

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## Acupuncture and related therapies for vasomotor symptoms in menopausal women: protocol of a systematic review and network meta-analysis

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**Review question / Objective:** We aim to present the evidence obtained via electronic databases, using network meta-analysis (NMA), of acupuncture-related therapies for the relief of VMSs, frequency of treatment-related AEs (such as bleeding or bruising) and of discontinuations due to AEs. We will analysis both direct and indirect randomized data and provide recommended rankings of different treatments for acupuncture and related therapies for VMSs in menopausal women.

**Condition being studied:** Acupuncture and related therapies for vasomotor symptoms in menopausal women. The research team comes from the acupuncture department of Hubei Provincial Hospital of Traditional Chinese Medicine, and all the team members have perfect clinical experience in treatments of menopausal women. Moreover, our team members have published nearly 10 meta-analyses, which can guarantee the successful completion of the current research.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 October 2021 and was last updated on 24 October 2021 (registration number INPLASY2021100090).

### INTRODUCTION

**Review question / Objective:** We aim to present the evidence obtained via electronic databases, using network meta-analysis (NMA), of acupuncture-related

therapies for the relief of VMSs, frequency of treatment-related AEs (such as bleeding or bruising) and of discontinuations due to AEs. We will analysis both direct and indirect randomized data and provide recommended rankings of different

treatments for acupuncture and related therapies for VMSs in menopausal women.

**Rationale:** Vasomotor symptoms (VMSs) are experienced by 68% to 82% of women transitioning through menopause. Hormone Therapy (HT) is the treatment of choice. Although it can improve some clinical symptoms quickly and effectively, it is accompanied by adverse reactions (eg, stroke, breast cancer, and cardiovascular disease), potential risk of long-term application, and relative contraindications in some women. Few women are willing to choose HT or other conventional treatments and there is a great need for alternative treatments without any or less adverse effects. Among all complementary therapies, acupuncture has gained more and more attention and is reported as an effective and safe method for many medical diseases.

**Condition being studied:** Acupuncture and related therapies for vasomotor symptoms in menopausal women. The research team comes from the acupuncture department of Hubei Provincial Hospital of Traditional Chinese Medicine, and all the team members have perfect clinical experience in treatments of menopausal women. Moreover, our team members have published nearly 10 meta-analyses, which can guarantee the successful completion of the current research.

## METHODS

**Search strategy:** We will systematically search the electronic databases PubMed, EMBASE, PsycINFO, CINAHL, Web of Science, the Cochrane Library, and four Chinese databases (CNKI, Wanfang, VIP, CBM) for eligible RCTs (from inception to September 31, 2021). All searches will be performed independently, and in duplicate. The search strategy for PubMed is provided in Table below, which will be adjusted in accordance with specific databases. The strategy will be confined to English or Chinese literature. Search strategies will be quality assured by cross-checking reference lists of highly relevant

papers and compared with search strategies in other systematic reviews.

**Participant or population:** Menopausal women.

**Intervention:** Acupuncture and related treatments (ie, manual acupuncture, electro-acupuncture, auricular acupoint stimulation, acupoint catgut embedding) alone or in combination.

**Comparator:** Either inactive (ie, sham acupuncture or usual care) or active (ie, hormone therapy).

**Study designs to be included:** The inclusion criteria of study are as follows: (1) RCTs enrolling women experiencing VMSs; (2) number of randomization participants greater than 30; (3) at least one of the following efficacy outcomes or safety endpoints was included: reduction in the frequency of daily hot flushes; reduction in the severity of daily hot flushes; menopause-related symptoms assessed using the MRS; quality of life (QoL) assessed using the MSQoL; treatment-related AEs; (4) participants in the experimental group have received acupuncture and related treatments (ie, manual acupuncture, electro-acupuncture, auricular acupoint stimulation, acupoint catgut embedding) alone or in combination; (5) studies with a control group, either inactive (ie, sham acupuncture or usual care) or active (ie, HT), were included.

**Eligibility criteria:** Studies will be included so long as inclusion criteria are met. The eligibility criteria are summarized using the PICOS approach (patients/participants, intervention, comparisons/control, outcomes, and study design type).

