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Blinding assessment in randomized sham-controlled trials of acupuncture: a protocol for a systematic survey

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Abstract

Introduction Although various sham acupuncture techniques have been employed to ensure blinding in randomized controlled trials (RCTs) of acupuncture, the effectiveness of blinding in these trials and its influence on trial effect size estimates remain unclear. The objectives of this study are: (1) to investigate the proportion and study characteristics of sham-controlled trials reporting on blinding assessment, (2) to assess the blinding effectiveness of different types of sham acupuncture, (3) to investigate the relationship between blinding effectiveness and effect sizes in acupuncture RCTs.

Methods and analysis We will conduct a systematic survey of randomized sham-controlled trials of acupuncture in humans published in PubMed and EMBASE. Paired investigators will independently determine eligibility and use pilot-tested standardized forms for data extraction. We will calculate the proportion of sham-controlled trials that assessed and reported blinding success and conduct descriptive analyses of general study characteristics, acupuncture treatment details, sham acupuncture details and blinding assessments for included trials. We will assess the effectiveness of blinding success using the James Blinding index (BI) and Bang BI, and pool data from included trials using random effects models. We will use Hedges' g, a standardized mean difference (SMD), with its 95% confidence interval (CI), to calculate treatment effects and use Pearson's r correlation coefficient to assess the relationship between blinding effectiveness and trial effect sizes.

Ethics and dissemination Ethical approval is not required. The findings of this study will be disseminated through peer-reviewed publications, conference presentations and condensed summaries for clinicians, health policymakers and guideline developers regarding the design, conduct, analysis and interpretation of blinded assessment of sham acupuncture RCTs.

Keywords: systematic survey, sham acupuncture, randomized controlled trial,

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blinding assessment

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study will use a rigorous review procedure with clearly defined criteria, comprehensive search strategies, and pilot-tested data extraction forms. Our study includes more sham-controlled trials of acupuncture than previous studies, making our findings more generalizable.
- This study will evaluate the effectiveness of blinding success and assess the relationship between blinding effectiveness and effect sizes in sham-controlled trials of acupuncture, which that have not been adequately investigated in previous studies.
- This study is based on published papers, and due to words constraints in journals, blind assessments conducted by investigators may not have been reported. This potential omission may affect the estimated proportion of sham-controlled trials reporting on blinding assessment.
- This study only uses the pain outcomes of acupuncture for chronic pain trials to explore the relationship between blinding effectiveness and trial effect sizes.

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BACKGROUND

Randomized controlled trials (RCTs) are widely regarded as the gold standard for evaluating the efficacy of healthcare interventions. Blinding, a crucial methodological component in RCTs, involves keeping participants and/or researchers unaware of treatment allocation to minimize bias (1). It can be classified as single-blind, double-blind or triple-blind depending on who is blinded. Successful blinding can not only enhances the validity and credibility of RCTs, but also assists readers in evaluating the quality of the results(2). Insufficient blinding may lead to an overestimation of patient-reported outcomes (3), with nonblinded patients exaggerating effect sizes by an average of 0.56 standard deviations (95% CI -0.71 to -0.41)(4). The Template for Intervention Description and Replication (TIDieR)-Placebo, a guide and checklist for reporting placebo and sham controls, recommends that trials should measure and report the success of blinding to aid in the interpretation and use of clinical study findings(5).

Acupuncture is a traditional Chinese medicine practice that involves inserting thin needles into specific points on the body to treat various health conditions(6). It has gained worldwide popularity as a complementary and alternative therapy, particularly for various pain conditions, leading to numerous RCTs assessing its efficacy(7). Blinding is particularly crucial in acupuncture trials since it often involves subjective outcomes(8). However, blinding in acupuncture trials presents unique challenges due to the physical manipulation and subjective experiences involved(9). The nature of acupuncture makes it difficult to develop a placebo procedure that is physiologically inert and indistinguishable from true treatment(10). To achieve blinding, various types of sham acupuncture have been employed in trials, such as inserting needles at non-acupuncture points or with minimal penetration, as well as using non-penetrating placebo devices like Streitberger and Park sham needle(11).

However, the effectiveness of binding of these sham acupuncture in acupuncture trials remains a topic of debate, with some studies suggesting that participants can still distinguish between real and sham acupuncture. For instance, a RCT on

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patients with neck pain found that 18% of participants in the non-penetrating acupuncture group, 19% in shallow puncture group convinced that they had received sham acupuncture treatment(12). An earlier survey, including published literature up to 2011, evaluated the blinding effectiveness of acupuncture trials using a blinding index and found that 61% of participants maintained ideal blinding(13). Furthermore, insufficient attention has been given to assessing and reporting blinding in practice. Several studies have shown that the success of blinding was assessed or reported in less than 10% of trials(4, 14), and methods for evaluating blinding were inconsistent and questionable(15); however, these results consisted mainly of trials in other fields of medicine, with only a few involving acupuncture trials. Although these efforts, it remains unclear in practice how many sham-controlled acupuncture trials report blinding assessment, what methods are used to evaluate the success of blinding, and whether there are differences in blinding effectiveness of different types of sham acupuncture and whether the blinding effectiveness affects the trial effect size.

Given the importance of blinding in RCTs to ensure the validity and quality of study results, we aim to conduct a systematic survey on the blinding assessment of sham-controlled acupuncture trials. In this study, we have three main objectives: (1) estimating the proportion and study characteristics of sham-controlled trials reporting on blinding assessment, (2) assessing the blinding effectiveness of different types of sham acupuncture while exploring potential influencing factors, (3) investigating the relationship between blinding effectiveness and trial effect sizes.

Methods

We will conduct a systematic survey of randomized sham-controlled trials of acupuncture conducted in humans and published in PubMed and EMBASE. The protocol was registered in the Open Science Framework (https://doi.org/10.17605/OSF.IO/B3U7K).

