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Warm needle acupuncture in primary osteoporosis management: a systematic review and meta-analysis

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ABSTRACT

Background Warm needle acupuncture (WNA) is commonly used in primary osteoporosis (OP) management in China. The evidence of its effectiveness needs to be systematically reviewed.

Objective The aim of the meta-analysis was to evaluate whether using WNA alone or combined with conventional medicine benefits primary OP.

Methods PubMed, Embase, the Cochrane Central Register, Medline, China National Knowledge Infrastructure, Wanfang and VIP databases were searched from their inception through 30 June 2016. RCTs applying WNA independently or as an adjunct to conventional medicine, compared with conventional medicine alone, were included. Primary outcomes were bone mineral density (BMD) of the lumbar vertebrae, femoral neck, Ward's triangle and greater trochanter. The secondary outcome was chronic pain measured by VAS score. Meta-analysis was conducted using RevMan V.5.3 software.

Results Nine RCTs involving 572 participants were included. When WNA was used as an adjunct to conventional medicine, meta-analysis revealed a statistical difference in favour of increasing BMD of the lumbar vertebrae (mean difference (MD)=0.06, 95% CI 0.03 to 0.08, P<0.001). WNA increased BMD of the femoral neck (MD 0.14, 95% CI 0.08 to 0.21, P<0.001) and greater trochanter (MD 0.09, 95% CI 0.04 to 0.15, P<0.001) when used alone, and additionally decreased VAS scores (MD=−1.10, 95% CI −1.14 to −1.06, P<0.001) when used as an adjunct to conventional medicine. However, the safety of WNA was not specifically reported.

Conclusions WNA may have beneficial effects on BMD and VAS scores of patients with primary OP. However, all included trials were at high risk of bias and of low quality. Further rigorous studies are needed to determine the effectiveness of WNA for primary OP treatment.

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INTRODUCTION

Osteoporosis (OP) is a disease that is characterised by decreased bone strength and a high risk of bony fractures. OP can strike at any age, but it is the main cause of fractures in elderly and postmenopausal women. OP is also called a 'silent disease', for it gradually progresses without any symptoms until bony fractures occur. Fractures occurring in the hip can be permanently disabling. According to a document produced by the National Osteoporosis Foundation, OP is a growing public health problem and economic burden worldwide because of its high morbidity. In the USA, approximately 10 million Americans are diagnosed with OP and 43.1 million are diagnosed with osteopaenia which is attributed to 2 million fractures annually.[1] Also, there were nearly 22 million women and 5.5 million men diagnosed with OP in the European Union in 2010.[2] The situation in low/middle income countries in Asia is even worse. In China, the OP population is expected to sharply increase to 212 million by 2050, resulting in a heavy burden on the social medical system.[3]

OP is a systematic bone disorder that results from the imbalance of bone resorption and bone formation.[4] In healthy bone, more than 10% of bone mass is remodelling in bone multicellular units by osteoclasts and osteoblasts at any time point.[5] OP occurs when osteoclasts are degrading the bone matrix faster than osteoblasts are rebuilding it. Inadequate peak bone mass, excessive bone resorption and inadequate formation of new bones have become the three key underlying mechanisms of OP.[6] Hormonal factors and changes in calcium metabolism related to ageing are thought to play important roles in the above mechanisms. Thus, the main purpose of primary OP management is to slow down the progress of OP and improve the quality of life of patients. The conventional medicines used in OP treatment include oestrogen, bisphosphonates and calcium.[7] Comprehensive therapy, including nutrition, proper

exercise, healthy lifestyle changes and fall prevention, is also recommended.[8 9]

However, due to the low efficiency and side effects of conventional medications, Chinese herbal medicines and alternative therapies are also used in China.[10 11] Many Chinese herbal medicines and their derivatives are considered useful for relieving OP symptoms in view of their oestrogenic properties.[12–14] Additionally, acupuncture, used as a tool for treating a wide spectrum of diseases, can also have potential benefits in OP by improving bone mineral density (BMD) and attenuating acute fracture-related pain.[15] The underlying mechanism may be related to increased serum 17-beta-oestradiol (E2), deoxypyridinoline and serum bone-specific alkaline phosphatase levels, and reduced serum levels of C-terminal cross-linking telopeptide of type I collagen (CTX-I).[16–19]

