

# Acupuncture for osteoporosis: study protocol for a randomized controlled trial

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## Study protocol

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# Abstract

**Background:** The rapid increase in the prevalence of osteoporosis and the rate of fractures after osteoporosis indicates that osteoporosis has become a serious global public health problem. A recent meta-analysis showed that oral alendronate and parenteral injection of zoledronate had no statistical significance in preventing postmenopausal hip fractures. Acupuncture and moxibustion are widely used in the treatment of osteoporosis due to their good analgesic effects. Early observation showed that integral adjustment of acupuncture and moxibustion therapy could improve the quality of life of patients with osteoporosis and prevent the occurrence of osteoporosis fractures. As the observation period of fracture is too long, it is necessary to carry out a large and strictly designed multi-center randomized trial covering the risk factors of fracture and fracture induction, so as to evaluate the effectiveness of acupuncture and moxibustion in the treatment of primary osteoporosis.

**Methods/Design:** A multicenter randomized controlled trial will be performed in three hospitals. 312 participants patients within primary osteoporosis will be divided into an experimental group and a control group randomly. The experimental group is treated with acupuncture and western medicine while the control group is treated with Western medicine. All the patients will receive a 3-month treatment and 6-month, and one year follow-ups. The primary outcome is the bone mineral density (BMD), the secondary outcome is Bone-derived alkaline phosphatase (BALP), bone glaprotein (BGP), visual pain scale score (VAS), Traditional Chinese Medicine (TCM) syndrome scores, quality of daily life score (QOL) and adverse events. Outcome measures (including primary and secondary outcome measures) are collected at baseline, 3 months of the intervention, Causes and number of falls are collected at 6 months and one year after the intervention.

**Discussion:** This study will provide clinical evidence for the treatment of primary osteoporosis with holistic adjustment acupuncture. This study will evaluate the synergistic effect of acupuncture treatment for primary osteoporosis and provide evidence for clinical treatment.

**Trial registration:** This trial was registered at Chinese Clinical Trial Registry, registration date: 5 August 2018. URL: <http://www.chictr.org.cn>, registration number: ChiCTR1800017581.

## Background

Osteoporosis (OP) is a systemic metabolic bone disease that results in increased bone fragility due to decreased bone density, decreased bone mass, and degeneration of bone tissue microstructure.

Osteoporosis occur at any age, but primary osteoporosis is more common in postmenopausal women and older men. According to the National Statistical Yearbook in 2015, the population that was over 60 years exceeds 210 million, accounting for about 15.5% of the total population<sup>[1]</sup>, with the increase of the elderly population, osteoporosis has developed into a health problem with significant physical, psychosocial, and economic consequences<sup>[2]</sup>. In 2016, the prevalence of osteoporosis in elderly people was about 36% in China, of which 23% were male and 49% were female<sup>[3]</sup>. Fractures in various parts of the body are

extremely occur after osteoporosis, especially for elderly women, the rapid decline in estrogen can easily lead to hip fractures after osteoporosis, which increases the risk of disability and death rate, brings hit hard of both psychological and physical for them, and has brought heavy economic burdens to families. The latest data from the International Osteoporosis Foundation (IOF) estimates that 200 million osteoporotic women in the world suffer from osteoporotic fracture every 3 seconds [4], The high prevalence of osteoporosis and the rapid increase in fracture rates indicates that osteoporosis has become a serious public health problem. As an independent risk factor for osteoporotic fractures [5], falls should also be taken seriously, some studies have shown that patients with osteoporosis have a significantly higher risk of falling and causing fractures than non-osteoporotic elderly [6]. It is necessary to track the causes of falls and the number of falls to evaluate the effectiveness of the anti-osteoporosis treatment.

