



# A meta-analysis of dietary inflammatory index and bone health status

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## Abstract

**Background** The inflammatory potential of diets is associated with several diseases and can affect bone health. We aimed to systematically review and pool the current evidence on the association of DII with bone health in observational studies.

**Methods** We searched PubMed and NLM Gateway (for Medline), Web of Science, Scopus and EMBASE up to December 16, 2020 for studies that examined the relationship between DII score and bone mineral density (BMD) or fracture. All observational studies were included in this meta-analysis. Heterogeneity between studies was evaluated using Cochran Q-statistic and I<sup>2</sup> statistics. Random effect meta-analysis method was used to pool the effect size. Stratified meta-analysis according to the type of study (cohort/ non-cohort) was performed to assess the relationship of DII with BMD and fracture.

**Results** In total, 13 articles were included in the present systematic review, including five cohorts, five cross-sectional, and three case-control studies. The total sample size of these studies was 211,938 individuals aged 5 to 85 years. According to random-effect meta-analysis, DII was associated with increased odds of fracture in non-cohort studies (pooled OR=1.42, 95%CI: 1.17, 1.67), but this association was not statistically significant in cohort studies (pooled OR=1.03, 95%CI: 0.97, 1.09). Moreover, only in non-cohort studies, the mean of BMD in subjects in the highest DII category was significantly lower than those in the lowest DII category (SMD: -9.59, 95%CI: -10.84, -8.33).

**Conclusions** Our findings showed that high score of DII can have devastating effects on bone health. Further longitudinal studies are necessary to confirm these findings among more diverse populations.

**Keywords** Dietary inflammatory index · Bone mineral density · Fracture · Meta-analysis · Osteoporosis

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## Introduction

Osteoporosis is an age-related metabolic bone disease characterized by bone mass reduction and alteration of bone architecture, which is the main risk factor of bone fragility and fracture [1]. The increasing prevalence of osteoporosis is a major concern of public health worldwide because of the increase in life expectancy and old age population [2]. It has been estimated that the number of people suffering from osteoporosis are more than 200 million in the world. According to the recent International Osteoporosis Foundation (IOF) report, 1 in 2 women over the age of 50 years and 1 in 5 men will experience osteoporotic fractures in their lifetime [3]. Osteoporosis and its related fracture impose a growing economic burden on affected individuals and the healthcare system [4].

Numerous risk factors including genetic and environmental susceptibility factors have been proposed to increase osteoporosis and fracture risk. Dietary pattern and nutrients

intake are the modifiable non-pharmacologic risk factors that improve bone health [5].

Chronic low grade of inflammation in the body is associated with increased risk of disorders including obesity [6], cancer [7], diabetes and metabolic syndrome [8], as well as poor bone health and age-related sarcopenia [9]. Dietary inflammatory index (DII) is a literature-based scoring system that determines the potential inflammatory status of an individual's diet based on the pro-and anti-inflammatory status of many specific foods and nutrients in the diet. A higher DII score represents a more pro-inflammatory diet, while a lower DII score indicates a more anti-inflammatory diet [10]. The first time, DII scores were introduced to the medical literature by Cavicchina [11] and colleges and then updated by Shivappa in 2017 [10]. In the generation of DII score, more than 1900 relevant articles published in the peer-reviewed journals were assessed to find the positive or negative association of nutrients and foods with specific inflammatory markers such as CRP [12], TNF-alpha [13], IL-1beta, IL-4, IL-6 and IL-10 [10, 14].

Although some previous studies reported an inverse association of high DII with lower BMD or increased fracture risk, other studies showed no association. In addition, there is inconsistency regarding the relationship between DII score and bone health status between men and women. Resent umbrella review confirmed that although several systematic review and meta-analysis studies have been assessed the relationship between DII and health outcomes [15], none of them evaluated the association of DII with bone health outcomes. Therefore, the current study conducted for systematically reviewing the evidence and a meta-analysis to pool the findings.