Eligibility criteria

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The inclusion criteria are:

1) The study is an RCT;

2) The participants are human with any disease or symptom;

3) The study assesses the effect of acupuncture (e.g., manual acupuncture, electroacupuncture);

4) The study uses sham acupuncture as control;

5) The study is a main study report.

Acupuncture interventions are defined as the insertion of needles into the skin or muscle with or without stimulation, excluding non-inserted techniques such as laser acupuncture. Sham acupuncture refers to sham, placebo, fake, or simulated treatments that differed from acupuncture in at least one aspect to skin penetration or point location.

The exclusion criteria are:

1) The participants are healthy volunteers;

2) The study is to investigate the neurological mechanism of acupuncture;

3) The study is reported as an abstract, research letter, protocol and short report.

Literature search

We will search PubMed and EMBASE to identify sham-controlled trials, with no restrictions on language. The search for relevant studies will involve using database-specific subject headings (such as MeSH terms) and free texts associated with acupuncture, sham acupuncture and RCT. The search strategy will be developed by two experience investigators (J.L., L.L) with reference to previous related studies(16, 17) (**Appendix 1**).

Study process

Paired investigators, who have received training in research methods, will screen titles/abstracts and full texts to determine eligibility, and collect data from all included trials, independently and in duplicate. We will use electronic forms, developed with Microsoft Access, for study screening and data extraction. The forms will undergo standardization and pilot-testing, accompanied by detailed

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written instructions to enhance reliability. Any disagreements will be settled through discussion, or consultation with a third researcher (J.Y or J.L).

Data abstraction

We will develop a data extraction questionnaire, which will initially be created by three experienced investigators (J.Y, J.L., and L.L) based on previous related studies(16, 17). Subsequently, the data extraction form will undergo a pilot phase where data from 10 eligible RCTs will be collected. A discussion session will follow to assess the appropriateness and applicability of the listed items, resulting in necessary revisions. Based on the revised form, we will extract the following information from each included trial.

General characteristics of study

We will extract information on the first author, publication year, journal name, type of design, multi-nationality (i.e., the trial was conducted in two or more countries), country of trial conducted, center involved (single or multicenter), symptoms or diseases, sample size, number of arms, randomization ratio, length of follow-up, registration information, availability of protocol, signed informed consent (i.e., whether to inform the patients that they have the same opportunity to receive acupuncture or sham acupuncture treatment), source of funding (private for profit, private not for profit, governmental, not funded). Additionally, we will record information regarding patients' prior experience with acupuncture in the inclusion/exclusion criteria of each trial (i.e., including patients who had never received acupuncture treatment, including patients who had not recently received acupuncture, including both patients with or without previous acupuncture experience, not reported).

Characteristics of acupuncture treatment

We will record characteristics of acupuncture treatment, including type of acupuncture (manual acupuncture, electroacupuncture), acupoint prescription (standardized point prescription, partially individualized prescription, fully individualized prescription), depth of insertion, needle retention time, frequency

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and duration of treatment, total treatment sessions, needle type (diameter, length). In addition, we will document information on participating acupuncturists, including the description of acupuncturists (qualification or professional affiliation, years of acupuncture practice, trained in acupuncture techniques), whether multiple acupuncturists were involved, whether multiple acupuncturists were randomly grouped, and communication of acupuncturist-patient. For electroacupuncture, we will also record information on the current.

Characteristics of sham acupuncture

We will record characteristics of sham acupuncture, including whether the rational or theory of sham acupuncture was described, type of acupoints (non-meridian and non-acupoints, non-disease-related acupoints, same acupoints as acupuncture group, not reported), insertion depth (non-penetrating, shallow/minimal needling, same insertion depth as acupuncture group, not reported), needle stimulation (no manipulation or without manual stimulation, same manipulation as acupuncture group, other, not reported), response sought (no de qi sensation or muscle response, same as acupuncture group, other, not reported), needle retention time (same as acupuncture group, other, not reported), frequency and duration of treatment (same as acupuncture group, other, not reported), patients posture (same as acupuncture group, other, not reported). Furthermore, we will record the needle type (i.e., diameter, material) used in sham acupuncture.

If the acupoints used in sham acupuncture were non-meridian and non-acupoints, we will record whether these points were predefined, the method of definition (near points, the midpoint between two acupoints, other, not reported), and whether the definition has a source or theoretical basis (based on TCM theory, expert/clinical experience, other, not reported). If the acupoints were non-disease-related acupoints, we will also record whether these points were predefined, the diseases associated with these points, and rational for selecting them.

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If the insertion depth of sham acupuncture was non-penetrating, we will record whether a sham acupuncture device was used, and the type of sham acupuncture device (e.g., Foam needle, Steiberger needle, Park needle, Takakura needle). If the insertion depth of sham acupuncture was shallow/minimal needling, we will record whether the shallow/minimal needling was predefined, and the insertion depth (less than 3mm, 3-5mm, more than 5mm).

For electroacupuncture as an intervention, we will record the electrical stimulation information of sham acupuncture (no electrical stimulation or without current, turn off/interrupt the current after a few minutes of electrical stimulation, low current electrical stimulation, not reported), and the equipment of electroacupuncture. If low current is used, we will record whether it was predefined, and specify the range of current (less than 0.2mA, 0.2-0.5mA, more than 0.5mA).