Warm needle acupuncture (WNA), a specialised form of acupuncture therapy, involves placement of an ignited moxa stick on the handle of the needle after inserting it into the body. It is now commonly used in clinical practice to treat OP in China, where it is anecdotally considered to be more effective than regular acupuncture. However, to our knowledge there has been no critical appraisal of the evidence for WNA in primary OP management. Therefore, the aim of this review was to systematically review the literature for randomised controlled trials (RCTs) examining the effect of WNA in the primary management of OP.

METHODS

Protocol and registration

The protocol and search strategy of the review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database on 1 August 2016 (registration no. CRD42016043899). It was conducted and reported according to the PRISMA guideline.

Eligibility criteria

We aimed to include all RCTs of WNA, whether applied alone or in combination with conventional medicine, in participants diagnosed with primary OP or osteopaenia, diagnosed according to World Health Organization (WHO) recommended criteria, regardless of age and gender. To be included, trials needed to have used BMD or visual analogue scale (VAS) pain score as outcome measures and to have been published in English or Chinese. Letters, case reports, reviews and commentaries were excluded, as were trials with participants diagnosed with secondary OP.

Outcomes

Primary outcome measures were BMD of the lumbar vertebrae, femoral neck, femoral Ward's triangle and femoral greater trochanter. The secondary outcome was chronic pain related to OP as measured on a VAS.

Search strategy

The following electronic bibliographic databases were searched from their inception until 30 June 2016: Medline, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), the Chinese VIP database and Wangfang database. MeSH and free text terms were employed for searching. The literature search was performed in English and Chinese. The following search terms were used individually or combined: "osteoporosis"; "osteopenia"; "bone loss"; "warming needle"; "moxibustion"; "acupuncture". Chinese search terms included "guzhishusong", "wenzhen", "aijiu", "zhenjiu" and "zhenci". Details of the search strategies for PubMed and Embase are shown in online supplementary appendix 1.

Study selection

Two authors selected the included trials according to the eligibility criteria independently. Disagreement was resolved by discussion.

Data extraction and management

The following information was extracted from the included trials: author, age, participants, duration of symptoms, interventions and outcomes. Any disagreement regarding the eligibility of a study was resolved by discussion with a third author.

Assessment of risk of bias

The Cochrane Collaboration's tool was used in order to assess the methodological quality of the selected studies, based on the following seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias.[20] The quality of the trials was assessed by two authors independently. Disagreement was resolved by discussion.

Data synthesis and analysis

The primary outcome was BMD of the lumbar vertebrae, femoral neck, femoral Ward's triangle and femoral greater trochanter. The secondary outcome was the VAS score for OP-related pain. The meta-analysis and statistical analyses were conducted using RevMan V.5.3 software (Cochrane, London, UK). Means and SDs for different outcomes were calculated and compared between groups. Continuous and dichotomous outcomes were presented as risk ratio (RRs), mean differences (MDs) and 95% CIs. Heterogeneity among studies was assessed using the Higgins I^2 test. A random effects model was applied if I^2 >50%; otherwise, a fixed effects model was used. In cases of obvious heterogeneity, subgroup analysis was conducted. Publication bias was also evaluated by determining if the data points formed a symmetric