## Methods

### Search strategy

To identify the eligible studies for this systematic review, relevant studies were selected through searching Web of Science, PubMed and NLM Gateway (for Medline), Scopus, and before December 16, 2020. We used the following keywords in this review: (“dietary inflammatory index” OR “pro-inflammatory diet” OR “anti-inflammatory diet” OR “pro-inflammatory dietary pattern” OR “anti-inflammatory dietary pattern” or “Inflammatory potential of diet”) AND (“osteoporosis” or “bone mineral density” or “BMD” or “bone mass” or “osteopenia” or “fracture risk” or “fracture”). The search had no restriction on publication date or language. In addition, the reference lists of relevant publications were reviewed to avoid missing any published data. The study protocol was registered in the international prospective register of systematic reviews database

[<http://www.crd.york.ac.uk/> PROSPERO, registration no: 2018CRD42018104324].

### Inclusion and exclusion criteria

The present study was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) protocol [16]. All observational studies that investigated the association between DII and bone health status, including BMD and fracture were eligible for inclusion. Studies that reported correlation coefficient, odds ratio (OR), hazard ratio (HR), standardized mean difference (SMD), along with 95% confidence interval (CI) for the association of DII with BMD changes or fracture were included in our meta-analysis. We excluded letters, comments, narrative reviews, and studies on nonhumans, and duplicated studies. The details of the study selection process are shown in Fig. 1.

