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The blinding status and characteristics in acupuncture clinical trials: a systematic reviews and meta-analysis

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Abstract

Background Sham acupuncture is a widely accepted control in acupuncture clinical trials. Given the nature of acupuncture, it is warranted to assess the blinding of sham-controlled trials. Despite the sham acupuncture design having been widely used, the overall blinding of sham acupuncture and the characteristics of blinding assessment in acupuncture trials are unclear. This research aims to assess the blinding status of acupuncture clinical trials and explore the blinding assessment characteristics in acupuncture trials.

Methods This meta-analysis included all the acupuncture clinical trials published in English that performed blinding assessments and reported the results. We searched PubMed, Embase, and Web of Science for randomized controlled trials (RCTs) from inception to April 2024. The primary outcome is Bang's Blinding Index (Bang's BI) and 95% credibility interval (CrI) was pooled using a Bayesian hierarchical model. The study adheres to the PRISMA guidelines.

Results Sixty-four eligible studies published from 1999 to 2024 were included. The mean of Bang's BI was − 0.24 (95% CrI − 0.34 to − 0.14, $tau^2 = 0.13$) for the sham acupuncture group and 0.41 (95% CrI 0.32 to 0.49, $tau^2 = 0.10$) for the verum acupuncture group. The characteristics of blinding showed that 62.50% of the trials had a Bang's BI greater than 0 in the verum group and less than 0 in the sham group; in 28.15% of the trials, the Bang's BI was greater than 0 in the verum group and greater than 0 in the sham group. Subgroup analysis revealed that area, number of research centers, treatment sessions, acupoints number, and evaluation timepoint can influence blinding results.

Conclusion Overall blinding status in current acupuncture clinical trials shows a majority correctly guessing for the verum group and opposite guessing for the sham group. However, in some acupuncture trials, the blinding of sham acupuncture might be compromised. Factors such as the Asian population, penetrating sham needling, and querying participants about their group assignment during the study increase the risk of unblinding and warrant careful consideration in sham acupuncture control design. Furthermore, researchers should closely monitor the blinding status of sham acupuncture and transparently report details of blinding assessments.

Systematic review registration PROSPERO CRD42023403595.

Keywords Acupuncture clinical trials, Blinding assessment, Bang's Blinding Index, Blinding status

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Background

Blinding is commonly employed to control measurement bias in clinical trials and enhances the validity and credibility of study findings [1]. Successful blinding can promote participant compliance and reduce the study dropout rate [2]. Unsuccessful blinding will increase the use of co-interventions and impact the study results [3]. Meanwhile, unsuccessful blinding may overestimate treatment effects and cause assessment bias, particularly for patient-reported outcomes such as pain or insomnia [3–5]. Acupuncture is a complex intervention that includes multiple procedures. Developing a sham acupuncture control that is indistinguishable from verum acupuncture is difficult. Sham acupuncture may not completely and effectively simulate the needling sensations required for participant blinding, especially for individuals with prior experience or knowledge of acupuncture [6]. Therefore, blinding assessments are essential for acupuncture clinical trials [7, 8]. The sham acupuncture reporting guidelines and checklist (The SHARE) [8] and the TIDieR-Placebo [9] require the assessment and detailed reporting of blinding in acupuncture clinical trials. Presently, fewer acupuncture clinical studies published in international journals conduct blinding assessments and report the results. However, most of those acupuncture clinical studies conducting the blinding assessment focus on specific diseases and cannot provide generalized and robust evidences for the quality and effectiveness of sham acupuncture control. Hence, it is necessary to assess the overall blinding effectiveness of sham acupuncture in acupuncture clinical trials [10].

At present, the methods of blinding assessment in acupuncture clinical trials are adapted from those used in pharmaceutical interventions. However, acupuncture's unique sensory experience distinguishes it from pharmaceutical interventions. Sham acupuncture designs aim to convince participants they are receiving real acupuncture, often by simulating the sensation of needle penetration. This simulated sensation can lead participants to guess their group assignment, making random guesses unlikely and potentially biasing the balance between groups. Therefore, the blinding effectiveness between verum acupuncture and sham acupuncture groups in acupuncture trials may differ from that in pharmaceutical trials. However, there is no related study about the blinding status of acupuncture trials by now. Our study comprehensively included all sham acupuncture control studies to assess the blinding status and the characteristics of blinding in acupuncture clinical trials.

