



Can increasing the prevalence of vegetable-based diets lower the risk of osteoporosis in postmenopausal subjects? A systematic review with meta-analysis of the literature



Ling-Feng Zeng^{a,b,c}, Wei-Yi Yang^a, Gui-Hong Liang^{a,b}, Ming-Hui Luo^a, Ye Cao^d, Hong-Yun Chen^a, Jian-Ke Pan^a, He-Tao Huang^c, Yan-Hong Han^c, Di Zhao^c, Jiong-Tong Lin^c, Sen-Rong Hou^c, Ai-Hua Ou^a, Zi-Tong Guan^e, Qi Wang^{a,*}, Jun Liu^{a,b,c,*}

^a The 2nd Affiliated Hospital of Guangzhou University of Chinese Medicine (Guangdong Provincial Hospital of Chinese Medicine), Guangzhou, 510120, China

^b Bone and Joint Research Team of Degeneration and Injury, Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou 510120, China

^c The Second Clinical College of Guangzhou University of Chinese Medicine, Guangzhou 510405, China

^d Department of Clinical Research/National Clinical Trials Institute, Sun Yat-sen University Cancer Center, Guangzhou 510060, China

^e World Federation of Chinese Medicine Societies, Beijing, 100101, China

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ABSTRACT

Objectives: Several epidemiological investigations have assessed the association between vegetable-based diet intake (VDI) and risk of osteoporosis in postmenopausal subjects (OPS), but the outcomes have been inconsistent. We performed a review of the updated literature to evaluate this correlation.

Methods: We searched for relevant studies published in September 2018 or earlier. Two researchers conducted eligibility assessment and data extraction. Discrepancies were resolved through consultation with a third expert. Pooled odds ratios (ORs) were calculated with 95% confidence intervals (CIs).

Results: Ten studies, which included 14,247 subjects, were identified. On comparing the highest category of VDI consumption with the lowest category of VDI consumption, the pooled OR for OPS was 0.73 (95% CI = 0.57–0.95), i.e., participants with a higher intake of vegetables had a 27% (95% CI = 5–43%) lower risk of OPS. Significant benefits were found on subgroup analyses of case-control studies (OR, 0.61 [95% CI, 0.48–0.78]), but not on subgroup analyses of cross-sectional studies (OR, 0.82 [95% CI, 0.57–1.16]). The synthesized effect estimates were in the direction of decreased risk of OPS on subgroup analyses of the femoral region (OR, 0.57, 95% CI = 0.41–0.80) and the lumbar spine (OR = 0.55, 95% CI = 0.38–0.81), but not on subgroup analyses of the calcaneus (OR = 0.85, 95% CI = 0.33–2.16) and the lumbar and/or femoral region (OR = 1.04, 95% CI = 0.79–1.38). Positive results were observed on pooled analyses of the Dual energy X-ray absorptiometry (DEXA) measurement method (OR, 0.72 [95% CI, 0.54–0.95]), but not on pooled analyses of the Standardized Quantitative Ultrasound (QUS) measurement method (OR, 0.85 [95% CI, 0.33–2.16]). This might have resulted from a type II error due to wide confidence intervals and less number of included studies.

Conclusion: This meta-analysis seemingly confirms that higher consumption of VDI was associated with a lower risk of OPS. Taken together, these results highlight the need for future high-quality design-based trials on quantified vegetable intake and OPS.

1. Introduction

Osteoporosis is a chronic disorder characterized by microstructural deterioration of bone tissue and decreased bone mineral density (BMD).^{1–2} It is one of the common health problems in the elderly population, and 55% of the subjects aged ≥ 50 years worldwide suffer

from the condition of osteopenia or osteoporosis.³ The lifetime risk of fracture of the hip, wrist, or vertebral regions caused by osteoporosis has been obviously identified. This fragility impacts patients' basic daily functionality and mobility more than their athletic ability, thus leading to personal tension and societal burden.⁴

Previous studies found that the average and maximum bone mass

* Corresponding authors at: The 2nd Affiliated Hospital of Guangzhou University of Chinese Medicine (Guangdong Provincial Hospital of Chinese Medicine) & Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou 510120, China; No.12 Dade Road, Yuexiu District, Guangzhou 510120, China.

E-mail addresses: wqme01@163.com (Q. Wang), liujungdtem@163.com (J. Liu).

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values in the female population were relatively lower than those in the male population, while bone loss was 10% higher than that in the latter.^{5–6} This promoted a tendency for osteoporosis in the female population, especially in postmenopausal women. As a result, their maximum bone mass was decreased by 40–50% due to hormonal changes at that time.^{5–7} Thus, it is important to explore the protective or risk factors of osteoporosis in postmenopausal subjects (OPS). Although specific anti-osteoporotic therapies, such as bisphosphonate, hormone replacement therapy, denosumab, and teriparatide, are available for the treatment and prevention of OPS, alternative and complementary therapies, such as nutrients from diet, still play an important role.⁸ Recent evidence showed that the benefits of some dietary supplements appear to be associated with the optimization of bone health and promotion of bone formation. The consumption of vegetable-based diets, as well as fruits, grains, and other foods from plant sources, may be correlated with a lower risk of OPS.⁹

Although a series of epidemiological studies has been performed to evaluate the association between vegetable-based diet intake (VDI) and the risk of OPS,^{10–19} the outcomes remain controversial. An inverse correlation between VDI and the risk of OPS was observed in 5 studies,^{10,13–16} whereas no association was found in other studies.^{11–12,17–19} The purpose of this present updated meta-analysis was to assess the association between VDI and the risk of OPS.

2. Materials and methods

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement²⁰ and other guidelines^{21–22} during conduction of assessments.

2.1. Literature search

Observational studies on OPS involving the VDI data were identified for this meta-analysis. Systematic searches were carried out by two reviewers for identifying potential articles that were published from inception to September 30, 2018 based on EmBase, PubMed, Web of Science, and Chinese CNKI databases. The approaches of using MeSH terms and free-text terms were applied for the above-mentioned databases with relevant key words, such as (“diet” OR “dietary pattern”) and (“vegetable” OR “Vegetables”) and (“osteoporosis OR bone OR fracture”) and (“postmenopausal” OR “postmenopause” OR “elderly”). Also, the reference lists of relevant articles were manually rechecked for this review. The final results of the literature search were updated on November 10, 2018.