Assessment of blinding

We will record whether blind design was explicitly reported (single-blind, double blind, not reported), whether it clearly reported who is blinded (patients, acupuncturists, outcome assessors, not reported), whether the success of blinding was assessed, who was assessed the success of blinding (patients, acupuncturists), and methods used to test for blinding (patients/acupuncturists were asked to guess their treatment allocation, other method). If the method was guessing treatment allocation, we will record when patients/acupuncturists were asked to guess (after the first treatment, at the end of trial, once during the trial, at multiple follow-up visits during trial, not reported), guessing options (acupuncture or sham acupuncture, acupuncture or sham acupuncture or uncertainty, other, not reported), and whether patients/acupuncturists rated the certainty of their guess using a continuous or Likert scale. Additionally, we will record whether before the trial volunteers were asked to evaluate the similarity between acupuncture and sham acupuncture that will be used in the trial, and reported the similarity results.

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We will also record the result and analysis of blinding assessment, including whether the results were reported, how the results were presented, statistical analysis methods for guessing treatment allocation (e.g., Chi-square or Fisher's exact test, Trend test, Kappa-value, James blinding index, Bang blinding index), conclusion of blinding (reported as successful blinding, reported as unsuccessful blinding, not reported), the reason for unsuccessful blinding (e.g., lack of effect in sham acupuncture group, side effects in acupuncture group), and whether the implications of unsuccessful blinding on interpreting results were discussed. Additionally, we will extract the data on the number or proportion of patients in each arm who correctly guessed their treatment assignment (i.e., contingency table).

Outcomes

We will use the pain outcomes of acupuncture for chronic pain (e.g., neck pain, shoulder pain, low back pain, osteoarthritis pain) trials to explore the relationship between blinding effectiveness and trial effect sizes. We will record the name of pain outcome, mean and standard deviation (SD) of changes from baseline pain intensity, and number of patients included for analyses in each treatment group.

Statistical analysis

We will calculate the proportion of sham-controlled trials assessing and reporting the success of blinding. Then, we will conduct descriptive analyses of general study characteristics, details of acupuncture treatment, details of sham acupuncture, and assessment of blinding for included trials. For all descriptive analyses, we will use frequencies (and percentages) for dichotomous variables, and mean (and SD) or median (and range) for continuous variables.

We will use James Blinding Index (BI) to assess the effectiveness of blinding success(18). James BI provides a comprehensive measure of blinding, with values ranging from 0 to 1, where 1 indicates complete blinding (successful blinding), 0 indicates complete unblinding (no blinding), and 0.5 indicates random guessing (ideal blinding)(19). If the upper bound of the confidence interval (CI) of James BI

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is below 0.5, unblinding may be claimed(19). Given the variability in study characteristics, we will use a random-effects model to pool James BI from included trials. We will also use Bang BI to assess the degree of blinding of each arm(20). Bang BI is directly interpreted as the extent of unblinding beyond chance and can capture different behaviors in different arms, with values ranging from -1 to 1, where 1 indicates all individuals guessed their assigned treatment correctly (complete unblinding), -1 indicates all individuals guessed incorrectly (opposite guessing), and 0 indicates random guessing (ideal blinding). We will calculate and pool the BI for each arm, that is, acupuncture BI and sham acupuncture BI. The statistical heterogeneity across the included studies will be examined using Cochrane's Q test and I^2 statistics. We will conduct several subgroup analyses to investigate heterogeneity when sufficient data are available, such as based on the type of disease, type of acupuncture, type of sham acupuncture, patients' prior experience with acupuncture.

We will calculate the treatment effect using Hedges'g, a standardized mean difference (SMD), with its 95% confidence interval (CI)(21). We will use Pearson's r correlation coefficient to assess the relationship between the blinding effectiveness and trial effect sizes. We will also use meta-regression to explore the relationship. All data analyses will be conducted using R software (version 4.3.2), with $p \leqslant 0.05$ considered statistically significant.

Discussion

The protocol describes a methodological study aimed at analyzing the blinding assessment in sham-controlled trials of acupuncture, including the blinding effectiveness of different types of sham acupuncture and its potential impact on trial effect sizes. By publishing the detailed study protocol, we aim to enhance transparency regarding our objectives and methods.

Strengths and limitations

Our study has several strengths. First, we will use rigorous review procedure that includes well-defined inclusion and exclusion criteria, comprehensive search

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strategies, and the use of pilot-tested standardized forms for study selection and data extraction. Additionally, calibration exercises and pilot data extraction will be conducted to ensure consistency between reviewers before proceeding with data abstraction. Second, our study will employ broad eligibility criteria without restrictions on the journal or publication year, which enhances the generalizability of our findings in comparison to previous studies. Finally, our study will address a series of unanswered questions regarding blinding assessment in sham-controlled trials of acupuncture that have not been adequately explored in prior research.

Our study also has some limitations. First, our study is based on published papers, given the space or words constraints in journals, it is possible that blind assessments conducted by investigators were not reported. This potential omission may impact the estimated proportion of sham-controlled trials reporting on blinding assessment. To address this concern, we plan to review the appendices and supplementary data files for any additional information provided. Second, there may be different methods to measure the success of blinding in practice. Guessing treatment allocation is a commonly used measurement method by researchers, and we will assess the blinding effectiveness of different types of sham acupuncture based on this measurement data. This may ignore data from other measurement methods, but we will extract and describe the results of other blind measurements. Third, although we will use SMD to combine pain intensity data from different chronic pain disorders, there may still be heterogeneity between studies, which may have compromised our findings. Finally, our search for eligible studies is limited to PubMed and EMBASE databases rather than including other search engines like CNKI which may potentially result in missing some trials. However, studies obtained from PubMed and EMBASE are characterized by sufficient sample size and representativeness since these databases are considered comprehensive and reliable sources.