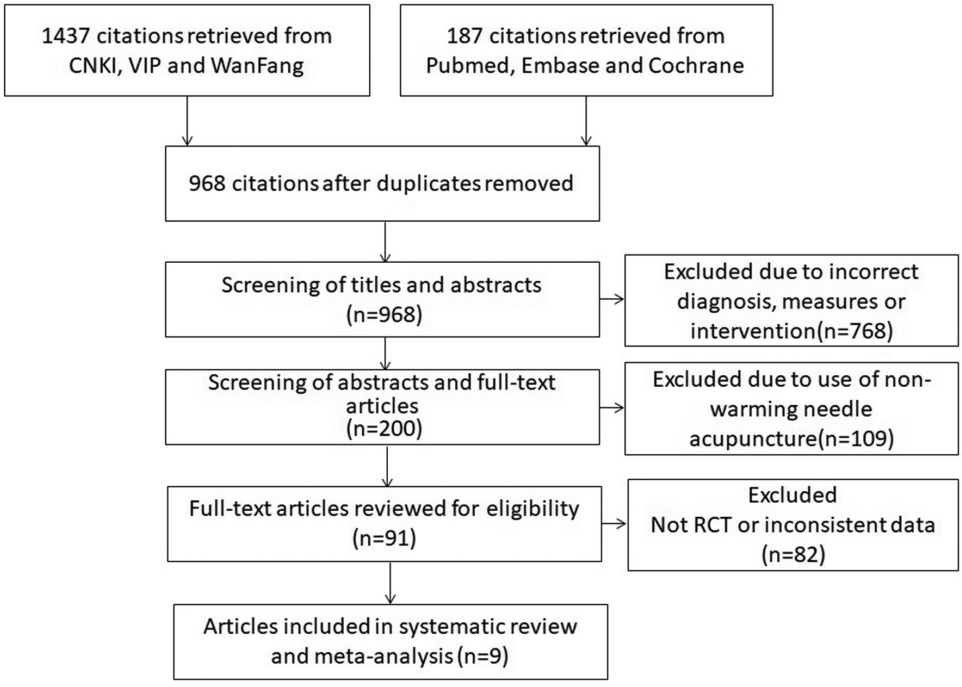

Figure 1 Flow diagram for study selection. CNKI, China National Knowledge Infrastructure; RCT, randomised controlled trial.

funnel-shaped distribution and had a one-tailed significance level of P>0.05 by Egger's test when included studies were ≥10.

RESULTS

Study selection

Of 1624 potential citations identified in the initial search, 656 duplicate articles were excluded (figure 1). A further 768 citations were excluded due to the lack of a primary OP diagnosis and BMD/VAS measurement. Then, 109 studies that used non-warming needle acupuncture were excluded. Eighty-two were either not RCTs or did not meet our inclusion criteria, and were thus excluded. Finally, nine studies were included for further qualitative and quantitative analyses.[21–29]

Study characteristics

The nine included studies involved 572 participants in total. Three hundred and three participants received WNA (alone or combined with conventional

Table 1 Main characteristics of included RCTs

First author (year)	Age (mean±SD)	Participants	Treatment group	Control group	Intervention duration	Outcomes	Adverse events
Luo (2015)[21]	54.8±6.2	36	(A) WNA (n=18)	(B) Osteoform capsules (n=18)	6 months	BMD	Not mentioned
Zhou (2014)[22]	T: 62.4±7.12 C: 61.4±8.06	60	(A) WNA + (B) (n=30)	(B) Risedronate (n=30)	1 month	BMD, VAS	Not mentioned
Cai (2014)[23]	T: 51±6 C: 50±6	90	(A) WNA (n=30)	(B) Caltrate D tablets (n=30)	1 month	BMD, VAS	Not mentioned
Wu (2012)[24]	T: 68±5.27 C: 68±5.27	55	(A) WNA + (B) (n=25)	(B) Caltrate D; alfacalcidol (n=30)	3 months	BMD, VAS	Not mentioned
Nong (2011)[25]	T: 67.8±6.83 C: 69.4±4.12	63	(A) WNA (n=32)	(B) Vitamin D2 calcium hydrogen phosphate (n=31)	3 months	BMD, VAS, BGP	Not mentioned
Ouyang (2011)[26]	T: 64.4±5.3 C: 65.6±6.6	55	(A) WNA + (B) (n=25)	(B) Alendronate (n=30)	6 months	BMD	Mentioned
Wang (2008)[27]	T: 61±4.6 C: 62±5.2	103	(A) WNA + (B) (n=73)	(B) Bone phosphorus capsule (n=30)	6 months	BMD, BGP, E2	Not mentioned
Liang (2007)[28]	T: 61.3 C: 61.3	80	(A) WNA (n=40)	(B) Caltrate D (n=40)	3 months	BMD	Not mentioned
Chen (2004)[29]	T: 58.1±7.25 C: 57.6±7.68	60	(A) WNA + (B) (n=30)	(B) Caltrate D (n=30)	6 months	BMD, E2	Not mentioned

