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NUTRITION, EXERCISE AND LIFESTYLE (S SHAPSES AND R DALY, SECTION EDITORS)

Fracture Risk in Vegetarians and Vegans: the Role of Diet and Metabolic Factors

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Abstract

Purpose of Review There is strong evidence that poor dietary intake of certain micro- and macro-nutrients can negatively affect bone health. It is unclear if diet is the primary culprit for poor bone health in the vegan population.

Recent Findings Plant-based diets are gaining public interest since they may improve metabolic health. Studies that examine vegetarians and vegans together show a lower bone mineral density (BMD), but not always increased fracture risk compared to omnivores. However, vegans consistently have higher risk of fracture at multiple bone sites, especially at the hip.

Summary There is higher fracture risk in vegans which may be due to calcium and vitamin D intake, as well as amount of dietary protein and quality. Other nutrients (B vitamins, Se, Zn, Fe, iodine) or physiological factors (lower body mass index, microbiome, or endocrine profile) may also play a role but have not been examined and require further study.

Keywords Bone · Diet · Fracture · Protein · Microbiome · Omnivore · Vegan · Vegetarian

Introduction

Plant-based dietary patterns, such as vegetarian and vegan diets, have gained significant attention and acceptance over the last decade due to concerns relating to climate change and sustainability, animal welfare, and personal health [1]. Vegetarian diets eliminate the consumption of meat, poultry, and fish, and depending on the subclassification may include dairy products and eggs. Vegan diets abstain from all animal products, including dairy and eggs. The prevalence of practicing vegan diets is about 1–2% of the population depending on the country, and the prevalence of vegetarians is about 5% in many countries yet is nearly 40% in India where it is widely accepted [2, 3]. Plant-based diets can reduce the risk of type 2 diabetes, cardiovascular disease, and all-cause mortality [4–6], which may be partly attributed to alterations in the gut microbiota, endocrine profile, and lower chronic inflammation. Although plant-based diets can increase the intake of certain nutrients that are important for metabolic health [7, 8], it is often reported that vegetarian, and especially vegan diets, can lead to a reduction in the intake of calcium (Ca), vitamin D, vitamin B_{12}, and protein [7, 9–11]. While a well-planned vegetarian or vegan diet can avoid nutrient insufficiencies [12], these frequently observed nutrient reductions can compromise bone health. This is important due to the rise in plant-based diets and the high risk of osteoporotic fracture in an aging population [13]. In this review, we will provide insight into the current evidence for lower bone mineral density (BMD) and higher fracture risk with a vegan diet, and what modifiable factors that can be considered in the field.

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Bone Health and Body Composition in Vegetarians, Vegans, and Omnivores

Fracture

Individuals who consume vegan and vegetarian diets have been shown to have an increased risk of fracture at multiple

sites, with more heterogeneous findings for any fracture risk in vegetarians [14•]. There are still few prospective studies examining fracture risk in vegans and vegetarians compared to omnivores (Table 1) [15–21]. Despite some evidence for increased fracture risk in vegetarians [21], a higher fracture risk is more consistently reported in vegans compared to omnivores [15, 16•, 17, 19••]. In addition, fracture has been reported at multiple sites [15, 19••, 20]. Incident fractures in one study reported increased wrist/arm, ankle, and foot fractures primarily due to falls in vegans [15], but most studies show higher risk of hip fracture ranging from 2.31 to 2.99 increased risk in vegans compared to omnivores (Table 1). Specifically, the EPIC trial (2020) reported that there was an increased risk of hip fracture in vegans (HR: 2.99, 95%CI 1.54, 5.82) and vegetarians (HR: 1.25, 95%CI 1.04, 1.50) compared to those who eat meat after controlling for body mass index (BMI), and Ca and protein intake [19••]. Fish eaters also had a higher risk of hip fracture (HR: 1.26, 95%CI 1.02–1.54) compared to meat eaters, but vegans had higher risk of total, leg, and vertebral fractures [19••]. In the sensitivity analysis of a recent study that discerned between vegetarians and vegans, there was an increased risk of hip fracture (HR: 1.28, 95%CI: 1.07, 1.78) in vegetarians compared to meat eaters [22]. A predominant site of fracture in younger vegetarians (army recruits) compared to omnivores is at the tibia due to stress fractures that occurred during basic training with high-intensity exercise [21].

