INPLASY PROTOCOL

To cite: Chen et al. Acupuncture and moxibustion combined with various external treatments of traditional Chinese medicine to prevent and treat primary osteoporosis： A systematic review and Network Meta-Analysis. Inplasy protocol 202140036. doi: 10.37766/inplasy2021.4.0036

Received: 06 April 2021

Published: 07 April 2021

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Support: **国家自然科学基金 (82060895).**

Review Stage at time of this submission: **Piloting of the study selection process.**

Conflicts of interest:
None declared.

Acupuncture and moxibustion combined with various external treatments of traditional Chinese medicine to prevent and treat primary osteoporosis： A systematic review and Network Meta-Analysis

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Review question / Objective: **Which external treatment combined with Acupuncture and moxibustion is the most effective treatment for osteoporosis patients? The aim of this systematic review and Network Meta-Analysis is to compare the effect of acupuncture and acupuncture combined with various external treatments of traditional Chinese medicine, to improve the existing treatment of acupuncture and moxibustion, to scientifically evaluate the efficacy of acupuncture and moxibustion in the treatment of osteoporosis and to provide the basis for clinical selection of acupuncture and moxibustion therapy in the treatment of osteoporosis, based on evidence-based medicine for systematic review and Network Meta-Analysis. Participant： Patients with primary osteoporosis Intervention： Acupuncture and moxibustion combined with various external treatments of TCM Comparison: Acupuncture, Traditional Chinese Medicine Decoction, Conventional Western Medicine Outcome: To improving the existing treatment of acupuncture and moxibustion, to scientifically evaluate the efficacy of acupuncture and moxibustion in the treatment of osteoporosis and to provide the basis for clinical selection of acupuncture and moxibustion therapy in the treatment of osteoporosis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 April 2021 and was last updated on 07 April 2021 (registration number INPLASY202140036).

INTRODUCTION

Review question / Objective: **Which external treatment combined with Acupuncture and moxibustion is the most effective treatment for osteoporosis patients? The aim of this systematic review and Network Meta-Analysis is to compare**

the effect of acupuncture and acupuncture combined with various external treatments of traditional Chinese medicine, to improve the existing treatment of acupuncture and moxibustion, to scientifically evaluate the efficacy of acupuncture and moxibustion in the treatment of osteoporosis and to provide the basis for clinical selection of acupuncture and moxibustion therapy in the treatment of osteoporosis, based on evidence-based medicine for systematic review and Network Meta-Analysis. Participant: Patients with primary osteoporosis Intervention: Acupuncture and moxibustion combined with various external treatments of TCM Comparison: Acupuncture, Traditional Chinese Medicine Decoction, Conventional Western Medicine Outcome: To improving the existing treatment of acupuncture and moxibustion, to scientifically evaluate the efficacy of acupuncture and moxibustion in the treatment of osteoporosis and to provide the basis for clinical selection of acupuncture and moxibustion therapy in the treatment of osteoporosis.

Rationale: (1) According to the epidemiological report of osteoporosis, the prevalence of osteoporosis and its social and economic burden are steadily increasing due to the aging world population. According to reports, more than 10 million people in the United States are affected by osteoporosis, which is expected to exceed 14 million by March 2020, and more than 200 million women worldwide have osteoporosis. (2) As the population ages, Osteoporosis has become an important public health problem in China. At present, China's population over 60 years old has exceeded 210 million (about 15.5% of the total population), Nearly 140 million people over the age of 65(about 10.1 per cent of the total population) are among the world's largest absolute numbers of older persons. Early epidemiological survey showed that the prevalence rate of osteoporosis among women over 50 years old in China was 20.7%, 14.4% men, The prevalence of osteoporosis in people over 60 years of age is significantly higher, Women are particularly prominent. It is estimated that nearly 70 million osteoporosis patients in China in 2006, More than 200 million people have lost bone mass. (3) With the development of modern biotechnology, more and more researchers use modern technology to study the OP of non-drug therapy at molecular biological level. These studies have found that external treatment of traditional Chinese medicine can not only significantly improve the clinical symptoms of patients, but also improve the bone metabolism index, maintain the balance of bone metabolism, and have great potential for OP prevention and treatment. Acupuncture and moxibustion combined with external treatment of traditional Chinese medicine are more, but many osteoporosis guidelines do not explain in detail the treatment of osteoporosis with acupuncture and moxibustion combined with a variety of external treatment of traditional Chinese medicine. This leads to the poor consistency of treatment protocols in many clinical studies of acupuncture and moxibustion for primary osteoporosis, which can not be effectively compared and popularized. At the same time, the experimental data of these studies are not reproducible and the sample size is small. In order to solve the above problems, it is necessary to introduce evidence-based medicine to integrate and analyze a large number of clinical studies of acupuncture and moxibustion combined with external treatment of primary osteoporosis, so as to provide a more reliable proof of the effectiveness of its treatment. To explore and improve the most effective treatment for primary osteoporosis with evidence-based medicine.