Methods

This meta-analysis was reported in accordance with the updated Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA 2020, 27-item checklist) guidelines (Supplementary eTable 1). The protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42023403595).

Literature search

Three English databases, PubMed, Embase, and Web of Science, were searched from inception to April 2024 for potentially relevant studies. The following search strategy for PubMed was used: ("acupuncture"[Mesh] OR "acupuncture therapy"[Mesh] OR "electroacupuncture"[Mesh] OR "meridians" [Mesh] OR "acupuncture points"[Mesh]) OR ("acupuncture"[Title/Abstract] OR "acupoint"[Title/Abstract] OR "acupuncture point"[Title/Abstract] OR "electroacupuncture"[Title/Abstract] OR "electro-acupuncture"[Title/Abstract] OR "needling"[Title/Abstract] OR "dry-needling"[Title/Abstract]). In addition, reference lists of included articles were manually searched.

Eligibility criteria and data collection

Included articles adhered to the following criteria: (1) single-blind or double-blind, randomized controlled trials of acupuncture in which participants were blinded, (2) reporting the Bang's BI or the guessed proportion or number of participants within each group, which can be used to calculate the Bang's BI. We excluded those articles with healthy participants. In addition, animal experiments, case series, cohort studies, and articles published as abstracts only, editorials, reviews, duplicate publications, or correspondence letters were excluded.

Two independent investigators (TL L and SJ L) conducted an initial screening based on the titles and abstracts. The final included literature was then determined by reading the full text. Information was collected from all studies by two independent investigators (TL L and ZY X); if there was a disagreement between two investigators, a third investigator (SY Y) was consulted to make the final decision. Information related to the sham acupuncture design of each study included sample size ($<100, \geq 100$), study region (Asia, non-Asia), study site (singer center, multicenter), the group name that referred to sham acupuncture during informed consent (sham treatment, placebo treatment, treatment), treatment sessions (≤ 10, 10–20, >20), treatment period and frequency, acupuncture experiences, age, gender, the number of dropouts, and acupuncturists qualifications.

Sham acupuncture characteristics included four aspects: penetration depth (no puncture, shallow), acupoint numbers, types of control needle (regular acupuncture needle, blunt needle), and location (acupoints or non-acupoints). The implementation process of sham acupuncture included manipulation or not, limitation of doctor-patient communication, the same acupuncturists in verum and sham groups, and acupuncturists' working years. For blinding assessments, the Bang's BI or the actual number of guessing group assignments in each group, blinding optimization measures, number of evaluations, and assessment time points were recorded. The efficacy of primary outcomes was also collected.

Risk of *bias* assessment

The risk of bias was assessed using the revised Cochrane risk-of-bias tool for randomized trials (ROB2). This tool evaluates five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain is judged as having a low, some concerns, or high risk of bias. The evaluation criteria are as follows: if all domains are assessed as low risk, then the overall risk is considered low risk. If there are some concerns in at least one domain but not high risk that would classify it as some concerns. If there are high risks in one or more domains, then the overall risk is considered high risk. Two investigators (TL L and LJ J) independently assessed the domains after identifying the included literature. A third investigator (SY Y) was consulted for a final decision if there was a disagreement.