There are multiple factors associated with vegan diets that may be responsible for fracture risk (Fig. 1). Besides the diet itself, reduced BMI and energy intake reported in vegans may increase fracture risk [23–26]. Discordant findings between studies may be due to the use of dietary supplements, which in general is reported to be higher in individuals who follow a plant-based diet [27]. In fact, it has been reported that vegans who supplement vitamin D and Ca do not have a higher fracture risk compared to vegetarians and omnivores [17]. Furthermore, when vegans and vegetarians consume higher quantities of protein, fracture risk is reduced [18] which is consistent with findings that older adults who eat more protein have been reported to have greater lean body mass (LBM), improved physical function, and reduced risk for falling [28]. Further research in vegans and vegetarians that considers LBM and physical function as confounders is needed for a greater understanding of the effect of plant-based and omnivorous diets on falls and, ultimately, fracture risk. Other factors that can affect fracture risk and study outcomes may be related to the length of follow up ranging from 2 years [16•, 20] to approximately 20 years [18, 19••], duration of adhering to a vegan or vegetarian diet, age group ranging 20 to 85 years [16•, 21], and the combination or separation of vegetarians and vegans, as well as biological sex in analyses [15, 16•, 18].

Bone Mineral Density

Plant-based diets have been associated with lower BMD which could increase the risk of osteoporotic fractures [29, 30]. A meta-analysis by Ho-Pham et al. in 2009 reported that vegans and vegetarians had approximately 4% lower BMD (spine, femoral neck or whole body), with the most pronounced effects in vegans compared to omnivores [31]. Two separate meta-analyses by Iguacel et al. [14•] and Li et al. [32•] also reported lower BMD in vegans and vegetarians compared to omnivores. Iguacel et al. [14•] reported that compared to omnivores, vegans and vegetarians had a significantly lower BMD (g/cm^2) at the lumber spine (− 0.03, 95%CI -0.05 to -0.02), femoral neck (− 0.04, 95%CI -0.05 to -0.02), and whole body (− 0.05, 95%CI -0.08 to -0.02), with larger effect sizes shown in vegans. Consistent with these findings [14•], a more recent meta-analysis [32•] reported similar lower BMD (g/cm^2) findings at the lumbar spine (− 0.04, 95%CI -0.05 to 0.02), femoral neck (− 0.04, 95%CI -0.06 to -0.02), and whole body (− 0.03, 95%CI -0.06 to -0.01) in vegans and vegetarians when compared to omnivores. In a recent cross-sectional study (n = 88), the bone microarchitecture was measured in vegans compared to omnivores [33]. The findings indicated lower total volumetric BMD and trabecular thickness at the tibia, and lower trabecular BMD and bone volume fraction at the radius and tibia in vegans compared to omnivores. In addition, a further subdivision of the two populations indicated that self-reported resistance training attenuated lower bone values in vegans compared to omnivores [33], which is interesting and should be addressed in larger studies. In addition, these diets may negatively impact bone turnover, but the data are limited with mixed findings [20, 27, 33–36]. In children, only one large study has examined the effect of a vegan and vegetarian diet on BMC. In this study, a 15% lower total body (less head) BMC was reported in these children compared to omnivores that remained significant after adjusting for lower height and weight z-scores [37]. This would indicate that skeletal growth may be compromised (shorter stature and lower bone mass). These studies indicate that both vegan and vegetarian diets can result in a lower BMD or BMC compared to omnivores in children and adults.

It is important to point out several nuances in previous plant-based diet studies examining BMD. For example, studies often group vegetarian and vegan diets together despite their different dietary restrictions. It is beneficial to specifically examine BMD and other bone outcomes in vegans apart from other vegetarians, as vegans are likely to be at a higher risk for lower BMD. Also, prior studies on vegetarians and vegans have mostly measured areal BMD alone in these populations, whereas more information about bone microarchitecture could help to predict fracture risk. In addition, vegetarians and vegans tend to have a lower BMI compared to omnivores [38], which alone can reduce BMD [39]. Interestingly, a study published in 2020 using

Table 1 Studies examining fracture risk in omnivores compared to vegetarian and/or vegan groups