BGP, bone Gla protein; BMD, bone mineral density; C, control group; E2, oestradiol; T, treatment group; WNA, warm needle acupuncture.

medicine), while 269 participants were treated with conventional medicine only. The characteristics of the included studies (including first author, age, participants, interventions, duration of intervention and outcome measurements) are shown in table 1. Of the nine included studies, four trials compared WNA with conventional medicine (comparative effectiveness) and five trials compared WNA combined with conventional medicine with conventional medicine alone (adjunctive effectiveness). All of them used BMD and VAS as outcome measures to determine treatment effects.

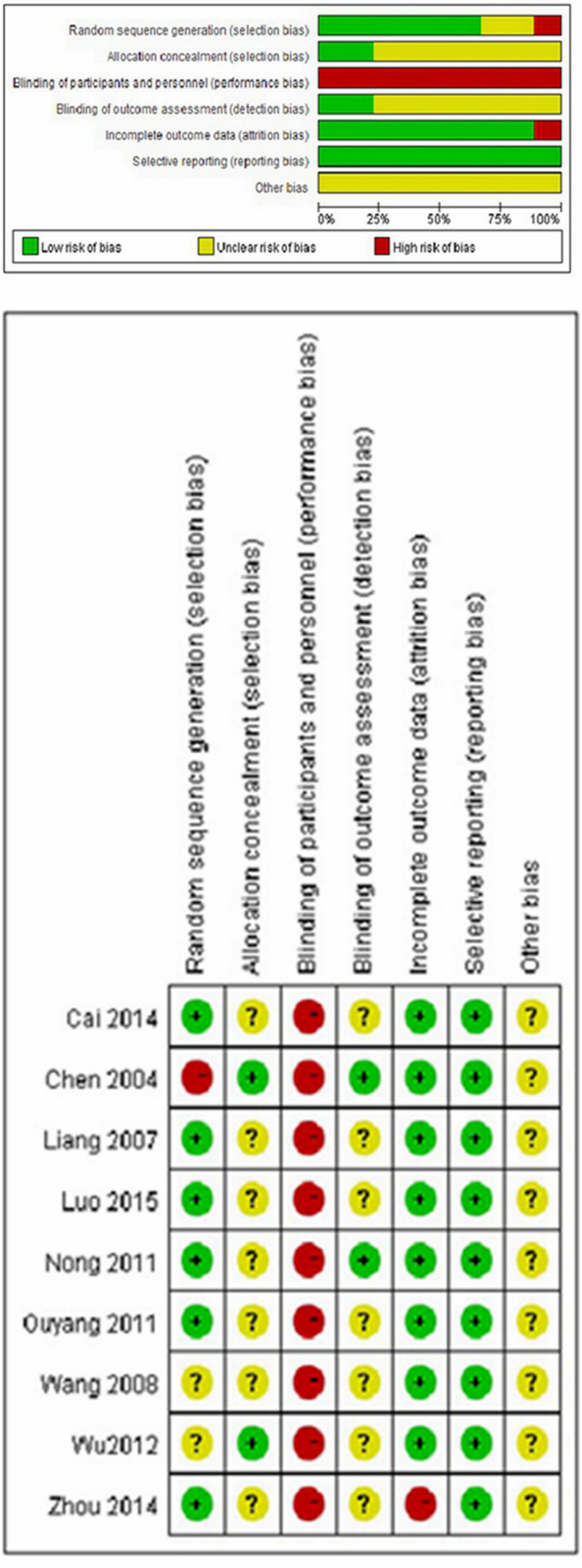

Figure 2 Risk of bias assessment.