2.2. Criteria for inclusion of studies in this review

Articles were included in this review if they met the following detailed items: 1) observational studies published in Chinese or English; 2) reported exposure to VDI or other vegetable-focused diets; 3) enrollment of subject groups with a high risk of OPS (e.g., age ≥ 55 years, females, etc.); 4) reported number of patients with OPS or BMD levels as the outcome; and 5) calculation of the odds ratios (ORs) for OPS by comparing the highest category of VDI consumption with the lowest category of VDI consumption, with 95% confidence intervals (CIs), or other information that can be used for drawing an inference. The exclusion criteria for the articles were as follows: i) previous documents of an animal experiment, review papers, and mechanistic studies; ii) lack of specified data on OPS; and iii) articles that were published as abstracts.

2.3. Data extraction

Two researchers extracted the data independently using standardized forms for literature collection. Attempts were made to resolve

discrepancies through consultation with a third expert. We did not collect unpublished data by contacting the potential authors. The extracted details included the first author's name, publication year, country where the study was performed, age, study design, sample size, number of cases, estimates of VDI, the measurement method for OPS, the measurement location of OPS, and the most adjusted ORs and 95% CIs for the highest versus lowest consumption. The Newcastle-Ottawa Scale (NOS) checklist was applied to assess the methodological quality of case-control and cohort studies, with the highest score of 9 points and higher scores reflecting better quality.²³ The Agency for Healthcare Research and Quality guidelines were used to evaluate the quality of cross-sectional studies.²⁴

2.4. Statistical analyses and data synthesis

In this meta-analysis, the risk estimates of OPS were determined across the highest category of VDI compared with the lowest. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a fixed-effects model (FEM) if no evidence of heterogeneity was found. Otherwise, a random-effects model (REM) was adopted for assessment. The I-squared (I²) statistic and the chi-square test were applied to explore the possible heterogeneity of the articles. The potential publication biases were inspected by the inspection of funnel plots. Subgroup analyses were performed for VDI and risk of OPS (based on the study design, the measurement location of OPS, the measurement method for OPS, etc.), with the aim to evaluate the possible influential factors. Statistical analyses were carried out using Stata SE, version 14.1 (Stata Corp, College Station, TX).

3. Results

3.1. Results of the search

Based on the inclusion criteria, 1936 publications were identified after database search. From among these 1936 publications, 1291 articles were excluded due to the following reasons: 174 publications were excluded due to duplication of authors or titles and 1117 studies were excluded because of their unmatched details (e.g., review articles (528), animal studies (219), laboratory studies (176), or other irrelevance to the current study (194)). Of the remaining 645 articles, 128 articles did not assess the correlation between VDI and OPS, 207 articles did not provide OR with 95% CI for this evaluation, 129 articles did not obtain data referring to female subjects, 12 articles were viewed as duplicate publications, and 69 articles recruited the subjects based on the hospital and not consecutively. Despite the attempts made to contact the authors (by e-mail or telephone), we did not receive any responses regarding the details. Finally, 10 eligible studies, including 4 case-control studies and 6 cross-sectional studies with a total of 14,247 subjects, were considered for further analysis^{10–19} (Fig. 1).

3.2. Characteristics at baseline and quality assessment

The basic characteristics of the included studies are shown in Table 1. The age of the participants was found to be equal to or greater than 55 years. The quality assessment score of studies by the Newcastle-Ottawa Scale (NOS) was not less than 5 points, thus revealing that the methodological qualities of the included studies were generally good.

3.3. Quantitative data synthesis

3.3.1. Meta-analysis of VDI and risk of OPS

A total of 10 articles^{10–19} reported the events of OPS, and the random effects meta-analysis displayed a significant difference between participants with the highest category of VDI consumption and the lowest category of VDI consumption. The OR for the OPS events between the two groups was 0.73 [95% CI, 0.57–0.95] (Fig. 2). The results