Study	Population n (age in years) [BMI (kg/m^2)]				Follow up (y)	Bone Site or Total	Fracture risk results	Fracture risk summary
	Omnivore	Vegetarian	Vegan	Sex				
Appleby et al. (2007)	Meat eaters: *n* = 19,249 (51 ± 12 y) [24.4 ± 3.9 kg/m^2] Fish eaters: *n* = 4901 (44 ± 13 y) [23.0 ± 3.4 kg/m^2]	*n* = 9420 (41 ± 13 y) [23.0 ± 3.5 kg/m^2]	*n* = 1126 (39 ± 13 y) [22.2 ± 3.0 kg/m^2]	M/F	5.2	Total	Vegans had increased risk of total fx compared to meat eaters. IRR: 1.30 (1.02–1.66)	↑ total fx risk in vegans [a]
Thorpe et al. (2008)[b,c,d]	*n* = 1142 (~ 50 y)	*n* = 718 (~50 y)	--	F	25	Wrist	No increased fx risk for vegetarians except those with low vegetable protein intake	No increased fx risk for vegetarians
Ho-Pham et al. (2012)	*n* = 93 (61 ± 9 y) [24 ± 3 kg/m^2]	--	*n* = 88 (62 ± 10 y) [24 ± 3 kg/m^2]	F	2	Vertebral	No increased fx risk in 2-year incidence for vegans versus omnivores. 5.7% (5 fxs out of 88 vegans) 5.4% (6 fxs out of 93 omnivores)	No increased fx risk (small study)
Dash and Kushwaha (2012)[b,d,e]	*n* = 6439 (~ 20 y)	2131 (~ 20 y)	--	M	5	Total	Stress fx occurred in 209 (9.8%) of vegetarians 395 (6.1%) of non-vegetarians	↑ total stress fx risk in vegetarians
Lousuebsakul-Matthews et al. (2014)[b,c,f]	n = 15,831 (~ 57 y) No fx: 81.5 ± 19.1 kg fx: 78.7 ± 18.3 kg	*n* = 13,524 (~ 57 y) No fx: 74.1 ± 16.4 kg fx: 68.4 ± 14.2 kg[e]	*n* = 3776 NR	M/F	≥ 2	Hip	Vegans had increased fx risk Age-adjusted rate per 1000 person-years: HR = 2.99[g]	↑ hip fx risk in vegans
Tong et al. (2020)	Meat eaters: *n* = 29,380 (50 ± 13 y) [24.5 ± 4.0 kg/m^2] Fish eaters: *n* = 8037 (43 ± 13 y) [23.0 ± 3.4 kg/m^2]	*n* = 15,499 (40 ± 14 y) [22.9 ± 3.5 kg/m^2]	*n* = 1982 (39 ± 14 y) [22.1 ± 3.0 kg/m^2]	M/F	17.6	Hip, leg, spine, total	Vegan had increased fx risk vs meat eaters (HR). Hip: 2.31 (95%CI 1.66–3.22) Leg: 2.05 (95%CI 1.23–3.41) Spine: 1.59 (95%CI 1.02–2.50) Total: 1.43 (95%CI 1.20–1.70)	↑ hip, leg, spine, and total fx risk in vegans
Thorpe et al. (2021)[b]	*n* = 14,656 (63 ± 11 y)	*n* = 12,008 (64 ± 11 y)	*n* = 2832 (63 ± 11 y)	M/F	8.4	Hip	In women, vegans had increased fx risk compared to vegetarians and omnivores. HR: 2.99 (95% CI 1.54, 5.82)	↑ hip fx risk in vegan women[h]
Webster et al. (2022)[i]	Meat eaters: *n* = 13,984 (53.3 ± 9.2 y) [25.3 ± 4.5 kg/m^2] Fish eaters: *n* = 3867 (49.7 ± 8.5 y) [23.3 ± 3.5 kg/m^2]	*n* = 4393 (48.3 ± 8.2) [23.3 ± 3.9 kg/m^2]	*n* = 130 NR	F	22.3	Hip	Women who eat a vegetarian diet had increased fx risk. HR: 1.28 (95%CI 1.07, 1.78) HR (c̄ vegans): 1.33 (95%CI 1.03, 1.71)	↑ hip fx risk in vegetarian women

Abbreviations: *fx*, fracture; *HR*, hazard ratio; *NR*, not reported; *IRR*, incidence rate ratio; including (c̄). All studies reported incident fractures, not specific to osteoporotic condition which is less common in age groups < 65 y reported in these studies. Total fracture means cumulative for all sites

