REVIEW

Dietary Patterns in Relation to Low Bone Mineral Density and Fracture Risk: A Systematic Review and Meta-Analysis

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ABSTRACT

Low bone mineral density (BMD) and osteoporosis-related fractures constitute a considerable public health burden. Several studies have demonstrated the association between diet and bone health. We performed a systematic review to provide an estimate of the association between different dietary patterns defined through the use of a posteriori methods and fracture or low BMD risk. A literature search on PubMed, Web of Science, and Scopus databases, up to March 2018, was performed to identify all eligible case-control, prospective, or cross-sectional studies involving subjects of both sexes and any age. Random-effects models were used. Heterogeneity and publication bias were evaluated. Stratified analyses were conducted on study characteristics. The meta-analysis includes 20 studies and identifies 3 prevalent dietary patterns: "Healthy," "Milk/dairy," and "Meat/Western." From the 10 studies on fracture, adherence to the "Healthy" pattern reduced the risk, particularly in older people (OR: 0.79; 95% CI: 0.66, 0.95; $P = 0.011$) and in Eastern countries (OR: 0.64; 95% CI: 0.43, 0.97; $P = 0.037$), whereas the risk increased with the "Meat/Western" pattern, especially for older people (OR: 1.11; 95% CI: 1.04, 1.18, $P = 0.001$), in those with hip fractures (OR: 1.15; 95% CI: 1.05, 1.25; $P = 0.002$), and in Western countries (OR: 1.10; 95% CI: 1.07, 1.14; $P < 0.0001$). Analyses on low BMD showed a reduced risk in the "Healthy" pattern, particularly for younger people (OR: 0.62; 95% CI: 0.44, 0.89; $P = 0.009$). The "Meat/Western" pattern increased low BMD risk, especially in older people (OR: 1.31; 95% CI: 1.05, 1.64; $P = 0.015$). The "Milk/dairy" pattern resulted in the strongest reduction in low BMD risk; when stratifying, this effect remained significant (e.g., older women—OR: 0.57; 95% CI: 0.46, 0.70; $P < 0.0001$). Nutrition is an important modifiable factor affecting bone health. The "Healthy" and "Milk/dairy" patterns are associated with a reduced risk of low BMD and fracture. In contrast, the "Western" pattern is inversely associated. *Adv Nutr* 2019;10:219–236.

Keywords: dietary pattern, bone mineral density, bone fracture, systematic review, meta-analysis

Introduction

Osteoporosis is a systemic skeletal disorder, characterized by low bone mineral density (BMD) and compromised bone strength (1, 2). Low BMD and osteoporosis-related fractures constitute an important socioeconomic and public health burden (3, 4). The risk of low BMD and bone fractures increases exponentially with age in both sexes and, as a result of the expanding aging population, the burden of osteoporotic fractures is expected to increase over the next few decades with a consequent economic impact on health care costs (3, 5). Osteoporotic fractures may result in significant disability, reduced quality of life, and increased risk of institutionalization and mortality (6–9).

Many factors contribute to BMD and osteoporosis, such as gender, physical inactivity, excessive alcohol consumption, smoking, loss of estrogen, and nutritional factors mainly related to adequate intakes of calcium and vitamin D (2). Several epidemiologic studies have explored the association of dietary habits on bone health, and the association of individual foods and nutrients with fracture and low BMD risk has been recently reviewed. A significant preventive effect has been described for the adequate intake of milk and dairy products (10, 11), fruits and vegetables (12), and dietary protein, both animal and plant (13, 14).

Dietary patterns have been recently applied in nutritional epidemiology to examine the relation between diet and chronic diseases rather than focusing on individual foods and

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Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances/.
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Abbreviations used: BMD, bone mineral density; FA, factor analysis; PCA, principal component analysis, PCFA, principal component factor analysis.

nutrients (15, 16). This strategy provides a closer representation of the actual conditions in which foods and nutrients are consumed and permits the effect of overall dietary habits to be evaluated. Dietary patterns have been defined by several statistical methods, which can be distinguished as a priori and a posteriori methods. A priori approaches define dietary indices and scores (i.e., glycemic index, Mediterranean score) on the basis of current nutritional knowledge of the healthy or unhealthy effects of various dietary constituents and identify a desirable pattern, the adherence to which could maximize health benefit. Conversely, a posteriori methods generate dietary patterns (i.e., Western, healthy, and dairy patterns) on the basis of available dietary data directly obtained from the studied population (15).

Dietary patterns extracted via a posteriori methods have the major limit that results obtained may be sample specific and influenced by subjective decisions. On the other hand, the a priori approach can prove more advantageous only if important dietary factors have been clearly defined to affect the outcome under study (15, 17). However, in the last few years, several epidemiologic studies have successfully investigated the relation between fracture or low BMD risk and different dietary patterns derived by a posteriori methods. Although the association of the aforementioned bone health outcomes with the Mediterranean score has been recently reviewed and estimated (18), to the best of our knowledge, there is no currently available meta-analysis considering the effect of dietary patterns defined by a posteriori methods on fracture and low BMD risk.

In this systematic review and meta-analysis, we selected studies addressing the association between the different dietary patterns defined through the use of a posteriori methods and fracture or low BMD risk and evaluated them to provide an estimate of the association.

Methods

In this study, the standard procedures for conducting and reporting meta-analysis according to MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement were followed (19, 20).

Search strategy and data source

We carried out a comprehensive literature search, without restrictions, up to March 2018 through the PubMed (http://www.ncbi.nlm.nih.gov/pubmed/), Web of Science (http://wokinfo.com/), and Scopus (https://www.scopus.com/) databases to identify all the original articles on the association between dietary patterns and BMD or bone fracture. The following search medical subject headings (MeSH) and key words were used: ("bone mineral density" OR BMD OR fracture OR "bone mass density" OR osteoporosis) AND ("dietary pattern" OR "eating pattern" OR "food pattern" OR "dietary habit" OR "dietary score" OR "dietary index" OR "nutrient pattern" OR "diet diversity" OR "diet variety" OR "diet quality" OR "diet index" OR "diet score"). In addition, the reference lists of included articles and recent relevant reviews were manually examined to identify additional relevant publications.

Eligibility criteria

Articles were included if they met the following criteria: *1*) evaluated the relation between dietary patterns derived by a posteriori methods such as principal component analysis (PCA), factor analysis (FA), principal component factor analysis (PCFA), and cluster analysis and by reduced rank regression (i.e., an integration of the a priori and the a posteriori approaches) and BMD and fracture risk; *2*) used a case-control, prospective, or cross-sectional study design; and *3*) presented OR, RR, or HR estimates with 95% CIs. If the same study was reported in several publications, we selected the publication reporting the largest number of individuals. For each potential included study, 2 investigators independently carried out the selection, data abstraction, and quality assessment. Disagreements were resolved by discussion or in consultation with the third author. Although useful for background information, reviews and meta-analyses were excluded. No studies were excluded for weakness of design or data quality.

Data extraction and quality assessment

From the selected studies, we extracted the following information: first author's last name, year of publication, country, study design, sample size (when possible, number of cases and controls; cohort size and incident cases), population characteristics (gender, age), duration of follow-up for cohort studies, fracture and BMD evaluation site, dietary assessment and dietary pattern identification methods (FA, PCA, and PCFA), characteristics of the dietary assessment method, name given to the dietary patterns and their characteristics, cutoff points of the different categories of adherence to the dietary pattern (dichotomy, tertile, quartile, and quintile), risk estimates with 95% CIs for the different categories of adherence, *P* values for trend, and adjustment for confounding factors. When multiple estimates were reported in an article, we pulled out those that adjusted for the most confounding factors. The study quality was assessed by a 9-star system, based on the Newcastle-Ottawa Scale method (21); the full score was 9 and a total score of $\geq$7 was used as the criterion for a high-quality study. To avoid selection bias, no study was excluded because of these quality criteria.

Statistical analysis

The overall effect-size statistic estimated was the average of the logarithm of the observed OR (approximated to RR, when necessary) associated with the highest compared with the lowest level of adherence to the different dietary patterns. We used a random-effects model to calculate the summary OR and 95% CI. We restricted the analysis to the a posteriori dietary patterns. Because the labeling of the patterns is arbitrary and the dietary patterns are population specific, we considered only those patterns sharing most foods with similar factor loadings. For inclusion in the meta-analysis, the 3 most common dietary patterns having a similar factor loading of principal components were identified in 8 studies (out of 10) considering as outcome the fracture risk (22–31) and in 10 studies considering the low BMD risk (32–41). The first pattern, named the "Healthy" dietary pattern, was characterized by a high loading of vegetables and fruits, poultry, fish, and whole grains. The selected articles were labeled as "Healthy" (24, 28), "Prudent" (26, 33, 34), "Fruit-vegetables-dairy" (25), "Vegetable-fruit-soy" (27), "Nutrient-dense" (29), "Vegetable" (30), "White-rice-kimchi" (32), "Chinese-Western" (35), "Fruit-milk-whole grains" (36), "Chinese traditional" (37), "Vegetables-soya sauce" (38), "Traditional-Korean" (39), "Traditional" (40), "Pattern 2" (31), and "Pattern 4" (41). The second pattern, named the "Meat/Western" dietary pattern, had a high loading of red meat, processed meat, animal fat, eggs, and sweets. The included articles were labeled as "Western" (26, 33, 40), "Western/convenience" (24), "Refined/westernized" (34), "Sweets-animal fat-low meat" (25), "Meat-dim-sum" (27), "High-fat" (28), "Energy-dense" (29), "Meat" (30, 35), "Meat-vegetable" (32), "Meat-alcohol-sugar" (38), "Eggs-meat-flour" (36), "Western food" (37), "Fast food" (39), "Pattern 3" (31), and "Pattern 1" (41). In addition, a "Milk/dairy" dietary pattern, characterized by a high loading of milk and dairy products, was identified in 7 articles, which labeled it as "Milk-cereal-whole grain" (32), "Dairy-fish" (34), "Fruit-milk-whole grains" (36), "Calcium food" (37), "Dairy-fruit" (38), "Milk-cereal" (39), and "Dairy" (40).

