



## Review Paper

# Association of obesity with bone mineral density and osteoporosis in adults: a systematic review and meta-analysis



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## ABSTRACT

**Objectives:** Results from previous studies investigating the association of obesity with bone mineral density (BMD) and osteoporosis (OP) are inconsistent. The purpose of the present study was to examine whether obesity is associated with BMD and the risk of OP.

**Study design:** This is a meta-analysis.

**Methods:** A computerised literature search was conducted using the PubMed, Web of Science, China National Knowledge Internet (CNKI) (Chinese) and Wanfang (Chinese) databases for relevant articles published in English or Chinese before the end of December 2017. Means with standard deviations and odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs) were computed to estimate the association between obesity and BMD and the risk of OP by using a random-effects model. In addition, a heterogeneity test and sensitivity analysis were conducted.

**Results:** Adults with obesity had higher BMD than healthy-weight subjects in both the lumbar spine and femoral neck measurement sites. Obesity was positively related to BMD in the two sites, with merged weighted mean difference (WMD) of 0.07 g/cm<sup>2</sup> in the lumbar spine (95% CI: 0.045, 0.095;  $P < 0.001$ ;  $P_{\text{heterogeneity}} < 0.001$ ;  $I^2 = 89.1\%$ ) and WMD of 0.087 g/cm<sup>2</sup> in the femoral neck (95% CI: 0.063, 0.112;  $P < 0.001$ ;  $P_{\text{heterogeneity}} < 0.001$ ;  $I^2 = 92.8\%$ ). General obesity was negatively related to femoral neck OP, indicating that obesity is a protective factor for OP, with a merged OR of 0.169 (95% CI: 0.132, 0.216;  $P < 0.001$ ;  $P_{\text{heterogeneity}} = 0.716$ ;  $I^2 = 0.0\%$ ).

**Conclusions:** Adults with obesity had significantly higher BMD than healthy-weight adults. Obesity was positively associated with BMD and negatively correlated with OP.

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## Introduction

Osteoporosis is a systemic skeletal disease that is characterised by reduced bone microstructure, bone mineral composition and bone matrix ratio, resulting in a series of adverse outcomes, including thinning of the bone, decreased trabecular bone number, increased bone fragility and increased fracture risk.<sup>1</sup> With the ageing population and prolongation of life expectancy, the incidence of osteoporosis is continually increasing, and it has become an important health problem globally.<sup>2</sup> A study involving US adults

aged  $\geq 50$  years reported that the prevalence of osteoporosis was 6–11%, whereas the prevalence of low bone mass ranged from 28% to 45% in 2013–14.<sup>3</sup> A meta-analysis of 33 articles revealed that the prevalence of osteoporosis in Chinese people aged  $>60$  years was 36%; comprising 23% men and 49% women.<sup>4</sup>

Obesity is the excessive or abnormal accumulation of fat within the body. Obesity is considered a chronic metabolic disease related to both environmental and genetic factors. The World Health Organization (WHO) defines obesity as a body mass index (BMI)  $\geq 30$  kg/cm<sup>2</sup>; however, in China, obesity is defined as a BMI  $\geq 28$  kg/cm<sup>2</sup>. According to the WHO, there are about 1.7 billion overweight people and 300 million people with obesity in the world, suggesting obesity has become a global health problem. The number of overweight people and people with obesity in China has increased fourfold in the past 20 years.<sup>5</sup>

The development of osteoporosis is related to many factors. An increasing number of epidemiological investigations show that obesity, metabolic syndrome and diabetes are associated with osteoporosis. Recent studies have shown that an increase in BMI is

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detrimental to bone mineral density (BMD) and bone formation.<sup>6,7</sup> A large stratified study including 13,000 adults (including both men and premenopausal and postmenopausal women) showed that body fat percentage was positively correlated with osteopenia and non-vertebral fractures.<sup>8</sup> However, other studies suggest that obesity may be a protective factor for osteoporosis, and the risk of osteoporosis in people with obesity is lower than that in people without obesity, thus creating the obesity paradox. In addition, a study based on the physical examination of people aged >50 years<sup>9,10</sup> showed that there may be a significant negative correlation between obesity and osteoporosis.