Statistical analysis

Bang's BI was employed to evaluate the status of blinding. In instances where the Bang's BI was explicitly reported, this information was extracted directly. Alternatively, if the Bang's BI was not reported, it was calculated based on the number of participants' guesses as to which treatment they received in each treatment [11, 12]. We used a Bayesian hierarchical model to calculate the posterior index of Bang's BI. For level one, the Bang's BI was assumed to be normal distribution $N(\theta, \sigma^2)$, σ^2 indicated as error in-study. For level two, the θ was modeled using a normal distribution $N(\mu,\tau^2)$. A non-informative priors N (0.0,1.03), a normal distribution with a mean of 0 and a large variance, was chosen for hyper-parameter μ and a non-informative priors Unif (0,1000) for τ(the variation between studies). Subsequently, we entered this model and ran 10,000 Markov Chain Monte Carlo iterations to estimate the Bang's BI and their corresponding 95% probability intervals (CrI). Whether the chain of values had converge to a stable posterior distribution was assessed by shrink factor (Rhat < 1.1) [13]. A sensitivity analysis was conducted for the pooled Bang's BI based on the actual BI index reported in both groups. We used a random effects model (I–V heterogeneity) to pool the actual Bang's BI. Cochran's Q test and the I^2 statistic were used to assess heterogeneity among the studies included in our meta-analysis. If the heterogeneity was greater than 50%, the source of heterogeneity was explored by subgroup analysis.

To ascertain the potential correlation between the success of blinding and the magnitude of the study's effect, treatment outcomes were normalized using Cohen's d values for correlation analysis. Spearman correlation coefficient was employed to examine the association between BI and treatment effect. To assess publication bias, a nonparametric trim-and-fill analysis was conducted of the funnel plot, run estimator, and imputing on the right. The Egger test was also calculated. All data analyses were performed using Stata 17(The Analysis Factor LLC, Ithaca, Athens) and R 4.3.1(The R Foundation for Statistical Computing, Vienna, Austria) software. All results with a two-sided $p < 0.05$ are considered statistically significant.

Results

A total of 11,519 studies were initially identified, of which 5799 duplicated pieces of literature were excluded. The remaining 5720 studies underwent screening based on titles and abstracts, excluding 4277 studies. Additionally, 1443 were left for full-text screening. After reading the full text, 827 studies were removed, leaving 616 potentially eligible articles. Further, 557 studies were excluded that lacked blinding assessments or data, and five further studies were included by updating the search before writing the manuscript. Finally, 64 studies were included. Figure 1 shows the flow chart of the literature screening procedure. All the included studies and the Bang's BI, sham modality, and primary outcomes are listed in Table 1.

The summarized blinding index for both group

The summarized posterior Bang's BI of the verum acupuncture group and sham acupuncture analyzed by Bayesian hierarchical models were 0.41 (95% CrI: 0.32 to 0.49, $tau^2 = 0.10$) and − 0.24 (95% CrI: − 0.34 to − 0.14, $tau^2 = 0.13$), respectively. The forest plots of the Bang's BI were presented in Figs. 2 and 3. The sensitivity analyses with pooled actual Bang's BI in both groups were 0.42 (95%CI: 0.34 to 0.50, $I^2 = 96.4\%$) and − 0.23 (95%CI: − 0.34 to − 0.13, $I^2 = 97.8\%$) for the verum group and the sham group, respectively. Forest plots of sensitivity analysis are shown in eFig. 1 and eFig. 2.