**Information sources:** PubMed, EMBASE, PsychINFO, CINAHL, Web of Science, the Cochrane library, four Chinese databases (CNKI, Wanfang, VIP, CBM) for eligible RCTs (from inception to September 31, 2021).

**Main outcome(s):** Efficacy outcomes are changes from baseline in daily hot flush

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frequency and severity, Secondary outcomes are menopause Rating Scale (MRS) and quality of life (QoL).

**Additional outcome(s):** Safety outcome is frequency or discontinued of treatment-related adverse events (AEs).

**Data management:** Data will be double extracted from each publication according to a standard data collection sheet, independently by two reviewers, including the following: (1) characteristics of included RCTs (eg, authors' names and year of publication, country, menopause status, and number of participants in each group); (2) intervention characteristics (eg, frequency and duration of acupuncture sessions, name of acupuncture points, and retention time); (3) clinical outcomes (eg, instruments, measurement time points, results, withdrawals, and adverse events). Any disagreements among researchers will be resolved by discussion with all authors until a consensus is reached.

**Quality assessment / Risk of bias analysis:** The methodological quality of RCTs will be evaluated by two authors using Cochrane risk-of-bias tool. The risk of bias tool consists of six domains: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and investigators; (4) blinding of the outcome assessment; (5) incomplete data; (6) selective outcome reporting. The discrepancies will reach a consensus by discussion among all authors. This tool provides a rating of 'high risk', 'low risk', and 'unclear risk' quality.

**Strategy of data synthesis:** We will perform both traditional pairwise meta-analyses and NMA. Statistical models for both fixed and random effects that allowed the inclusion of multi-arm trials and accounted for the correlation between arms in the trials with any number of trial arms will be used. The Review Manager (Version 5.3, Cochrane Collaboration, Oxford, UK) will be used for pairwise meta-analyses.  $I^2$  test and  $I^2$  will be calculated for the assessment of heterogeneity. A random effects model will be used if  $I^2 > 50\%$ , otherwise a fixed effect model will be chosen. We will

calculate the odds ratios and corresponding 95% confidence intervals (CI) according to the date of efficacy outcomes. Mean differences (MD) or standard mean difference (SMD) between treatments may also be considered for continuous data. The forest plots will be drawn to illustrate the relative strength of curative effects. In pairwise meta-analyses, the effects of acupuncture and related therapies on daily hot flush frequency and severity, MRS and QoL will be examined. A class effect model will be selected for the NMA with the underlying assumption that the effectiveness of different treatments under the same class would be comparable. We will use WinBUGS (Version 1.4.3, MRC Biostatistics Unit, Cambridge, UK) for NMA. The continuous outcome will be measured by an SMD with a 95% CI for indirect comparisons. The overall ranking will be determined by network meta-analysis according to overall effect sizes. Subgroup analysis will be performed based on the specified outcomes. The rank of each outcome will be calculated by the surface under the cumulative ranking curve (SUCRA), which will be used STATA software. (Version 13.0; Stata Corporation, College Station, Texas). Higher SUCRA scores mean the higher rank of the treatment. AZ value and its corresponding p-value were calculated, and an R value less than 0.05 indicated a statistically significant difference.

**Subgroup analysis:** In case of possible important heterogeneity, we will explore the possible sources using subgroup and meta-regression analyses. Factors such as interventions, control group, baseline measures, sample size, age and sex will be conducted.

**Sensitivity analysis:** Sensitivity analyses will be performed on evidence quality evaluated by the Cochrane Collaboration's risk of bias tool. The meta-analysis will be repeated, and lower quality studies will be excluded.

**Language:** English and Chinese.

**Country(ies) involved:** China.

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**Other relevant information:** None.

**Keywords:** Vasomotor symptoms, menopausal women, systematic review, network meta-analysis.

**Contributions of each author:**

**Author 1 - Xia Chen -** The author contributed to the conception, design, data interpretation, manuscript revision for critical intellectual content, and supervision of the study.

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