Most common symptoms of osteoporosis include pain, spinal deformity and fragile fractures. The purpose of anti-osteoporosis treatment is to reduce pain, prevent fractures, and improve the quality of life of patients. Currently the main prevention and treatment methods for osteoporosis include anti-OP drugs and basic treatments such as nutrition, sun exposure, sports, calcium supplements or vitamin D [7], among them, bisphosphonates are the most widely used in clinical practice, such as alendronate sodium, zoledronate sodium, risedronate sodium, etc. Some studies have shown that alendronate can reduce bone loss, increase bone density, and reduce fracture risk [8]. However, some studies have also shown that these drugs do not reduce all types of fractures, and patients with fragile fractures who rely on medications have an increased risk of re-fracture after the first two years of fracture [9], In addition, the use of bisphosphonates may bring rare side effects such as joint pain, jaw necrosis, etc. patients have poor compliance, the long-term effective evidence is poverty in clinical practice [10-11], so that the finding of effective complementary and alternative therapies is a challenge for future clinicians. Acupuncture is a traditional green treatment method in China. Because of its low side effects and obvious analgesic effect, it is widely used clinically in the adjuvant treatment of osteoporosis. Studies have shown that moxibustion plus anti-osteoporosis drugs may be more effective in alleviating osteoporotic pain, increase bone density in the femoral neck, and improve bone calcium and bone alkalinity phosphatase levels compared with anti-osteoporosis drugs alone [12]. Cochrane evaluation also shows that acupuncture may be an effective method of preventing osteoporosis. Compared with western medicine alone, mild acupuncture is more effective than electroacupuncture and ordinary acupuncture [13], but the effectiveness and safety are still lack of high quality evidence. We have integrated warm acupuncture, skin acupuncture, and cupping as a holistic treatment in the previous clinical research, which has a certain effect on reducing patients' pain, increasing bone density, and improving quality of life, but more favorable evidence is needed.

A carefully designed, multicenter, randomized controlled trial incorporating quality of life and fracture occurrence (including falls of risk factors for fractures in the elderly) into efficacy evaluation indicators is necessary to assess the effectiveness of acupuncture in the treatment of osteoporosis.

## Methods/design

### Study design

This is a multicenter, randomized, patient and assessor-blinded trial. A target sample of 312 participants will be recruited from the acupuncture clinic at Yunnan Provincial hospital of Traditional Chinese Medicine , Kunming Minicipal Hospital of Traditional Chinese Medicine , Yuxi Minicipal Hospital of Traditional Chinese Medicine. The present protocol followed the SPIRIT guidelines and fulfilled the SPIRIT checklist(Additional file 1). The flow chart is shown in Fig.1. The protocol is in line with the principles of the Declaration of Helsinki and has been approved by Institution review board (IRB) of Yunnan Provincial hospital and Traditional Chinese Medicine (approval no.2018-003-01). This trial was registered at the Chinese Clinical Trial Registry (ChiCTR1800017581). Any changes which need to be made in the trial protocol will be communicated to all researchers, the ethics committees, and the trial registry. Each participant will sign an informed consent. Participants will be recruited into the study only once and will not receive any monetary compensation for their participation.

In the early stage, we will make the inclusion and exclusion criteria known to target population through posters, WeChat and Internet. The team leader will give lectures on osteoporosis in three hospitals, interact with osteoporosis patients, and improve the enthusiasm of patients to participate in the study. In the meantime, we will explain the eligibility criteria to interested patients, and the participants will sign an informed consent form when they have a clear and comprehensive understanding of the trials they will participate in, such as the benefits they may gain, the potential risks they may encounter, the settings of the acupuncture group and the interventions that will be conducted on them, and so on. The participants will be randomly assigned to the acupuncture group or drug group. We will pay particular attention to baseline characteristics such as age, sex, menopause time, bone density, time of first detection of fractures, level of risk for falls, exercise habits, ethnic distribution, smoking and drinking history.

This study will be performed over a period of 16 months: 1 month of preparation, 3 months of treatment, and 12 months of post-treatment follow-up. All eligible patients will be randomly divided to either an acupuncture group or a control group receiving standard western medicine treatment. Outcomes will be assessed at baseline, after 3-months treatment and at the 6-month and 12-month of the follow-up. Table 1 illustrate the time schedule of enrollment, interventions, assessments, and participant visits.

### **Randomization and blinding**

The researchers are unable to predict the allocation of patients, and no changes in allocation are allowed after randomization. The "computer pseudo-random number generation method" will be used to generate pseudo-random numbers, and the patients numbered from 1 to 312 will be given the pseudo-random numbers each. Participants with their pseudo-random numbers ranked in the even-numbered position will be included in the acupuncture group, and the rest will be included in the control group. Randomized allocations of acupuncture or control groups will be generated by independent researchers using computer software. Computer-generated treatment codes are placed in sealed, opaque envelopes and distributed by dedicated study nurses, who will be trained before the trial and will not participate in treatment or care.