In the WHO classification, osteoporosis is diagnosed based on the T-score, which expresses the BMD of the individual as a standard deviation score compared with the mean value in a healthy young person. The specific classification criteria are that people who have T-scores of  $-1.0$  or above have normal BMD, those with T-scores between  $-1.0$  and  $-2.5$  have osteopenia and those who have T-scores of  $-2.5$  or lower have osteoporosis. There is a lack of consistency in the results from previous studies regarding the relationship between obesity and BMD or osteoporosis.

Because obesity is usually determined by anthropometric parameters and is currently defined by BMI<sup>10</sup> (which was considered a more important indicator of obesity than body weight), this meta-analysis uses BMI (which is in line with the majority of previous studies) to examine the correlation between obesity and BMD as well as osteoporosis.

## Methods

### Search methods

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.<sup>11</sup> A computerised literature search was conducted using the PubMed, Web of Science, CNKI (Chinese) and Wanfang (Chinese) databases for relevant articles investigating the association of general obesity or BMI with BMD or osteoporosis that were published in English or Chinese before the end of December 2017. The following Medical Search Headings search terms ('obesity' AND 'bone density' AND 'osteoporosis') and free texts ('body weight' OR 'body mass index' OR 'BMI' AND 'bone mineral density' OR 'bone mineral densities' OR 'bone mineral content' OR 'bone mineral contents' OR 'osteoporoses' OR 'bone diseases') were used. At the same time, reference lists of identified articles were manually searched to identify any additional relevant articles. The literature search was updated in December 2018.

### Inclusion and exclusion criteria

Studies were included if they (i) were original studies of the general population; (ii) measured BMD of the lumbar spine and/or femoral neck by dual-energy X-ray absorptiometry (DXA); and (iii) included specific diagnostic criteria for obesity and osteoporosis.

Studies were excluded if they (i) were published twice or multiple times; (ii) did not provide access to the full text; (iii) were based on a particular population (e.g., children, pregnant women, volunteers, patients with non-simple obesity or only patients with obesity or osteoporosis); (iv) were comments, reviews or editorials; (v) had incomplete data; or (vi) focused on fracture. For articles published multiple times, only the article that provided the most comprehensive data was included.

### Data extraction and quality assessment

Two individuals independently assessed the methodological quality of the studies using an 11-item checklist, which was recommended by the Agency for Healthcare Research and Quality. An item would be scored '0' if it answered 'no' or 'unclear'; if it answered 'yes', then the item would be scored '1'. Article quality was assessed as follows: low quality = 0–3; moderate quality = 4–7; high quality = 8–11.

Two researchers conducted the search and screening of the articles independently and following strict guidelines. Any disagreements were resolved through discussion and with adjudication by a third reviewer if necessary. The following information from the articles was extracted: journal name, first author name, publication year, research type, research population, age, sample size, sample source, research area, outcome variables, number of people with obesity and people without obesity, BMD (mean and standard deviation) and odds ratios (ORs) with corresponding 95% confidence intervals (CIs).

### Statistical analyses

Means with standard deviations and ORs with corresponding 95% CIs were merged, respectively. Weighted mean difference (WMD) and 95% CI were chosen as the effect indicator when the data type was mean  $\pm$  standard deviation, for reasons that have been described previously.<sup>12</sup> When the literature provides multiple subgroup data, these can be merged to get total data for further analysis,<sup>13</sup> and subgroup data can be used in subgroup analysis. The random-effects model was used in this study; it considers not only the heterogeneity within the study but also the heterogeneity between studies and can provide conservative conclusions.<sup>14</sup>

Heterogeneity was examined using the standard Q test and I<sup>2</sup> test.<sup>15</sup> If significant heterogeneity ( $P \leq 0.1$  or I<sup>2</sup> >75%) existed among studies, a Galbraith plot and sensitivity analysis (by excluding one study at a time) were conducted to explore potential sources of heterogeneity. Subgroup analyses were conducted by sex, region, study quality and sample source (population/hospital) for exploration of heterogeneity.