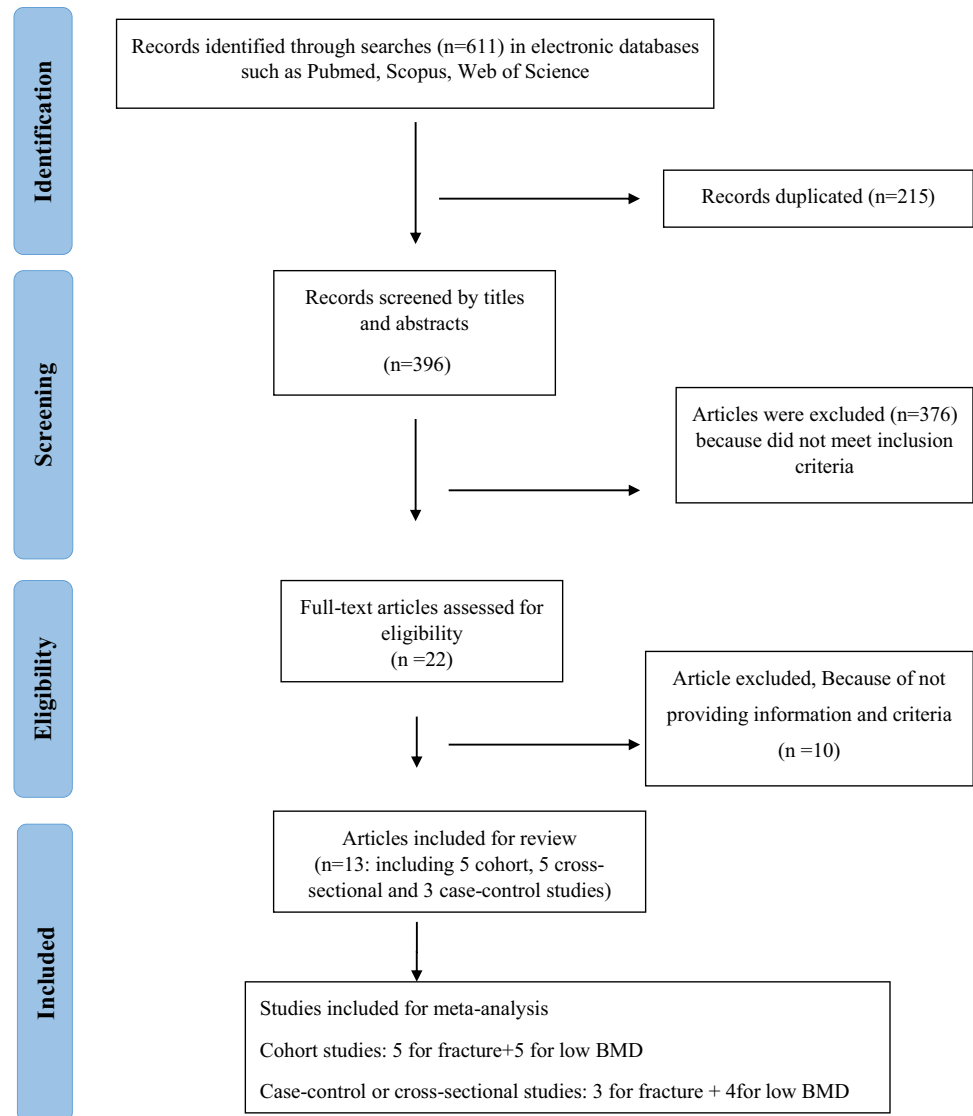
### Data extraction

Two reviewers independently assessed the titles, abstracts and full texts of articles retrieved from the systematic searches. All articles that clearly did not meet the inclusion criteria were rejected. The selected articles were analyzed by reading the full text, and the eligible ones were then identified. In all refinement steps if there was disagreement between the two reviewers during the study selection process, the issue was resolved through discussion or in consultation with a third reviewer.

Data were extracted using a checklist, which was included the following information: first author, country, mean age, gender, sample size, study population, type of study, duration of follow up (for cohort studies), the tool for assessing DII, unit of comparison of DII (categorical/continuous), bone health status (BMD/fracture) and methods of measurement, relevant effect size (OR, HR, Beta coefficient, Pearson correlation and SMD), and adjusted confounders. If a study reported both outcomes (BMD and fracture), it was considered as two separated studies in the meta-analysis.

### Assessment of study quality

The quality of studies was assessed using the Newcastle-Ottawa Quality Assessment Scale designed for cohort, case-control, or cross-sectional studies [17]. This scale consists of three portions of the selection, comparability, and outcomes/exposures, and studies earned maximum nine points. According to this scale, nine stars can be allocated to each study. In the present study, the publications with Newcastle-Ottawa scale  $\geq 7$  were considered high quality.

**Fig. 1** Flow diagram of the study selection process

## Statistical analysis

Heterogeneity between studies was assessed using Chi-square-based Q test and  $I^2$  statistics. Due to severe heterogeneity between studies, random effect meta-analysis proposed by Der-Simonian and Laird was used to pool the effect size. OR and HR with their 95% CI were used as effect size for the association of DII with fracture. Association of DII with BMD was presented as SMD with 95% CI. Publication bias was evaluated using Egger's tests, and the results of Egger's test were statistically significant at  $P < 0.1$ . Stratified meta-analysis according to the type of study (cohort/ non-cohort), sex, and definition of DII (categorical/ continuous) was performed to assess the association of DII with BMD and fracture. Sensitivity analysis was performed to assess the effect of removing any of the studies or group of studies on the pooled estimate. All the Analyses were conducted using

the statistical software STATA 11.0 (Stata Corp., College Station, TX, USA) for the meta-analysis.

## Results

### Findings from the systematic review

A flow diagram for the process of studies selection is presented in Fig. 1. Out of 611 articles in the initial search, after excluding 215 articles for duplication, 396 articles were screened by title and abstracts. Of these, finally, 13 articles fulfilled our inclusion criteria, including five cohorts, five cross-sectional, and three case-control studies in the present systematic review. These studies included 211,938 individuals with the age range of 5 to 85 years. The selected articles were published between 2016 and 2019. The duration of

cohort studies to investigate the association of DII and fracture varied from 7.9 to 11.4 years, while this duration for DII and BMD varied 5 months to 10 years. Out of these studies, five studies were conducted in the USA, two in Korea, two in China, one in Australia, one in Brazil, one in Spain, and one in Iran. Eight studies were performed on both males and females, and four studies on females. Four studies reported results for the association of DII score with fracture, three studies for BMD, and one study provided data for the association of DII with both fracture and BMD. In addition, three studies mentioned other markers of bone health status, including knee osteoarthritis, QUS of the right calcaneous, and cortical bone peripheral. In most studies, BMD was measured by X-ray absorptiometry (DXA), except in one study in which BD was measured by QUS. The fracture was assessed in the hip, lower arm, wrist, spine, non-vertebral, and total.