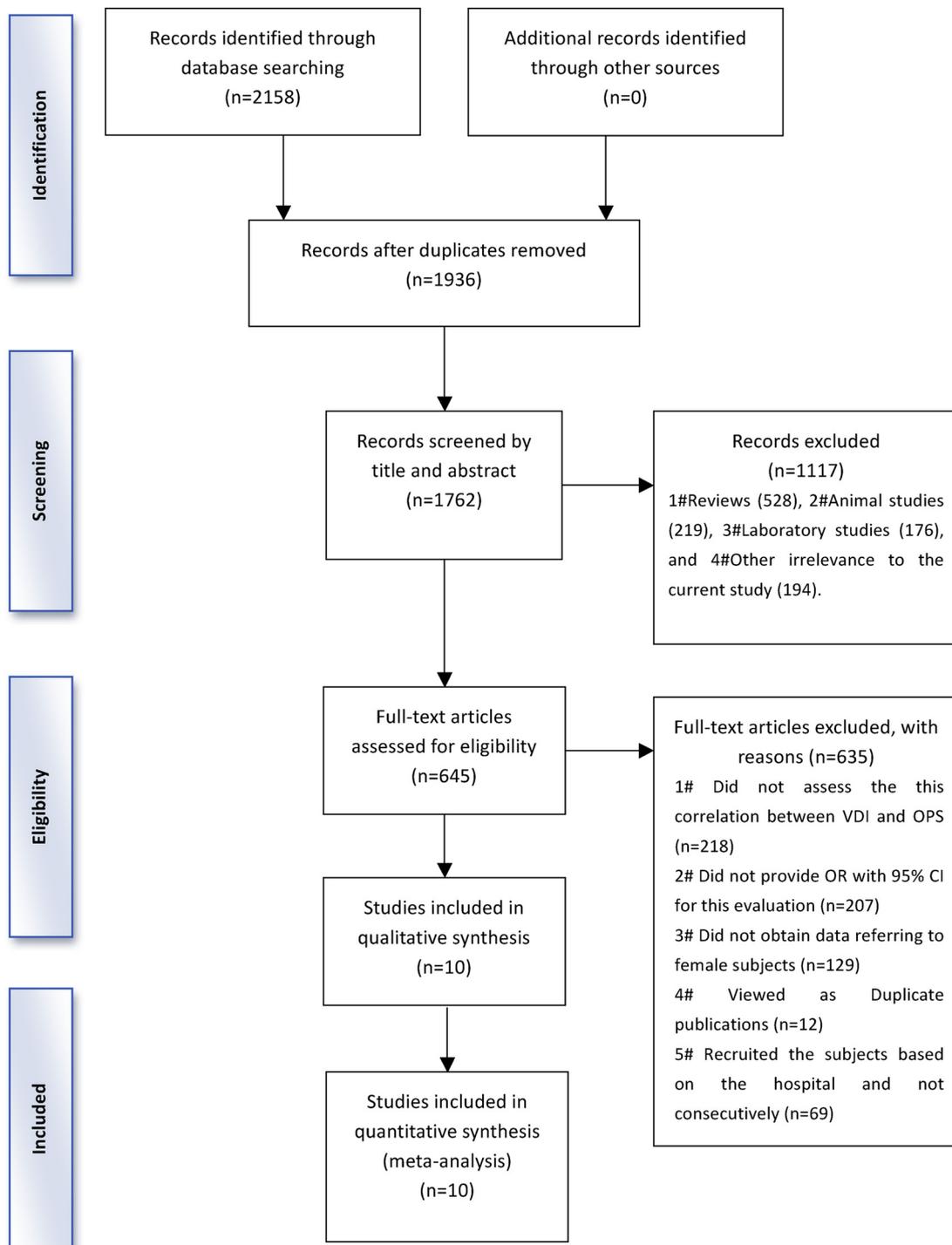


Fig. 1. Flow diagram of the trial selection process.

OPS = osteoporosis in postmenopausal subjects; VDI = vegetable-based dietary intake.

revealed that the subjects with a higher intake of vegetables had a 27% (95% CI 5–43%) lower risk of OPS. The pooled effect estimates for VDI were in the direction of lower risk of OPS.

Subgroup analyses stratified by the study design

Significant changes were observed in the subgroup analyses stratified by the study design for the correlation between VDI and risk of OPS (Fig. 3). Two studies^{13,16} with a case-control design and three studies^{10,14–15} with a cross-sectional design reported an association between increasing vegetable intake and lower risk of OPS, while other studies^{11–12,17–19} failed to show such a relationship. The evidence

synthesis for the risk of OPS appeared to be much lower in the case-control studies (OR, 0.61 [95% CI, 0.48–0.78]) and overall effects (OR, 0.73 [95% CI, 0.57–0.95]). However, no protective effect was identified for the pooled results in cross-sectional studies (OR, 0.82 [95% CI, 0.57–1.16]) involving VDI and risk of OPS (Fig. 3).

3.3.2. Subgroup analyses stratified by the measurement location of OPS

Ten articles^{10–19} reported the effects of the measurement location on VDI and risk of OPS. Risk reduction of OPS was found in the pooled results of 2 studies^{13,16} that performed measurements in the femoral

Table 1
Characteristics of the 10 studies included in the meta-analysis.

First author, year (sources)	Study population	Age(yrs), mean ± SD/range	Study design	Cases/ Sample size	OR (95%CI) for highest vs. lowest category	Estimates of VDI	Measurement method of OPS	Measurement location of OPS	Maximum adjustment available
Liu NJ, 2016	China	62.39 ± 8.98	Cross-sectional	539/1903	0.54 (0.35, 0.89)	SQFFQ	QUS	Calcaneus	Age, education, exercise, smoking, alcohol intake, medical and therapy history.
Park HM, 2011	South Korea	59.76 ± 0.59/50-70	Case-control	72/144	0.53 (0.17, 1.61)	FFQ	DEXA	Lumbar and/or femoral region	Age, BMI, energy, and hormone replacement therapy.
Shin S and Joung H, 2013 (Femoral neck)	South Korea	64.1 ± 9.5	Cross-sectional	827/3735	0.79 (0.51, 1.21)	24 h recall of dietary intakes	DEXA	Lumbar and/or femoral region	Age, BMI, energy intake, parathyroid hormone, serum 25-hydroxyvitamin D, smoking, alcohol intake, moderate physical activity, supplement use and oral contraceptive use.
Shin Sand Joung H, 2013 (Lumbar spine)	South Korea	64.1 ± 9.5	Cross-sectional	1132/3735	1.22 (0.86, 1.74)	24 h recall of dietary intakes	DEXA	Lumbar and/or femoral region	Age, BMI, energy intake, parathyroid hormone, serum 25-hydroxyvitamin D, smoking, alcohol intake, moderate physical activity, supplement use and oral contraceptive use.
Wang J, et al., 2011	China	50-65	Case-control	152/460	0.63 (0.42, 0.93)	SQFFQ	DEXA	Femoral region	Age, total energy and other common risk factors of OPS.
Ma XF, et al., 2010	China	50-65	Cross-sectional	111/281	0.37 (0.16, 0.84)	FFQ	DEXA	Lumbar spine	Age, education level, house income, obesity, physical activity, the number of births, cereal grains intake, beans and bean products intake, fruit intake, livestock intake, poultry intake, fish or seafood intake, eggs intake, dairy product intake, nut intake and drink intake.
Lan XZ and Zhang Q, 2011	China	50-65	Cross-sectional	110/282	0.42 (0.19, 0.94)	FFQ	DEXA	Lumbar spine	Age, BMI, the number of births, dietary factors of non-vegetables and other common risk factors of OPS.
Li N, et al., 2011	China	56.1 ± 3.8/50-65	Case-control	115/281	0.47 (0.26, 0.84)	FFQ	DEXA	Femoral region	Age, weight and other common risk factors of OPS.
Li HT, et al., 2014	China	50-65	Case-control	43/282	0.68 (0.49, 1.05)	FFQ	DEXA	Lumbar spine	Age, BMI, age at menarche and other common risk factors of OPS.
Fang YF, 2011	China	61.1 ± 9.4/40-79	Cross-sectional	125/643	1.40 (0.75, 2.59)	FFQ	QUS	Calcaneus	Age, age at menarche, occupation, BMI and physical activity.
Shin A, et al., 2010	South Korea	53.7 ± 5.8	Cross-sectional	302/2501	1.24 (0.87, 1.77)	FFQ	DEXA	Lumbar and/or femoral region	Age, BMI, alcohol consumption, smoking, physical activity, age at menarche, age at menopause, education level, house income, menopause duration and menopause causes.

Annotation: SQFFQ = Semi-quantitative Food Frequency Questionnaire; FFQ = Food Frequency Questionnaire; DEXA = Dual energy X-ray absorptiometry; QUS = Standardized Quantitative Ultrasound; OPS = Osteoporosis of postmenopausal subjects; VDI = Vegetable-oriented dietary intake; BMI = Body mass index; OR = odds ratio; CI = confidence interval.

