ABSTRACT

Introduction As populations age, osteoporosis has become a hot topic of global public concern. The beneficial effects of traditional Chinese exercises on the musculoskeletal system have been demonstrated. However, previous research findings on osteoporosis are inconsistent, and it is unclear which type of exercise and its frequency and duration have the best effect on osteoporosis. This study aims to investigate the most appropriate exercise modality for people with osteoporosis through systematic evaluation and network meta-analysis to guide clinical practice.

Methods and analysis The Cochrane Library, Web of Science, MEDLINE, Embase, China Biomedical Literature, China Knowledge Network, China Science and Technology Journal and Wanfang databases will be searched until January 2022. The language of the articles should be English or Chinese. All clinical randomised controlled trials on the effect of traditional Chinese exercises on osteoporosis will be included. We will use RevMan, Stata and GeMTC software to complete our network meta-analysis. We will perform risk of bias assessment, subgroup analysis and sensitivity analysis to correct the results. Finally, we will use the Grading of Recommendations Assessment, Development and Evaluation guideline development tool and Confidence in Network Meta-Analysis (CINeMA, a new method for assessing CINeMA results) approach to evaluate the reliability of our final results.

Ethics and dissemination All data for this study will be obtained from published studies, so no ethical review will be needed. We will publish the results of the study in a peer-reviewed journal.

PROSPERO registration number CRD42022323622.

INTRODUCTION

Osteoporosis (OP) is a progressive systemic skeletal disease characterised by low bone mass and microarchitectural degeneration of bone tissue, leading to increased bone fragility and fracture susceptibility. It is a common bone disease that affects more than 200 million patients worldwide. Taking the UK as an example, among women over 50 years of age, the proportion of women suffering from OP is 21.8%, and the proportion will continue to increase with age. Currently, approximately 54,000 new fragility fractures occur each year in the UK, creating a considerable financial burden, costing more than £4.7 billion a year and accounting for more than 2.4% of total healthcare costs. As demographics change, the risk of fragility fractures will rise rapidly. OP is already a global public health problem, and its early prevention and treatment are crucial.

Physical exercise is recommended as a low-cost and safe non-pharmacological intervention strategy to maintain musculoskeletal health. Current studies have shown that exercise can improve bone mineral density (BMD) and balance in patients to prevent falls, thereby reducing fragility fractures. With cultural exchange, traditional Chinese exercises (TCEs) have spread worldwide and flourished. TCEs, including Tai Chi, Qigong,
Baduanjin and Wuqinxi, are defined as moderate-intensity to low-intensity aerobic exercises that improve limb strength and human health.\textsuperscript{13} They combine balance and coordinated movements based on traditional aerobic exercises and are good for mental health. Studies have shown that participants who perform TCEs have higher levels of completion and greater persistence.\textsuperscript{15} TCEs are now considered to be of great value in the prevention and treatment of many chronic diseases, including OB.\textsuperscript{16} 17

According to related studies, TCEs substantially improve balance, reduce the incidence of fractures among OP patients, and increase BMD in elderly individuals. Tai Chi is considered to be superior to single-factor training programmes, such as endurance and resistance. It is better at building physical coordination, improving muscle mass, and reducing the risk of falls among older adults.\textsuperscript{18} In particular, Tai Chi may have longer-term fall prevention benefits in terms of walking posture adjustment and training.\textsuperscript{19} In terms of improving BMD, several meta-analyses in recent years have shown beneficial effects of Tai Chi in improving BMD in postmenopausal women.\textsuperscript{20–22} Qigong can improve flexibility and lower limb stability, improve body coordination and stability to reduce the risk of falls and is effective in improving pain in joints and other areas of the body.\textsuperscript{23} A randomised controlled trial (RCT) showed that Baduanjin (a form of Qigong that consists of eight independent, simple, subtle and smooth movements) increased BMD and decreased interleukin-6 (IL-6) levels in middle-aged women.\textsuperscript{24} A recent clinical study confirmed that Baduanjin is an effective, safe and beneficial exercise to improve the physical and mental health of patients with postmenopausal OP.\textsuperscript{25} Previous studies have found Wuqinxi to be effective in increasing BMD in patients with primary OP.\textsuperscript{26} However, these studies have problems such as small sample sizes in single studies and heterogeneity among studies. Currently, the efficacy of TCEs for OP is not clear, and the results regarding improvements in BMD in OP patients remain inconsistent.\textsuperscript{15} 17 The lack of evidence-based studies on the efficacies of different TCEs in treating OP makes it difficult to guide clinical practice. Moreover, information on the effect of the frequencies and durations of TCEs on OP is lacking. Currently, the optimal exercise prescription for patients with OP is unknown.