Publication bias was evaluated by Egger's test; a P-value of <0.1 shows the funnel plot as asymmetrical and indicates that there is publication bias.<sup>16</sup> A contour-enhanced funnel plot was also performed to analyse whether the publication bias caused the asymmetry of the funnel plot. All analyses were performed using the STATA software package (version 11.0). A two-tailed  $P < 0.05$  was considered statistically significant.

## Results

### Characteristics of the included studies

In total, 2957 studies were identified from four electronic databases. Only 17 articles met the inclusion criteria and were included in the meta-analysis; of these, the study outcome was mean BMD in 22 studies of 14 articles and the outcome was OR of osteoporosis in 6 studies of 5 articles. Fig. 1 details the selection and exclusion process.

The characteristics of the included studies are listed in Table 1. All the studies were cross-sectional. In total, three articles described stratified analyses by sex; eight articles included only women, and six included only men. Most of the study participants were Asians and were middle-aged to older adults. Among the 17 included articles, five were of high quality, 12 were of moderate quality and there were no articles with a low-quality rating.

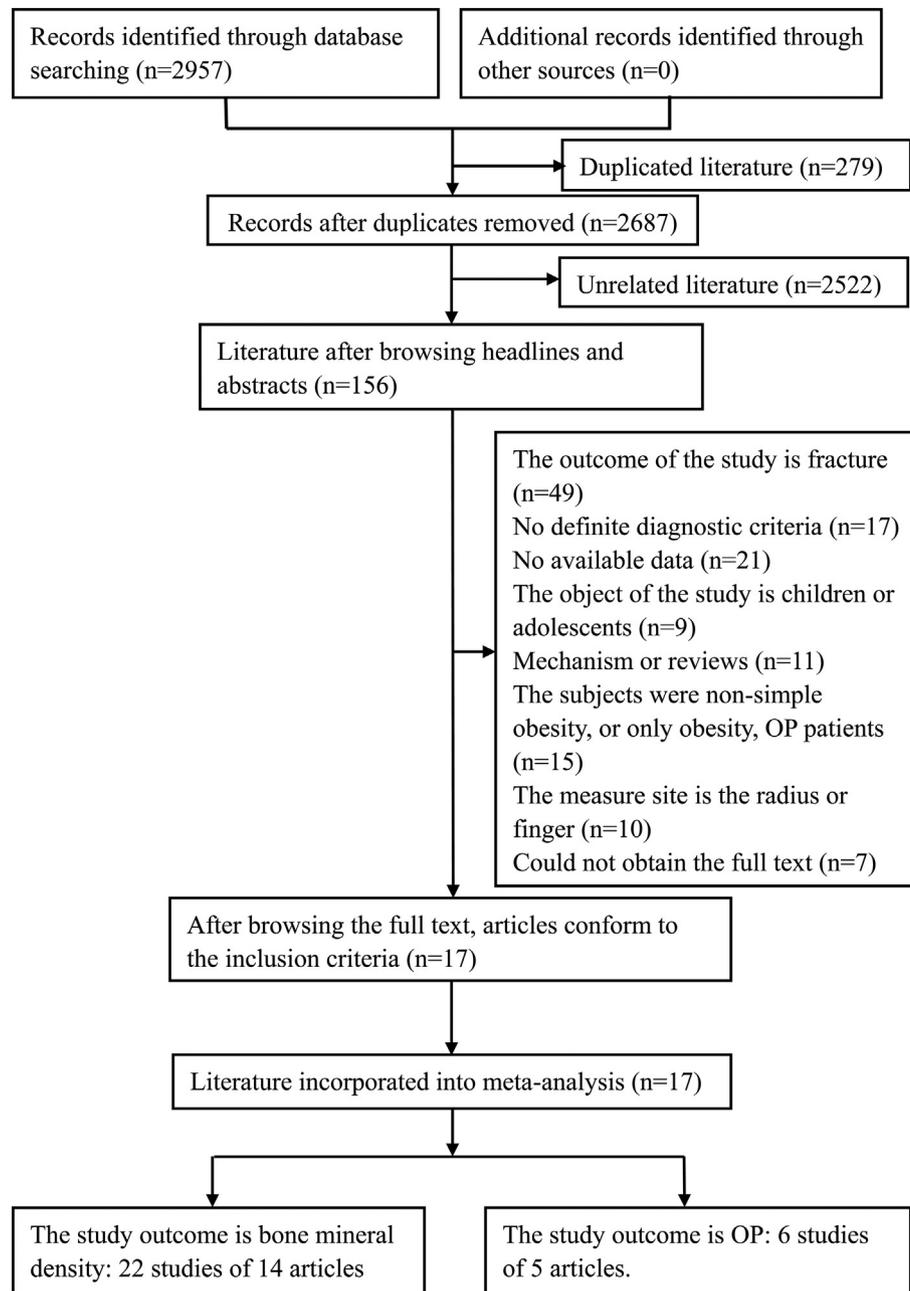


Fig. 1. Flow chart of the literature screening process. OP, osteoporosis.