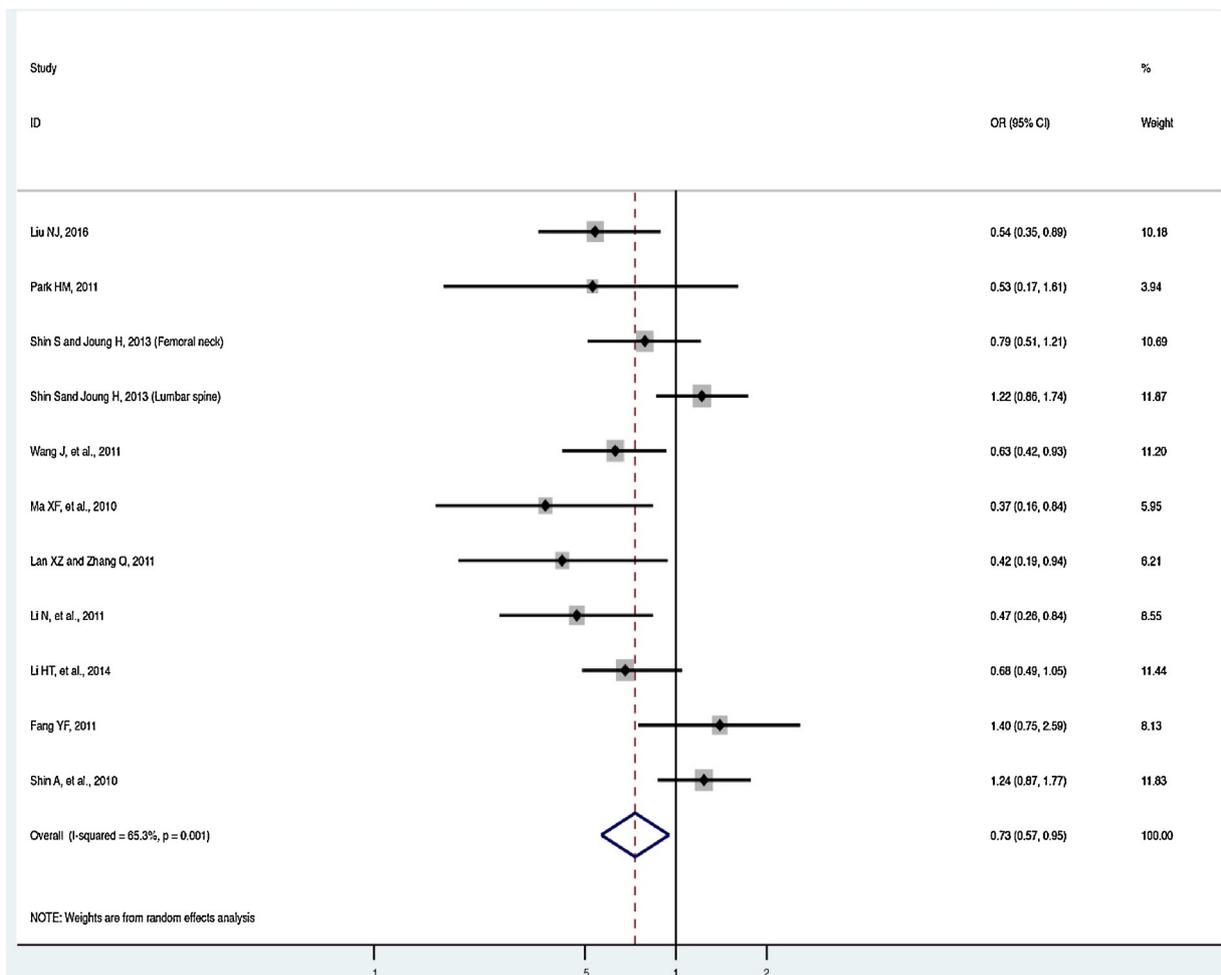


Fig. 2. Forest plots (random effects model) in the meta-analysis of vegetable intake and risk of OPS. Squares indicate study-specific risk estimates (size of the square reflects the study-specific statistical weight); horizontal lines indicate 95% CIs; the diamond indicates the summarized odds ratio with its 95% CI. OR = odds ratio; CI = confidence interval; OPS = osteoporosis in postmenopausal subjects.

region (OR = 0.57, 95% CI = 0.41–0.80) and 3 studies^{14–15} that performed measurements in the lumbar spine (OR = 0.55, 95% CI = 0.38–0.81). However, there were no positive effects in the synthesized data of 2 studies^{10,18} that performed measurements in the calcaneus (OR = 0.85, 95% CI = 0.33–2.16) and 3 studies^{11–12,19} that performed measurements in the lumbar and/or femoral region (OR = 1.04, 95% CI = 0.79–1.38) (Fig. 4).

3.3.3. Subgroup analyses stratified by the measurement method for OPS

The OR magnitude of OPS in 8 studies^{11–17,19} with the Dual energy X-ray absorptiometry (DEXA) measurement method (OR, 0.72 [95% CI, 0.54–0.95]) and overall effects (OR, 0.73 [95% CI, 0.57–0.95]) involving vegetable intake seemed to be in the direction of lower risk of OPS. However, no statistically significant correlations were observed in the pooled analyses of 2 studies^{10,18} with the Standardized Quantitative Ultrasound (QUS) measurement method (OR, 0.85 [95% CI, 0.33–2.16]) (Fig. 5). This might have resulted from a type II error due to wide confidence intervals and smaller number of included studies.

3.3.4. Publication bias analysis

We generated funnel plots to assess the publication bias, with ORs constructed from the studies involving VDI and risk of OPS. In the absence of publication bias, most of the points could be symmetrically located around the vertical line directed at the pooled ORs. No obvious evidence of publication bias was identified in the assessment of VDI and risk of OPS (Fig. 6).