The chi-square–based Cochran's Q statistic and the I^2 statistic were used to evaluate heterogeneity in results across studies (42). The I^2 statistic yields results ranging from 0% to 100% (I^2 = 0–25%, no heterogeneity; I^2 = 25–50%, moderate heterogeneity; I^2 = 50–75%, large heterogeneity; and I^2 = 75–100%, extreme heterogeneity) (43). The results of the meta-analysis may be biased if the probability of publication is dependent on the study results. We used the methods of Begg and Mazumdar (44) and Egger et al. (45) to detect publication bias. Both methods tested for funnel plot asymmetry, the former being based on the rank correlation between the effect estimates and their sampling variances and the latter on the intercept from regression of standard normal deviates against precision. If a potential bias was detected, we further conducted a sensitivity analysis to assess the robustness of combined effect estimates, and the possible influence of the bias, and to correct the bias. We also conducted a sensitivity analysis to investigate the influence of a single study on the overall risk estimate, by omitting 1 study at a time. We considered the funnel plot to be asymmetric if the intercept of Egger's regression line deviated from 0, with a P values <0.05. The statistical program ProMeta version 3.0 (Internovi) was used for the analyses.

Results

Study selection

From the primary literature search through the PubMed (n = 134), Web of Science (n = 137), and Scopus ($n = 346$) databases, and after removing duplicates ($n = 212$), we identified 405 records for title and abstract revision (Figure 1). Among these, 328 articles were excluded because they did not investigate the association between dietary patterns and the outcomes of interest. Seventy-seven articles were subjected to full-text revision. Manual searching of reference lists of both selected articles and recent relevant reviews led to the identification of 5 additional items. Subsequently, 62 articles were excluded because they did not meet the inclusion criteria as follows: 30 studies on dietary patterns determined by a priori methods, 29 studies not reporting the risk estimation, and 3 studies on adherence to nutrient dietary patterns. Therefore, at the end of the selection process, 20 studies were included for the identification of the different dietary patterns in the systematic review and meta-analysis (22–41). Ten studies considered the fracture risk (22–31) and 10 studies the risk of low BMD (Figure 1) (32–41).

Study characteristics and quality assessment

The general characteristics of the 10 studies evaluating the association between adherence to different dietary patterns with fracture risk are shown in **Supplemental Table 1**. Three studies were conducted in China (23, 27, 28), 2 in the United States (26, 31), and 1 each in Italy (22), Sweden (24), the Netherlands (25), Canada (29), and Japan (30). One was a cross-sectional study (22), 8 were cohort studies (23–27, 29–31), and 1 was a case-control study (28). These studies were published between 2010 and 2017. Four studies were conducted in women and men together (20,654 individuals) (22, 23, 25, 30), 4 studies were on women and men separately (113,753 women and 65,161 men) (26–29), and 2 studies were on women only (56,861) (24, 31). One study was conducted in young women (aged 18–26 y) (31) and reported data on all stress fractures, 1 study was on an adult population (≥18 y) (23), and the others were on older subjects (>30 y). Five studies considered hip fracture (10,012 cases) (24–28), 4 studies evaluated the number of fractures at any site (2733 cases) (22, 23, 25, 30), and 1 study considered all low-trauma clinical fractures excluding skull, face, hands, and feet (29). The fractures were assessed by radiographic imaging (22, 28, 31), questionnaire (23, 25, 26, 29), and linkage with a registry/database (24, 27, 30). Eight studies used an FFQ (67–170 items) (24–31), and 2 studies used a 24-h dietary recall (22, 23) to collect dietary information and to define the food groups (27–38 groups). Eight of the identified studies derived dietary patterns through an a posteriori method (PCA, PCFA, and FA) (22–24, 26–30), and 2 used a method that integrated "a priori" and "a posteriori" approaches (reduced rank regression) (25, 31). Five studies reported the association of fracture risk with 2 different dietary patterns (23, 25–27, 29), 1 study considered 3 dietary patterns (30), 3 studies considered 4 dietary patterns (24, 28, 31), and 1 study considered 6 different dietary patterns (22).

Table 1 shows the general characteristics of studies evaluating the association between adherence to different dietary patterns with low BMD risk. Five studies were

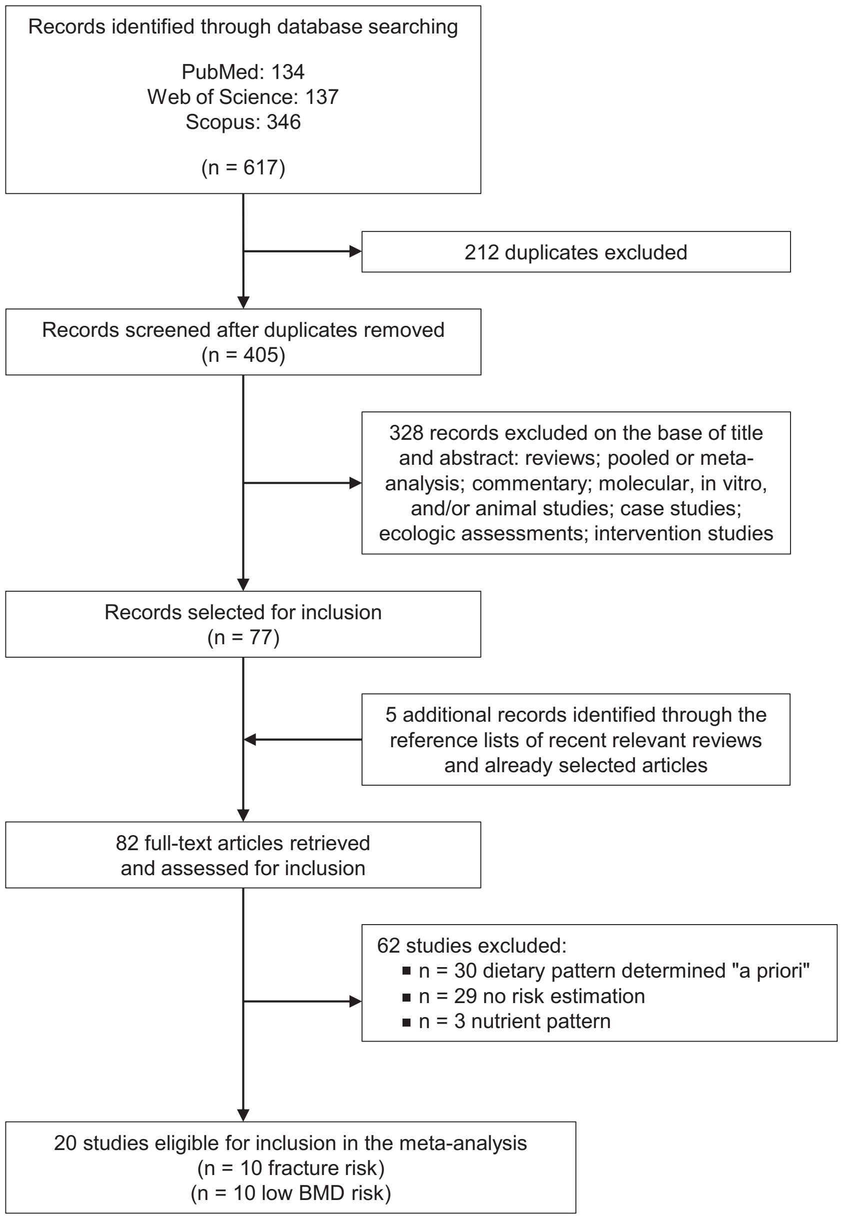

FIGURE 1 Flow diagram of the systematic literature search on dietary patterns and bone fracture and low BMD risk. BMD, bone mineral density.