### Quantitative data synthesis

#### Obesity and BMD

Twelve studies<sup>17–25,30–32</sup> reported the differences of lumbar spine BMD between healthy-weight adults and adults with obesity, and pooled results (Fig. 2A) show that adults with obesity had a higher level of BMD than healthy-weight participants, that is, obesity was positively correlated with BMD (merged WMD: 0.07 g/cm<sup>2</sup>; 95% CI: 0.045, 0.095;  $P < 0.001$ ;  $P_{\text{heterogeneity}} < 0.001$ ;  $I^2 = 89.1\%$ ). Similar significant results were found from twelve studies<sup>17,18,21–25,28–32</sup> that reported the differences of femoral neck BMD between healthy-weight adults and adults with obesity (Fig. 2B) (merged WMD: 0.087 g/cm<sup>2</sup>; 95% CI: 0.063, 0.112;  $P < 0.001$ ;  $P_{\text{heterogeneity}} < 0.001$ ;  $I^2 = 92.8\%$ ).

#### Obesity and osteoporosis

Three studies<sup>17,30,33</sup> reported the ORs and 95% CIs of osteoporosis in the femoral neck. Compared with healthy-weight individuals, adults with obesity had a lower risk of osteoporosis, suggesting obesity was a protective factor for osteoporosis (merged OR = 0.169; 95% CI: 0.132, 0.216;  $P < 0.001$ ;  $P_{\text{heterogeneity}} = 0.716$ ;  $I^2 = 0.0\%$ ) (Fig. 3B). However, the pooled results of three studies<sup>26,27,30</sup> reporting the ORs and 95% CIs of osteoporosis in the lumbar spine were not statistically significant (Fig. 3A).

#### Subgroup and sensitivity analyses

Significant heterogeneity was seen among studies investigating the differences in BMD between healthy-weight adults and adults

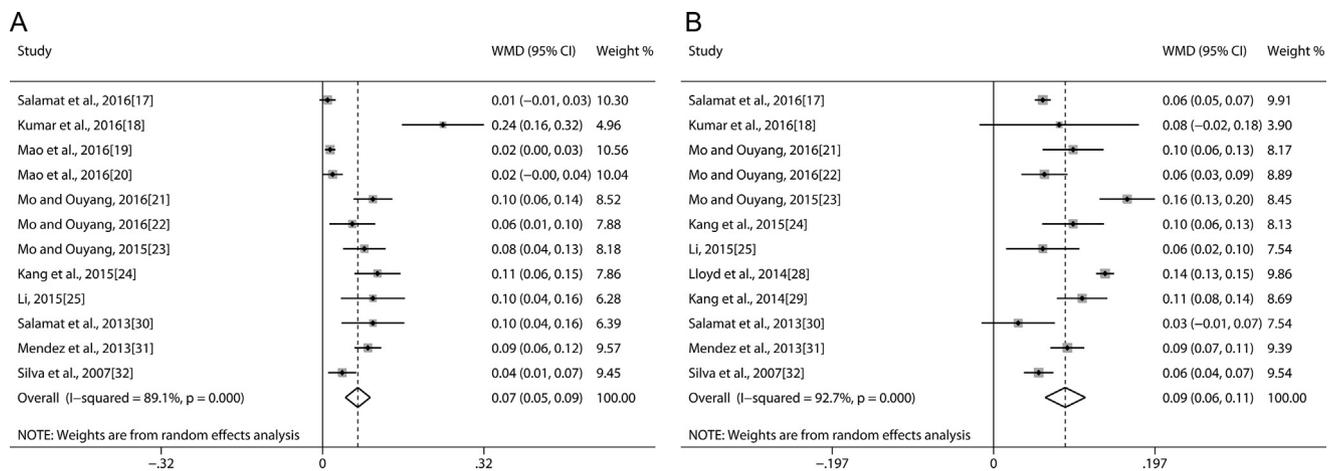
**Table 1**  
Details of the included studies.