Implications of this study

Blinding is a critical component in RCTs to minimize bias and ensure the validity of study results. However, blinding in acupuncture trials presents unique challenges

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due to the nature of the intervention. Regrettably, there has been insufficient emphasis on evaluating and reporting blinding effectiveness in practice(22). Although an earlier study examined the blinding effectiveness in sham acupuncture RCTs(13), it remains unclear regarding the status of blinding in sham-controlled acupuncture trials in practice. This study will investigate the extent of blinding evaluation and reporting in current sham-controlled acupuncture trials, analyze their study characteristics, so as to identify the strengths and limitations of different methods for assessing the success of blinding, highlight more appropriate practices, and provide recommendations for enhancing blinding evaluation in future acupuncture trials.

Furthermore, diverse sham acupuncture techniques were employed in the trial to ensure blinding, such as needle insertion at non-acupoints or with minimal penetration, and the use of non-penetrating placebo devices(11). However, a standardized or universally accepted sham procedure for acupuncture trials remains elusive(23). While some studies have investigated the effectiveness of different types of sham acupuncture in terms of blinding(24, 25), most have focused on non-penetrating placebo devices, leaving the blinding effectiveness of other forms such as shallow needling at non-acupoints unclear. This study will comprehensively summarize various types of sham acupuncture, provide detailed descriptions of their characteristics, evaluate the impact of different sham acupuncture on blinding effectiveness, and explore the relationship between blinding effectiveness and trial effect sizes. The findings of this study will contribute to the comprehension of which sham procedure would be most appropriate for future acupuncture research.

By publishing the detailed study protocol, we aim to enhance transparency regarding our research objectives and methods. The findings of this study may have significant implications for the design, implementation, analysis, and interpretation of blinding in acupuncture clinical trials, enhancing the methodological rigor and quality of acupuncture research.

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Contributors JY, JL, YF, LL, and XS conceptualized the study. All authors contributed the design of this protocol and approved the manuscript.

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#1:"acupuncture therapy"[MeSH Terms] OR "acupuncture treatment"[Title/Abstract] OR "Acupuncture"[Title/Abstract] OR "Pharmacopuncture"[Title/Abstract] OR "Acupotomy"[Title/Abstract] OR "Acupotomies"[Title/Abstract] OR "Acupoint"[Title/Abstract] OR "Acupoints"[Title/Abstract] OR "needle therapy"[Title/Abstract] OR "electroacupuncture"[Title/Abstract] OR "filiform needle"[Title/Abstract] OR "fire needle"[Title/Abstract] OR "scalp acupuncture"[Title/Abstract] OR "body acupuncture"[Title/Abstract] OR "needle warming therapy"[Title/Abstract] OR (("precipitating factors"[MeSH Terms] OR ("precipitating"[All Fields] AND "factors"[All Fields]) OR "precipitating factors"[All Fields] OR "trigger"[All Fields] OR "triggers"[All Fields] OR "triggerable"[All Fields] OR "triggered"[All Fields] OR "triggering"[All Fields] OR "triggerings"[All Fields]) AND "point"[Title/Abstract]) OR "dry needling"[Title/Abstract] OR "dry needle"[Title/Abstract]

#2: "sham acupuncture"[Title/Abstract] OR "placebo acupuncture"[Title/Abstract] OR "pseudo-acupuncture"[Title/Abstract] OR "non penetrating acupuncture"[Title/Abstract] OR "minimal acupuncture"[Title/Abstract] OR "superficial acupuncture"[Title/Abstract] OR "simulated acupuncture"[Title/Abstract] OR "sham"[Title/Abstract] OR "placebo"[Title/Abstract]

#3: "randomized controlled trial"[Publication Type] OR "Randomized"[Title/Abstract] OR "placebo"[Title/Abstract]

#4:#1 and #2 and #3

EMBASE

#1: ('acupuncture'/exp OR acupuncture) AND ('therapy'/exp OR therapy)

#2: 'Acupuncture Treatment':ab,ti or 'Acupuncture':ab,ti or 'Pharmacopuncture':ab,ti or 'Acupotomy':ab,ti or 'Acupotomies':ab,ti or ' Acupoint':ab,ti or 'Acupoints':ab,ti or 'needle therapy':ab,ti or 'electroacupuncture':ab,ti or 'filiform needle':ab,ti or 'fire needle':ab,ti or 'scalp acupuncture':ab,ti or 'body acupuncture':ab,ti or 'needle warming therapy':ab,ti or 'triggers point':ab,ti or 'dry needling':ab,ti or 'dry needle':ab,ti

#3:'simulated acupuncture':ab,ti or 'placebo acupuncture':ab,ti or 'pseudo-acupuncture':ab,ti or 'non-penetrating acupuncture':ab,ti or 'minimal acupuncture':ab,ti or 'superficial acupuncture':ab,ti or 'simulated acupuncture':ab,ti or 'sham':ab,ti or 'placebo':ab,ti

#4:'Randomized controlled trial':ab,ti or 'randomized':ab,ti or 'placebo':ab,ti or 'RCT':ab,ti

#5: #1 or #2

#6: #3 AND #4 AND #5

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Blinding assessment in randomized sham-controlled trials of acupuncture: protocol for a systematic survey

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Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Research methods, Rehabilitation medicine, Evidence based practice
Keywords:	Randomized Controlled Trial, Acupuncture, Systematic Review

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Blinding assessment in randomized sham-controlled trials of acupuncture: protocol for a systematic survey

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Abstract

Introduction: Although various sham acupuncture techniques have been employed to ensure blinding in randomized controlled trials (RCTs) of acupuncture, the effectiveness of blinding in these trials and its influence on trial effect size estimates remain unclear. The objectives of this study are: (1) to investigate the proportion and study characteristics of sham-controlled trials reporting on blinding assessment, (2) to assess the blinding effectiveness of different types of sham acupuncture, (3) to investigate the relationship between blinding effectiveness and effect sizes in acupuncture RCTs.