Participants in this study will be informed that they will receive acupuncture with medication or medication only. The acupuncturists in the acupuncture group and the physicians in the control group will receive a

pre-experimental training session, and we are unable to apply the principle of blindness to them. However, acupuncturists and physicians are not involved in the measurement of results or statistical analysis, and the specific details of their treatment cannot be disclosed to the assessor or participant. Before the statistical analysis is completed, the statisticians know nothing about the group allocation which may cause biases.

### **Inclusion criteria**

Participants who meet all the following requirements will be allowed for enrollment:

1. Meet the diagnostic criteria of traditional Chinese medicine: "Diagnosis and Treatment Program for Osteoporosis in the Key Specialty Cooperation Group of the State Administration of Traditional Chinese Medicine", the dialectical classification conforms to spleen and kidney yang deficiency, liver and kidney yin deficiency, qi stagnation and blood stasis;
2. Meet the diagnostic criteria of western medicine: refer to the 2017 guidelines for diagnosis and treatment of primary osteoporosis compiled by the Chinese Medical Association, patients with primary osteoporosis aged 60-80 years;
3. Willing to receive acupuncture treatment for 3 months;
4. Sign the informed consent and agree to accept the research treatment plan and obey the research arrangement.

### **Exclusion criteria**

Participants meeting any of the following criteria will be excluded:

1. report to have participated in other clinical trials in the past three months at the beginning of the study;
2. report to have taken osteoporosis drugs or received acupuncture treatment in the past three months;
3. report to have secondary osteoporosis;
4. report to have serious heart, liver and kidney diseases;
5. report to have hematological system diseases;
6. report to have hemiplegia, physical disability, prolonged confinement to bed;
7. report to have other serious chronic, consumptive diseases;
8. report to have severe mental or cognitive impairment.

### **Criteria for case exclusion and dropout**

Participants would be excluded or dropped out if they meet any of the criteria below:

1. do not follow medical advice in treatment;
2. quit by themselves during the test;
3. become ineligible for the trial because of physical reasons.

## **Acupuncture and the control group**

### **Acupuncture group**

Patients in the acupuncture group will receive standard pharmacological treatment same as the control group, and receive acupuncture two times a week for 12 weeks for a total of 24 treatment sessions. Patients will receive treatment in supine position for 20 min per session. The treatment will be provided by licensed acupuncturists holding acupuncture physician certifications in China with at least 3 years of clinical experience. Disposable, sterile needles with a diameter of 0.25 mm and a body length of 40 mm (Huatuo, Suzhou, China) will be used. Based on TCM theory and our clinical experience, acupoints used here are unilateral BL11 (Dayu), BL23 (Shenshu), and St36 (Zusanli). In addition, for participants with kidney deficiency GV4 (Ming Men) and KI (Taixi) are inserted; for those with spleen-deficiency SP6 (Sanyinjiao) and BL20 (Pi Shu) are punctured; for those with blood stagnation BL17 (Geyu) and SP6 (Sanyinjiao) are used. (Table 2). The exact location and depth of needling for each point will be determined based on the 2006 People's Republic of China National Standard (GB/T 12346–2006) *Acu-Points Name and Location* <sup>[14]</sup>. After insertion, all points will be manually stimulated by lifting and thrusting the needle every 10 min to elicit the “deqi”, warm acupuncture will be used, fix the 2 cm-long moxa-stick on the handle of the needle and light it at the root of the needle, the needles will be retained for 20 min.

The parameters of the skin needle are set as follows: Qixing needle: tapping along the first side line of the urinary bladder meridian in the back; moderate stimulation will be applied for the blood stasis type, until redness of the skin and petechiae is observed in the tapping part; mild stimulation was used for the rest of the syndromes until redness in the skin is observed.