[a] No increased fx risk in vegans who consumed > 525 mg Ca/d. [b] BMI not reported by diet group. [c] Age estimated from results in study; [d] vegetarian groups may include vegans; not specified. [e] Stress fractures of army recruits; age not reported; estimated by using mean national age of army recruits (19.7 y). [f] Weight differs between fx and no fx group; $p < 0.05$; [g] no 95%CI reported. [h] No increased fx risk in vegans who supplemented with vitamin D and Ca. [i] Sample size, age, and BMI estimates for vegetarians include vegans (*n* = 130), of which 5 vegans were fx cases

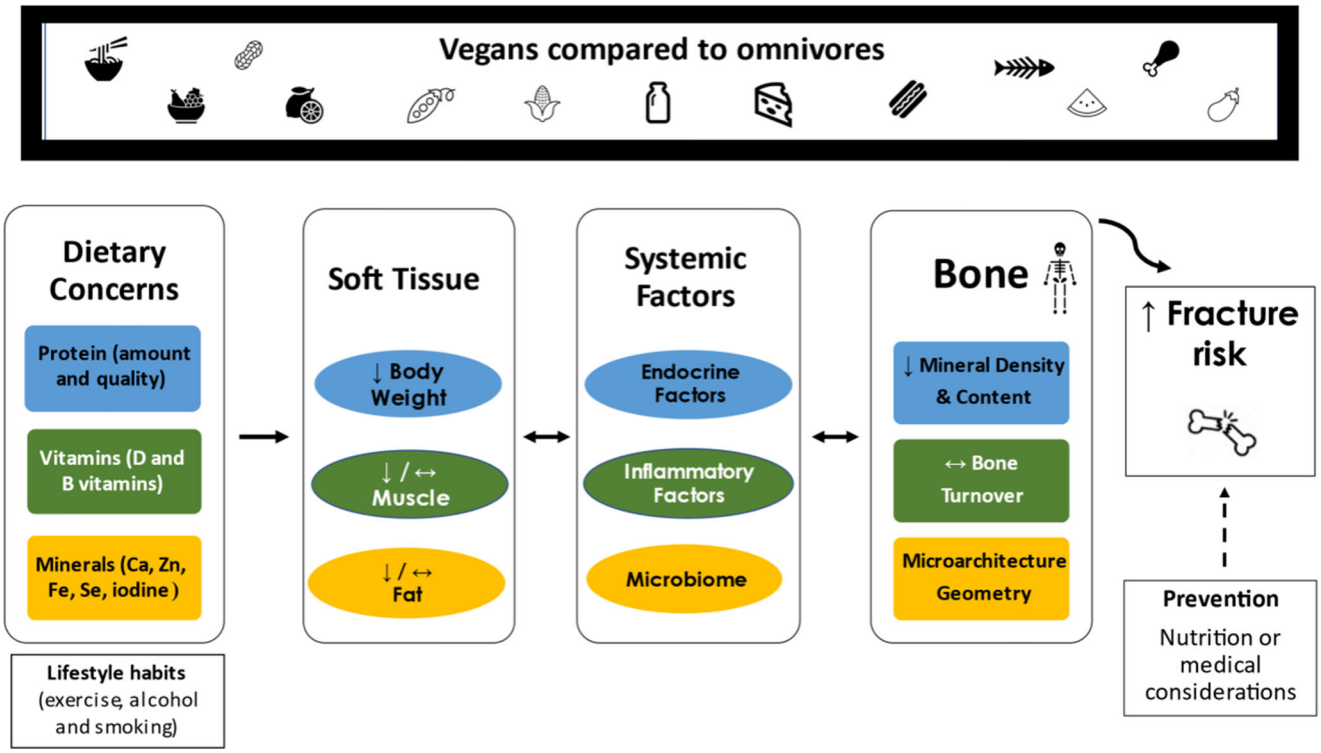

Fig. 1 Overview of potential factors related to fracture risk

NHANES data concluded that vegetarians and vegans had lower hip BMD compared to those who eat meat, however, after adjusting for BMI, these findings became nonsignificant [40•].