Author(s), year <sup>a</sup>	Sample size	Sample source	Age in years (mean ± SD)	Sex	Region	Site of BMD assessment	Outcome variable	Quality score <sup>b</sup>
Salamat et al., <sup>17</sup> 2016	3392	Population	54.9 ± 11.6	Men and women	Isfahan, Iran	LS and FN	BMD, OP	8
Kumar et al., <sup>18</sup> 2016	170	Population	Premenopausal women: 32.51 ± 7.22, postmenopausal women: 53.8 ± 7.3	Women	North India	LS and FN	BMD	6
Mao et al., <sup>19</sup> 2016	2072	Hospital		Women	Jilin, China	LS	BMD	7
Mao et al., <sup>20</sup> 2016	934	Hospital		Women	Changchun, China	LS	BMD	7
Mo and Ouyang, <sup>21</sup> 2016	273	Hospital	Obese group: 66.58 ± 4.29, control group: 65.97 ± 4.69	Men	Changsha, China	LS and FN	BMD	6
Mo and Ouyang, <sup>22</sup> 2016	269	Hospital	Obese group: 58.49 ± 7.05, control group: 57.71 ± 7.41	Women	Changsha, China	LS and FN	BMD	6
Mo and Ouyang, <sup>23</sup> 2015	189	Hospital	Obese group: 38.51 ± 7.35, healthy group: 38.24 ± 8.17	Men	Changsha city, China	LS and FN	BMD	6
Kang et al., <sup>24</sup> 2015	260	Population	Healthy group: 64.0 ± 16, obese group: 60.9 ± 13.8	Men	China	LS and FN	BMD	8
Li, <sup>25</sup> 2015	131	Hospital	63.96 ± 7.60	Women	Anhui, China	LS and FN	BMD	7
Sun et al., <sup>26</sup> 2014	2498	Population	48.5 ± 10.0	Men and women	Xinjiang, China	LS	OP	7
Yang, <sup>27</sup> 2014	423	Hospital	58.3 ± 5.6	Women	Hubei, China	LS	OP	6
Lloyd et al., <sup>28</sup> 2014	1996	Population	Healthy group: 63.7 ± 10.4, obese group: 61.3 ± 8.9	Men	US	FN	BMD	8
Kang et al., <sup>29</sup> 2014	277	Population	Healthy group: 64.7 ± 17.1, obese group: 61.2 ± 14.5	Men	Jinan, China	FN	BMD	8
Salamat et al., <sup>30</sup> 2013	144	Population	62.6 ± 8.1	Men	Isfahan, Iran	LS and FN	BMD, OP	7
Méndez et al., <sup>31</sup> 2013	495	Hospital	Healthy group: 59.6 ± 7.55, obese group: 59.7 ± 6.9	Women	Mexico	LS and FN	BMD	9
Silva et al., <sup>32</sup> 2007	588	Hospital	Healthy group: 53.9 ± 4.0, obese group: 54.5 ± 3.7	Women	Rio de Janeiro, Brazil	LS and FN	BMD	7
Barrera et al., <sup>33</sup> 2004	845	Population	75.6 ± 4.3	Men and women	Santiago, Chile	FN	OP	6

BMD, bone mineral density; FN, femoral neck; LS, lumbar spine; OP, osteoporosis; SD, standard deviation.

<sup>a</sup> Listed in the order of publication (most recent to oldest).

<sup>b</sup> Agency for Healthcare Research and Quality (AHRQ) quality score: low quality, 0–3; medium quality, 4–7; high quality, 8–11.