Condition being studied: This study was supported by the National Science Foundation of China under Grant (numbers:82060895). Professor Zhao Rong, (Corresponding author of the study, has more than 20 years of clinical experience in the treatment of osteoporosis and can provide guidance on the problems encountered in the study. Yunnan University of Chinese medicine has a strong team of teachers and sufficient

financial support, which can provide great help in the research process.

METHODS

Search strategy: (1)Research subjects: Clinical randomized controlled trials of acupuncture combined with external treatment of primary osteoporosis published in Chinese or English medical journals before December 2020. (2) Database Chinese Biomedical Literature Database (CBM), China Zhiwang (CNKI) (1979-2020.12), Wanfang Journal Database (1982-2020.12), Vip Chinese Journal Full Text Database, (Excerpta Media database,) Medical Literature Database EMBASE) (1974-2020.1), PubMed Medical Literature Retrieval Service (1966-2020.12), WOS database Web of science, WOS)(-2020.12). Track and consult relevant literature, manual retrieval, etc. in the references of clinical trial report papers or reviews. (3) Search keywords: Osteoporosis, Primary Osteoporosis, postmenopausal Osteoporosis, senile Osteoporosis, acupuncture, acupuncture treatment, acupoint treatment, Tuina, warm needle, warm needle treatment, electro-acupuncture, electroacupuncture treatment, electrical needle, electrical needle treatment, Acupoint injection, Moxibustion.

Participant or population: Type of study: acupuncture, massage, cupping and other external Chinese medicine treatment of primary osteoporosis clinical randomization controlled or semi-randomized controlled trials in Chinese or English Subjects: According to the Guidelines for Diagnosis and Treatment of Primary Osteoporosis (2017), Clinical Research on New Medicines of Traditional Chinese Medicine Guidelines and the Expert Consensus on the Diagnostic Criteria for Osteoporosis in China (Third Draft ,2014 Edition), patientsdiagnosed with primary osteoporosis.

Intervention: Acupuncture and moxibustion (including warm needle, electroacupuncture, acupoint catgut embedding, etc.) treatment and the treatment of acupuncture and moxibustion combined with external treatment of traditional Chinese medicine, including massage, cupping, seven-star needle, acupoint application, moxibustion, etc.

Comparator: The control measures acupuncture or acupuncture combined drugs or acupuncture combined drugs (including traditional Chinese medicine and conventional western medicine) or conventional drugs or acupuncture combined with other external treatment of traditional Chinese medicine

Study designs to be included: Type of study: acupuncture, massage, cupping and other external Chinese medicine treatment of primary osteoporosis clinical randomization controlled or semi-randomized controlled trials in Chinese or English Subjects: According to the Guidelines for Diagnosis and Treatment of Primary Osteoporosis (2017), Clinical Research on New Medicines of Traditional Chinese Medicine Guidelines and the Expert Consensus on the Diagnostic Criteria for Osteoporosis in China (Third Draft ,2014 Edition),patients diagnosed with primary osteoporosis.

Eligibility criteria: Type of Study: Clinical Randomization of Acupuncture, Massage, Cupping and other External Treatment Methods for Primary Osteoporosis The language of the literature is Chinese or English. Subjects: According to the Guidelines for Diagnosis and Treatment of Primary Osteoporosis (2017), Clinical Research on New Medicines of Traditional Chinese Medicine Guidelines and the Expert Consensus on the Diagnostic Criteria for Osteoporosis in China (Third Draft ,2014 Edition), patients diagnosed with primary osteoporosis. 3 Interventions: RCT of acupuncture treatment (including warm acupuncture, electroacupuncture, catgut embedding, etc.) in experimental group Research and acupuncture combined with external treatment of TCM (including massage, cupping, seven-star acupuncture, acupoint application, moxibustion At the same time, the control

group was acupuncture combined with external therapy. 4 Outcome indicators: Main outcome indicators: BMD (BMD), overall clinical efficiency. Secondary outcome indicators: VAS score, TCM syndrome score, serum metabolic index, etc.

Information sources: Database: Chinese Biomedical Literature Database (CBM), China Zhiwang (CNKI)(1979-2020.12), Wanfang Journal Database (1982-2020.12), Vip Chinese Journal Full Text Database, (Excerpta Media database,) Medical Literature Database EMBASE) (1974-2020.1), PubMed Medical Literature Retrieval Service (1966-2020.12), WOS database Web of science, WOS)(-2020.12). Follow up and consult relevant documents, manual search, etc. in clinical trial reports or reviews. Disputable documents can be included or not through group discussion; Missing data processing: actively contact the original author through email and other ways to obtain.