Risk of bias assessment

The quality of the trials was generally low according to the Cochrane Collaboration's risk of bias tool (figure 2). Over half of the included studies were at high risk of selection and detection bias due to unclear random sequence generation, allocation concealment and blinding of outcome assessors. None of the published reports mentioned whether an intention-to-treat analysis was performed. As none of the trials aimed to determine efficacy and therefore did not include a sham acupuncture arm, blinding of participants and therapists was not deemed to be applicable for this review.

Type of outcomes

Of nine included studies, six trials measured BMD of the lumbar vertebrae.[21 23 25 27–29] Three trials additionally quantified BMD of the neck, Ward's triangle and greater trochanter of the femur.[21 25 29] In terms of secondary outcomes, four trials assessed pain using the VAS scale.[22–25]

BMD of lumbar vertebrae

Six trials[23 24 26–29] providing completed numerical data for BMD of lumbar vertebrae in the experimental and control groups were included in a meta-analysis. Due to the low heterogeneity among these studies (I^2=16%, P=0.27; I^2=0%, P=0.96), a fixed effects model was applied. As shown in figure 3A, the pooled results yielded evidence of effectiveness with respect to lumbar BMD in favour of WNA when used as an adjunct to conventional medicine (MD 0.06, 95% CI 0.03 to 0.08). However, WNA did not appear to be effective at increasing lumbar BMD when used as an independent intervention compared with a conventional medicine control group (MD −0.06, 95% CI −0.19 to 0.07).

BMD of femoral neck, Ward's triangle and greater trochanter

Three trials[21 25 29] reported on BMD of the femoral neck, Ward's triangle and greater trochanter. Two of these trials[21 25] compared WNA with conventional medicine and were combined in a meta-analysis (figure 3). Due to a high level of heterogeneity for the femoral Ward's triangle (I^2=87%, P=0.006), a random effects model was used for the parameters. By contrast, a fixed effects model was used to analyse the data pertaining to the femoral neck (I^2=26%, P=0.24)