The parameters of the cupping are set as follows: moving cupping: smear the tapping spot evenly with Vaseline and move the cup along the first lateral line of urinary bladder meridian back and forth until red blood stasis appears on the skin, according to the patient's tolerance (feeling comfortable, without an obvious pain). Retaining cupping: Leave the cup for 8 to 10 minutes in Dazhui, Shenshu, and a severely painful area.

### **Control group**

The patients in the control group will receive standard pharmacological treatment. Patients with osteoporosis will take Alendronate Sodium Tablets 10mg (once per day, taken with a glass of warm water before breakfast) for 12 weeks. However, no acupuncture treatment was given during the study period. They will be evaluated at each visit.

### **Outcome assessment**

Patients will be carefully examined before the treatment and after the last treatment (three months after the first acupuncture treatment). Evaluation and follow-up will be conducted at the timepoints of 3 months, 6 months and 1 year after acupuncture treatments.

The primary outcome measure of this trial is the bone mineral density (BMD). BMD was measured by a dual energy X-ray absorptiometry (manufacturer: DMS, France; model: CHALLENGER C 313). BMD of the lumbar vertebrae (L1-L4) in the two groups will be measured before and after treatment. Mean value of BMD will be collected, and the rate of its change will be used to assess the effectiveness. BMD change rate ( $\Delta$ ) = (BMD after treatment - BMD before treatment) / BMD before treatment  $\times$  100%.

The secondary outcome measures include Bone-derived alkaline phosphatase (BALP), bone gla protein (BGP), visual pain scale score (VAS), Traditional Chinese Medicine (TCM) syndrome scores, quality of daily life score (QOL) and adverse events.

Bone metabolism markers: serum bone-derived alkaline phosphatase (BALP) levels, serum osteocalcin levels (BGP). The fasting venous blood was collected before treatment, one course of treatment and at the end of treatment respectively. The enzyme-linked immunosorbent assay (ELISA) (biocell enzyme standard instrument) was used to determine BGP and BALP.

Pain score. The pain score will be assessed for the lower back. A Visual Analogue Scale (VAS) will be used to measure each group before and after treatment (see Attached table 2). VAS is a 10 cm line with a scale of 0-10, with 0 being no pain and 10 being the worst pain. The subject will be asked to mark their current pain level on the line. The examiner scores the VAS by measuring the distance from the zero point to the point the subject marks. The unit is centimeter (CM).

Quality of life: Based on Quality of Life (QOL) and 36-Item Short Form Survey (SF-36), combined with the specificity of osteoporosis and clinical situations, a self-rating scale in line with Chinese ethnicity was developed (see Attached table 1). Previous studies have shown that it has good applicability<sup>[15-16]</sup>. The scale is answered by the patient without the physician be involved. The total score of 54 points or less is defined as a normal quality of life, >54-70 points as decreased quality of life, 71 -80 points as the quality of life decreased obviously, and > 80 points as a serious decline in quality of life. Self-control design will be conducted before and after treatment. A decrease in the score of  $\geq$  20 points is defined as an improvement in the quality of life.

Clinical symptoms of TCM: symptom quantitative score will be used, which is based on "Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine"<sup>[17]</sup>. Four levels are used to assess the severity of symptoms, which include no, mild, moderate and severe. a specific score will be given to each level (see attached Table 3). Effectiveness assessment: clinical recovery: TCM symptoms disappear, symptom score decreases by  $\geq$ 95%; remarkable effectiveness: TCM symptoms and signs are improved significantly, symptom score decreases by  $\geq$ 70%; effectiveness: TCM symptoms and signs improve, symptom score decreases by  $\geq$ 30%; No effectiveness: TCM symptoms and signs are not improved or aggravated, and the symptom score reduces by <30%.

## **Safety evaluation**

During the study, adverse events (AEs) are defined as any unexpected or undesired harmful effect resulting from acupuncture or pharmacological treatment. A research assistant (GL) will be required to record all the

AEs, including information on the time of occurrence, severity, duration, measurement, management, and its outcome, in a case report form (CRF). Any serious adverse events (SAEs) will be immediately reported to the principal investigator (JHS) and the Medical Ethics Committee within 24 h. The Acupuncture Department of Yunnan Province Hospital of TCM will be responsible for the treatment of all the AEs.