Body Weight and Soft Tissues

Vegetarians and vegans tend to have lower body weight and LBM [20, 24, 41] compared to omnivores, which by itself, can reduce BMD and increase fracture risk [42]. In the UK Biobank cohort, body weight, fat mass, and LBM were lower among vegans and vegetarians as compared to meat eaters, and this study also found lower BMD and grip strength in these groups [43]. In contrast, Ho-Pham et al. [44] examined Buddhist nuns and found no significant difference between vegans and omnivores in lean or fat mass which may reflect a different lifestyle or pattern of eating than the general population. Notably, in this study [44], there was also no difference in BMD at multiple sites either, unlike most other studies [20]. While some studies examining BMD in vegans and vegetarians have adjusted for body weight or BMI [40•, 43], none to our knowledge have adjusted for LBM. In children, there are no differences for LBM (z-score) in vegans and vegetarians, but vegan children have reduced BMI, height, and weight z-scores [37]. Overall, the evidence for lower LBM in adult vegans is largely consistent. Future research examining bone outcomes should consider covariates, such as body weight and LBM, which would advance our understanding of fracture risk in these populations.

Dietary Mechanisms Regulating Bone by Diet Pattern

Plant-based diets have been regarded as healthier dietary patterns compared to omnivore diets due to a reduction in saturated fat, cholesterol, and calorie intake, with an overall increase in fruits and vegetables. In fact, multiple diet quality scores have determined that vegetarian and vegan diets have higher diet quality scores than omnivorous diets [45–47]. However, these a priori indices were constructed to prevent only certain chronic diseases (i.e., heart disease, diabetes) and do not necessarily predict bone health [48]. As such, one group of researchers developed a food group-based BMD diet score to estimate bone health indicating dairy, fish, and a plant-based food pattern was better than one high in meat [49]. Importantly, the elimination and replacement of animal-based foods with plant-based foods can lead to an alteration in essential nutrients, which may be both beneficial and potentially harmful to overall health.

Plant-based dietary patterns, while generally higher in K, Mg, and vitamin K, can be associated with reductions in dietary intake of Ca, vitamin D, B vitamins, and protein. In addition, multiple other minerals, such as Zn, Fe, Se, and iodine can also be compromised [8, 26, 50]. The reduction of some of

these nutrients, including Ca, Zn, B_{12}, Se, and protein are often uniquely associated with vegan diets, which may lead to a deficiency and negative effects on bone health. To make matters worse, several commonly consumed plant-based foods contain compounds that can reduce Ca or protein absorption (that is described further below). In addition, intestinal Ca absorption can also be negatively affected by a reduced intake of vitamin D that is reported in vegans [9]. On the other hand, a greater fruit and vegetable intake in plant-based diets is known to increase flavonoid and polyphenol intake, and attenuate diet acidity, which could be beneficial to bone health, although this is not consistently reported [51–54]. Thus, plant-based dietary patterns, especially vegan diets, may negatively affect bone health due to reduced intake and absorption of key bone-supporting nutrients.

Nutrients of Concern in Plant-Based Diets That Impact Bone Health

Dietary Protein

Adequate protein intake is important for bone health [55] and in vegan diets, it is generally lower than in vegetarian and omnivorous diets [26]. Dietary protein stimulates the synthesis of insulin-like growth factor [56, 57], improves Ca balance and absorption [58], and reduces circulating parathyroid hormone [59]. A predominant source of protein in vegan diets is from soy whereas in vegetarians, the primary source is from dairy with smaller amounts from soy [26]. The digestible indispensable amino acid score (DIAAS), reflecting protein quality, of most plant-based proteins is reduced compared to animal-based proteins [60]. Overall, the reduction in protein quality of plant-based foods is due to the lower amount of certain indispensable amino acids, including leucine, lysine, and/or methionine [61], as well as the presence of protein digestion inhibitors, such as trypsin inhibitors or tannins [62]. In addition, plant-based proteins have been shown to be less anabolic for LBM than animal proteins [61]. However, soy is a unique protein because it has a similar DIAAS score as meat and dairy [63] and contains isoflavones with estrogenic activities that may benefit BMD [64, 65]. Vegans can achieve adequate intake of the amino acids lacking in some plant-based protein sources by consuming a combination of plant proteins with complementary amino acid compositions to support anabolism [61]. Furthermore, the processing of protein in plant-based foods may increase the bioavailability of amino acids [66]. For instance, soy has 84% bioavailability compared to soy protein isolate that is 96% bioavailability [66].