Methods and analysis: We will search PubMed and EMBASE from inception to 1 January 2025 to identify RCTs that compared acupuncture with sham acupuncture in humans with any disease or symptom, with no restrictions on language. Paired investigators will independently determine eligibility and use pilot-tested standardized forms for data extraction. We will calculate the proportion of sham-controlled trials that assessed and reported blinding success and conduct descriptive analyses of general study characteristics, acupuncture treatment details, sham acupuncture details and blinding assessments for included trials. We will assess the effectiveness of blinding success using the James Blinding index (BI) and Bang BI, and pool data from included trials using random effects models. We will use Hedges' g, a standardized mean difference (SMD), with its 95% confidence interval (CI), to calculate treatment effects. We will use Pearson's r correlation coefficient to assess the relationship between blinding effectiveness and trial effect sizes when variable distributions meet the assumptions of normality and linearity; otherwise, we will consider employing non-parametric tests. When sufficient data are available, we will also use random-effects meta-regression to explore the relationship.

Ethics and dissemination: Ethical approval is not required. The findings of this study will be disseminated through peer-reviewed publications, conference presentations and condensed summaries for clinicians, health policymakers and guideline developers regarding the design, conduct, analysis and interpretation of

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blinded assessment of sham acupuncture RCTs.

Study registration: Open Science Framework (https://doi.org/10.17605/OSF.IO/B3U7K).

Keywords: systematic survey, sham acupuncture, randomized controlled trial, blinding assessment

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study will evaluate the effectiveness of blinding success and assess the relationship between blinding effectiveness and effect sizes in sham-controlled trials of acupuncture.
- The study will use a rigorous review procedure with clearly defined criteria, comprehensive search strategies, and pilot-tested data extraction forms.
- The study will be based on published papers, which may have unreported blinding assessments due to journal constraints, which could affect the estimated proportion of sham-controlled trials reporting on blinding assessment.
- This study will use only the pain outcomes of acupuncture for chronic pain trials to explore the relationship between blinding effectiveness and trial effect sizes.

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INTRODUCTION

Randomized controlled trials (RCTs) are widely regarded as the gold standard for evaluating the efficacy of healthcare interventions. Blinding, a crucial methodological component in RCTs, involves keeping participants and/or researchers unaware of treatment allocation to minimize bias(1). It can be classified as single-blind, double-blind or triple-blind depending on who is blinded. Successful blinding can not only enhances the validity and credibility of RCTs, but also assists readers in evaluating the quality of the results(2). Insufficient blinding may lead to an overestimation of patient-reported outcomes(3), with nonblinded patients exaggerating effect sizes by an average of 0.56 standard deviations (95% CI -0.71 to -0.41)(4). The Template for Intervention Description and Replication (TIDieR)-Placebo, a guide and checklist for reporting placebo and sham controls, recommends that trials should measure and report the success of blinding to aid in the interpretation and use of clinical study findings(5).

Acupuncture is a traditional Chinese medicine practice that involves inserting thin needles into specific points on the body to treat various health conditions(6). It has gained worldwide popularity as a complementary and alternative therapy, particularly for various pain conditions, leading to numerous RCTs assessing its efficacy(7). Blinding is particularly crucial in acupuncture trials since it often involves subjective outcomes(8). However, blinding in acupuncture trials presents unique challenges due to the physical manipulation and subjective experiences involved(9). The nature of acupuncture makes it difficult to develop a placebo procedure that is physiologically inert and indistinguishable from true treatment(10). To achieve blinding, various types of sham acupuncture have been used in trials, such as inserting needles at non-acupuncture points or with minimal penetration to mimic the physical sensation of needling, which can potentially induce a therapeutic effect, as well as using non-penetrating placebo devices like Streitberger and Park sham needle, which may not fully achieve patient blinding (11).

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The effectiveness of binding of sham acupuncture in acupuncture trials remains a topic of debate, with some studies suggesting that participants can still distinguish between real and sham acupuncture. For instance, a RCT on patients with neck pain found that 18% of participants in the non-penetrating acupuncture group, 19% in shallow puncture group convinced that they had received sham acupuncture treatment(12). An earlier survey, including published literature up to 2011, evaluated the blinding effectiveness of acupuncture trials using a blinding index and found that 61% of participants maintained ideal blinding(13). Moreover, insufficient attention has been given to assessing and reporting blinding in practice. Several studies have shown that the success of blinding was assessed or reported in less than 10% of trials(4, 14), and methods for evaluating blinding were inconsistent and questionable(15); however, these results consisted mainly of trials in other fields of medicine, with only a few involving acupuncture trials. Additionally, a recent study proposed an exploratory principle and protocol for the blinding assessment without practical validation(16). Although these efforts, it remains unclear in practice how many sham-controlled acupuncture trials report blinding assessment, what methods are used to evaluate the success of blinding, and whether there are differences in blinding effectiveness of different types of sham acupuncture and whether the blinding effectiveness affects the trial effect size.

Given the importance of blinding in RCTs to ensure the validity and quality of study results, we aim to conduct a systematic survey on the blinding assessment of sham-controlled acupuncture trials. In this study, we have three main objectives: (1) estimating the proportion and study characteristics of sham-controlled trials reporting on blinding assessment, (2) assessing the blinding effectiveness of different types of sham acupuncture while exploring potential influencing factors, (3) investigating the relationship between blinding effectiveness and trial effect sizes.

METHODS AND ANALYSIS

We will conduct a systematic survey of randomized sham-controlled trials of

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acupuncture conducted in humans and published in PubMed and EMBASE. The protocol was registered in the Open Science Framework (https://doi.org/10.17605/OSF.IO/B3U7K).

Eligibility criteria

The inclusion criteria are:

1) The study is an RCT;

2) The participants are human with any disease or symptom;

3) The study assesses the effect of acupuncture (e.g., manual acupuncture, electroacupuncture);

4) The study uses sham acupuncture as control;

5) The study is a main study report.