**Fig. 2.** Forest plots showing the effects of obesity on bone mineral density of (A) the lumbar spine and (B) the femoral neck. CI, confidence interval; WMD, weighted mean difference.

with obesity. Subgroup analyses by region, study quality and sample source (population/hospital) showed no significant differences; however, subgroup analyses by gender showed that men with obesity had a higher level of BMD than women. Nevertheless, heterogeneity remained after subgroup analysis (Supplement Table 1). Therefore, sensitivity analyses by removing one study at a time (Supplement Figure 1) were performed, and a Galbraith diagram (Supplement Figure 2) was produced. The results indicated that nine studies (studies by Salamat et al.,<sup>17</sup> Kumar et al.,<sup>18</sup> Mao et al.,<sup>19</sup> Mo and Ouyang,<sup>21</sup> Mo and Ouyang,<sup>23</sup> Kang et al.,<sup>24</sup> Lloyd

et al.,<sup>28</sup> Méndez et al.<sup>31</sup> and Silva et al.<sup>32</sup>) may be the sources of high heterogeneity. After eliminating these nine studies, heterogeneity significantly decreased or even disappeared, and the results remained consistent (Supplement Figure 3).

#### Publication bias

Significant publication bias existed among twelve studies reporting the differences of BMD in the lumbar spine between healthy-weight adults and adults with obesity (Egger's test:

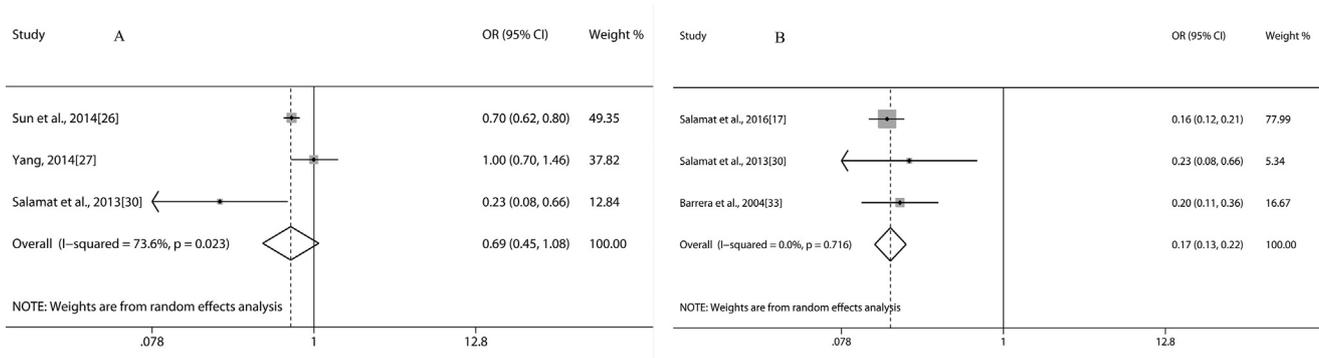


Fig. 3. Forest plots showing the effects of obesity on osteoporosis of (A) the lumbar spine and (B) the femoral neck. CI, confidence interval; OR, odds ratio.

$P < 0.001$ ) (Fig. 4). Contour-enhanced funnel plots (Supplement Figure 4) indicated that the missing studies were located in a statistically significant area, suggesting that asymmetry may not be caused by publication bias.

**Discussion**

Osteoporosis and obesity are important public health concerns among the middle-aged and elderly population.<sup>34,35</sup> Previous studies have shown that obesity is associated with the risk of osteoporosis;<sup>36,37</sup> however, the results are inconsistent, which may be due to small sample sizes and different study methods. A meta-

analysis can provide more reliable evidence than separate research by summarising a number of study results to overcome the shortcomings of small sample sizes and inadequate statistical efficacy.<sup>38</sup> Hence, we conducted a meta-analysis to assess the association of general obesity with BMD and osteoporosis.