conducted in Korea (32, 36, 38–40), 2 in China (35, 37), and 1 each in Australia (33), Mexico (34), and Iran (41). Nine were cross-sectional studies (32–39, 41) and 1 was a cohort study (40). These studies were published between 2012 and 2017. Five studies were conducted in women and men together (11,086 individuals) (33–35, 37, 39), 1 study was on women and men separately (1102 women and 716 men) (36), 3 studies were on women only (5359) (38, 40, 41) and 1 study was on men only (1351) (32). Four studies were conducted in young subjects (aged 10–25 y; 4456 subjects) (32, 35, 37, 39), and the other studies were on older subjects (>20 y; 15,158 subjects) (33, 34, 36, 38, 39, 41). Three studies evaluated the BMD in 1 site: calcaneus (35, 37) and whole body (33); 5 studies considered 2 sites: whole pelvis and lumbar spine (36), femur and lumbar spine (38, 39, 41), and radius and tibia (40); and 2 studies considered 3 sites: whole body, lumbar spine, and whole body less head (32) and whole body, hip, and lumbar spine (34). In 7 studies BMD was evaluated by DXA (32–34, 36, 38, 39, 41), whereas in 3 studies BMD was estimated measuring the speed of sound with an ultrasound bone densitometer (35, 37, 40). Subjects were classified in the low-BMD groups either on the basis of the *z* score in 3 studies (32, 35, 39) or the *T* score in 6 studies (33, 34, 36–38, 40). In 1 study, the low-BMD group included those subjects with a BMD value below the median (41). To assess the dietary habits and to derive the food groups (18–39) defining the dietary patterns, 6 studies used an FFQ (103–168 items) (33–35, 37, 40, 41), 2 studies used a 24-h dietary recall (32, 38),

TABLE 1 General characteristics of included studies in the meta-analysis of dietary patterns and low BMD risk[1]

Study, year (ref)	Study design, location	Population, age	BMD site	BMD definition method	Dietary pattern assessment and identification method	Dietary pattern type and characteristics	Percentile of adherence to dietary patterns	OR/RR (95% CI)	*P*-trend	Matched or adjusted variables	NOS score
Shin et al., 2017 (32)	Cross-sectional, Korea	1351 males, 10–25 y	Whole body Lumbar spine (L 1–4) Whole body less head	DXA scan low BMD: *Z* score ≤−2.0	24-h dietary recall EIG >1.3 20 food groups PCFA Loading >0.2 3 factors, VE 25.7%	1. Meat and vegetable: vegetables, potatoes, mushrooms, oils, seasonings, meat, noodles, ramen, eggs, shellfish, beverages	Tertile 1 Tertile 3	1.00 (Ref.) 0.75 (0.30, 1.84)	0.623	Age, body size, energy intake, serum 25(OH)D, residence region, household income, physical activity	8
						2. White rice and kimchi: white rice, soy, kimchi, fruits, fish, seaweed, seasonings	Tertile 1 Tertile 3	1.00 (Ref.) 0.68 (0.30, 1.53)	0.649		
						3. Milk-cereal and whole grain: milk, dairy products, whole grains, cereals, bread, cakes, sweet snacks, eggs	Tertile 1 Tertile 3	1.00 (Ref.) 0.36 (0.16, 0.81)	0.018		
Melaku et al., 2016 (33)	Cross-sectional, Australia	1066 individuals, >50 y	Whole body	DXA scan low BMD: *T* score ≤ −2.5	FFQ, SA 39 food groups PCA Varimax rotation EIG > 1 Loading > 0.2 2 factors, VE 17%	1. Prudent: fruits, vegetables, sugar, nut-based milk, fish, legumes, high-fiber bread	Tertile 1 Tertile 3	1.00 (Ref.) 0.52 (0.33, 0.83)	0006	Age, sex, BMI smoking, alcohol, marital status, income, health literacy, leisuretime, job-related physical activity, diabetes mellitus, family history of osteoporosis, energy intake	7
						2. Western: processed and red meat, snacks, takeaway foods, jam, beer, soft drinks, white bread, poultry, potato with fat, high-fat dairy products, eggs	Tertile 1 Tertile 3	1.00 (Ref.) 1.68 (1.02, 2.77)	0044		
Denova-Gutiérrez et al., 2016 (34)	Cross-sectional, Mexico	6915 individuals, 20–80 y	Whole body Hip Lumbar spine (L 1–4)	DXA scan low BMD: *T* score ≤ −1.0	116-item FFQ 22 food groups PCA Varimax rotation EIG >1.5 Factor loading ≥0.2 3 factors, VE 26.1%	1. Prudent: fresh vegetables, fruit, tomato, oils, legumes, fish, whole grains	Quintile 1 Quintile 5	Whole body 1.00 (Ref.) 0.83 (0.63, 1.07)	0.252	Age, gender, BMI, height, multivitamin use, smoking, physical activity, energy intake. For women: estrogen use, age of menarche, parity, menopause	7
							Quintile 1 Quintile 5	Hip 1.00 (Ref.) 0.71 (0.44, 0.97)	0.025		
							Quintile 1 Quintile 5	Lumbar spine 1.00 (Ref.) 0.80 (0.68, 0.94)	0.031		

(*Continued*)

TABLE 1 *Continued*

Study, year (ref)	Study design, location	Population, age	BMD site	BMD definition method	Dietary pattern assessment and identification method	Dietary pattern type and characteristics	Percentile of adherence to dietary patterns	OR/RR (95% CI)	*P*-trend	Matched or adjusted variables	NOS score
						2. Refined/westernized: red meat, fats, sugar, sweets, soft drinks, eggs, refined grains, alcoholic beverages	Quintile 1 Quintile 5	Whole body 1.00 (Ref.) 1.74 (1.10, 2.76)	0.016		
							Quintile 1 Quintile 5	Hip 1.00 (Ref.) 1.91 (1.19, 3.04)	0.004		
							Quintile 1 Quintile 5	Lumbar spine 1.00 (Ref.) 1.61 (1.06, 2.45)	0.027		
						3. Dairy and fish: fish and other seafood, dairy foods, whole grains, milk	Quintile 1 Quintile 5	Whole body 1.00 (Ref.) 0.51 (0.40, 0.66)	<0.001		
							Quintile 1 Quintile 5	Hip 1.00 (Ref.) 0.86 (0.67, 1.12)	0.252		
							Quintile 1 Quintile 5	Lumbar pine 1.00 (Ref.) 0.69 (0.56, 0.85)	<0.001		
Yang et al., 2016 (35)	Cross-sectional, China	1590 individuals, 11–17 y	Right calcaneus	Ultrasound bone densitometer, speed of sound (m/s) *Z* score "normal"	FFQ, IA 24 food groups FA Varimax rotation EIG > 1.5 Factor loading ≥ 0.4 3 factors, VE 65.6%	1. Chinese and Western: rice, rice products, flour, flour products, whole grains, fresh vegetables, fresh fruit, poultry, eggs, freshwater fishes, shrimps, deep-sea fish, milk, dairy products, beans, bean products, nuts, snacks, sugar, barbecue	Tertile 1 Tertile 3	1.00 (Ref.) 0.42 (0.29, 0.56)		Sex, passive smoking, drinking, calcium	7
						2. Westernization structure: rice, rice products, flour, flour products, fresh fruit, fat meat, hamburgers, fried foods, processed products, snacks, Coke, Sprite, coffee, ice cream, instant noodles, barbecue	Tertile 1 Tertile 3	1.00 (Ref.) 0.98 (0.79, 1.22)			
						3. Meat: fat meat, beef, mutton, poultry, animal liver, freshwater fishes, shrimps, deep-sea fish, processed products	Tertile 1 Tertile 3	1.00 (Ref.) 1.07 (0.76, 1.50)			

(*Continued*)

TABLE 1 *Continued*

Study, year (ref)	Study design, location	Population, age	BMD site	BMD definition method	Dietary pattern assessment and identification method	Dietary pattern type and characteristics	Percentile of adherence to dietary patterns	OR/RR (95% CI)	*P*-trend	Matched or adjusted variables	NOS score
Shin et al., 2014 (36)	Cross-sectional, Korea	1818 individuals (1102 women, 716 men), ≥ 30 y	Whole pelvis Lumbar spine	DXA scan low BMD: *T* score ≤ −1.0	3-d food record 22 food groups PCA Varimax rotation EIG >1.5 Factor loading >0.2 4 factors, VE 31.1%	1. Rice and kimchi: white rice, kimchi, garlic, onions, fish, shellfish, legumes, vegetables, mushrooms	 Quartile 1 Quartile 4 Quartile 1 Quartile 4	Women 1.00 (Ref.) 1.05 (0.67, 1.67) Men 1.00 (Ref.) 0.62 (0.35, 1.10)	0.6667 0.1855	Age, body size, energy intake, smoking, alcohol, physical activity, menopausal status (women)	7
						2. Eggs, meat and flour: oil, seasoning, eggs, processed meats, meat, poultry, noodles, dumplings, bread, snacks	 Quartile 1 Quartile 4 Quartile 1 Quartile 4	Women 1.00 (Ref.) 1.06 (0.65, 1.72) Men 1.00 (Ref.) 0.65 (0.36, 1.18)	0.835 0.2667		
						3. Fruit, milk, and whole grains: fruits, potatoes, whole grains, dairy foods, vegetables, mushrooms, nuts	 Quartile 1 Quartile 4 Quartile 1 Quartile 4	Women 1.00 (Ref.) 0.45 (0.28, 0.72) Men 1.00 (Ref.) 0.38 (0.22, 0.67)	0.0128 0.0004		
						4. Fast food and soda: pizza, hamburgers, French fries, soda, coffee, sweet fruit juice	 Quartile 1 Quartile 4 Quartile 1 Quartile 4	Women 1.00 (Ref.) 0.80 (0.50, 1.29) Men 1.00 (Ref.) 1.47 (0.81, 3.09)	0.2386 0.1327		
Mu et al., 2014 (37)	Cross-sectional, China	1319 individuals, 16–20 y	Right calcaneus	Ultrasound bone densitometer, speed of sound (m/s) low BMD: *T* score ≤ −1.0	FFQ, IA 19 food groups FA Varimax rotation EIG >1.5 Factor loading >0.3 4 factors, VE 51.1%	1. Western food: hamburger, fried food, nuts, snack food, cola, coffee, sugars	Tertile 1 Tertile 3	1.00 (Ref.) 1.09 (0.62, 1.93)		Sex, physical activity, passive smoking, alcohol, calcium supplements, BMI	8
						2. Animal protein: pork, mutton, beef, poultry meat, animal liver	Tertile 1 Tertile 3	1.00 (Ref.) 1.04 (0.73, 1.49)			