4. Discussion

4.1. Summary of evidence

Our meta-analysis included 10 studies involving 14,247 subjects. Quantitative synthesis of these observational studies demonstrated that there was a significant association between VDI and risk of OPS on comparing the highest category with the lowest category. Participants with a higher intake of vegetables had a 27% (95% CI = 5–43%) lower risk of OPS. Significant benefits were found on subgroup analyses of case-control studies, but not on subgroup analyses of cross-sectional studies. The synthesized effect estimates were in the direction of decreased risk of OPS on subgroup analyses of the femoral region and the lumbar spine, but not on subgroup analyses of the calcaneus and the lumbar and/or femoral region. Additionally, positive results were observed on pooled analyses of the DEXA measurement method, but not on pooled analyses of the QUS measurement method. In all, our meta-analysis seemingly confirmed the inverse correlation between VDI and risk of OPS, i.e., increased vegetable intake could lower the risk of OPS.

Due to the defects in the methodological quality among the articles included, the absolute association between VDI and risk of OPS could not be definitely validated by the existing evidences. Therefore, the current interpretation of recommendations for clinical decision-making should be performed cautiously. Further high-quality design-based trials with detailed indexes of quantification are needed to verify these findings.

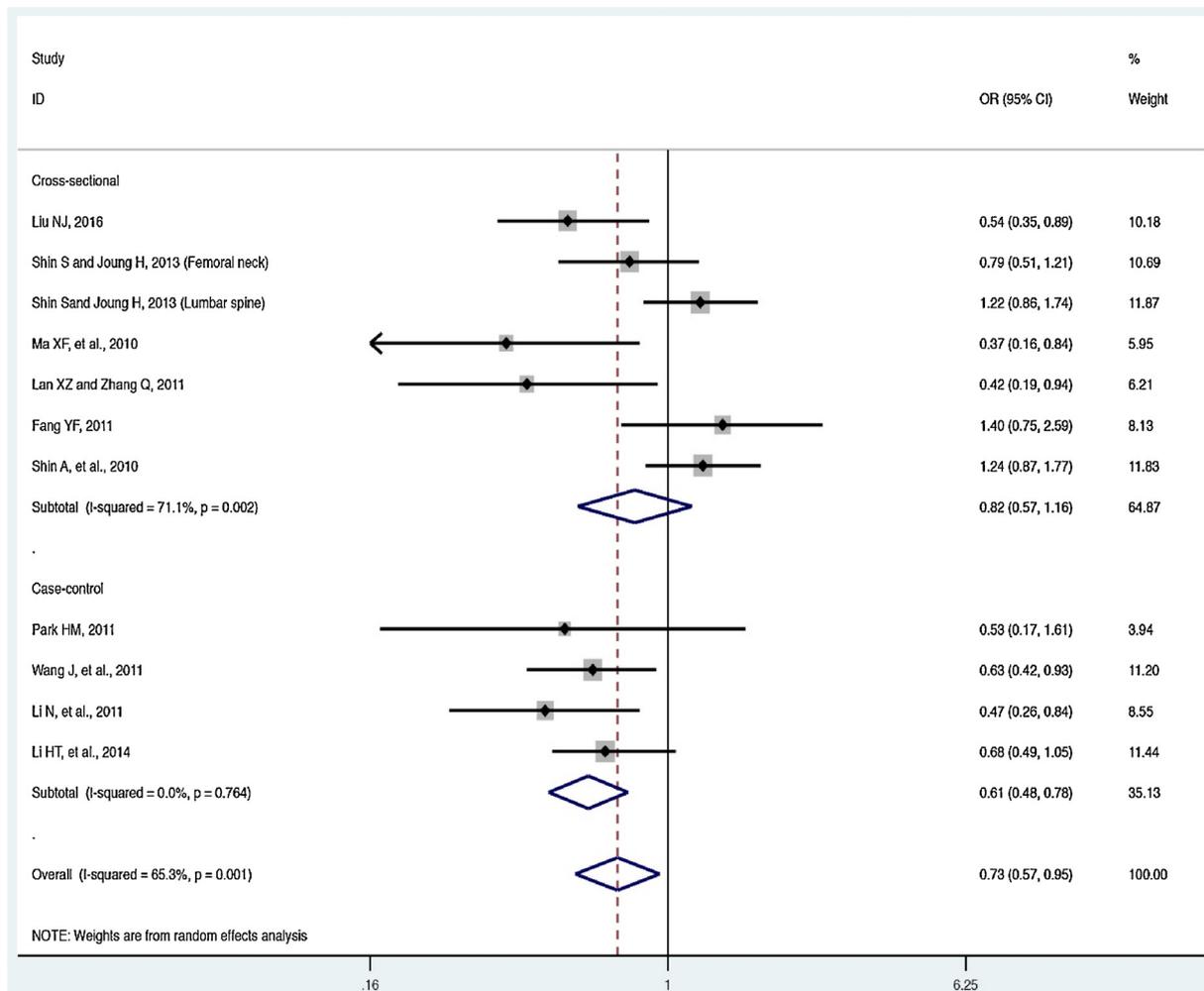


Fig. 3. Subgroup analyses stratified by the study design for the correlation between vegetable intake and risk of OPS: (A) Case-control; (B) Cross-sectional. Squares indicate study-specific risk estimates (size of the square reflects the study-specific statistical weight); horizontal lines indicate 95% CIs; the diamond indicates the summarized odds ratio with its 95% CI. OR = odds ratio; CI = confidence interval; OPS = osteoporosis in postmenopausal subjects.

4.2. Comparison of the findings with other results in the literature

Although a number of articles related to plant-based food and risk of OPS, ranging from case reports, case series, and controlled trials to randomized controlled trials, have been published, a meta-analysis focusing on the association between the consumption of vegetable-based diets and OPS has not been performed. To our knowledge, this is the first review to explore the role of VDI and the risk of OPS by retrieving and updating the relevant documents that have already been reported.