Regarding the studied population, two studies have been conducted on postmenopausal women, four studies on healthy adults, one study on healthy adolescents, two studies on older adults, one study on subjects at risk of osteoarthritis, and 1 study on lactating women. The score of DII was assessed by food frequency questionnaire (FFQ) with different number items, including 48-item FFQ to 168-items FFQ in eight studies. Three studies used 24-hour recall, and two studies used 72- hours recall questionnaire to calculate the DII score. In all included studies, DII was categorized as tertile, quartile, and quintile. However, in five studies, DII was considered as continuous value.

### Finding from meta-analysis

As noted above, four cohort studies were regarding the association of DII and fracture. Orchard et al., measured risk of fracture in total, hip and lower arm and Kim et al., study that measured risk of total fracture in females and in both gender were considered as three and two separate studies, respectively. In Verones et al., study the association of fracture were assessed with DII as per 1SD and as comparison Q5to Q1 of DII in males, females and both gender. Therefore, the results of this study were included in the meta-analysis as six separate studies. Cervo et al., the study evaluated the risk of fracture in two bone sites in males and females. Finally, 15 studies were included in systematic review. The total sample size of included studies was 174,882 subjects in cohort studies and 22,687 subjects in non-cohort studies. However, the association between DII and risk of fracture was not statistically significant in the cohort (pooled OR=1.03, 95%CI: 0.97-1.09, I<sub>2</sub>=75.5, P<0.001), in non-cohort studies, DII was associated with an increased risk of fracture (pooled OR=1.42, 95%CI: 1.17-1.67, I<sub>2</sub>=55.9, P=0.04). The analysis of DII score as a categorical variable also showed that individuals with the highest score of DII were 53% more prone

to experience fracture than subjects who had the lowest DII score (Tables 1, 2, 3 and 4).

The results of the Egger test for association of DII with fracture show that publication bias does not exist (coefficient: 0.96; P = 0.25), and the funnel plot was symmetric.

Moreover, according to random-effect meta-analysis, the mean of BMD in subjects in the highest DII category was significantly lower than those in the lowest DII category (SMD: -9.59, 95%CI: -10.84,-8.33) in non-cohort studies. In cohort studies this association was not statistically significant (SMD: 0.141, 95%CI: -0.08, 0.36).

### Quality assessment

The quality assessment of included studies was performed by two independent reviewers using Newcastle–Ottawa Scale (NOS). Any discrepancy between reviewers was resolved by a third reviewer. The qualitative assessment results showed that six studies had a high quality, and the remains had a moderate quality. Also, no low quality studies were observed.

### Sensitivity analysis

Sensitivity analysis showed that excluding any individual studies could not significantly change the pooled estimate of DII association with fracture and BMD.

### Discussion

The results of our study revealed that DII was associated with bone health outcomes (fracture and BMD). The risk of fracture was significantly higher in individuals who had the most pro-inflammatory diet (highest DII score) in comparison with those with an anti-inflammatory diet (lowest DII score). Moreover, the mean of BMD in subjects in the highest DII category was significantly lower than those in the lowest DII category. Dietary intake is one of the main environmental determinants of the inflammatory status of the body. DII is the literature-derived tool, which is generated by the association of nutrients and inflammatory markers, including pro- and anti-inflammatory foods.

By evaluating the other indexes of healthy dietary patterns such as Mediterranean diet, DASH, or HEI by using the pro-and anti-inflammatory categories of foods in DII, it is revealed that individuals with low DII score more probably consume healthy dietary patterns with more anti-inflammatory and antioxidant nutrients [29–31]. In evaluating of DII score, foods including red or processed meat, French fries, hydrogenated fats, which are known as unhealthy foods, are considered in pro-inflammatory group. Moreover, healthy foods such