### **Sample size calculation and statistical analysis**

According to our previous research results<sup>[15]</sup>, which showed that, among 36 patients with primary osteoporosis in each group 28 cases gained an increase in their quality of life in the acupuncture group after a course of treatment (2 times a week, 3 months for a course of treatment), and 18 cases gained an increase in their quality of life in the drug group. In this proposal, two groups are set up, set  $\alpha=0.05$ ,  $1-\beta=0.90$ . According to the literature estimation, the effective rate of the drug group was 50%, that of the acupuncture group was 78%, and the expected loss to follow up was less than 10%. According to the formula for sample size of each group<sup>[18]</sup>  $n=1/1-f*[2*Z_{\alpha}+Z_{\beta}]^2*p*(1-p)/|p_0-p_1|^2$  in which  $p_0=50%$ ,  $p_1=78%$ ,  $p=(p_0+p_1)/2=64%$ ,  $Z_{\alpha}=1.65$ (one-sided),  $Z_{\beta}=1.28$ . After calculation, the sample size of acupuncture group or drug group is 155.7 (), so 312 cases of osteoporosis patients are needed in this study, with 156 cases in each group.

Statistical analysis of all data in this study will be performed by a specialized statistician, who is blinded to the treatment allocation. All data will be analyzed by blinded statisticians using SPSS20.0 (SPSS Inc., Chicago, IL, USA). First, collect and compare baseline data. All participants randomly assigned to each group will be included in the analysis, and the intention to treat analysis (ITT) will be used. The randomly assigned patients, regardless of whether they complete the treatment or not, should be finally included in the assigned group for statistical analysis of efficacy. For the data of classified variables, "count n (percentage, %)" or "percentage (numerator/denominator, n/ n)" will be used for the statistics, and the Chi-square test will be used to compare rates between groups. For the data of numerical variables, the one-sample Kolmogorov-Smirnov Test will be used to verify whether the data is normally distributed. The data that is normally distributed will be expressed as "Mean $\pm$ SD", and the Mean comparison between the two groups will be tested using the t-test. Data that is not normally distributed will be described as Median [lower quartile, upper quartile] (Median [Q1, Q3]) of Tukey's Hinges ; Comparison of distributions between two groups will be performed using the Mann-Whitney U Test from Nonparametric Test. A two-sided p value of less than 0.05 will be considered statistically significant for all analyses.

### **Data management and monitoring**

All the researchers will focus on and sign to protect the individual privacy of the participants. The raw data will be collected and cross-checked by two researchers (Huang M and Lai MX). The database software EpiData (version 3.1) will be used for the data management. All the management will be performed in compliance with the study Standard Operation Process (SOP).

The Department of Science and Technology in Yunanan University of TCM, which is not taking part in the study, will be responsible for the monitoring. The CRFs, protocol compliance, data management, treatment

administration and AEs will be monitored independently during the study.

## Discussion

The treatment of osteoporosis is a long-term process, and non-drug treatment is more consistent with the needs of patients. Pain is one of the major symptoms of osteoporosis, and acupuncture therapy is widely used in the adjuvant therapy of osteoporosis for its obvious analgesic effect<sup>[19]</sup>. Although the Cochrane review suggested that acupuncture might be an effective treatment for osteoporosis, more favorable evidence is needed to assess its effectiveness<sup>[13]</sup>.

Osteoporosis can be classified into the category of Guwei (bone atrophy-flaccidity) and Guku (bone wilt) in TCM, which is closely related to "kidney deficiency", "spleen deficiency" and "blood stasis", and results from aging when the overall function declines. At present, the acupuncture and moxibustion treatment of osteoporosis mostly was applied in a manner of single acupuncture and moxibustion therapy. In this study, we use needle warming moxibustion, cupping therapy and skin acupuncture for kidney deficiency, spleen deficiency and blood stasis, respectively, to regulate the meridians, musculo-tendinous and cutaneous regions of the meridian system, and to adjust the overall function of the body by stimulating the functions of the meridian system, so as to treat osteoporosis. Our previous experimental results indicated that acupuncture therapy with Zusanli, Dazhu and Shenshu as the main acupoints could increase femur's resistance to external forces in rats with osteoporosis<sup>[20]</sup>, Clinical studies<sup>[15-16]</sup> and that the holistic adjustment acupuncture therapy has a certain effect on pain relief, increase in bone density and improvement of quality of life. However, rigorously designed large, multicenter, randomized, controlled trials are still needed to verify the evidence.