Some underlying biochemical hypotheses or other biological mechanisms might exist, which play a vital role in the progression of pathogenesis. First and foremost, phytonutrients (especially the domains of polyphenols) can be used to modulate bone metabolism in osteoclasts and osteoblasts.²⁵ A series of different polyphenols has been found in the vegetable-based diets. The present evidence shows that flavones within the polyphenols can be used to stimulate the regulatory machinery involving osteoprotegerin (OPG), receptor activator of nuclear factor- κ B ligand (RANKL), and receptor activator of nuclear factor- κ B (RANK), which plays a vital role in the osteoclasts and osteoblasts. 17β -oestradiol and Daidzein at low concentrations (nmol L⁻¹) function as accelerators of osteoblast differentiation²⁶; thus preserving the balance of bone remodeling, and preventing osteoporosis to a large extent.^{9, 27–28} Second, large amounts of potassium and magnesium are present in vegetable-based food.^{29–30} Consequently, a diet rich in vegetables resulted in a decreased load of dietary acids. Previous

literature highlighted that an increased acid load could act as an inhibitor of the functioning of osteoblasts, thus promoting the activity of osteoclasts, reducing bone formation, and increasing bone resorption.^{31–32} Increased intake of vegetable-based diets can influence bone health and prevent OPS.³³ Last, but not least, vegetable plants are rich in vitamin C, vitamin K, and other nutrients, and they have also been found to play important roles in the synthesis of bone matrix in subjects.^{28, 34}

4.3. Meaning of the study for possible clinical use

Additive benefits were observed in the participants with OPS after taking VDI into consideration, i.e., a positive link potentially exists between vegetable-based diets and OPS. However, there were some caveats for the evidence in this meta-analysis. One of the most important points is the potential errors in detailed quantification of nutrient intake. The nutrient intake was mostly not estimated by any definite judgments, but it was replaced by performing measurements with dietary questionnaires (i.e., Semi-quantitative Food Frequency Questionnaire, Food Frequency Questionnaire, etc.) in relevant terms. To some extent, more or less of a nutrient might be inferred to be associated with better or worse outcomes. However, the description of actual quantities and intervals of VDI in the observational articles was insufficient to allow any specific inferences to be drawn. Furthermore, the exposures in the observational studies were selected by the

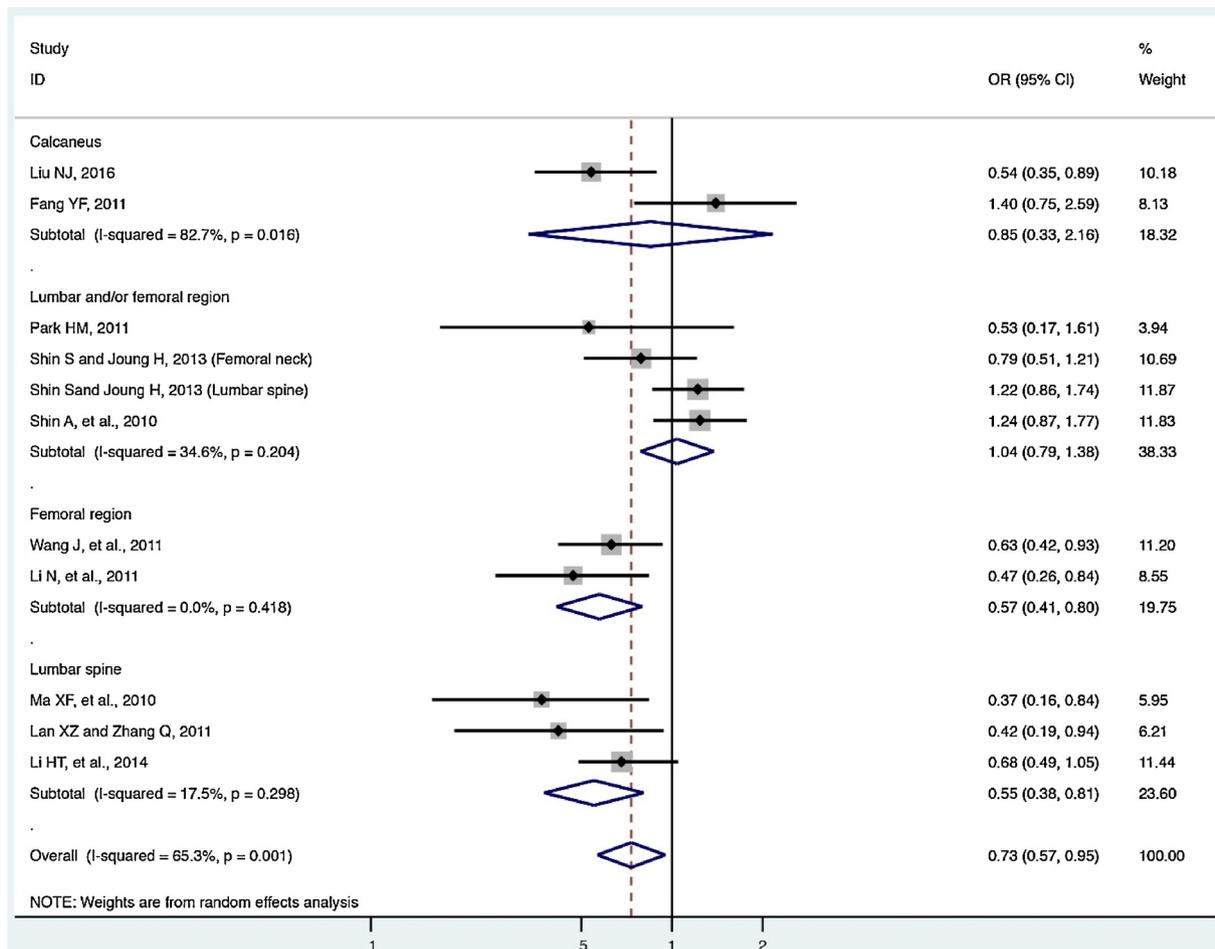


Fig. 4. Subgroup analyses stratified by the measurement location of OPS for the correlation between vegetable intake and risk of OPS: (A) Femoral region; (B) Lumbar spine; (D) Lumbar and/or femoral region; (C) Calcaneus. Squares indicate study-specific risk estimates (size of the square reflects the study-specific statistical weight); horizontal lines indicate 95% CIs; the diamond indicates the summarized odds ratio with its 95% CI. OR = odds ratio; CI = confidence interval; OPS = osteoporosis in postmenopausal subjects.

participants (not by the researchers), which could have resulted in potentially uncontrolled confounding. The issues of possible bias and confounding could be fully resolved through randomized controlled trials (RCTs) because this type of study design was considered to be the ideal method to assess the effects of VDI and risk of events. However, due to the relatively long duration of preclinical conditions or other types of OPS, it was almost impossible for the investigators in the clinical environment to carry out such trials based on primary prevention by way of diet patterns. Moreover, the progression of OPS could be the result of participants' observation exposure beginning in old age or their life-long exposures. However, the length of latency periods in participants with OPS, (i.e., the adoption of diets prevented or delayed the development of this disorder), might be long enough, lasting for decades, which appeared to be uncertain on the basis of the present evidence. As for the articles on association between VDI and OPS, this study was conducted in the participants with mean age ≥ 50 years and an advanced stage in the latency durations of OPS was noted in this age group. Thus, the evidence focusing on diet intakes and effects on varied course of disorders were relatively limited. In addition, diet patterns reported in the articles could indicate the actions of preclinical OPS. Also, the exposures reported might have been affected by preclinical OPS-related disorders.^{35–37} All of the above-mentioned factors could have resulted in bias associations or inaccurate interpretations.