Protein from soy-meat analogues (which include eggs and dairy), meat or fish indicate that higher intakes can reduce hip fracture risk by 40–64% compared to those who do not consume these foods, such as vegans [16•]. However, legume intake was also associated with a reduced fracture risk among those who consumed higher quantities [16•] which would be expected to especially benefit vegans. While studies indicate that dietary protein from dairy intake increases BMD, it is unclear if there is a benefit of consuming protein from animal or plant-based sources on fracture risk [67]. These findings may be confounded by Ca content and vitamin D fortification and explain current evidence indicating no differential effect of protein source on fracture [68].

Calcium

The greater Ca content, bioavailability, and absorption from animal sources (e.g., dairy) compared to plant-based foods could compromise total Ca balance in vegans compared to vegetarians and omnivores. Intestinal absorption of dietary Ca is about 25–30% and will depend on several factors, such as age, estrogen status, 1-25-dihydroxyvitamin D level [69], calorie intake [70, 71], and differences between individual foods. The bioavailability of Ca in plant sources is reduced to about one third of the efficiency of dairy foods due to binding to oxalic, phytic, and tannic acids [72, 73]. In addition, total Ca intake in an adult vegan can range from 300 to 600 mg/day [7, 20] which is markedly lower than the recommended intake of 1000–1200 mg/day [74]. In addition, the quantity of plant-based Ca sources required to achieve the recommended intake for Ca would be about 6 cups bok choy or kale per day (compared to 3.5 servings of dairy) (Fig. 2) [69]. Nuts are not in this figure as they were not specifically examined in the absorption studies, but many nuts and especially almonds are good sources of Ca (about 96 mg/serving or 1/4 cup) [75]. Furthermore, there are multiple calcium-fortified foods that can be consumed by vegans with high absorption (Fig. 2). In fact, calcium-fortified orange juice has the highest Ca absorption of all non-dairy foods, which is likely due to its low pH that increases Ca bio-accessibility and absorption [76]. Overall, these highly absorbed Ca-fortified foods would be good choices for vegans to maintain Ca balance and bone health.

Vitamin D

Most studies report that vegans and vegetarians consume lower amounts of vitamin D, which is not surprising since the highest vitamin D sources are from fatty fish and fortified dairy products [77–79]. Vitamin D_2 from plants compared to vitamin D_3 in animal sources may be less bioavailable due to