Acupuncture interventions are defined as the insertion of needles into the skin or muscle with or without stimulation, excluding non-inserted techniques such as laser acupuncture. Sham acupuncture refers to sham, placebo, fake, or simulated treatments that differed from acupuncture in at least one aspect to skin penetration or point location. This systematic survey has no disease or condition restriction, but for investigating the relationship between blinding effectiveness and trial effect sizes, this analysis will be limited on trials involving pain-related disorders.

The exclusion criteria are:

1) The participants are healthy volunteers;

2) The study is to investigate the neurological mechanism of acupuncture;

3) The study is reported as an abstract, research letter, protocol and short report.

Literature search

We will search PubMed and EMBASE to identify randomized sham-controlled trials from inception to 1 January 2025, with no restrictions on language. The search for relevant studies will involve using database-specific subject headings (such as MeSH terms) and free texts associated with acupuncture, sham acupuncture and RCT. The search strategy will be developed by two experience

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investigators (J.L., L.L) with reference to previous related studies(17, 18) (**Appendix 1**).

Study procedures

Paired investigators, who have received training in research methods, will screen titles/abstracts and full texts to determine eligibility, and collect data from all included trials, independently and in duplicate. We will use electronic forms, developed with Microsoft Access, for study screening and data extraction. The forms will undergo standardization and pilot-testing, accompanied by detailed written instructions to enhance reliability. Any disagreements will be settled through discussion, or consultation with a third researcher (J.Y or J.L).

Data abstraction

We will develop a data extraction questionnaire, which will initially be created by three experienced investigators (J.Y, J.L., and L.L) based on previous related studies(17, 18). Subsequently, the data extraction form will undergo a pilot phase where data from 10 eligible RCTs will be collected. A discussion session will follow to assess the appropriateness and applicability of the listed items, resulting in necessary revisions. Based on the revised form, we will extract the following information from each included trial.

General characteristics of study

We will extract information on the first author, publication year, journal name, type of design, multi-nationality (i.e., the trial was conducted in two or more countries), country of trial conducted, center involved (single or multicenter), symptoms or diseases, sample size, number of arms, randomization ratio, length of follow-up, registration information, availability of protocol, signed informed consent (i.e., whether to inform the patients that they have the same opportunity to receive acupuncture or sham acupuncture treatment), source of funding (private for profit, private not for profit, governmental, not funded). Additionally, we will record information regarding patients' prior experience with acupuncture in the inclusion/exclusion criteria of each trial (i.e., including patients who had

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never received acupuncture treatment, including patients who had not recently received acupuncture, including both patients with or without previous acupuncture experience, not reported).

Characteristics of acupuncture treatment

We will record the characteristics of acupuncture treatment according to the STRICTA guideline(19). Including the rationale or theory of acupuncture, type of acupuncture (manual acupuncture, electroacupuncture), number of needle insertions per subject per session (mean and range), names or location of points used, acupoint prescription (standardized point prescription, partially individualized prescription, fully individualized prescription), depth of insertion, response sought (de qi, muscle twitch response, other, not reported), needle retention time, frequency and duration of treatment, total treatment sessions, needle type (diameter, length). In addition, we will document information on participating acupuncturists, including the description of acupuncturists (qualification or professional affiliation, years of acupuncture practice, trained in acupuncture techniques), whether multiple acupuncturists were involved, whether multiple acupuncturists were randomly grouped, and communication of acupuncturist-patient. For electroacupuncture, we will also record information on the current.

Characteristics of sham acupuncture

We will record characteristics of sham acupuncture, including whether the rational or theory of sham acupuncture was described, type of acupoints (non-meridian and non-acupoints, non-disease-related acupoints, same acupoints as acupuncture group, not reported), insertion depth (non-penetrating, shallow/minimal needling, same insertion depth as acupuncture group, not reported), needle stimulation (no manipulation or without manual stimulation, same manipulation as acupuncture group, other, not reported), response sought (no de qi sensation or muscle response, same as acupuncture group, other, not reported), needle retention time (same as acupuncture group, other, not reported), frequency and duration of treatment (same as acupuncture group,

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other, not reported), patients posture (same as acupuncture group, other, not reported). Furthermore, we will record the needle type (i.e., diameter, material) used in sham acupuncture.

If the acupoints used in sham acupuncture were non-meridian and non-acupoints, we will record whether these points were predefined, the method of definition (near points, the midpoint between two acupoints, other, not reported), and whether the definition has a source or theoretical basis (based on TCM theory, expert/clinical experience, other, not reported). If the acupoints were non-disease-related acupoints, we will also record whether these points were predefined, the diseases associated with these points, and rational for selecting them.

If the insertion depth of sham acupuncture was non-penetrating, we will record whether a sham acupuncture device was used, and the type of sham acupuncture device (e.g., Foam needle, Steiberger needle, Park needle, Takakura needle). If the insertion depth of sham acupuncture was shallow/minimal needling, we will record whether the shallow/minimal needling was predefined, and the insertion depth (less than 3mm, 3-5mm, more than 5mm).

For electroacupuncture as an intervention, we will record the electrical stimulation information of sham acupuncture (no electrical stimulation or without current, turn off/interrupt the current after a few minutes of electrical stimulation, low current electrical stimulation, not reported), and the equipment of electroacupuncture. If low current is used, we will record whether it was predefined, and specify the range of current (less than 0.2mA, 0.2-0.5mA, more than 0.5mA).