This is the first systematic review and network meta-analysis (NMA) of TCEs for OP. Through this study, we will summarise the evidence of the use of TCEs in the treatment of OP, clarify its effects on BMD, bone metabolism, fracture, pain and functional levels of OP patients, and provide ideas for OP exercise therapy. There is still a gap in the field of FITT (frequency, intensity, time and type) of TCEs that are most appropriate for patients with OP. We will compare the efficacy of different FITT components for patients with OP by using a NMA. Our findings will provide evidence for the optimal exercise treatment plan for patients with OP.

**METHODS**

This study protocol will be presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for the Protocol.\textsuperscript{28} This protocol is registered with PROSPERO under registration number CRD42022323622.

**Eligibility criteria**

Inclusion criteria: We will use the Population, Intervention, Outcome and Study design principle to evaluate the studies (Table 1).

Exclusion criteria: Studies meeting any of the following conditions will be excluded.

1. Animal studies or case reports (non-randomised controlled trials);
2. Incomplete data or unavailable full text;
3. Control group intervention consisting of TCEs or (4) duplicate studies.

**Data sources and search strategies**

Data sources: We will conduct literature searches in the Cochrane Library, Web of Science, MEDLINE, Embase,
China Biomedical Literature, China Knowledge Network, China Science and Technology Journal and Wanfang databases. The time period will be from the inception of the database to January 2022. The language of the articles should be English or Chinese. The following terms with their synonyms will be used for the database search: Qigong or Taiji or Taijiquan or Baduanjin or TCE or OP or Bone Loss. The types of articles will be limited to randomised controlled studies. Box 1 shows the search strategy on PubMed. This search strategy can also be used in the Cochrane Library, Web of Science and Embase. When necessary, the search string will be adapted to perfectly fit each database. We will search the China Biomedical Literature Database, China Knowledge Network, China Science and Technology Journal Database and Wanfang Database after the above terms and synonyms are replaced using Chinese.

Search process
The literature search and screening will be conducted independently by two authors (HC and RZ). In case of any disagreement, the decision will be made by the corresponding author (YY). First, we will use Endnote software to manage the literature and remove duplicates. Then, we will read through the titles and abstracts of the studies for the next screening step. During this process, we will document the reasons for removal. Finally, the studies included in this review will be selected by reading the full text. References to previous similar studies will be viewed for supplementation. Figure 1 illustrates this process.

Data extraction
A data extraction form will be designed before two authors (HC and KY) independently extract the data from the selected studies. The extracted data will have detailed information about the authors, year of publication, study population, interventions and outcomes. If disagreements occur between the two authors performing the data extraction, they will be resolved by the corresponding author (YY). The finalised information will be summarised in a table and reviewed.

The following items will be extracted:
1. Study characteristics, including the first author, country and year of publication.
2. Study design, including randomisation methods, blindness and allocation concealment.
3. Participants, including sample size, age range, sex ratio, diagnostic criteria and baseline status of various indicators of OP.
4. Interventions, including type of intervention, frequency of exercise, duration and other measures.
5. Outcomes, including all outcome measures, such as primary and secondary outcomes, completion time point, number of drop-outs, the time that the subjects performed the TCEs and adverse events.