The measurement of biochemical indicators of bone turnover can timely reflect the state of bone metabolism in the whole body. BGP is the highest non-collagen protein in bones and is secreted by osteoblasts. BALP is one of the human serum alkaline phosphatase (ALP) isoenzymes, which can be used as an indicator of clinical osteoblast activity and overall bone formation. Anti-osteoporosis treatment usually uses the various detection indicators before treatment as the baseline value. Among them, the change of biochemical markers of bone turnover can be measured for at least 3 months of drug treatment, and judged based on the minimum meaningful change value (LSC)<sup>[21]</sup>. The "Clinician's Guide to Preventing and Treating Osteoporosis" states<sup>[22]</sup> that BMD testing is performed 1 to 2 years after starting osteoporosis medication, and thereafter every 2 years. However, in some special clinical situations, more frequent BMD tests may be needed. Taking into account the time of this project and considering the patient's compliance with acupuncture, tentatively determined various indicators were tested in this experiment after 3 months. As an independent risk factor for osteoporotic fractures, falls were recored at 6-months and one year followed up time. After osteoporosis, a series of physical and psychological problems occur, which affects the quality of life of patients. It is increasingly important to use simple and feasible scales to assess the life quality of patients. However, there is currently no "gold standard" validity standard test. Therefore, our team developed universal quality of life scale (MOS SF-36) which is based on the World Health Organization (WHO) Quality of Life Scale (QOL) and the United States Medical Outcomes Research Group

(Medi-cal outcomes Study (MOS)), according to the specificity of osteoporosis in Chinese residents and the actual clinical situation, a self-assessment scale consistent with the Chinese race has been developed, which has been widely used and promoted in clinic<sup>[14]</sup>.

The most common complication of osteoporosis is vertebral fracture, which occurs in regions rich in cancellous bone, namely, vertebral body, hip (femoral neck and femoral trochanter), radial distal end and metaphyseal end of long tubular bone. The mortality of patients with osteoporotic hip fracture is as high as 30%<sup>[6]</sup>. Elderly postmenopausal women are the group with high prevalence of osteoporosis, and are also a high-risk group for falls. Falls not only cause physical injuries, but also cause psychological fear. A cohort study by Faulkner KA et al. of men older than 65 who lived in communities in the U.S. revealed that, compared with men who had had no falls, the risk of non-vertebral, lower extremity fractures was significantly higher in men with one, two or more falls, respectively<sup>[23]</sup>. The IOF working group reviewed the currently available interventions to prevent osteoporosis, indicating the primary basic interventions to prevent hip fractures: preventing falls and correcting nutritional deficiencies<sup>[24]</sup>. In 2012, Chinese Center for Disease Control and Prevention (China CDC) launched "Special Action for Secondary Prevention of Osteoporotic Fractures", which included falls as an important factor in prevention and control. As it would take a long time to observe fractures to occur, falls may serve as an important factor of fractures risk. In this trial the number and reason of falls are taken as a factor to assess whether fractures are likely to occur.

According to Guidelines for Diagnosis and Treatment of Primary Osteoporosis (2017), the prevention and treatment measures of primary osteoporosis mainly include basic measures, medication and rehabilitation treatments. Both medication and rehabilitation treatment need to be based on basic prevention and treatment. Therefore, in this study we need to instruct patients of both the acupuncture group and drug group in nutrition, sun exposure, exercises, supplementation with calcium or vitamin D and other basic treatments, and the results will be included in the statistical analyses. Under strict quality control, this study is expected to assess whether acupuncture therapy (including warm acupuncture, skin acupuncture and cupping) is an adjuvant treatment for osteoporosis. Our research is also expected to confirm whether acupuncture is effective in reducing pain, improving quality of life, and preventing falls or fractures.