Assessment of blinding

We will record whether blind design was explicitly reported (single-blind, double blind, not reported), the subject of binding (patients, acupuncturists, outcome assessors, not reported), whether the success of blinding was assessed, who was

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assessed the success of blinding (patients, acupuncturists), and methods used to test for blinding (patients/acupuncturists were asked to guess their treatment allocation, other method). If the method was guessing treatment allocation, we will record when patients/acupuncturists were asked to guess (after the first treatment, at the end of trial, once during the trial, at multiple follow-up visits during trial, not reported), guessing options (acupuncture or sham acupuncture, acupuncture or sham acupuncture or uncertainty, other, not reported), and whether patients/acupuncturists rated the certainty of their guess using a continuous or Likert scale. Additionally, we will record whether before the trial volunteers were asked to evaluate the similarity between acupuncture and the sham acupuncture that will be used in the trial, and reported the similarity results.

We will also record the result and analysis of blinding assessment, including whether the results were reported, how the results were presented, statistical analysis methods for guessing treatment allocation (e.g., Chi-square or Fisher's exact test, Trend test, Kappa-value, James blinding index, Bang blinding index), conclusion of blinding (reported as successful blinding, reported as unsuccessful blinding, not reported), the reason for unsuccessful blinding (e.g., lack of effect in sham acupuncture group, side effects in acupuncture group), and whether the implications of unsuccessful blinding on interpreting results were discussed. Additionally, we will extract the data on the number or proportion of patients in each arm who correctly guessed their treatment assignment (i.e., contingency table).

Outcomes

To evaluate the relationship between blinding effectiveness and trial effect sizes, we will use the pain outcomes from acupuncture for chronic pain trials (e.g., neck pain, shoulder pain, low back pain, osteoarthritis pain). We will record the name of pain outcome, mean and standard deviation (SD) of changes from baseline pain intensity, and number of patients included for analyses in each treatment group.

Statistical analysis

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We will calculate the proportion of sham-controlled trials assessing and reporting the success of blinding. Then, we will conduct descriptive analyses of general study characteristics, details of acupuncture treatment, details of sham acupuncture, and assessment of blinding for included trials. For all descriptive analyses, we will use frequencies (and percentages) for dichotomous variables, and mean (and SD) or median (and range) for continuous variables.

We will use James Blinding Index (BI) to assess the effectiveness of blinding success(20). James BI provides a comprehensive measure of blinding, with values ranging from 0 to 1, where 1 indicates complete blinding (successful blinding), 0 indicates complete unblinding (no blinding), and 0.5 indicates random guessing (ideal blinding)(16). If the upper bound of the confidence interval (CI) of James BI is below 0.5, unblinding may be claimed(16). Given the variability in study characteristics, we will use a random-effects model to pool James BI from included trials. We will also use Bang BI to assess the degree of blinding of each arm(21). Bang BI is directly interpreted as the extent of unblinding beyond chance and can capture different behaviors in different arms, with values ranging from -1 to 1, where 1 indicates all individuals guessed their assigned treatment correctly (complete unblinding), -1 indicates all individuals guessed incorrectly (opposite guessing), and 0 indicates random guessing (ideal blinding). We will calculate and pool the BI for each arm, that is, acupuncture BI and sham acupuncture BI. The statistical heterogeneity across the included studies will be examined using Cochrane's Q test and I^2 statistics. We will conduct several subgroup analyses to investigate heterogeneity when sufficient data are available, such as based on the type of disease, type of acupuncture, type of sham acupuncture, patients' prior experience with acupuncture, subject of blinding.

We will calculate the treatment effect using Hedges'g, a standardized mean difference (SMD), with its 95% confidence interval (CI)(22). We will use Pearson's r correlation coefficient to assess the relationship between blinding effectiveness and trial effect sizes when variable distributions meet the assumptions of normality and linearity; otherwise, we will consider employing non-parametric

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tests, such as Spearman's rank correlation coefficient. When sufficient data are available, we will also use meta-regression to explore the relationship while accounting for several potential confounding variables, such as the type of sham acupuncture, type of sham acupoints, insertion depth, needle stimulation, and patient' prior experience with acupuncture. These variables will be incorporated as covariates within a random-effects model to accommodate inter-study heterogeneity and account for intra-study variability. All data analyses will be conducted using R software (version 4.3.2), with $p \leqslant 0.05$ considered statistically significant.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

Ethical approval is not required. The findings of this study will be disseminated through peer-reviewed publications, conference presentations and condensed summaries for clinicians, health policymakers and guideline developers regarding the design, conduct, analysis and interpretation of blinded assessment of sham acupuncture RCTs.

DISCUSSION

The protocol describes a methodological study aimed at analyzing the blinding assessment in sham-controlled trials of acupuncture, including the blinding effectiveness of different types of sham acupuncture and its potential impact on trial effect sizes. By publishing the detailed study protocol, we aim to enhance transparency regarding our objectives and methods.

Our study has several strengths. First, we will use rigorous review procedure that includes well-defined inclusion and exclusion criteria, comprehensive search strategies, and the use of pilot-tested standardized forms for study selection and data extraction. Additionally, calibration exercises and pilot data extraction will be conducted to ensure consistency between reviewers before proceeding with data

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abstraction. Second, our study will employ broad eligibility criteria without restrictions on the journal or publication year, which enhances the generalizability of our findings. Finally, our study will address a series of unanswered questions regarding blinding assessment in sham-controlled trials of acupuncture that have not been adequately explored in prior research.