Risk of bias assessment
All included studies will be assessed for risk of bias using the Cochrane Collaboration’s Risk of Bias tool. The risk of bias for each domain will be categorised as low, unclear or high. The risk of bias will be evaluated with RevMan software (V.5.4). Risk of bias includes the following main areas:
1. Random sequence generation (selection bias): Whether the method for generating random assignment sequences is described in detail so that different assignment groups can be assessed for comparability.
2. Allocation concealment (selection bias): Whether the method of concealing the random allocation scheme is described in detail, and whether the allocation method of the intervention is predicted before and during the assignment.
3. Blinding of participants and personnel (performance bias): Whether all methods of blinding subjects and experimenters are described in detail and all information relevant to whether the blinding method is effective is provided.
4. Blinding of outcome assessment (detection bias): Whether all methods of blinding outcome assessors are described in detail and all relevant information about whether the blinding method is effective is provided.
5. Incomplete outcome data (attrition bias): Whether the completeness of outcome data for each primary outcome, including participants lost to follow-up and excluded from analysis, is described; whether participants were reported for lost to follow-up and excluded from the analysis, the number of people in each intervention group (compared with the number at the time of enrolment), and whether the reason for loss
to follow-up and exclusion was reported, and whether the data included in the analysis are described by the systematic reviewer.

6. Selective reporting (reporting bias): Whether how the evaluator checked for possible selective outcome reports and what the conclusions were are described.

7. Other bias: Whether there are other factors that cause bias.

Data analysis
For all statistical results, a p<0.05 is considered statistically significant.

If the outcome indicator is a dichotomous variable, ORs with 95% CIs will be used for the effect size. If the outcome indicator is a continuous variable, mean differences (MDs) or standardised MDs with 95% CIs will be used for the effect size. If there are unclear or missing data, efforts will be made to contact the first author or corresponding author for more information, and if not, we will exclude the study.

Pairwise meta-analyses: If there are more than two studies on the same pair of interventions, we will use RevMan (V.5.4) software for pairwise meta-analysis. Heterogeneity among trials will be identified by the $\chi^2$ test and reported as $I^2$ statistics. If $I^2<50\%$, this indicates good homogeneity between experiments and a fixed model will be used. If $I^2>50\%$, heterogeneity is indicated and a random effects model will be used. We will use the contribution matrix to show the impact of each pairwise meta-analysis on the results.

NMA: We will use Stata (V.16.0) software to plot a network for each outcome, where each node represents an intervention and the line between nodes represents a direct comparison between the two, with the size of the nodes and lines proportional to the number of included studies.

We will use GeMTC (V.0.14.3) software and Markov chain Monte Carlo to perform Bayesian NMA to compare multiple interventions simultaneously. We intend to set the initial parameters of GeMTC as follows: 4 simulation...
chains, 10 steps (refinement interval), 50,000 iterations and the first 20,000 iterations for annealing to eliminate the influence of the initial values. We will use the Brooks-Gelman-Rubin statistical method to evaluate convergence. Convergence among the included studies will be expressed as a potential scale reduction factor (PSRF), which indicates good convergence when the PSRF is close to or equal to 1. The split node method will be used for each loop in the NMA to compare the agreement between direct and indirect evidence. A p > 0.05 indicates consistency. Probability ranking charts can help us assess the efficacy of various interventions. We will use the surface under the cumulative ranking curve (SUCRA) to obtain the ranking of all interventions.

### Examination of assumptions

The assumptions of NMA include homogeneity, transitivity, and inconsistency.

The transferability assumption is a prerequisite for NMA and will be investigated by examining the distribution of potential influential modifiers (participant characteristics: age, sex, disease severity at baseline; interventions: duration of treatment, frequency of treatment).

Heterogeneity among studies will be assessed by I² statistics. If I² > 75%, it indicates high heterogeneity and we will investigate the source of heterogeneity. If the heterogeneity cannot be eliminated, we will only perform a general statistical description without data synthesis.

We will evaluate the overall inconsistency by comparing the results of the consistency model with those of the inconsistency model; the node-splitting method will be used to evaluate the inconsistency of each loop.

### Subgroup and sensitivity analysis

We will analyse the possible causes of heterogeneity or inconsistency using subgroup analysis and sensitivity analysis methods.