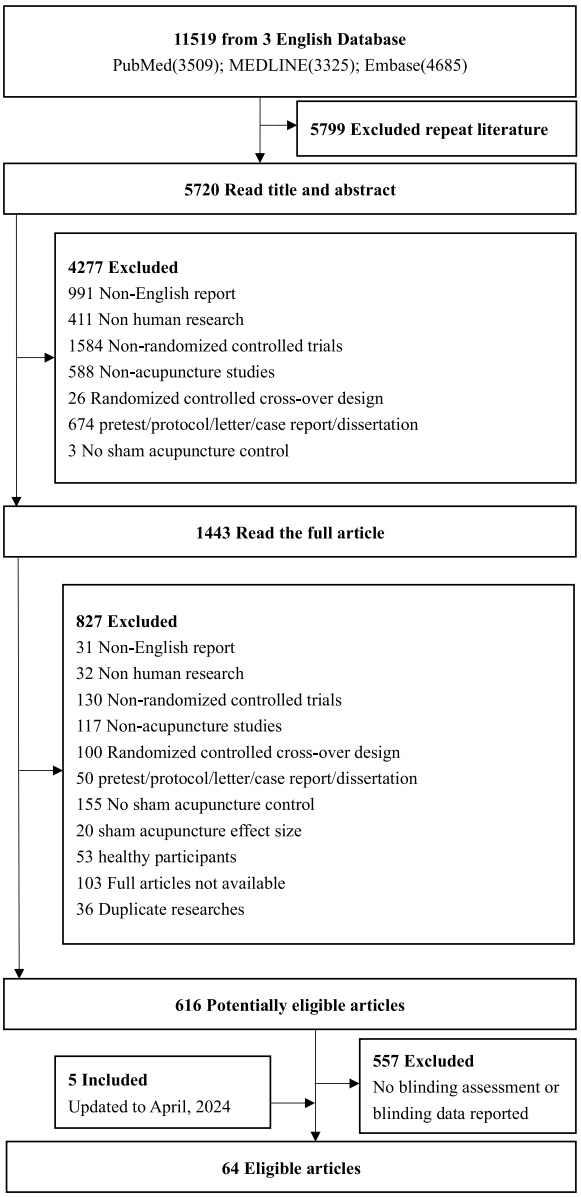

Fig. 1 Study flow diagram

The characteristics of blinding in acupuncture trials

For the verum acupuncture group, 90.60% of trials had a Bang's BI greater than 0, and only 6 trials exhibited a Bang's BI smaller than 0. In contrast, for the sham acupuncture group, 65.60% of trials had a Bang's BI smaller than 0, while 34.40% of trials had a Bang's BI greater than 0. There were four scenarios based on the combination of Bang's BI values between the verum and sham acupuncture groups. Scenario 1, where the BI was greater than 0 in the verum acupuncture group and less than 0 in the sham group, comprised 62.50% of the trials. Scenario 3, with BIs greater than 0 in both the verum and sham acupuncture groups, accounted for 28.15% of the trials. Detailed scenarios of blinding in acupuncture trials are shown in Table 2.

Relationship between Bang's BI and treatment effect sizes

The results of Spearman correlation analysis indicated insufficient evidence to support an association between the success of blinding and treatment effect sizes ($r=0.00$, $p=0.94$). In scenario 1, the results showed that Bang's BI and treatment effect are independent ($r=0.05$, $p=0.77$). Similarly, in scenario 3, the correlation between Bang's BI and treatment effect was also found to be non-significant ($r=-0.43$, $p=0.08$).

Subgroup analysis in sham acupuncture group

Subgroup analysis revealed that area ($p=0.04$, $I^2=75.60\%$), number of study centers ($p=0.03$, $I^2=78.80\%$), treatment sessions ($p=0.00$, $I^2=90.60\%$), acupoints number ($p=0.04$, $I^2=74.90\%$), and evaluation timepoint ($p=0.00$, $I^2=84.00\%$) can influence participants' perceptions of the treatment they received within the sham group (eTable 2).

Risk of *bias* and publication *bias*

The overall risk of bias was categorized as either "of some concern" or "high." According to our results, 13 included studies had an overall low risk of bias, 27 studies had a moderate risk, and 24 studies had a high risk. The Risk of Bias assessment (RoB2) of all the included studies can be found in Supplementary eFig. 3, eFig. 4, and eTable 3. Additionally, neither the funnel plot nor the Egger test ($p=0.15$) showed publication bias (Supplementary eFig. 5).

Discussion

As a non-pharmacological intervention, acupuncture presents challenges in achieving blinding [77]. Assessing the success of blinding in acupuncture clinical trials is crucial. This study represents the first comprehensive evaluation of the status and characteristics of blinding, as well as factors influencing blinding in sham-controlled trials. Our findings revealed that, in the verum acupuncture group, Bang's BI was greater than 0, approaching 1, suggesting that a high proportion of participants in this group correctly identified they received the real treatment. Conversely, in the sham acupuncture group, Bang's BI was smaller than 0, indicating that more participants in this group believed that they received real acupuncture. Regarding associations between Bang's BI and treatment effect sizes, our results revealed insufficient evidence to support a significant association. Factors such as study area, number of research centers, treatment sessions, number of acupoints, and evaluation time