This study showed that adults with obesity had a higher level of BMD than healthy-weight participants, when taking into account both the lumbar spine and femoral neck measurements, that is, obesity was positively correlated with BMD. Subgroup analysis by sex showed that the association was more significant in men with obesity, suggesting that obesity, especially in men, could increase BMD. One possible explanation for the difference seen between

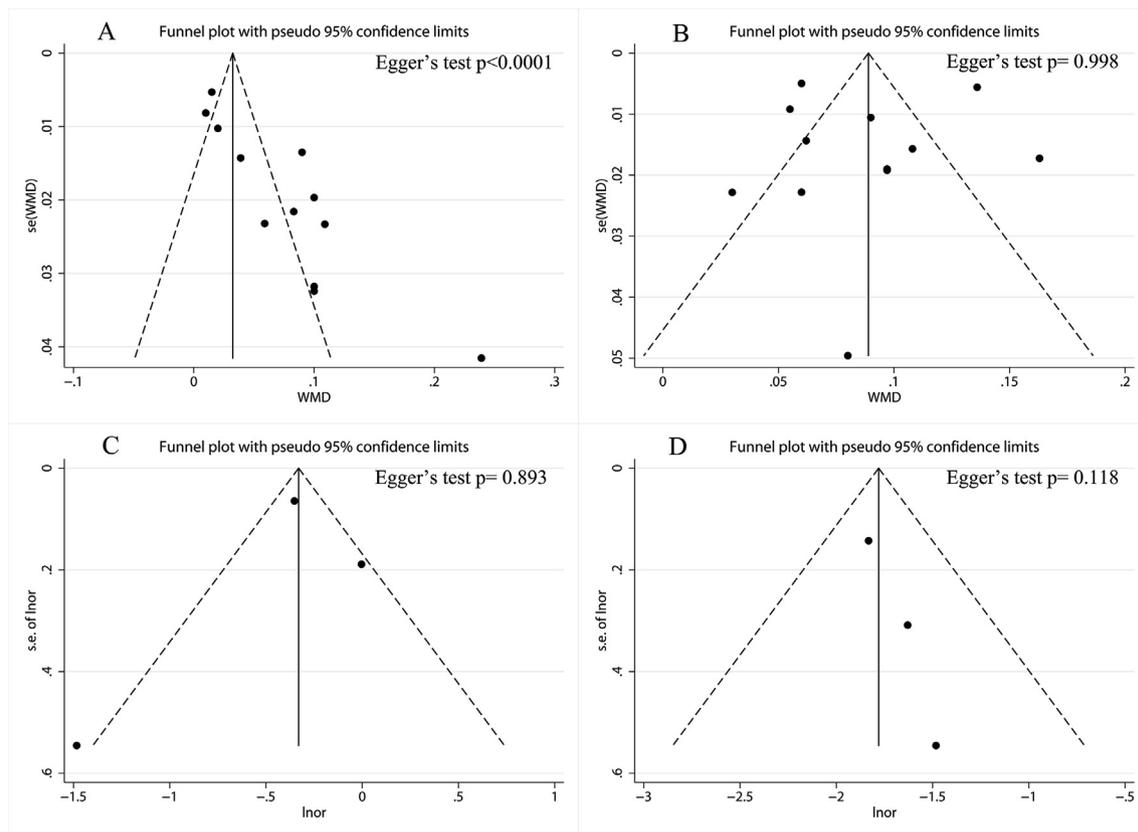


Fig. 4. Funnel plots showing the relationship between obesity and bone mineral density (BMD) and osteoporosis. (A) Twelve studies reported on the differences in lumbar spine BMD between healthy-weight adults and adults with obesity; (B) 12 studies reported on the differences in femoral neck BMD between healthy-weight adults and adults with obesity; (C) three studies reported on the odds ratio (OR) and 95% confidence interval (CI) of osteoporosis in the lumbar spine between adults with obesity and healthy-weight adults; (D) three studies reported on the OR and 95% CI of osteoporosis in the femoral neck between adults with obesity and healthy-weight adults. InOR, xxx ; se, standard error; WMD, weighted mean difference.

men and women may be a result of the changes in hormone levels before and after menopause in women, which has an impact on BMD. We did not find statistical significance between obesity and lumbar spine osteoporosis, which may be due to insufficient studies being included in this meta-analysis. It should be noted that increased body weight leads to augmented mechanical stimulation on bone, which promotes osteoblast activation and bone formation. However, this mechanical stimulating effect mainly exists in the weight-bearing bones, which might partly explain why there was no significant association between obesity and lumbar spine osteoporosis. In addition, there was a negative correlation between obesity and osteoporosis in the femoral neck, indicating obesity was a protective factor for osteoporosis.