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Two subgroup analyses will be performed to determine the effect of exercise frequency and duration on outcomes. Based on previous experience, the study duration will be divided into three subgroups, <12 months vs 12–18 months vs ≤18 months. Based on the characteristics of TCE, we will classify >4 times/week as high frequency and ≤4 times/week as low frequency. Then, we will perform a subgroup analysis to explore the most appropriate frequency of exercise. If there are enough studies, we will also perform a subgroup analysis of the participants’ age and sex ratios, severity of OP at baseline, pain level, types of primary OP and types of drugs. We will perform sensitivity analyses and exclude RCTs with low methodological quality and remove incomplete data.

### Assessment of publication bias

In paired meta-analyses, we will use funnel plots to assess small study effects and publication bias when there are at least 10 studies. For publication bias in the NMA (NMA), we will use a comparison-adjusted funnel plot and Egger’s test to assess the risk of publication bias.

### Quality of evidence

We will use the Grading of Recommendations Assessment, Development and Evaluation guideline development tool to assess the quality of the evidence and to specify the recommended level of evidence. In addition, we will use Confidence in NMA (a free, open-source software to assess the confidence level of NMA results) to assess the credibility of the results of this NMA. Without compromising statistical and methodological rigour, this software simplifies and accelerates the process of evaluating the results of large, complex networks for assessing the confidence level of treatment effect estimates in NMAs.

### Patient and public involvement

This review will not recruit patients, and they will not be directly involved in the design and implementation of this study.

### Ethics and dissemination

All data for this study will be obtained from published studies, so no ethical review will be needed. The completed study will be published in a peer-reviewed journal and the findings will be further disseminated through presentation at an appropriate forum or conference.

### DISCUSSION

OP is a disabling disease whose prevention and treatment necessitate an individual rehabilitation plan because of its associated pain-restricted mobility, including severe fragility fractures. Exercise is currently recognised as a non-pharmacological treatment for the prevention and treatment of OP, and major organisations have emphasised the importance of physical activity or exercise for the prevention of bone loss, falls and fractures. The exact mechanism by which exercise improves bone health is not fully understood. However, we have found that mechanical loads induced by exercise create mechanical stress in the bone, which can trigger biological, bone-building responses that ultimately strengthen the bone. The influence of muscle tissue on bone mass involves all cellular elements responsible for bone tissue metabolism, such as chondrocytes, osteocytes, osteoblasts and osteoclasts. Muscle contractions caused by exercise can increase myokine secretion, which promotes bone formation. There is a strong interaction between bone and muscle tissue, so exercise is an effective strategy for improving bone health. However, the dosage and optimal exercise prescription for patients with OP is unclear, which is an entry point for future research.
As light to moderate exercises, TCEs are safe, effective and economical. They combine balance and coordination capacity on the basis of aerobic exercise and emphasise the physical–psychological connection.\(^{38}\) Because of this, these traditional sports are very popular among people of all ages in China and have become quite popular around the world in recent years.\(^{39}\) Evidence has demonstrated the effectiveness of TCEs in improving cardiopulmonary and musculoskeletal system function and quality of life in older adults.\(^{13,14,23}\) A number of studies have found TCEs to have a positive effect in increasing BMD, relieving pain, improving muscle mass and preventing falls in patients with OP.\(^{18,21,24,40}\) However, there are some studies with inconsistent results.\(^{15,27,41}\) This may be the result of low-quality research methods, small sample sizes in individual studies, or high heterogeneity between studies.\(^{20}\)

At present, the effect of TCEs on OP, especially BMD, is still unclear. In addition, each of these TCEs has its own unique style that may affect OP differently. For example, Wuqinxi emphasises breath control and mental regulation during exercise. Baduanjin emphasises the stretching of the muscles of the whole body, and Tai Chi emphasises the stability of the lower body.\(^{42}\) At the same time, studies on exercise frequency and duration have conducted preliminary explorations, but the results are not clear.\(^{43}\) The existence of these problems affects practical applications and is also the key to our subsequent research.

We will summarise the available evidence to clarify this issue through a systematic review. We hope to compare and rank the effects of various different TCE types on OP through this NMA and perform subgroup analysis on exercise dosage to clarify the optimal exercise modality for OP. Through our work, we hope to provide evidence-based medical guidance to support practice. Our research will support the development of individualised exercise therapies for patients with OP.

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Competing interests None declared.

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REFERENCES