**Table 1** Studies included in systematic review and meta-analysis of DII and fracture

First author (year)	country	Mean (SD) age (range)	gender	Sample size	Study population (health status)	Type of study	Follow up (number of incident case)	Dietary inflammatory index tool	Unit of comparison	Bone health status (methods of measurement)	Effect size measure (95%CI)	Adjusted for*
T.Orchard (2017)[18]	USA	63 (50-79)	F	10,290	Postmenopausal women	Cohort	11.4±3.3 y (total=47,974 hip=3738)	122- item FFQ	Q4 vs. Q1 (2.98 vs. -3.63)	Hip fracture (self-reported or medical record) Lower arm fracture (self-reported or medical record) Total fracture (self-reported or medical record)	HR= 1.02 (0.92-1.14) HR* = 0.92 (0.86-0.98) HR* = 0.95 (0.92-0.98)	1,2,3,4,5,6,7,8,9, 10,11,12,13,14,15, 16,17,18,19
N. Veronese (2017)[19]	USA	60.6 (9.1) 45-79	F/M	3648 M=1577 F=2071	With or at risk of knee osteoarthritis	Cohort	8 y (560= 198 M, 362 F)	70- item FFQ	Per 1-SD increment DII (1.68 points) Q5 vs. Q1	Fracture (self-reported)	F HR* = 1.14 (1.02-1.27) M HR= 0.95 (0.82-1.11) Overall HR=1.22 (0.91-1.64) F HR* = 1.46 (1.02-2.11) M HR=0.91 (0.54-1.54)	1, 2, 3, 4, 21, 24, 26,27,28,29
H.S kim (2018)[20]	Korea	52.34(8.24) 40-79	F/M	159,846 M=57,740 F=102,106	Healthy adults	Cohort	7.9 years (2572= 148 M, 2424 F)	106- item FFQ	Q5vs.Q1 (-9.12 to -0.98) vs. (2.1762 to 7.1055)	Fracture (self-report )	Total HR* = 1.33 (1.12-1.58) F HR* = 1.33 (1.11- 1.59) M HR=1.32 (0.64-2.71)	1, 3, 4, 5, 14, 26,30, 31

Table 1 (continued)

First author (year)	country	Mean (SD) age (range)	gender	Sample size	Study population (health status)	Type of study	Follow up (number of incident case)	Dietary inflammatory tool	Unit of comparison	Bone health status (methods of measurement)	Effect size measure (95%CI)	Adjusted for*
MM.Cervo (2019)[21]	Australia	63.0 (7.5) 51-79	F/M	1098 M=559 F=538	Non-institutionalized older adults	Cohort	10 years (total=566)	74-item FFQ	1- unit increase in E-DII	Any fracture (self-report) Non-vertebral fracture (self-reported)	M HR* = 1.090 (1.011-1.017) F HR* = 0.878 (0.800-0.964) M HR = 1.074 (0.995-1.159) F HR = 0.911 (0.827-1.003)	1,4,31,32,34,35
ZQ.Zhang (2017)[22]	70.62 (7.55) 52-83	F/M	2100 F=781 M=269	Elders	Case-control (case=1050 control=1050)	NA	79- item FFQ	Q4 vs. Q1	Hip fracture (self-report)	Total OR* = 2.44 (1.73-3.45) Female OR* = 2.08 (1.38-3.12) Male OR* = 4.30 (1.89-9.80)	3, 4, 5, 8, 21, 23, 27,32	
M. Mori-moto (2019)[23]	Brazil	57.9 (13.5) ≥40	F/M	2269 F=1585 M=684	Healthy adults	Cross-sectional	NA	24-hr recall	Q4 vs.Q1 (>1.89 vs. ≤0.49)	low impact fracture (self-report)	OR: 0.98 (0.8-1.21)	
M. Mazidi (2017)[24]	USA	47.43 (0.27)	F/M	18,318 F= 8921 M=9397	Healthy adults	Cross-sectional	NA	24-h diet recall	Q4 vs. Q1	Hip fracture* Wrist* spine*	OR;1.00(0.94-1.06) OR;1.03(0.97-1.09) OR;1.00(0.94-1.07)	1,2,3,4,5,21,33

QUS: Quantitative ultrasonometry, Y: years, F: females, M: males, M: males, FFQ: food frequency questionnaire, HR: hazard ratio, OR: odds ratio, Q: quartile, T: tertile, DII: dietary inflammatory index, E-DII: Energy adjusted dietary inflammatory index, BD: Bone density