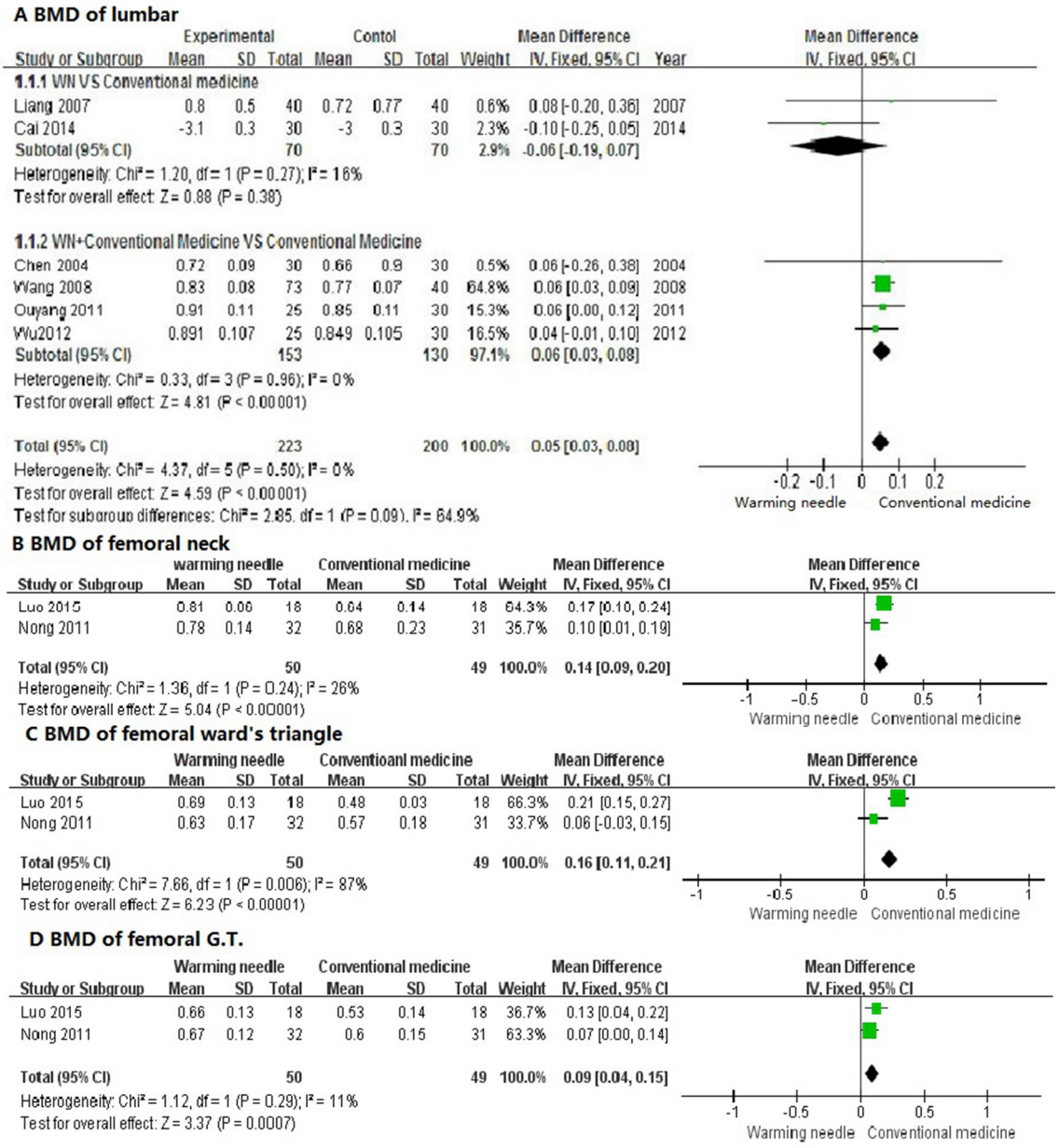

Figure 3 BMD, bone mineral density; WNA, warm needle acupuncture.

and greater trochanter (I^2=11%, P=0.29) due to lower heterogeneity. Compared with the control group, WNA increased BMD of the femoral neck (MD 0.14, 95% CI 0.08 to 0.21, P<0.001) and the greater trochanter (MD 0.09, 95% CI 0.04 to 0.15, P<0.001) but not the femoral Ward's triangle (MD 0.14, 95% CI −0.01 to 0.2, P=0.07) (shown in figure 3B–D).

VAS pain score

Four included trials (two comparative effectiveness and two adjunctive effectiveness studies) assessed analgesic effects of WNA on patients with OP by measurement of VAS scores.[22–25] A random effects model was employed due to high heterogeneity in this outcome measure (I^2=81%, P=0.15). As shown in figure 4, the pooled results showed that WNA generated a small reduction in VAS pain score when used as an adjunct to conventional medicine (MD −1.10, 95% CI −1.14 to −1.06, P<0.001) while no significant difference was found between WNA and conventional medicine when compared directly (MD −1.72, 95% CI −4.03 to 0.60, P=0.15).

DISCUSSION

This systematic review and meta-analysis summarised available RCTs examining the effect of WNA, applied independently or as an adjunct to conventional medicine, in primary OP management. Nine studies were included in this review. According to limited data derived from the included trials, WNA used independently or as an adjunct to conventional medicine