This experiment is a clinical study, so acupuncturists and participants will know whether to use acupuncture treatment. We will conduct trials in three public Chinese medicine hospitals to ensure sufficient source of patients

## **Trial status**

This trial was registered at Chinese Clinical Trial Registry, registration date: 10 August 2018, registration number: ChiCTR1800017581. At the time of initial manuscript submission, recruitment had already started (1 August 2018), but it has not been completed. The last patient is expected to be included in the study in 1 August 2020. I confirm that this the protocol version number 1.0 is the version registered at the date that I have provided.

# Abbreviations

OP=Osteoporosis,BMD=bone mineral density,BGP=bone gla protein,BALP=bone alkaline phosphatase,IOF=international foundation for osteoporosis,GCP=Good Clinical Practice,VAS=visual pain scale score,QOL=quality of daily life,TCM=Traditional Chinese Medicine, ITT=intention to treat analysis,LSC=least significant change; BALP=Bone-derived alkaline phosphatase,BGP= bone glaprotein

# Declarations

## 1. Ethics approval and consent to participate

The research plan has already been clinical trials of traditional Chinese medicine hospital ethics committee approval in Yunnan province, China (grant no. (2018) (003) - 01). Central ethical approval has been confirmed from ethics committee of Yunnan provincial hospital of traditional Chinese medicine ethics committee (ref approval no. (2018) (003) - 01) and we will not begin recruiting at other centres in the trial until local ethical approval has been obtained. The research registered on the Chinese clinical trial registry (<http://www.chictr.org.cn/>, ID: ChiCTR1800017581). Each participant will sign an informed consent form. Patients will be enrolled in the study and will be recruited only once and will not receive any financial compensation for their participation in the study.

## 2. Consent for publication

All subjects participating in the image acquisition signed the consent form and consent for publication.

## 3. Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

## 4. Competing interests

The authors declare that they have no competing interests.

## 5. Funding

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## 6. Authors' contributions

Zhao R and Wang ZH is the chief designers of this trial. Zhao R drafted the protocol. Wang XY, Li JY and Yang J provided clinical advice. Huang M and Lai MX are the coordinators and responsible for the screening and enrollment of patients. Huang M, Lai MX, Wang YF, Yang ZG, Ren ZQ and Mei R are involved in the recruitment of patients. Yang J, Ren ZQ and Huang M drew pictures. Huang M and Lai MX revised the manuscript. All authors have read and approved the final version of the manuscript.

## 7. Acknowledgements

The authors will acknowledge all the participants in this study.

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## Tables

Table 1 Overview of study visits

		STUDY PERIOD							
		Enrollment	Allocation	Post-allocation			Close out	Follow-up	
	Time point (month)	-1	0	1	2	3		6	12
PREPARATION	Enrollment								
	Informed consent	√							
	Eligibility screen	√							
	Allocation		√						
INTERVENTION	Acupuncture group			√	√	√			
	control group			√	√	√			
ASSESSMENT	BMD(L1-4)	√				√			
	T; BP; P; R	√		√		√			
	BALP;BGP	√				√			
	Quality of Life Questionnaire	√				√			
	Fall Fractures			√	√	√	√	√	√
	VAS	√		√		√			
	TCM syndrome	√							
	Data analysis						√		
Adverse events			√	√	√				

T: body temperature, BP: blood pressure, P: pulse rate, R: respiration.

Table 2 Acupuncture point selection

Point	Location
<b>BL11(Dazhu)</b>	In the spinal region, under the spinous process of the first thoracic spine, 1.5 cun lateral to the posterior midline
<b>BL23(Shenshu)</b>	1.5 cun beside the spinous process of the second lumbar spine
<b>ST36(Zusanli)</b>	At the anterior aspect of the leg 3 cun inferior to ST35 (Dubi) on the line connecting ST35(Dubi) to ST41 (Jiexi)
<b>DU04(Mingmen)</b>	Between the spinous processes of the second and third lumbar vertebrae
<b>BL20(Pishu)</b>	Under the spinous process of the eleven thoracic spine on the back, 1.5 cun beside the midline
<b>SP06(Sanyinjiao)</b>	On the tibial aspect of the leg posterior to the medial border of the tibia, 3 cun superior to the prominence of the medial malleolus
<b>LU11(Taixi)</b>	On the posteromedial aspect of the ankle in the depression between the prominence of the medial malleolus and the calcaneal tendon
<b>BL17(Geshu)</b>	Under the spinous process of the seventh thoracic spine on the back, 1.5 cun beside the midline.