Another key point focuses on the issues of methodological formulation. The OPS participants have been identified on the basis of conventional guidelines for osteoporosis. However, the detection of

similar data did not always indicate the qualified outcomes. Some of the guidelines did not guarantee consistency with the integrity of osteopenia or osteoporosis among subjects in relation to low bone mass. Thus, some institutes have attempted to explore some potential criteria for the provisional diagnosis of above status.^{38–39} Furthermore, a series of scaling scores have been developed to assess the subsequent disorders in patients in relation to low bone mass so as to better evaluate the impacts or to create tracks for the development of this disorder.^{37,40–41} With respect to the detailed assessment of OPS participants, several domains should be further improved for structured interview methods and similar rating scales, especially for the measurement of self-report approaches for OPS participants in serious stages. In other words, the bias report concerning tension or worries experienced by OPS participants themselves, the under-reported symptoms by the participants, and the over-reported symptoms by the caregivers might be possibly identified and observed in the real clinical context. Thus, positive measures should be taken by the investigators to reduce the risk and to assess the sources of informative outcomes.

4.4. Limitation of the review

Certain information on the correlation between VDI and risk of OPS could be identified in this meta-analysis. However, several limitations were noted. First, the difference in the measurement locations of OPS also affected the outcomes to some extent. Second, the pooled effect estimates (i.e., ORs) from the articles, in which OPS was identified by

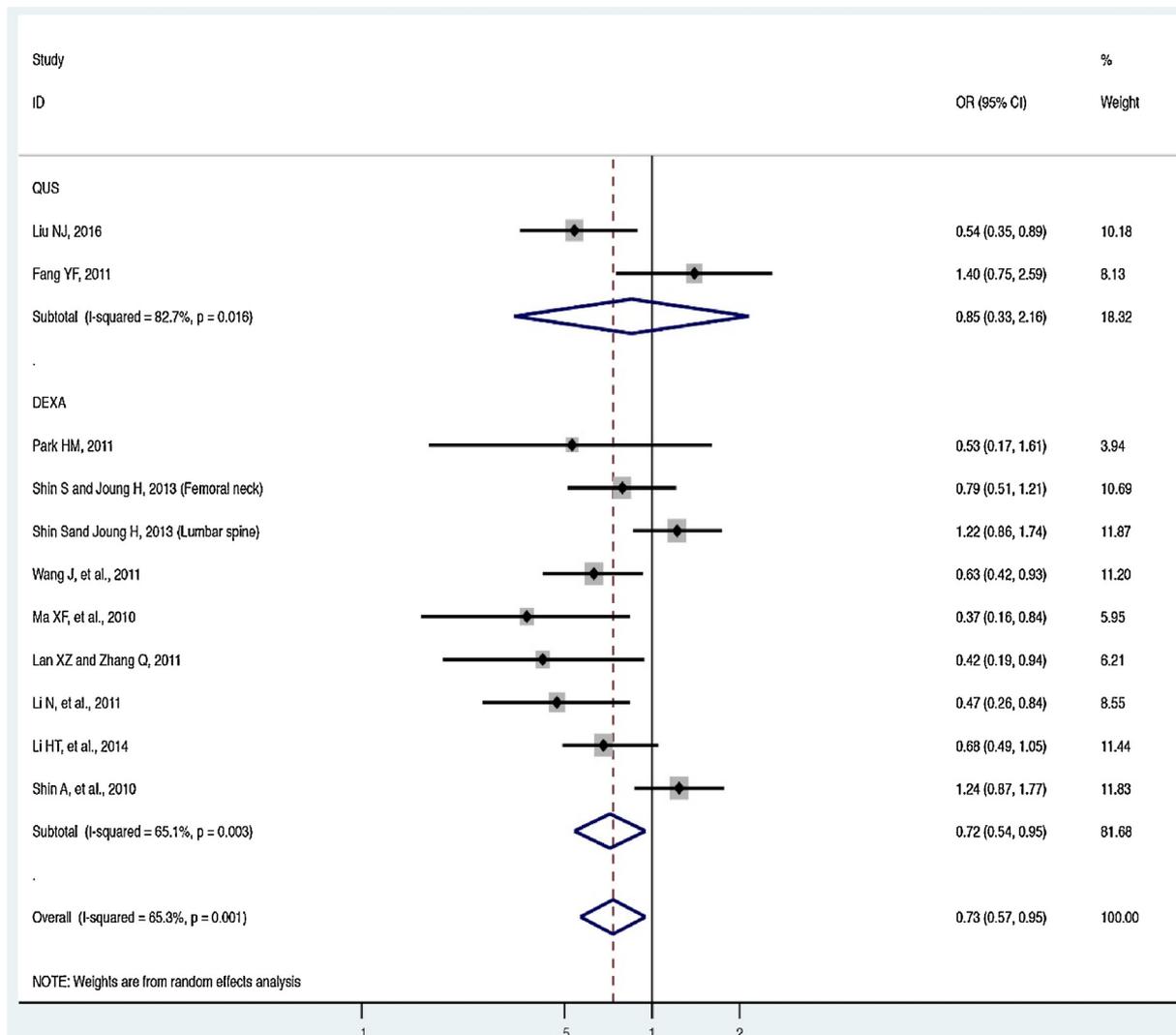


Fig. 5. Subgroup analyses stratified by the measurement method of OPS for the correlation between vegetable intake and risk of OPS: (A) QUS; (B) DEXA. OR = odds ratio; CI = confidence interval; DEXA = Dual energy X-ray absorptiometry; QUS = Standardized Quantitative Ultrasound; OPS = osteoporosis in postmenopausal subjects.

quantitative ultrasound at the calcaneus and the lumbar and/or femoral region, were found to be statistically insignificant. As in several articles on OPS, the examination was performed by quantitative ultrasound at the calcaneus and the lumbar and/or femoral region in this study, thus the potential reasons for the results could not be further explored. Third, most of the articles included in this review were designed as cross-sectional studies, and this limited the establishment of a causal association to a large degree. Fourth, evidence for this review was collected from a maximized search of previously reported observational articles. However, we could not rule out the possibility that a few qualified articles might have been ignored in the initial retrievals, which could have been the possible sources of potential bias. Fifth, although control approaches have been used for underlying confounders in the eligible articles, several leftover confounders might have not been fully eliminated. Sixth, the detection time-points for OPS were not standardized among the included studies. Seventh, due to limited sample sizes of the included studies, the assessment of publication bias was required for further evidence.