\* 1-age, 2-race, 3- BMI, 4-smoking, 5- physical activity, 6-DII (baseline),7-CT(clinical trial assignment), 8-parental history of fracture, 9-personal history of fracture at age 55 years or older, 10-region, 11-diabetes, 12-female hormone use, 13-NSAID use, 14-total calcium intake, 15- corticosteroid use (screening), 16-inflammatory bowel disease,17- rheumatoid arthritis, 18-weight, 19-height, 20- parity, 21- education, 22- fragility fracture history, 23- supplement intake, 24-antiresorptive drug use, 25- age at menarche, 26- total energy intake, 27-yearly income,28-Charlson comorbidity Index,29-physical activity scale for the elderly, 30-gender, 31-alcohol consumption, 32- calcium supplement, 33-C-reactive protein, 34-percentage body fat, 35- step per day,36-baseline T-score, 37- feeding modes, 38- time of complementary foods, 39-stage of sexual maturation, 40-muscle cross-sectional area., 41-postmenopausal period, 42- vitamin D, 43- CES-D, 44-use of medications for Knee OA



as fruits, vegetables and fish oils are categories as anti-inflammatory foods [32]. In considering single nutrients or foods individually, the results of a National survey on the Korean population showed that fat consumption (pro-inflammatory item) was an independent predictor of osteoporosis [33]. In another study, a low chance of having low BMD was observed in adolescents with high consumption of milk and cereals in their dietary pattern [34]. In other studies, low dietary intake of folate, total fibers, vitamin B6, potassium, vitamin A and foods such as milk and cereals were correlated with high likelihood of having low BMD [35, 36].

Other studies have reported that better adherence to the Mediterranean diet was associated with a lower risk of bone fracture [37]. Similar results were found regarding DASH and HEI with decreasing the risk of fracture [38].

There is a growing body of literature reporting positive correlation between pro-inflammatory foods such as red or processed meat, butter, and saturated fats or oils with the increased blood circulation of inflammatory markers including C-reactive proteins (CRP), TNF-alpha, E-selectin, soluble vascular cell adhesions molecules [39, 40]. It is well established that rheumatoid arthritis [41] and cystic fibrosis as chronic inflammatory diseases negatively affect bone health status [42]. In addition, as we know, low grade inflammation in the body potentially increases the risk of chronic disorders such as diabetes, insulin resistance, cancer, metabolic syndrome, asthma, cardiovascular disease, and also osteoporosis which is the main risk factor of bone fracture [43]. Consistent with this hypothesis, previous studies have shown that serum level of TNF-gamma is positively and the neutrophil/lymphocyte ratio (NLR) is negatively correlated with BMD [44]. Inflammatory cytokines such as TNF-alpha, CRP, increase the activity of osteoclasts. In addition, systematic inflammation in the body may elevate the osteoclast activities by endorsing ligand-RANK release [45]. As we know, calcium and vitamin D are the main dietary factors that influence the health status of bones. It was demonstrated that increased inflammation in the intestinal decreases the absorption of calcium and phosphorous by up regulating the synthesis of 1,25(OH)2D and suppressing the expression of vitamin D receptors [46].

To the best of our knowledge, this study was the first meta-analysis that assessed the relationship between DII score and bone health outcomes, including low BMD and fracture risk. This study has some limitations. In this review, we included all types of studies and analysis separately as cohort and non-cohort studies. The first limitation of this review measured the low BMD and risk of fracture in the different bone sites in included studies.

## Conclusions

Our findings showed that high score of DII can have devastating effects on bone health. Further longitudinal studies are necessary to confirm these findings among more diverse populations. This knowledge could have implications for dietary advice provided to those at risk of osteopenia or osteoporosis. Further research is warranted to confirm these findings among more diverse populations.

**Authors' contributions** HA and MQ contributed to the conceptualization of the systematic review. ET, AM and JM conducted the data sereaching. HA, ET, JM and AM conducted the data screening and quality assessment. ET and HA conducted the data extraction and drafted the manuscript. MQ performed meta-analysis and drafted the manuscript. All authors provided critical review of drafts and have read and approved the final manuscript.

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**Data availability** No additional data are available.

## Declarations

**Ethics approval and consent to participate** This systematic review and meta-analysis study was not performed on human or animal subjects. The Ethics council of National Institute for Medical Research Development (NIMAD), Tehran, Iran.