Table 3, cited on page 9, was omitted by the authors in this version of the manuscript.

## Figures

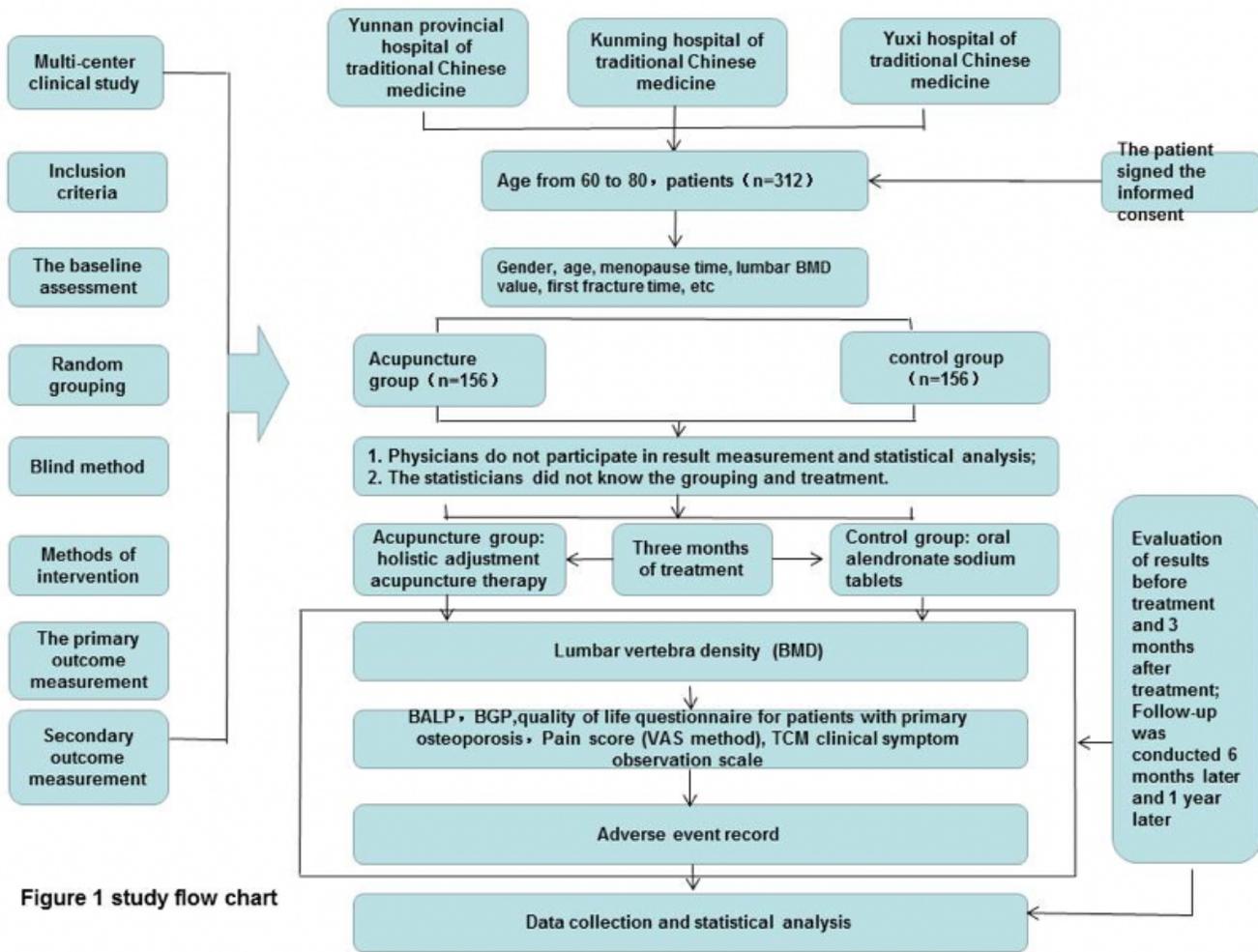


Figure 1 study flow chart

## Figure 1

Study flow chart

## Supplementary Files

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