(*Continued*)

TABLE 1 *Continued*

Study, year (ref)	Study design, location	Population, age	BMD site	BMD definition method	Dietary pattern assessment and identification method	Dietary pattern type and characteristics	Percentile of adherence to dietary patterns	OR/RR (95% CI)	*P*-trend	Matched or adjusted variables	NOS score
						3. Calcium food: milk, dairy products, beans, bean products, fresh fruit, eggs, fish, shrimp, kelp laver, sea fish	Tertile 1 Tertile 3	1.00 (Ref.) 0.59 (0.41, 0.87)			
						4. Chinese traditional: grains, fresh vegetables and fruits, pork	Tertile 1 Tertile 3	1.00 (Ref.) 0.78 (0.55, 0.89)			
Shin and Joung, 2013 (38)	Cross-sectional, Korea	3735 women post-menopausal, 64.1 ± 9.5 y	Femoral neck Lumbar spine (L 1–4)	DXA scan low BMD: *T* score ≤ −2.5	24-h dietary recall, IA 20 food groups PCA Varimax rotation EIG >1.5 Factor loading >0.2 4 factors, VE 30.9%	1. Meat, alcohol and sugar: oils, starch syrup and sugar, meat and its products, alcohol	 Quintile 1 Quintile 5 Quintile 1 Quintile 5	Femoral neck 1.00 (Ref.) 0.89 (0.60, 1·31) Lumbar spine 1.00 (Ref.) 0.78 (0.57, 1·07)	0.6602 0.1988	Age, BMI, energy intake, parathyroid hormone, serum 25(OH)D, smoking, alcohol, physical activity, supplement, oral contraceptive	8
						2. Vegetables and soya sauce: vegetables, mushrooms, soya sauce, red pepper, garlic, onion, legumes, white rice	 Quintile 1 Quintile 5 Quintile 1 Quintile 5	Femoral neck 1.00 (Ref.) 0.79 (0.51, 1.21) Lumbar spine 1.00 (Ref.) 1.22 (0.86, 1.74)	0.0689 0.9823		
						3. White rice, kimchi and seaweed: white rice, seaweed, kimchi, fish, shellfish	 Quintile 1 Quintile 5 Quintile 1 Quintile 5	Femoral neck 1.00 (Ref.) 1.14 (0.80, 1.64) Lumbar spine 1.00 (Ref.) 1.40 (1.03, 1.90)	0.9435 0.0479		
						4. Dairy and fruit: legumes, milk, dairy foods, flour, bread, fruits, nuts	 Quintile 1 Quintile 5 Quintile 1 Quintile 5	Femoral neck 1.00 (Ref.) 0.80 (0.54, 1.19) Lumbar spine 1.00 (Ref.) 0.47 (0.34, 0.65)	0.1763 0.0001		
Shin et al., 2013 (39)	Cross-sectional, Korea	196 adolescents, 12–15 y	Femur Lumbar spine (L 1–4)	DXA scan low BMD: *T* score ≤ −1.0	6-d food record, IA 24 food groups FA Varimax rotation EIG >1.25 Factor loading >0.25 4 factors, VE 28.4%	1. Traditional Korean: rice, other grains, fish, shellfish, legumes, soy sauce, soybean pastes, seaweed, kimchi	 Tertile 1 Tertile 3 Tertile 1 Tertile 3	Femur 1.00 (Ref.) 0.86 (0.35, 2.14) Lumbar spine 1.00 (Ref.) 0.58 (0.23, 1.48)	0.8072 0.3556	Age, sex, BMI, weight loss attempts, pubertal status, physical activity	6

(*Continued*)

TABLE 1 *Continued*

Study, year (ref)	Study design, location	Population, age	BMD site	BMD definition method	Dietary pattern assessment and identification method	Dietary pattern type and characteristics	Percentile of adherence to dietary patterns	OR/RR (95% CI)	*P*-trend	Matched or adjusted variables	NOS score
						2. Fast food: carbonated drinks, French fries, hamburgers, biscuits, cookies, pizza, fried chicken		Femur	0.5933		
							Tertile 1	1.00 (Ref.)			
							Tertile 3	0.76 (0.29, 1.99)			
								Lumbar spine	0.6281		
							Tertile 1	1.00 (Ref.)			
							Tertile 3	0.81 (0.31, 2.10)			
						3. Milk and cereal: milk, yogurt, cereal, bread		Femur	0.3705		
							Tertile 1	1.00 (Ref.)			
							Tertile 3	0.71 (0.29, 1.72)			
								Lumbar spine	0.0461		
							Tertile 1	1.00 (Ref.)			
							Tertile 3	0.36 (0.14, 0.93)			
						4. Snacks: sauce, seasonings, chocolate, ice cream, gum, candy, seeds, nuts, fruits, vegetables, sandwiches, simple sugar		Femur	0.6707		
							Tertile 1	1.00 (Ref.)			
							Tertile 3	1.27 (0.51, 3.15)	0.8534		
								Lumbar spine			
							Tertile 1	1.00 (Ref.)			
							Tertile 3	1.23 (0.47, 3.20)			
Park et al., 2012 (40)	Cohort, Korea Follow-up 4 y	1464 post-menopausal women, 40–69 y Cases: 324 radius, 390 tibia	Radius Mid-tibia	Ultrasound bone densitometer, speed of sound (m/s) low BMD: *T* score ≤ 2.5	103-item FFQ 18 food groups FA Varimax rotation EIG >1.0 Factor loading >0.2 3 factors, VE 33.9%	1. Traditional: rice, kimchi, vegetables, fruits		Radius	0.0674	Age, residual area, physical activity, passive smoking	7
							Quintile 1	1.00 (Ref.)			
							Quintile 5	1.46 (1.00, 2.13)			
								Tibia	0.0095		
							Quintile 1	1.00 (Ref.)			
							Quintile 5	1.82 (1.12, 2.96)			
						2. Dairy: milk, dairy products, green tea		Radius	0.0554		
							Quintile 1	1.00 (Ref.)			
							Quintile 5	0.63 (0.42, 0.93)			
								Tibia	0.0483		
							Quintile 1	1.00 (Ref.)			
							Quintile 5	0.56 (0.35, 0.90)			
						3. Western: noodles, breads, sugar, fat		Radius	0.0428		
							Quintile 1	1.00 (Ref.)			
							Quintile 5	1.46 (1.02, 2.10)			
								Tibia	0.0628		
							Quintile 1	1.00 (Ref.)			
							Quintile 5	1.46 (0.91, 2.33)			

(*Continued*)

TABLE 1 *Continued*

Study, year (ref)	Study design, location	Population, age	BMD site	BMD definition method	Dietary pattern assessment and identification method	Dietary pattern type and characteristics	Percentile of adherence to dietary patterns	OR/RR (95% CI)	*P*-trend	Matched or adjusted variables	NOS score
Karamati et al., 2012 (41)	Cross-sectional, Iran	160 post-menopausal women, 50–85 y	Femoral neck Lumbar spine (L 1–4)	DXA scan low BMD: BMD below the median	168-item FFQ 25 food groups PCFA Varimax rotation EIG >1.0 Factor loading >0.3 6 factors, VE 48.27%	1. Pattern: fat dairy products, organ meats, red meat, processed meats, nonrefined cereals	2 categories	Femoral neck 1.84 (0.87, 3.88) Lumbar spine 2.29 (1.05, 4.96)	0.11 0.04	Age, BMI, physical activity, parity, smoking, education, fragility fracture history, history of hormone replacement therapy, supplement intake, antiresorptive drug use, age at menarche, relative accuracy of energy reporting	7
						2. Pattern: French fries, mayonnaise, sweets, desserts, vegetable oils	2 categories	Femoral neck 2.83 (1.31, 6.09) Lumbar spine 0.73 (0.35, 1.54)	<0.01 0.41		
						3. Pattern: hydrogenated fats, pickles, eggs, soft drinks	2 categories	Femoral neck 0.75 (0.36, 1.56) Lumbar spine 0.67 (0.33, 1.44)	0.44 0.32		
						4. Pattern: vegetables, low-fat dairy products, fruits, fruit juices, legumes, fish	2 categories	Femoral neck 0.90 (0.44, 1.86) Lumbar spine 0.72 (0.35, 1.50)	0.78 0.39		
						5. Pattern: condiment, potatoes	2 categories	Femoral neck 0.76 (0.35, 1.63) Lumbar spine 0.68 (0.31, 1.46)	0.48 0.32		
						6. Pattern: snacks, tea, coffee, poultry, nuts.	2 categories	Femoral neck 1.01 (0.49, 2.10) Lumbar spine 0.82 (0.39, 1.73)	0.98 0.6		

[1] BMD, bone mineral density; EIG, eigenvalues; FA, factor analysis; IA, interviewer administered; NOS, Newcastle-Ottawa Scale; PCA, principal component analysis; PCFA, principal component factor analysis; ref, reference; Ref., referent; SA, self-administered; VE, variance explained; 25(OH)D, 25-hydroxyvitamin D.

and 2 studies used a 3-d and 6-d food record, respectively (36, 39). One study reported the association of low BMD risk with 2 different dietary patterns (33), 4 studies considered 3 dietary patterns (32, 34, 35, 40), 4 studies considered 4 dietary patterns (33–36), and 1 study considered 6 different dietary patterns (41).