Our study also has some limitations. First, our study based on published papers may have unreported blind assessments by investigators due to journal constraints, which could affect the estimated proportion of sham-controlled trials reporting on blinding assessment. To address this concern, we plan to review the appendices and supplementary data files for any additional information provided. Second, there may be different methods to measure the success of blinding in practice. Guessing treatment allocation is a commonly used measurement method by researchers, and we will assess the blinding effectiveness of different types of sham acupuncture based on this measurement data. This may ignore data from other methods, but we will extract and describe the results of other blind measurements. Third, although we will use SMD to combine pain intensity data from different chronic pain disorders, there may still be heterogeneity between studies, such as variations in patient baseline characteristics, which may have compromised our findings. Finally, our search for eligible studies is limited to PubMed and EMBASE databases rather than including other search engines like CNKI which may potentially result in missing some trials. However, studies obtained from PubMed and EMBASE are characterized by sufficient sample size and representativeness since these databases are considered comprehensive and reliable sources.

Blinding is a critical component in RCTs to minimize bias and ensure the validity of study results. However, blinding in acupuncture trials presents unique challenges due to the nature of the intervention. Regrettably, there has been insufficient emphasis on evaluating and reporting blinding effectiveness in practice(23). Although an earlier study examined the blinding effectiveness in sham acupuncture RCTs(13), it remains unclear regarding the status of blinding in sham-

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controlled acupuncture trials in practice. This study will investigate the extent of blinding evaluation and reporting in current sham-controlled acupuncture trials, analyze their study characteristics, so as to identify the strengths and limitations of different methods for assessing the success of blinding, highlight more appropriate practices, and provide recommendations for enhancing blinding evaluation in future acupuncture trials.

Furthermore, diverse sham acupuncture techniques were employed in the trial to ensure blinding, such as needle insertion at non-acupoints or with minimal penetration, and the use of non-penetrating placebo devices(11). However, a standardized or universally accepted sham procedure for acupuncture trials remains elusive(24). While some studies have investigated the effectiveness of different types of sham acupuncture in terms of blinding(25, 26), most have focused on non-penetrating placebo devices, leaving the blinding effectiveness of other forms such as shallow needling at non-acupoints unclear. This study will comprehensively summarize various types of sham acupuncture, provide detailed descriptions of their characteristics, evaluate the impact of different sham acupuncture on blinding effectiveness, and explore the relationship between blinding effectiveness and trial effect sizes. The findings of this study will contribute to the comprehension of which sham procedure would be most appropriate for future acupuncture research.

By publishing the detailed study protocol, we aim to enhance transparency regarding our research objectives and methods. The findings of this study may have significant implications for the design, implementation, analysis, and interpretation of blinding in acupuncture clinical trials, enhancing the methodological rigor and quality of acupuncture research.

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Contributors: JY, JL, YF, LL, and XS conceptualized the study. All authors contributed the design of this protocol and approved the manuscript. YF (Yong Fu) is the guarantor for this study.

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Patient consent for publication: Not applicable.

Provenance and peer review: Not commissioned; externally peer reviewed.

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#1:"acupuncture therapy"[MeSH Terms] OR "acupuncture treatment"[Title/Abstract] OR "Acupuncture"[Title/Abstract] OR "Pharmacopuncture"[Title/Abstract] OR "Acupotomy"[Title/Abstract] OR "Acupotomies"[Title/Abstract] OR "Acupoint"[Title/Abstract] OR "Acupoints"[Title/Abstract] OR "needle therapy"[Title/Abstract] OR "electroacupuncture"[Title/Abstract] OR "filiform needle"[Title/Abstract] OR "fire needle"[Title/Abstract] OR "scalp acupuncture"[Title/Abstract] OR "body acupuncture"[Title/Abstract] OR "needle warming therapy"[Title/Abstract] OR (("precipitating factors"[MeSH Terms] OR ("precipitating"[All Fields] AND "factors"[All Fields]) OR "precipitating factors"[All Fields] OR "trigger"[All Fields] OR "triggers"[All Fields] OR "triggerable"[All Fields] OR "triggered"[All Fields] OR "triggering"[All Fields] OR "triggerings"[All Fields]) AND "point"[Title/Abstract]) OR "dry needling"[Title/Abstract] OR "dry needle"[Title/Abstract]

#2: "sham acupuncture"[Title/Abstract] OR "placebo acupuncture"[Title/Abstract] OR "pseudo-acupuncture"[Title/Abstract] OR "non penetrating acupuncture"[Title/Abstract] OR "minimal acupuncture"[Title/Abstract] OR "superficial acupuncture"[Title/Abstract] OR "simulated acupuncture"[Title/Abstract] OR "sham"[Title/Abstract] OR "placebo"[Title/Abstract]

#3: "randomized controlled trial"[Publication Type] OR "Randomized"[Title/Abstract] OR "placebo"[Title/Abstract]

#4:#1 and #2 and #3

EMBASE

#1: ('acupuncture'/exp OR acupuncture) AND ('therapy'/exp OR therapy)

#2: 'Acupuncture Treatment':ab,ti or 'Acupuncture':ab,ti or 'Pharmacopuncture':ab,ti or 'Acupotomy':ab,ti or 'Acupotomies':ab,ti or ' Acupoint':ab,ti or 'Acupoints':ab,ti or 'needle therapy':ab,ti or 'electroacupuncture':ab,ti or 'filiform needle':ab,ti or 'fire needle':ab,ti or 'scalp acupuncture':ab,ti or 'body acupuncture':ab,ti or 'needle warming therapy':ab,ti or 'triggers point':ab,ti or 'dry needling':ab,ti or 'dry needle':ab,ti

#3:'simulated acupuncture':ab,ti or 'placebo acupuncture':ab,ti or 'pseudo-acupuncture':ab,ti or 'non-penetrating acupuncture':ab,ti or 'minimal acupuncture':ab,ti or 'superficial acupuncture':ab,ti or 'simulated acupuncture':ab,ti or 'sham':ab,ti or 'placebo':ab,ti

#4:'Randomized controlled trial':ab,ti or 'randomized':ab,ti or 'placebo':ab,ti or 'RCT':ab,ti

#5: #1 or #2

#6: #3 AND #4 AND #5

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