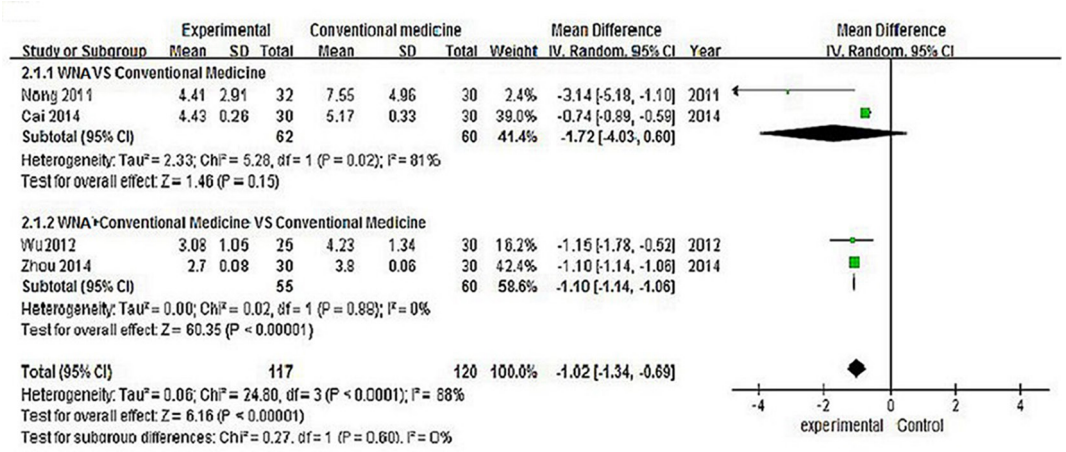

Figure 4 VAS pain score. WNA, warm needle acupuncture.

may lead to a beneficial increase in lumbar or femoral BMD and reduction in VAS scores. However, the poor quality of the evidence and very high risk of bias of the included trials are major limitations of the data, dspite the fact it should arguably have been easy to blind outcome assessors for the primary outcome measure of BMD, which is highly objective in nature. Thus, the finding of a benefit of WNA in OP treatment is unlikely to be conclusive and therefore further evidence is needed.

In the present review, nine RCTs involving 572 participants were included. When WNA was compared with conventional medicine), meta-analysis revealed a statistical difference in favour of increasing BMD of the lumbar vertebrae and femoral Ward's triangle, and attenuated VAS scores, when WNA was used as an adjunct to conventional medicine. Moreover, WNA increased BMD of the femoral neck and greater trochanter when applied alone. However, there are many limitations of this review that must be acknowledged. First, all of the included trials inadequately reported randomisation and none of them reported the details of random allocation or allocation concealment, which may have led to selection bias. Second, none of the included trials mentioned whether a blinding method was used, although it can be assumed there was no masking given the absence of a sham acupuncture control capable of blinding participants. Third, all of the trials used a small sample size and had significant methodological limitations. Fourth, only one of them mentioned adverse events. Thus, we cannot draw a definitive conclusion as to whether WNA might be a promising (i.e. safe and effective) method of attenuating osteoporotic syndromes such as low BMD and related chronic pain.

Although the clinical effect of WNA in primary OP treatment remains inconclusive, preclinical research and clinical studies in related fields are encouraging. According to recent studies, acupuncture and relative supplemental therapies are effective at treating orthopaedic ageing-related degenerative diseases. For example, electroacupuncture (EA) appeared to prevent the degeneration of articular cartilage, at least partly though the regulation of matrix metalloproteinase (MMP)-13 and inhibition of mitogen-activated protein kinases (MAPK)s in the cartilage of rats with osteoarthritis.[30] Ren and colleagues found that both acupuncture and moxibustion increased reproductive endocrine function in male rats with partial androgen deficiency of the ageing male,[31] , commonly known as andropause or late-onset hypogonadism, which is a series of symptoms related to testosterone deficiency such as sexual degeneration, osteopaenia and OP. Other research in animal models has demonstrated that the effect of EA and mild moxibusion on gene expression and proinflammatory cytokines may be useful for treating age-related diseases.[32 33] Thus, WNA (as a modified acupuncture therapy that combines acupuncture and thermal stimulation) may similarly alleviate OP via similar underlying mechanisms of action.

In summary, WNA may have beneficial effects on BMD and VAS scores of patients with primary OP. However, all included trials were at high risk of bias and of low quality. Further rigorous studies are needed to determine the effectiveness of WNA for primary OP treatment.

Contributors DL and YL contributed equally to data analysis and manuscript preparation. YW, RM and LW were responsible for data collation, extraction and management. RG registered the protocol in the PROSPERO database. WF was responsible for protocol design.

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Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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