Main outcome(s): The clinical effective rate was divided into two categories, using ratio ratio (odds ratio ,OR) or risk ratio (Risk Ratio ,RR) and 95% confidence interval (95% CI) as statistics. BMD was a continuous variable, analyzed using mean difference (mean difference,MD) and 95% confidence interval (95% CI) as statistics.

Additional outcome(s): VAS score was a continuous variable, using mean difference (mean difference,MD) and 95% confidence interval (95% CI) as statistics. The incidence of adverse reactions was divided into two categories, using ratio ratio (odds ratio ,OR) or risk ratio (Risk Ratio ,RR) and 95% confidence interval (95% CI) as statistics.

Data management: Document screening: The selected database is searched according to the search scheme specified by the project, and the obtained literature is screened by two research members independently by reading the title and abstract, and the literature that may meet the inclusion criteria is read in full to determine whether it meets the inclusion criteria. The process: The literature management software Noteexpress was used to sort out the preliminary retrieved literatures, and delete the duplicated literatures and non-journal literatures; The titles and abstracts of the literature were read to eliminate the literature that obviously did not meet the inclusion criteria; Download the full text for further analysis and screening; Through the pre-set inclusion exclusion criteria, the selected documents were reviewed and screened, and the number and reasons of culling were recorded; Disputable documents can be included or not through group discussion; Missing data processing: actively contact the original author through email and other ways to obtain; Basic data extraction: Two researchers independently extracted the data. During the extraction process, the original data were retained for review. The extraction contents include: the title and author of the literature, the baseline data of the study subjects (gender and mean age), random grouping method, blind method (study subjects and treatment methods), intervention measures, measurement indexes, outcome data, adverse reactions and their shedding data, as well as the analysis and treatment methods.

Quality assessment / Risk of bias analysis: Literature quality assessment: A modified JADAD scale was used to evaluate the methodological quality of the included studies. Specific entries included: reference to randomization, correct random methods, reference to hidden points, reference to blind methods, correct blind methods, description of inclusion or exclusion criteria, description of missing or withdrawn persons and reasons, description of sample size estimation, safety evaluation, description of statistical methods, description of funding or sponsorship. According to the above items, 1-3 is divided into low quality and 4-7 is high quality. Applying the Cochrane bias risk assessment tool to assess the risk of inclusion in the literature, The risk bias

consists of 6 entries in 5 aspects: selective bias, measurement bias, implementation bias, reporting bias and other bias, The criteria for the degree of literature bias are low risk, unclear and high risk, And the quality of the study from high to low into three grades: A: low bias, That is, fully meet the quality standards of 4 or more entries (low risk), Less likely to be biased; Grade B: moderate bias, Full compliance with 2 or 3 entry quality standards (low risk), Moderate likelihood of bias; Grade C: highly biased. One of the entries and above is completely non-compliant (high risk), or only 1 or no entry quality standard fully met (low risk), High probability of bias.

Strategy of data synthesis: Using the Review Manager 5.3 recommended by the Cochrane collaboration network for Meta analysis, And draw risk bias map (as shown in figure 2) and forest map. If there were more than 10 studies in each group, Funnel graph analysis can be drawn to describe and evaluate the publication bias included in the study. For the included studies, chi-square and heterogeneity tests, When P>0.1 and I2P>50, The heterogeneity among the included studies is small, Adopt fixed effect model; When P50, The heterogeneity among the included studies is large, Using random effects, And should be included in the study sensitivity analysis or subgroup analysis to find the source of heterogeneity, If the heterogeneity can not be reduced, Only descriptive analysis of the results was carried out. Binary variables, (odds ratio,) Use ratio OR or hazard ratio (Risk Ratio,); and RR) and 95% confidence intervals (95% CI) were analyzed as statistics; Continuous variables, Average difference (mean difference,) used MD) and 95% confidence intervals (95% CI) were analyzed as statistics. ㈪STATA 16.0 software STATA software is a set of integrated statistical software that can be used for data management, data analysis and professional chart drawing. It has many functions, including balanced repetition, polynomial Probi mode and linear mixed model.

Subgroup analysis: The control measures were conventional western medicine or single external treatment of traditional Chinese medicine or single Chinese medicine clinical randomized controlled study.

Sensitivity analysis: If the heterogeneity between the included studies is large, the heterogeneity analysis is carried out from the research object, treatment method, control method, outcome index and so on. The heterogeneity of the research was eliminated to reduce the heterogeneity among the included studies, and if the inhibition could not be reduced after exclusion, the statistical results of the included studies were described only.

Language: Language restrictions in English or Chinese.

Country(ies) involved: Areas mainly include Chinese mainland and all areas where acupuncture is used.

Keywords: acupuncture, primary osteoporosis, random controlled trials, systematic review, network Meta-analysis.

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