**Consent for publication** Not applicable.

**Competing interests** Ehsaneh Taheri, Armita Mahdavi-Gorab, Jalal Moloudi, Hamid Asayesh, Mostafa Qorbani declare that they have no conflict of interest.

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**Table 2** Studies included in systematic review and meta-analysis of DII and BMD

First author (year)	country	Mean age (range)	gender	Sample size	Study population (health status)	Type of study	Follow up (number of incident case)	Dietary inflammatory index tool	Unit of comparison	Bone health status (methods of measurement)	Effect size measure (95%CI)	Adjusted for*
T. Orchard (2017)[18]	USA	63 (50-79)	F	8303	Postmenopausal women	Cohort	6 years	122-item FFQ	Q4 vs. Q1	BMD (DXA) Hip	After multivariable adjustment, women with the least inflammatory dietary pattern (Q1) had a more positive overall change in hip BMD ( <i>p</i> for linear trend < 0.001)	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19
MMi,Cervo (2019)[21]	Australia	63.0 (7.5) 50-79	F/M	1098	Non-institutionalized older adults	Cohort	10 years	74-item FFQ	1 - unit increase in E-DII	BMD (DXA) Femoral neck Total Hip lumbar spine (DXA)	M B=-0.001 (-0.008 to 0.006) F B=-0.002 (-0.009 to 0.005) M B=-0.009 (-0.017 to -0.000) F B=-0.007 (-0.016 to 0.001) M B=-0.013 (-0.024 to -0.002) F B=-0.009 (-0.019 to 0.001)	1,4,31,32,34,35



**Table 2** (continued)

First author (year)	country	Mean age (range)	gender	Sample size	Study population (health status)	Type of study	Follow up (number of incident case)	Dietary inflammatory tool	Unit of comparison	Bone health status (methods of measurement)	Effect size measure (95%CI)	Adjusted for*
Y.Zhou (2019)[25]	china	31.72 (4.50)	F	150	Lactating women	Cohort	5 months	48-item FFQ	DII Tertiles	BD (QUS)	Mean (SD) BD changes T1: 0.05 (0.3) T2: 0.00 (0.3) T3: -0.1 (0.4)	3,5,21,26,36,37,38
N.Shivappa (2016)[26]	Iran	60 (8.4) 50-85	F	160	Postmenopausal women	Cross-sectional	NA	168-item FFQ	DII (continuous) DII > -0.06 vs. DII ≤ -0.06	BMD(DXA) lumbar spine femoral neck lumbar spine femoral neck	OR*=1.64 (1.11- 2.43) OR=1.29 (0.86- 1.93) OR*=2.30 (1.05- 5.07) OR=1.22 (0.55- 2.72)	1,3,4,5,9, 12, 20, 21,23,24,25
M. Mazidi (2017)[24]	USA	47.43 (0.27)	F/M	18,318 M=9397 F=8921	Healthy adults	Cross-sectional	NA	One 24-h diet recall	Q1 vs Q4	BMD (DXA)	Standardized mean difference of BMD	1,2,3,4,5,21,33
W.Na (2019) [27]	Korea	63.65 (8.44) ≥50	F	2778	Postmenopausal women	cross-sectional study	NA	24-h dietary recall	DII Tertiles T1 (-5.15 to 0.84) vs. T3 (3.05 to 6.35)	BMD (DXA) Total femur Femur neck Lumbar spine (L1-L4)	OR= 1.27 (1.00-1.62) OR*= 1.43 (1.10-1.86) OR= 1.11 (0.87-1.49)	1,3,4,5,12,27,32,41,42

Y: years, F: females, M:males, FFQ: food frequency questionnaire, HR: hazard ratio, Q: quartile, T: tertile, DII: dietary inflammatory index, E-DII:Energy adjusted dietary inflammatory index, BD: Bone density  
QUS: Quantitative ultrasonometry