Significant heterogeneity was noted among studies investigating the differences in BMD between healthy-weight adults and adults with obesity. Thus, subgroup analyses were carried out based on the characteristics of the study, but the source of heterogeneity was not found. Sensitivity analyses and the Galbraith diagram showed that nine studies (studies by Salamat et al.,<sup>17</sup> Kumar et al.,<sup>18</sup> Mao et al.,<sup>19</sup> Mo and Ouyang,<sup>21</sup> Mo and Ouyang,<sup>23</sup> Kang et al.,<sup>24</sup> Lloyd et al.,<sup>28</sup> Méndez et al.<sup>31</sup> and Silva et al.<sup>32</sup>) had significant impact on the results. Although the selected studies explored the relationship between obesity and BMD or osteoporosis in adults, the majority of study participants were aged >50 years and were postmenopausal women. Among 12 studies investigating the differences in femoral neck BMD between healthy-weight adults and adults with obesity, four studies (studies by Salamat et al.,<sup>17</sup> Mo and Ouyang,<sup>23</sup> Silva et al.<sup>32</sup> and Lloyd et al.<sup>28</sup>) had high heterogeneity. Of these, the studies by Salamat et al.<sup>17</sup> and Mo and Ouyang<sup>23</sup> obtained data from participants of different age groups, including men aged <50 years and premenopausal women. Therefore, age may be one of the sources of heterogeneity; however, owing to the lack of data grouped by age, subgroup analysis could not be carried out.

The relationship between obesity and osteoporosis has received wide attention, and there are several possible mechanisms to explain the complex relationship between adipose tissue and bone. First, adipose tissue is thought to secrete a variety of 'fat factors' that affect metabolism, bone and cardiovascular function.<sup>39</sup> Furthermore, adipose tissue is one of the main sources of the aromatic enzyme that synthesises oestrogen from the androgen precursor, which plays an important role in maintaining bone balance and preventing osteoporosis.<sup>40</sup> In addition, recent studies suggest that bone cells can express some specific hormone receptors, such as osteocalcin and osteopontin. These bone factors can affect body weight and blood glucose level.<sup>41</sup> Therefore, as an endocrine target organ, bone is also an endocrine organ, which may affect the function of other organs. Finally, adipocytes and osteoblasts all originate from a mesenchymal stem cell with multiple differentiation potentials. Under the influence of cell transcription factors, the cells have the tendency to differentiate into adipocytes and osteoblasts.<sup>42</sup> In addition, the fact that individuals with obesity require bones with more weight-bearing abilities must also be considered.

In this study, a comprehensive search strategy and strict inclusion and exclusion criteria were used to ensure the comprehensiveness and quality of the literature search. BMD was measured by DXA in all included studies, which ensured accuracy and precision of the measurement results. Our study also has several limitations. First, BMD is related not only to obesity but also to age and the menopause status of women. However, because of the lack of specific data, this study did not examine the effect of age or menopause status on BMD. Second, cross-sectional studies mostly found a significantly higher BMD in adults with obesity. Given the nature of cross-sectional studies and the lack of evidence on the

long-term consequences of adult obesity on BMD, more prospective research should be performed in this field.

There was a strong positive correlation between obesity and BMD, both in the lumbar spine and femoral neck measurement sites, and this association was more significant in men with obesity. Furthermore, obesity was negatively correlated with osteoporosis, indicating that obesity was a protective factor for osteoporosis.

## Author statements

### Author contributions

D.Q., Y.L., X.L., X.Z., X.Q. and H.Z. made substantial contributions to the implementation and technical completion of the study. D.Q., Y.L., X.L., G.Z. and C.W. contributed to conception and design of the study. D.Q., Y.L. and X.Z. critically revised the manuscript and helped draft the final version. D.Q., Y.L., X.Q. and H.Z. conducted the statistical analysis, interpreted the data and prepared the manuscript. All authors read and approved the final manuscript.

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### Ethical approval

Ethics approval was obtained from the Zhengzhou University Life Science Ethics Committee, and written informed consent was obtained from all participants (ethics approval code: [2015] MEC (S128)).

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### Competing interests

None declared.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhe.2019.11.001>.

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