The Newcastle-Ottawa Scale score for each study is shown in the Supplemental Table 1 and Table 1. The study-specific range of quality score was from 6 to 9, the median was 7 (for both low BMD and fracture) and means were 6.9 and 7.3 for fracture and low BMD, respectively.

Meta-analysis on fracture risk

We identified 2 common dietary patterns that had similar factor loadings of the principal components “Healthy” and “Meat/Western,” respectively. Eight out of 10 articles included in the systematic review were used for the overall risk estimation (24–31). Two studies were excluded because the first did not report the risk associated with dietary patterns of interest (22), and the second reported 2 dietary patterns that could not be clearly assumed to fall into either “Healthy” or “Meat/Western” dietary patterns (23). The associations between the highest intake compared with the lowest intake categories of the “Healthy” and “Meat/Western” dietary patterns with fracture risk are shown in **Figure 2**. The overall analysis showed a reduction in fracture risk associated with the “Healthy” pattern (OR: 0.79; 95% CI: 0.66, 0.93; $P = 0.007$), whereas an increment of fracture risk was associated with the “Meat/Western” pattern (OR: 1.11; 95% CI: 1.05, 1.17; $P < 0.001$) (**Table 2**). Considering the “Healthy” pattern, stratification according to the geographic area showed a reduced fracture risk only in the Eastern countries (OR: 0.64; 95% CI: 0.43, 0.97; $P = 0.037$). The results did not essentially change when the study by Nieves et al. (31) in young female runners (aged 18–26 y) was excluded (Table 2). The heterogeneity in the “Healthy” pattern analysis was extremely high. Stratifying by gender, a stronger adherence to the “Healthy” pattern reduced the fracture risk in both women and men. The analysis performed by fracture site showed a significant decrease in the hip fracture risk only, and this preventive effect was preserved in the further fractionation by gender, although without statistical significance (Table 2). Considering the “Meat/Western” pattern, the analysis stratified according to gender showed an increment in the fracture risk in women only (Table 2). In addition, the “Meat/Western” pattern was not significantly associated with the fractures in any site other than hip, and further fractionation by gender showed a significant result for women only (Table 2). The analysis stratified according to the geographic area showed an increased fracture risk in the Western countries only (OR: 1.10; 95% CI: 1.07, 1.14; $P < 0.0001$). The stratification by study design resulted in a weaker association between the adherence to “Healthy” and “Meat/Western” patterns and a significantly lower (OR: 0.82; 95% CI: 0.69, 0.98; $P = 0.026$) and higher (OR: 1.10; 95% CI: 1.06, 1.15; $P < 0.0001$) risk of fractures, respectively, in the cohort studies. In contrast to the “Healthy” pattern, the “Meat/Western” pattern results did not show any heterogeneity (Table 2). No evidence of publication bias could be detected for risk in any case, as evidenced by both the Egger and Begg tests (Table 2) and funnel plot asymmetry (data not shown). Sensitivity analyses suggested that the estimates were not substantially modified by any single study. In particular, small changes were found in the risk estimates after removal of the outlier studies by Zeng et al. (28) (OR: 0.82; 95% CI: 0.69, 0.98; $P = 0.026$) and by Monma et al. (30) (OR: 0.76; 95% CI: 0.64, 0.91; $P = 0.003$) on the “Healthy” pattern. Moreover, the fracture risk estimates associated with the “Meat/Western” pattern ranged from 1.09 (95% CI: 1.03, 1.15; $P = 0.002$) to 1.13 (95% CI: 1.06, 1.20; $P < 0.001$), omitting the study by Warensjö-Lemming et al. (24) and by Langsetmo et al. (29), respectively.

Meta-analysis on low BMD risk

We identified 3 common dietary patterns that were named “Healthy,” “Meat/Western,” and “Milk/dairy”. The “Healthy” and “Meat/Western” patterns were identified in all 10 articles included in the systematic review (32–41), whereas the “Milk/dairy” pattern was identified in only 7 studies (32, 34, 36–40). The associations between the highest intake compared with the lowest intake categories of the “Healthy,” “Meat/Western,” and “Milk/dairy” patterns with low BMD risk are shown in **Figure 3**. When data from all the studies were pooled together, a reduction in low BMD risk was associated with the “Healthy” pattern (OR: 0.82; 95% CI: 0.69, 0.98; $P = 0.028$) with high heterogeneity ($I^2 = 66.36\%$, $P < 0.0001$) (**Table 3**). Stratifying the analysis by age, we found that in younger subjects (<30 y) (32, 35, 37, 39) this dietary pattern showed a preventive effect (OR: 0.62; 95% CI: 0.44, 0.89; $P = 0.009$) (Table 3). On the contrary, the overall analysis on the “Meat/Western” pattern showed an increased risk of low BMD (OR: 1.22; 95% CI: 1.02, 1.45; $P = 0.028$), which was enhanced in older subjects (OR: 1.31; 95% CI: 1.05, 1.64; $P = 0.015$) and lost in younger individuals (Table 3). In contrast, the “Milk/dairy” pattern was always associated with a reduced low BMD risk, regardless of age (Table 3). The age stratification decreased the heterogeneity in the older subgroup for each dietary pattern. Due to the small amount of data, only a few subgroup analyses could be performed. For instance, regarding gender, the analysis was performed only in women, and low BMD risk was not associated with the “Healthy” or “Meat/Western” patterns, whereas it was reduced by adherence to the “Milk/dairy” pattern (Table 3). For the “Healthy” and “Meat/Western” patterns we found no association between low BMD and geographic area. “Milk/dairy” showed a reduced risk of low BMD in Eastern countries (OR: 0.54; 95% CI: 0.47, 0.63; $P < 0.0001$). Stratifying the analysis according to the BMD measurement site, an evident effect was observed only in the whole body when considering both the “Healthy” and “Meat/Western” patterns. Instead, in the case of the “Milk/dairy” pattern the preventive effect was significant in all strata groups considered (Table 3). In general, no evidence of publication bias could be detected for risk, as evidenced

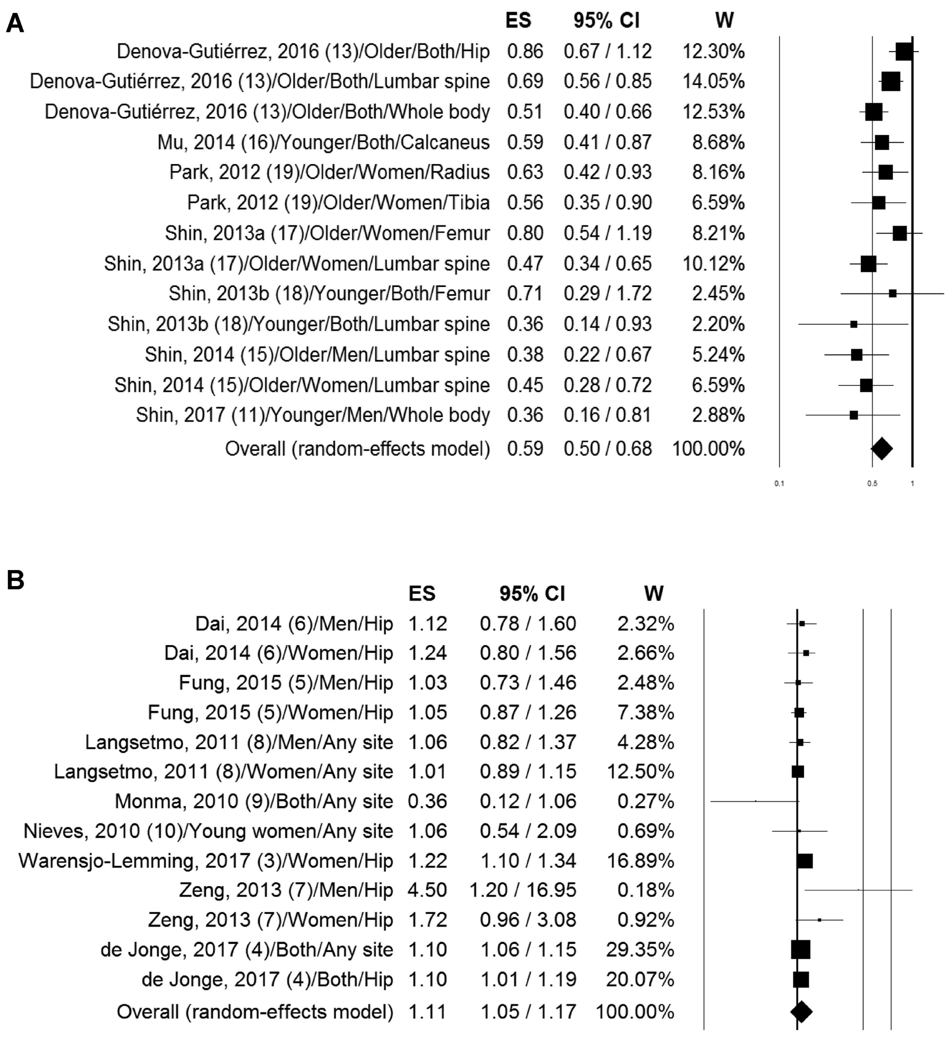

FIGURE 2 Forest plots of the association between "Healthy" (A) and "Meat/Western" (B) dietary patterns and fracture risk. ES, effect size.