5. Conclusion

This updated meta-analysis seemingly confirms that a higher consumption of VDI was associated with a lower risk of OPS. Taken

together, these results highlight the need for future high-quality design-based clinical trials on vegetable intake with specified quantification and OPS.

Authors' contributions

Liu J and Wang Q conceived and designed the study. The literature searches, trial selection, critical appraisal, data extraction, as well as contacting authors for additional data were conducted and performed by Zeng LF, Yang WY, Luo MH, Lin JT and Guan ZT. Cao Y, Chen HY, Huang HT, Hou SR and Zeng LF carried out analysis and interpretation of the data. Zeng LF, Liang GH, Han YH, Zhao D, Pan JK and Liu J drafted the article. Liu J, Ou AH and Zeng LF further revised the manuscript. Zeng LF (Zeng Ling-Feng), Yang WY (Yang Wei-Yi) and Liang GH (Liang Gui-Hong) contributed equally to this work. The final version of the manuscript were read and approved by Liu J, Zeng LF, Yang WY, Liang GH, Luo MH, Cao Y, Chen HY, Pan JK, Huang HT, Han YH, Zhao D, Lin JT, Hou SR, Guan ZT, Wang Q, and Ou AH.

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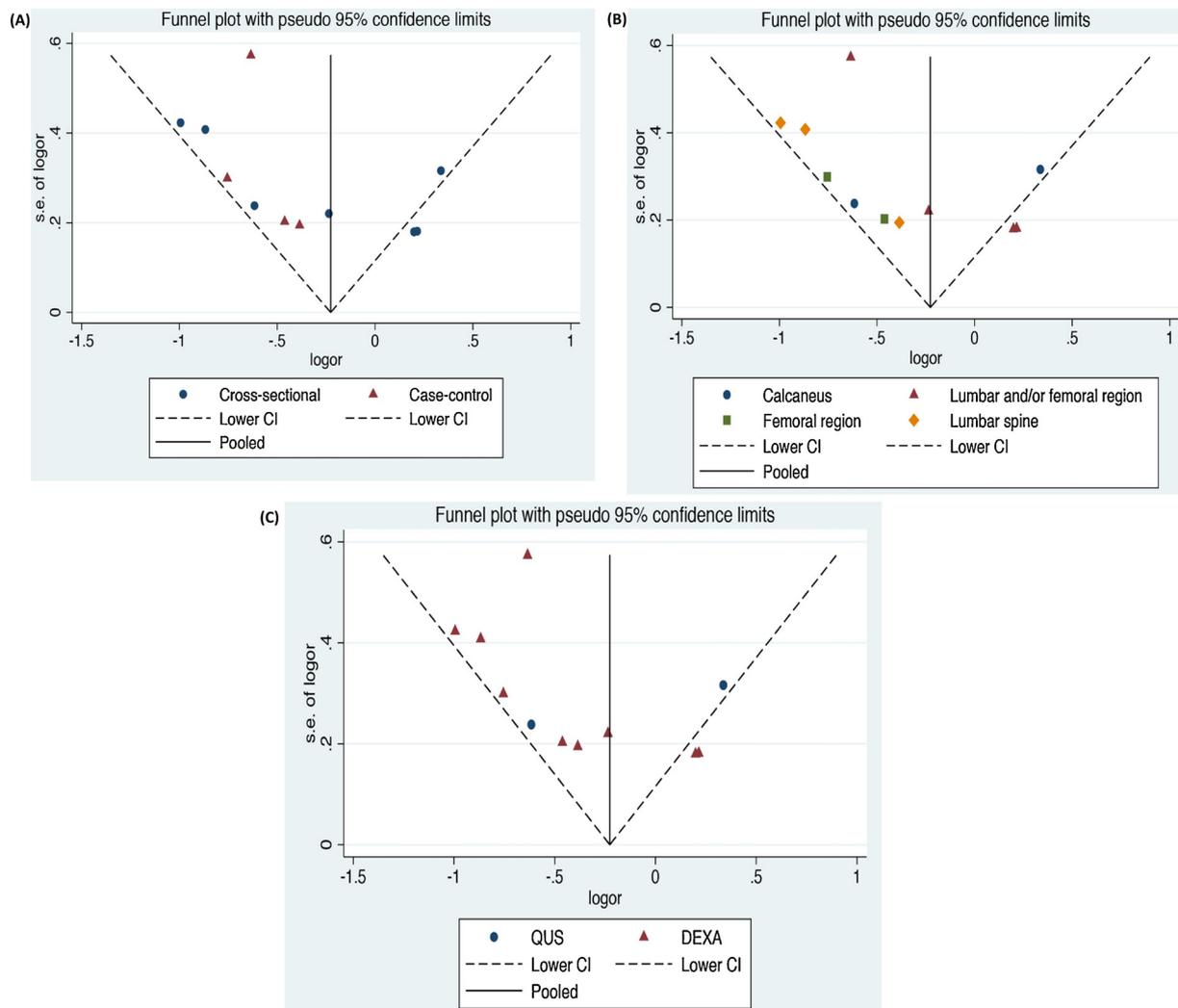


Fig. 6. Publication bias in the studies included in the meta-analysis. Funnel plot in the meta-analysis of vegetable intake and risk of OPS: (a) Study design; (b) Measurement location of OPS; (c) Measurement method of OPS. OR = odds ratio; S.E. = standard error; DEXA = Dual energy X-ray absorptiometry; QUS = Standardized Quantitative Ultrasound; OPS = osteoporosis in postmenopausal subjects. In the absence of publication bias, the points should be symmetrical about the vertical line directed at the pooled ORs. A reasonably symmetrical distribution suggests the absence of publication bias.

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Competing interests

The authors declare that they have no competing interests.

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