monroe DG. Estrogen and the skeleton. *Trends Endocrinol Metab* 2012;23:576-81.
84. Cauley JA. Estrogen and bone health in men and women. *Steroids* 2015;99:11-5.
85. Sahni S, Broe KE, Tucker KL, McLean RR, Kiel DP, Cupples LA, et al. Association of total protein intake with bone mineral density and bone loss in men and women from the Framingham Offspring Study. *Public Health Nutr* 2014;17:2570-6.
86. Setchell KD, Cassidy A. Dietary isoflavones: Biological effects and relevance to human health. *J Nutr* 1999;129:758S-67S.
87. Brandi ML. New treatment strategies: Ipriflavone, strontium, Vitamin D metabolites and analogs. *Am J Med* 1993;95:69S-74S.
88. Arjmandi BH, Alekel L, Hollis BW, Amin D, Stacewicz-Sapuntzakis M, Guo P, et al. Dietary soybean protein prevents bone loss in an ovariectomized rat model of osteoporosis. *J Nutr* 1996;126:161-7.
89. Potter SM, Baum JA, Teng H, Stillman RJ, Shay NF, Erdman JW Jr. Soy protein and isoflavones: Their effects on blood lipids and bone density in postmenopausal women. *Am J Clin Nutr* 1998;68:1375S-9S.
90. Anderson JJ. Plant-based diets and bone health: Nutritional implications. *Am J Clin Nutr* 1999;70:539S-42S.
91. Ho SC. Body measurements, bone mass, and fractures. Does the East differ from the West? *Clin Orthop Relat Res* 1996;323:75-80.
92. Tobias JH, Cook DG, Chambers TJ, Dalzell N. A comparison of bone mineral density between Caucasian, Asian and Afro-Caribbean women. *Clin Sci (Lond)* 1994;87:587-91.
93. Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 1990;323:878-83.
94. Haytowitz D, Lemar L, Pehrsson P, Exler J, Patterson K, Thomas R, et al. USDA National Nutrient Database for Standard Reference, Release 24. Washington, DC, USA: US Department of Agriculture; 2011.
95. Cappuccio FP, Kalaitzidis R, Duneclift S, Eastwood JB. Unravelling the links between calcium excretion, salt intake, hypertension, kidney stones and bone metabolism. *J Nephrol* 2000;13:169-77.
96. DiNicolantonio JJ, Mehta V, Zaman SB, O'Keefe JH. Not salt but sugar as aetiological in osteoporosis: A review. *Mo Med* 2018;115:247-52.