by both the Egger and Begg tests (Table 3) and funnel plot asymmetry (data not shown). The sensitivity analyses, carried out separately in younger and older individuals, indicate that the estimates were in 2 cases substantially modified by omitting a single study. In particular, excluding the results by Park et al. (40), the preventive effect of the "Healthy" dietary pattern on older people became significant (OR: 0.81; 95% CI: 0.71, 0.93; $P = 0.003$), with low heterogeneity ($I^2 = 21.62\%$, $P = 0.244$) and no evident publication bias (Egger test: $P = 0.787$; Begg test: $P = 0.531$). In addition, the low BMD estimates associated with the "Meat/Western" dietary pattern ranged from 1.18 (95% CI: 0.92, 1.53; $P = 0.192$) to 1.48 (95% CI: 1.23, 1.79; $P < 0.0001$), excluding the articles by Denova-Gutiérrez et al. (34) and Shin et al. (38), respectively. No significant changes in the risk estimates were found after removal of any single study in the case of the "Milk/dairy" pattern in respect to low BMD.

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis investigating the effect of dietary patterns identified by a posteriori methods on low BMD and fracture risk. In the 20 selected articles, we found common combinations of different foods and identified 3 prevalent dietary patterns: "Healthy," "Meat/Western," and "Milk/dairy." The results indicate that both the "Healthy" and "Milk/dairy" patterns are associated with a decreased risk of low BMD, whereas the "Meat/Western" pattern shows a significant positive association with low BMD risk. Moreover, the "Healthy" pattern has a significant preventive effect on fracture risk, whereas the "Meat/Western" pattern significantly increases the fracture risk.

Similarly to our results, healthy dietary patterns are associated with lower risk for all clinical cardiovascular end points, except for stroke (46), and reduce cognitive decline and the risk of dementia (47). In addition, the "Western" dietary pattern is positively associated with an increment of cancer risk in different sites (48–54).

In our meta-analysis, the "Meat/Western" pattern was positively associated with increases of 22% and 11% in low BMD and fracture risk, respectively. This pattern is characterized by a high consumption of red meat, processed meat,

A

	ES	95% CI	W
Denova-Gutiérrez, 2016 (13)/Older/Both/Hip	0.71	0.44 / 0.97	6.76%
Denova-Gutiérrez, 2016 (13)/Older/Both/Lumbar Spine	0.80	0.68 / 0.94	9.62%
Denova-Gutiérrez, 2016 (13)/Older/Both/Whole body	0.83	0.63 / 1.07	8.42%
Karamati, 2012 (20)/Older/Women/Femur	0.90	0.44 / 1.86	3.69%
Karamati, 2012 (20)/Older/Women/Lumbar Spine	0.72	0.35 / 1.50	3.64%
Melaku, 2016 (12)/Older/Both/Whole body	0.52	0.33 / 0.83	5.99%
Mu, 2014 (16)/Younger/Both/Calcaneus	0.78	0.55 / 0.89	8.72%
Park, 2012 (19)/Older/Women/Radius	1.46	1.00 / 2.13	6.97%
Park, 2012 (19)/Older/Women/Tibia	1.82	1.12 / 2.96	5.71%
Shin, 2013a (17)/Older/Women/Femur	0.79	0.51 / 1.21	6.32%
Shin, 2013a (17)/Older/Women/Lumbar Spine	1.22	0.86 / 1.74	7.29%
Shin, 2013b (18)/Younger/Both/Femur	0.86	0.35 / 2.14	2.68%
Shin, 2013b (18)/Younger/Both/Lumbar Spine	0.58	0.23 / 1.48	2.57%
Shin, 2014 (15)/Older/Men/Lumbar Spine	0.62	0.35 / 1.10	4.85%
Shin, 2014 (15)/Older/Women/Lumbar Spine	1.05	0.67 / 1.67	6.04%
Shin, 2017 (11)/Younger/Men/Whole body	0.68	0.30 / 1.53	3.13%
Yang, 2016 (14)/Younger/Both/Calcaneus	0.42	0.29 / 0.56	7.59%
Overall (random-effects model)	0.82	0.69 / 0.98	100.00%

B

	ES	95% CI	W
Denova-Gutiérrez, 2016 (13)/Older/Both/Hip	1.91	1.19 / 3.04	6.65%
Denova-Gutiérrez, 2016 (13)/Older/Both/Lumbar spine	1.61	1.06 / 2.45	7.36%
Denova-Gutiérrez, 2016 (13)/Older/Both/Whole body	1.74	1.10 / 2.76	6.77%
Karamati, 2012 (20)/Older/Women/Femur	1.84	0.87 / 3.88	3.85%
Karamati, 2012 (20)/Older/Women/Lumbar spine	2.29	1.05 / 4.96	3.65%
Melaku, 2016 (12)/Older/Both/Whole body	1.68	1.02 / 2.77	6.25%
Mu, 2014 (16)/Younger/Both/Calcaneus	1.09	0.62 / 1.93	5.45%
Park, 2012 (19)/Older/Women/Radius	1.46	1.02 / 2.10	8.24%
Park, 2012 (19)/Older/Women/Tibia	1.46	0.91 / 2.33	6.64%
Shin, 2013a (17) /Older/Women/Femur	0.89	0.60 / 1.31	7.78%
Shin, 2013a (17) /Older/Women/Lumbar spine	0.78	0.57 / 1.07	8.99%
Shin, 2013b (18)/Younger/Both/Femur	0.76	0.29 / 1.99	2.64%
Shin, 2013b (18)/Younger/Both/Lumbar spine	0.81	0.31 / 2.10	2.66%
Shin, 2014 (15)/Older/Men/Lumbar spine	0.65	0.36 / 1.18	5.18%
Shin, 2014 (15)/Older/Women/Lumbar spine	1.06	0.65 / 1.72	6.42%
Shin, 2017 (11)/Younger/Men/Whole body	0.75	0.30 / 1.84	2.90%
Yang, 2016 (14)/Younger/Both/Calcaneus	1.07	0.76 / 1.50	8.58%
Overall (random-effects model)	1.22	1.02 / 1.45	100.00%

C

	ES	95% CI	W
Denova-Gutiérrez, 2016 (13)/Older/Both/Hip	0.86	0.67 / 1.12	12.30%
Denova-Gutiérrez, 2016 (13)/Older/Both/Lumbar spine	0.69	0.56 / 0.85	14.05%
Denova-Gutiérrez, 2016 (13)/Older/Both/Whole body	0.51	0.40 / 0.66	12.53%
Mu, 2014 (16)/Younger/Both/Calcaneus	0.59	0.41 / 0.87	8.68%
Park, 2012 (19)/Older/Women/Radius	0.63	0.42 / 0.93	8.16%
Park, 2012 (19)/Older/Women/Tibia	0.56	0.35 / 0.90	6.59%
Shin, 2013a (17)/Older/Women/Femur	0.80	0.54 / 1.19	8.21%
Shin, 2013a (17)/Older/Women/Lumbar spine	0.47	0.34 / 0.65	10.12%
Shin, 2013b (18)/Younger/Both/Femur	0.71	0.29 / 1.72	2.45%
Shin, 2013b (18)/Younger/Both/Lumbar spine	0.36	0.14 / 0.93	2.20%
Shin, 2014 (15)/Older/Men/Lumbar spine	0.38	0.22 / 0.67	5.24%
Shin, 2014 (15)/Older/Women/Lumbar spine	0.45	0.28 / 0.72	6.59%
Shin, 2017 (11)/Younger/Men/Whole body	0.36	0.16 / 0.81	2.88%
Overall (random-effects model)	0.59	0.50 / 0.68	100.00%