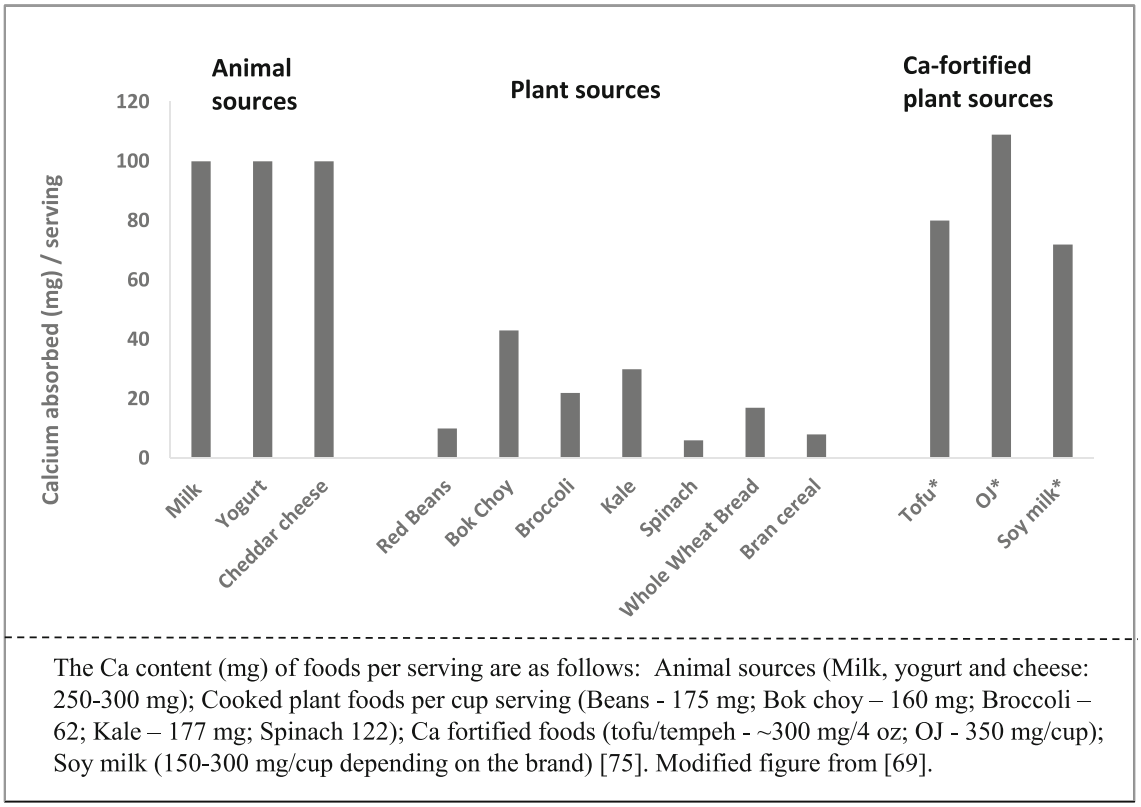

Fig. 2 Calcium absorption/serving for animal and plant-based foods. The Ca content (mg) of foods per serving are as follows: animal sources (milk, yogurt and cheese: 250–300 mg); cooked plant foods per cup serving (beans, 175 mg; bok choy, 160 mg; broccoli, 62; kale, 177 mg; Spinach 122); Ca-fortified foods (tofu/tempeh, ~ 300 mg/4 oz; OJ, 350 mg/cup); soy milk (150–300 mg/cup depending on the brand) [75] (modified figure from [69])

the interactions with certain nutrients and arrangement within the food matrix [80]. However, this should not compromise vitamin D status since intestinal absorption does not differ between the two (D_2 or D_3), and both can raise serum levels of serum 25-hydroxyvitamin (25OHD) to a similar degree [81]. Similar to Ca, the bioavailability of vitamin D_2 or D_3 is affected by food intake. Specifically, the amount of fat and possibly the type of fat (increased with MUFA, decreased with PUFA) may affect absorption of vitamin D [82]. Because vegans tend to have lower fat intake [45, 83–85] and higher PUFA intake compared to omnivores [26], this may compromise vitamin D absorption and Ca absorption. This has never been studied specifically in vegans, but it might be one hypothesis to explain their poor bone health.

Mechanisms Altered by Diet That Regulate Bone

Vitamin D and PTH

Most studies examining the role of vitamin D on bone outcomes in vegetarians are limited to dietary intake [83], whereas only a few examine circulating levels of 25-hydroxyvitamin D (25OHD) and other bone regulating hormones [8, 27, 85]. Low dietary intake of vitamin D may explain the lower serum 25OHD concentrations reported in vegans and vegetarians compared to omnivores [10]. In this same small study, only vegans ($n = 6$) had an elevated parathyroid hormone (PTH) and a negative effect on BMD compared to lactovegetarians ($n = 6$) and omnivores ($n = 16$) [10]. Similar results were reported by another study [34] that showed vegans had lower serum 25OHD, which were accompanied by higher levels of serum PTH and bone turnover markers compared to omnivores. Meanwhile, another study [27] found that even though vegans had lower dietary intake of vitamin D, their serum 25OHD levels were comparable to those on an omnivorous diet, but the vegan group still trended towards having higher circulating PTH and bone resorption. Importantly, a low vitamin D status has been reported in vegans despite 77% supplementing with vitamin D [84], and low circulating 25OHD levels may associate with high PTH, which could partially explain the higher fracture risk in vegans. Serum Ca is not a marker of bone status, but is associated with a physiological response, including elevated serum PTH and decreased urinary Ca excretion [10, 27] and, if altered in vegans, could indirectly explain the poor bone health. Overall, vegan diets may lead to lower 25OHD levels and

elevated PTH, but it is not clear if this mechanism contributes to low BMD and fracture risk in this population since studies are limited in number with generally have smaller sample sizes. Nevertheless, the lower dietary vitamin D and Ca intake is a concern, indicating that consumption of supplements or fortified foods could benefit vegans.

Inflammatory Cytokines

Low-grade inflammation reflected by slightly higher circulating inflammatory cytokines, such as C-reactive protein (CRP), interleukin-6 (IL-6), or tumor necrosis factor-alpha levels, is associated with increased risk of numerous chronic diseases including osteoporosis [86–88]. Importantly, osteoclastogenesis and bone resorption are modulated by pro-inflammatory cytokines, and inflammation may lead to bone loss [89]. In fact, elevated markers of inflammation have been reported to be associated with a higher risk of osteoporotic fracture [90]. In addition, a large body of data indicates that pro-inflammatory diets can lower lumbar spine and hip BMD and increase the risk of osteoporotic fractures [91]. This may be explained by evidence that plant-based diets, and especially vegan diets [92•], can favorably modulate inflammatory biomarker profiles (e.g., lower CRP and IL-6 concentrations), and lower neutrophils, monocytes, and platelets [93–96], which can protect against a range of chronic inflammatory diseases [97, 98]. Overall, while inflammatory biomarker profiles may be improved by a vegan diet, there is limited evidence whether this contributes to bone health in this population.