\* 1-age, 2-race, 3- BMI, 4-smoking, 5- physical activity, 6-DII (baseline),7-CT(clinical trial assignment), 8-parental history of fracture, 9-personal history of fracture at age 55 years or older, 10-region, 11-diabetes, 12-female hormone use, 13-NSAID use, 14-total calcium intake, 15- corticosteroid use (screening), 16-inflammatory bowel disease,17- rheumatoid arthritis, 18-weight, 19-height, 20- parity, 21- education, 22- fragility fracture history, 23- supplement intake, 24-antiresorptive drug use, 25- age at menarche, 26- total energy intake, 27-yearly income,28-Charlson comorbidityIndex,29-physical activity scale for the elderly, 30-gender, 31-alcohol consumption, 32- calcium supplement, 33-C-reactive protein, 34-percentatge body fat, 35- step per day,36-baseline T-score, 37- feeding modes, 38- time of complementary foods, 39-stage of sexual maturation, 40-muscle cross-sectional area., 41-postmenopausal period, 42- vitamin D, 43- CES-D, 44-use of medications for Knee OA

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**Table 3** Quality assessment of included studies on dietary inflammatory index and bone health

Cohort Studies										
Author/year	Representativeness of exposed cohort	Selection of no exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Study controls for age, sex, and marital status	Study controls for any additional factors	Assessment of outcome	Followed up long enough for outcome to occur (> 15 years)	Adequacy of follow-up of cohort	Total score
T. Orchard (2017)[18]	*	*	*	*	-	*	*	-	*	7
N. Veronese (2018)[19]	*	*	*	-	*	*	*	-	*	7
H.S kim (2018)[20]	*	*	*	*	*	*	*	-	*	8
Yalin Zhou (2019)	-	*	*	*	*	*	*	-	-	6
N. Veronese (2018) [19]	*	-	*	*	*	*	*	-	-	6
MM.Cervo (2019)[21]	*	-	*	*	*	*	*	-	*	7
Zhou (2019)[25]	-	*	*	*	*	*	*	-	-	6
Case-Control Studies										
Zhang ZQ (2017)[22]	*	*	*	*	-	*	*	*	-	7
Cross-Sectional Studies										
Author/year	Representativeness of the sample	Representativeness of cases	Selection of controls	Definition of controls	Ascertainment of (risk factor)	Study controls for any additional factor	Assessment of exposure	Assessment of the outcome	Statistical test	Total score
W.Na (2019)[27]	*	*	*	-	**	*	**	**	*	7
Morimoto M (2019)[23]	*	*	*	-	**	*	*	-	*	6
Mazidi M (2017) [24]	*	*	*	-	**	*	**	**	*	9
Coleley L.M (2019)[28]	-	*	*	-	**	*	-	**	*	6

**Table 3** (continued)

kim (2018)[20]	-	*	-	**	*	6
Shivappa (2016)[26]	-	*	-	**	**	8

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**Table 4** Meta-analysis of dietary inflammatory index and fracture

Impairment	Number of study	Sample size	Pooled Effect size % (95% CI)	Model	Heterogeneity assessment		
					I <sup>2</sup> %	Q test	P-value
Fracture in Cohort studies							
Overall	15	174882	1.03 (0.97-1.09)	Random	75.5	57.19	<0.001
By sex							
Male	5	59876	0.97 (0.85-1.09)	Random	65.4	11.57	0.021
Female	8	115005	1.02 (0.95-1.09)	Random	79.7	34.49	<0.001
Both sex	2	163494	1.29 (1.10-1.49)	Random	----	----	----
Definition of DII							
Categorical	9	173784	1.06 (0.97-1.15)	Random	71.5	28.03	<0.001
Continuous	6	4746	1.006 (0.92- 1.09)	Random	80.6	25.73	<0.001
Fracture in non-Cohort studies							
Overall	7	22687	1.42 (1.17-1.67)	Random	55.9	13.60	0.04
By sex							
Male	1	269	4.30 (0.3-48.25)	Random	----	----	----
Female	1	781	2.08 (1.21- 2.95)	Random	----	----	----
Both sex	5	22687	1.33 (1.12-1.56)	Random	52.5	8.41	0.03
Definition of DII							
Categorical	6	20418	1.53 (1.20- 1.86)	Random	55.1	11.14	0.07
Continuous	1	2269	1.18 (0.96-1.40)	Random	----	----	----