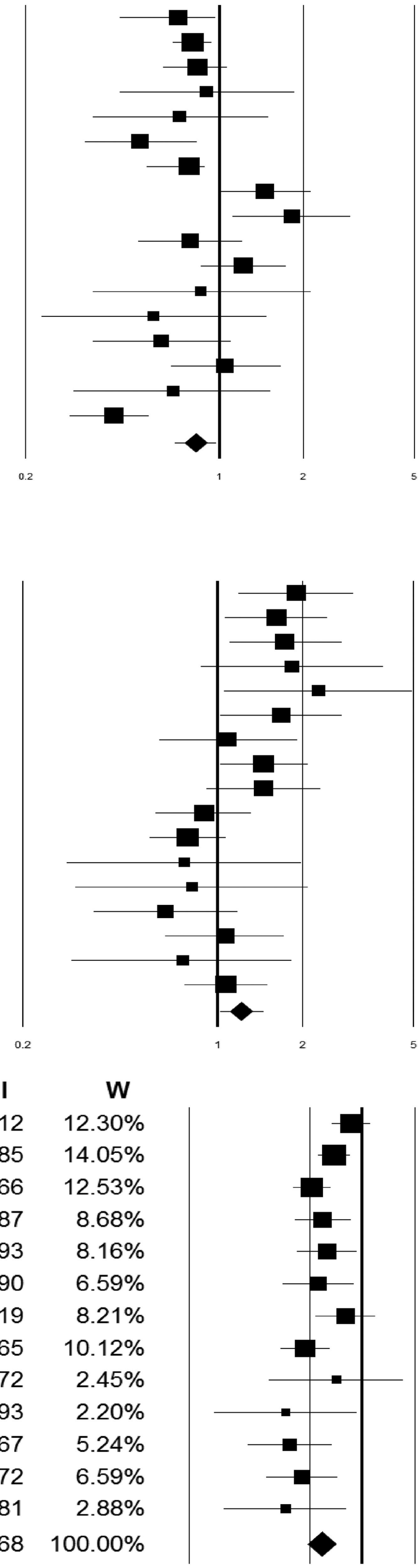

FIGURE 3 Forest plots of the association between "Healthy" (A), "Meat/Western" (B), and "Milk-dairy" (C) dietary patterns and low BMD risk. BMD, bone mineral density; ES, effect size.

TABLE 2 Stratified analysis of the bone fracture risk estimates associated with dietary patterns[1]

Dietary pattern[2]	Combined risk estimate		Test of heterogeneity			Publication bias, *P*	
	OR (95% CI)	*P*	*Q*	I^2, %	*P*	Egger test	Begg test
"Healthy"							
All ($n = 13$)	0.79 (0.66, 0.93)	0.007	154.06	92.2	<0.0001	0.235	0.625
Eastern countries[3] ($n = 5$)	0.64 (0.43, 0.97)	0.037	11.95	66.5	0.018	0.855	0.327
Western countries ($n = 8$)	0.84 (0.69, 1.02)	0.083	129.24	94.6	<0.0001	0.481	0.805
Excluding subjects <30 y[4] ($n = 12$)	0.79 (0.66, 0.95)	0.011	153.06	92.8	<0.0001	0.267	0.784
Women ($n = 6$)	0.73 (0.55, 0.96)	0.025	63.29	92.1	<0.0001	0.705	0.573
Men ($n = 4$)	0.72 (0.54, 0.96)	0.025	6.99	57.1	0.072	0.23	0.497
Hip fractures ($n = 8$)	0.71 (0.55, 0.91)	0.007	65.61	89.3	<0.0001	0.773	0.216
Women ($n = 4$)	0.70 (0.47, 1.04)	0.075	50.42	94.1	<0.0001	0.69	1.000
Men ($n = 3$)	0.64 (0.40, 1.02)	0.062	6.03	66.8	0.046	0.46	0.117
Any site fractures ($n = 5$)	0.91 (0.80, 1.04)	0.157	9.45	57.7	0.051	0.654	1.000
Cohort studies ($n = 11$)	0.82 (0.69, 0.98)	0.026	145.88	93.1	<0.0001	0.395	0.938
Older subjects ≥50 y ($n = 8$)	0.88 (0.77, 0.99)	0.038	19.09	63.3	0.008	0.126	0.621
"Meat/Western"							
All ($n = 13$)	1.11 (1.05, 1.17)	<0.001	17.45	31.2	0.133	0.753	0.329
Eastern countries[3] ($n = 5$)	1.25 (0.83, 1.89)	0.279	10.11	60.4	0.039	0.865	0.624
Western countries ($n = 8$)	1.10 (1.07, 1.14)	<0.0001	6.37	0.0	0.497	0.634	0.805
Excluding subjects <30 y[4] ($n = 12$)	1.11 (1.04, 1.18)	0.001	17.43	36.9	0.096	0.725	0.337
Women ($n = 6$)	1.13 (1.01, 1.26)	0.029	8.18	38.9	0.146	0.778	0.851
Men ($n = 4$)	1.12 (0.88, 1.42)	0.365	4.57	34.4	0.206	0.054	0.174
Hip fractures ($n = 8$)	1.15 (1.05, 1.25)	0.002	9.91	29.4	0.193	0.24	0.083
Women ($n = 4$)	1.19 (1.07, 1.32)	0.002	3.59	16.4	0.309	0.729	0.497
Men ($n = 3$)	1.22 (0.80, 1.87)	0.359	4.46	55.2	0.107	0.077	0.117
Any site fractures ($n = 5$)	1.06 (0.97, 1.16)	0.176	5.58	28.3	0.233	0.148	0.327
Cohort studies ($n = 11$)	1.10 (1.06, 1.15)	<0.0001	10.91	8.34	0.365	0.392	0.586
Older subjects ≥50 y ($n = 8$)	1.08 (1.00, 1.17)	0.044	12.45	43.8	0.087	0.931	1.000

[1] The analysis was performed when ≥3 data were available. The risk estimates were calculated through the use of the random-effects model.
[2] The number of data included in the analysis is indicated in parentheses.
[3] The risk was calculated excluding the studies conducted in Italy (22), Sweden (24), the Netherlands (25), the United States (26, 31), and Canada (29).
[4] The data on young runners reported in the study by Nieves et al. (31) were excluded.

eggs, refined grains, and sweets. These foods are plausibly the main cause of the observed adverse effect on bone mineralization and fracture risk. Thus, strong adherence to the "Western" diet involves a high intake of fat, protein, refined carbohydrates, sodium, and phosphorus (55). A high-fat diet can affect bone remineralization, reducing the absorption of dietary calcium (56), and the resulting obesity may play a role in decreasing osteoblast differentiation and bone formation (57). Adequate protein intake is essential for bone matrix formation and maintenance (58), and higher intakes of proteins are associated with a reduced risk of hip fracture (59). As animal proteins are rich in "sulfur amino acids," their metabolism contributes to endogenous acid production, and the acidic load produced is neutralized by calcium with bone resorption (60). The complex role of protein in bone health probably depends on other dietary factors and the presence of other nutrients in the diet (61). Several studies reported a reduced risk of fractures associated with a high intake of calcium and proteins (62, 63). Even though the effect of dietary protein intake alone and with supplemental calcium with or without vitamin D on bone health is related to positive trends on BMD at most bone sites, a recent meta-analysis reported insufficient evidence supporting a protective effect for fractures (64). The concept of calcium balance is more important than the amount of calcium contained in a food, and a positive balance has been demonstrated to preserve bone health (56, 58). The calciuria related to a high intake of sodium leads to increased bone remodeling and bone loss (65). Moreover, the excessive intake of inorganic phosphorus contained in food additives may affect endocrine regulation of the calcium balance (55).

In our study, the "Healthy" pattern was associated with a reduced risk of low BMD (−18%) and fractures (−21%). Healthy dietary patterns are characterized by high consumption of fruit and vegetables, which are rich in the micronutrients necessary for bone health, including potassium and magnesium, vitamin C, vitamin K, folate, and carotenoids (54, 66). Potassium and magnesium contribute to the acid-base balance in the body, preventing bone loss (67, 68) and reducing osteoporotic fracture risk (69). As a result of its many biological functions, vitamin C plays an important role in bone health, suppressing osteoclast activity and acting as a cofactor for osteoblast differentiation and collagen formation (70, 71). Carotenoids and other antioxidants reduce oxidative stress, preserving bone health (72); vitamin K is involved in bone health and osteoporosis prevention (73), whereas the risk of fractures associated with hyperhomocysteinemia is indirectly affected by folate and vitamin B-12 (74, 75). Healthy dietary patterns are also characterized by high intake of fish and seafood, which are rich in PUFAs, especially n−3 (ω-3) fatty acids, which are known to have an anti-inflammatory impact that benefits bone (76).