Gut Microbiota

The human gut microbiota is a complex ecosystem within the intestines that is associated with the regulation of the host's immune system, nutrient absorption, and production of nutrients that can also influence the host's bone health [99, 100]. Germ-free mice display altered bone mass compared to conventionally raised mice [101, 102], and bone strength is negatively affected by these gut microbiota alterations [103]. The gut microbiota can be altered by many external factors, including dietary intake, age, lifestyle, and antibiotic use, with perturbations associated with several chronic diseases, including bone health. Interestingly, strain-specific probiotic supplementation of *Bacteroides* or *Lactobacillus* has been shown to ameliorate bone loss in ovariectomized murine models [104, 105] and positively affect acute Ca metabolism in humans [106]. In human studies, the gut microbiota has been associated with reduced BMD and higher fracture incidence; however, the association of specific microbial alterations is not consistently reported [107–110].

Plant-based diets can cause an alteration in the gut microbiota due to the change in nutrient intake, such as higher fiber and reduced saturated fats. Several cross-sectional studies have reported alterations in microbiota composition between vegetarians and vegans compared to omnivores [111–113]. In addition, randomized crossover trials have shown rapid alterations in microbial diversity and abundance with omnivorous or plant-based diets [114, 115]. However, a recent systematic review was unable to consistently associate plant-based diets with a specific microbiota composition compared to omnivores [116•]. This may be partially attributed to the heterogeneity between the analyzed studies, including differences in geographical location and methodological procedures. Indeed, associations or changes of gut microbiota composition tend to vary between studies. A reduction in the abundance of *Bacteroides* for vegans was reported in some [117], but not all [112, 113, 115, 118] studies, with one study [114] reporting an increase following an omnivorous diet. In addition, early evidence suggested that the abundance of *Lactobacillus* was reduced in vegan diets [119]. This could be partly explained by the elimination of common dietary sources of *Lactobacillus*, such as fermented dairy products; however, more recent studies reported no differences in the abundance of *Lactobacillus* between vegans, vegetarians, or omnivores [117, 118]. Furthermore, others have suggested that prebiotic fibers (possibly higher in the vegan diet) may offer an alternative approach to enhance Ca absorption [120] which may be due to an altered gut microbiota to ultimately improve bone health [121]. While the gut microbiota can affect BMD, bone strength, and fracture in murine models, further research in human trials is necessary that uses consistent methodological procedures (e.g., sequencing libraries) to elucidate its role in bone health.

Conclusion

Adequately planned vegetarian diets, including vegan diets, can provide many health benefits that are largely attributed to the lower intake of saturated fat and higher intake of fiber and phytochemicals [122]. However, the lower intake of protein and Ca (and other micronutrients) may be factors leading to the lower BMD and higher risk of hip fracture in vegans compared to omnivores. This is despite evidence that vegans generally have a healthy lifestyle, including some reports suggesting greater physical activity than individuals following other dietary patterns [15, 123]. The evidence for poor bone health in vegans is consistent over a wide range of ages including higher incident fracture in middle-aged and older adults, higher stress fractures in young army recruits, and attenuated height in vegan children. In contrast, vegetarian diets that include dairy and eggs show limited evidence that it compromises bone health. Whether modest solutions, such as advising vegans to consume more high-quality proteins and nutrient fortified foods while including other lifestyle

recommendations (e.g., resistance exercise) can maintain bone health should be examined. In addition, it is possible that the intake of prebiotic fibers can improve Ca absorption and attenuate fracture risk. Overall, there is a growing interest in plant-based and vegan diets due to environmental and ethical reasons, besides the health benefits. However, clinical guidance is needed to prevent unintended side effects, such as increased osteoporosis risk. Future studies should include not only large cohort studies but also well-designed randomized controlled intervention trials that separate vegans from other vegetarians to address bone health and fracture risk.

Declarations

Conflict of Interest The authors declare no conflict of interest.

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Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

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