TABLE 3 Stratified analysis of the low BMD risk estimates associated with dietary patterns[1]

	Combined risk estimate		Test of heterogeneity			Publication bias, *P*	
Dietary pattern[2]	**OR (95% CI)**	***P***	***Q***	**I^2, %**	***P***	**Egger test**	**Begg test**
"Healthy"							
All (*n* = 17)	0.82 (0.69, 0.98)	0.028	47.6	66.4	<0.0001	0.897	0.742
DXA only[3] (*n* = 13)	0.81 (0.73, 0.90)	0.0001	12.2	1.5	0.431	0.561	0.329
Eastern countries[4] (*n* = 11)	0.88 (0.66, 1.16)	0.367	42.5	76.5	<0.0001	0.845	0.938
Gender							
Women (*n* = 7)	1.14 (0.90, 1.44)	0.281	10.2	40.9	0.119	0.348	0.453
Both sexes (*n* = 8)	0.69 (0.57, 0.82)	<0.0001	15.7	55.5	0.028	0.311	0.138
Bone site							
Femur (*n* = 3)	0.82 (0.58, 1.16)	0.267	0.1	0.0	0.95	0.348	0.602
Lumbar spine (*n* = 6)	0.87 (0.70, 1.07)	0.185	7.42	32.6	0.192	0.962	0.851
Whole body (*n* = 3)	0.70 (0.51, 0.96)	0.026	3.01	33.5	0.222	0.574	0.602
Younger (*n* = 5)	0.62 (0.44, 0.89)	0.009	9.36	57.3	0.053	0.918	0.624
Both sexes (*n* = 4)	0.61 (0.40, 0.94)	0.023	9.34	67.9	0.025	0.893	0.497
Excluding subjects <30 y (*n* = 12)	0.91 (0.75, 1.09)	0.289	29	62	0.002	0.644	1.000
Gender							
Women (*n* = 7)	1.14 (0.90, 1.44)	0.281	10.2	40.9	0.119	0.348	0.453
Both sexes (*n* = 4)	0.76 (0.66, 0.88)	<0.001	3.47	13.5	0.325	0.232	0.042
Bone site							
Lumbar spine (*n* = 5)	0.89 (0.71, 1.11)	0.293	6.76	40.8	0.149	0.794	1.000
"Meat/Western"							
All (*n* = 17)	1.22 (1.02, 1.45)	0.028	32.5	50.8	0.009	0.749	0.934
DXA only[3] (*n* = 13)	1.20 (0.95, 1.53)	0.132	30	60	0.003	0.693	0.903
Eastern countries[4] (*n* = 11)	1.00 (0.85, 1.18)	0.957	12.6	20.9	0.245	0.507	0.586
Gender							
Women (*n* = 7)	1.21 (0.92, 1.59)	0.181	14.7	59.2	0.023	0.069	0.099
Both sexes (*n* = 8)	1.38 (1.12, 1.71)	0.002	9.42	25.7	0.224	0.444	0.458
Bone site							
Femur (*n* = 3)	1.05 (0.65, 1.70)	0.829	3.21	37.7	0.201	0.761	0.602
Lumbar spine (*n* = 6)	1.07 (0.74, 1.53)	0.733	14	64.2	0.016	0.619	0.851
Whole body (*n* = 3)	1.50 (1.01, 2.22)	0.042	2.8	28.7	0.246	0.045	0.117
Younger (*n* = 5)	1.00 (0.77, 1.29)	0.991	1.13	0.0	0.89	0.037	0.142
Both sexes (*n* = 4)	1.02 (0.78, 1.34)	0.864	0.71	0.0	0.871	0.123	0.042
Excluding subjects <30 y (*n* = 12)	1.31 (1.05, 1.64)	0.015	29	62.1	0.002	0.155	0.337
Gender							
Women (*n* = 7)	1.21 (0.92, 1.59)	0.181	14.7	59.2	0.023	0.069	0.099
Both sexes (*n* = 4)	1.73 (1.37, 2.17)	<0.0001	0.3	0.0	0.96	0.545	0.497
Bone site							
Lumbar spine (*n* = 5)	1.10 (0.74, 1.64)	0.642	13.8	70.9	0.008	0.453	0.624
"Milk/dairy"							
All (*n* = 13)	0.59 (0.50, 0.68)	<0.0001	22	45.3	0.038	0.113	0.464
DXA only[3] (*n* = 10)	0.57 (0.47, 0.70)	<0.0001	21.8	58.6	0.01	0.177	0.788
Eastern countries[5] (*n* = 10)	0.54 (0.47, 0.63)	<0.0001	9.44	4.71	0.397	0.367	0.421
Gender							
Women (*n* = 5)	0.57 (0.46, 0.70)	<0.0001	5.4	25.9	0.249	0.851	1.000
Both sexes (*n* = 6)	0.64 (0.52, 0.79)	<0.0001	10.3	51.2	0.068	0.574	0.573
Bone site							
Lumbar spine (*n* = 5)	0.50 (0.38, 0.66)	<0.0001	8.48	52.8	0.076	0.057	0.624
Younger (*n* = 4)	0.54 (0.40, 0.72)	<0.0001	2.24	0.0	0.525	0.457	0.497
Both sexes (*n* = 3)	0.57 (0.41, 0.79)	<0.0001	1.17	0.0	0.557	0.752	0.602
Excluding subjects <30 y (*n* = 9)	0.60 (0.50, 0.71)	<0.0001	18.9	57.7	0.015	0.232	0.297
Gender							
Women (*n* = 5)	0.57 (0.46, 0.70)	<0.0001	5.4	25.9	0.249	0.851	1.000
Both sexes (*n* = 3)	0.67 (0.51, 0.89)	0.005	8.27	75.8	0.016	0.995	0.602
Bone site							
Lumbar spine (*n* = 4)	0.52 (0.39, 0.69)	<0.0001	7.58	60.4	0.056	0.069	0.174

[1] The analysis was performed when ≥3 data were available. The risk estimates were calculated through the use of the random-effects model. BMD, bone mineral density.
[2] The number of data included in the analysis is indicated in parentheses.
[3] The risk was calculated excluding the studies in which BMD was estimated by measuring the speed of sound by ultrasound bone densitometry (35, 37, 40).
[4] The risk was calculated excluding the studies conducted in Australia (33), Mexico (34), and Iran (41).
[5] The risk was calculated excluding the studies conducted in Mexico (34).

Other characteristic components of a healthy dietary pattern are poultry and whole grains. Indeed, substituting red meat intake with poultry and fish is associated with a healthier inflammatory biomarker profile (77, 78), which is relevant as inflammation is associated with the overproduction of various cytokines and leads to excessive bone degradation and bone loss (79, 80). Moreover, a high consumption of whole grains, providing beneficial nutrients for bone health (81), is also related to lower inflammatory levels (78).

High adherence to the "Milk/dairy" pattern is positively associated with a reduced (−41%) risk of low BMD. Dairy products are rich in calcium and magnesium, both of which play a structural role in bone health and are a relevant source of proteins, vitamin D, vitamin B-12, riboflavin, zinc, and potassium (10, 65, 82). Vitamin D not only stimulates the absorption of calcium but is also related to BMD and bone turnover. Vitamin D deficiency leads to mineralization defects, osteoporosis, and fractures (83). Milk and dairy products showed a significant inverse association with bone turnover markers and a positive association with bone mineralization. Moreover, fortified dairy products induce more favorable changes and more beneficial effects on bone metabolism than does calcium supplementation alone (10).

The main limitation of this meta-analysis is that dietary patterns, other than the 3 we discussed ("Healthy," "Meat/Western," and "Milk/dairy"), could be related to bone health. Moreover, other limitations are represented by the difference in population, site, and method of BMD measurement and covariates, resulting in heterogeneity. The high heterogeneity may be correlated to the wide variability in dietary data collection and analysis, in the identification of the dietary patterns, and in the various and not uniformly adjusted confounding factors used to estimate the risk. In particular, the identification of dietary patterns is influenced by methodologic issues, such as the classification of foods into groups, the number of factors and the assessment method used (FA and PCA are subjective techniques with opportunities for variation at almost every step) (15). In our analysis, heterogeneity is more evident in the results regarding the "Meat/Western" pattern, probably due to the difficulty in characterizing this pattern. Other limitations could be linked to the fact that pooled findings were directly driven by the included studies, which present their own weaknesses in study design. Hence, these aspects may have affected the reproducibility of the associations between dietary patterns and bone outcomes. In addition, risk estimates were adjusted for different potential confounders. Because dietary intakes vary greatly in relation to sex, race/ethnicity, and societal factors, it has been necessary to consider our findings in different geographic contexts. We analyzed the impact of adherence to the "Healthy" and "Meat/Western" pattern in Eastern and Western countries. No significant association was identified between the identified dietary pattern and the geographic context for low BMD risk. We found a significant preventive effect of the "Healthy" pattern on fracture risk in Eastern countries (−37%). Notably, in Western countries, where the adherence to the "Meat/Western" pattern is strongest, this pattern significantly increased fracture risk (+10%), whereas in Eastern countries this association lost significance. To further advance this field of research, and considering that all the studies included in this meta-analysis were cross-sectional, future studies are needed to determine the impact of dietary patterns upon BMD loss. In addition, it will be important to further investigate the association between dietary patterns and bone health in different geographic contexts not yet described.

In conclusion, a beneficial impact on bone health is attributed to the "Healthy" and "Milk/dairy" patterns, which emphasize the intake of fruit, vegetables, whole grains, poultry and fish, nuts and legumes, and low-fat dairy products and avoid the consumption of soft drinks, fried foods, meat and processed products, sweets and desserts, and refined grains. In contrast, the unhealthy "Western" dietary pattern is inversely associated with bone health. Overall, adherence to a healthy dietary pattern consisting of the aforementioned food groups can improve BMD and decrease fracture risk (84). Nutrition is an important modifiable factor that affects bone health (low BMD and fracture). Considering that most of the osteoporotic fractures occur among women (85), and the strongest impact of dietary patterns on fractures among older women observed in our study, much emphasis should be placed on the importance of a healthy dietary pattern in this population. Public health efforts to adopt healthy dietary patterns and to provide guidance for nutritional intervention may reduce the burden and disability of low BMD and osteoporotic fractures.

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