Table 1 Characteristics of trials included for the main analyses

Year, name	Sample size	BI of acupuncture	95%CI		BI of Sham acupuncture	95%CI		Sham treatment	Primary outcome
			Lower	Upper		Lower	Upper		
1999, Liao, L X [14]	39	0.47	0.22	0.73	0.05	−0.17	0.27	Empty plastic needle tube	The pain rescue time
2002, Nabeta, T [15]	34	0.41	0.1	0.75	−0.18	−0.54	0.2	Blunt needle	Visual analog scale (VAS)
2004, Berman, B M [2]	381	0.58	0.5	0.66	−0.49	−0.56	−0.39	Disposable needle	The Western Ontario and McMaster Universities (WOMAC), Osteoarthritis Index
2005, Park, J [16]	116	0.47	0.33	0.61	−0.31	−0.49	−0.13	Blunt needle	Barthel ADL score
2006, Diener, H C [17]	607	0.13	0.05	0.21	0.19	0.11	0.26	Disposable needle	Migraine days
2006, Smith, C [18]	228	0.19	0.1	0.28	0	−0.1	0.1	Streiberger needle	Pregnancy rate
2007, Endres, H C [19]	413	−0.16	−0.27	−0.05	−0.04	−0.16	0.08	Disposable needle	Pain score
2007, Haake, M [20]	774	−0.01	−0.01	0.01	0.11	0.04	0.18	Disposable needle	Von Korff Chronic Pain Grade Scale7
2008, Alecrim-A, J [21]	36	0.26	0.02	0.5	−0.12	−0.35	0.11	Disposable needle	Percentage of patients with ≥ 50% reduction in migraine attack frequency
2008, Deng, G [22]	108	0.08	−0.24	0.4	0.19	−0.13	0.5	Dummy studs	Pain score
2008, Elden, H [23]	115	0.63	0.51	0.75	−0.63	−0.76	−0.51	Streiberger needle	Visual analog scale (VAS)
2008, Goldman, R H [24]	123	0.43	0.24	0.62	−0.63	−0.8	−0.47	Blunt needle	Pain score
2008, Jubb, R W [25]	68	0.17	−0.09	0.43	0.29	0.07	0.5	Blunt needle	The Western Ontario and McMaster Universities (WOMAC), Osteoarthritis Index
2008, Smith, C A [26]	364	−0.03	−0.14	0.09	0.01	−0.01	0.12	Disposable needle	Change in Bishop score
2009, Chae, Y Y [27]	20	0.8	0.49	1.11	−0.6	−0.95	−0.25	Park needle	Behavioral Tests frequency
2010, Modlock, J [28]	125	−0.1	−0.22	0.1	−0.05	−0.19	0.1	Park needle	Participant had undergone delivery or was in active labour
2010, Tong, Y Q [29]	63	0.32	0.27	0.37	−0.65	−0.69	−0.61	Disposable needle	F-wave minimum latency
2010, White, P [30]	147	0.92	0.84	0.99	−0.85	−0.96	−0.75	Streitberger needle	Visual analog scale (VAS)
2011, Kim, D Il [31]	54	0.82	0.63	1.1	−0.47	−0.78	−0.18	Disposable needle	Hot flush scores
2011, Lee, S W H [32]	90	0.22	−0.01	0.47	−0.56	−0.76	−0.35	Disposable needle	Visual analog scale (VAS)
2011, Ma, W Z [33]	233	0.92	0.88	0.96	−0.87	−0.92	−0.82	Pragmatic placebo needles	Visual analog scale (VAS)
2011, Smith, C A [34]	92	0.17	−0.02	0.37	0.15	−0.03	0.33	Blunt needle	Pain score
2012, Chung, K F [35]	20	0	−0.52	0.52	0.11	−0.43	0.66	Streitberger needle	Hospital Anxiety and Depression Scale (HADS)
2012, Enblom, A [36]	215	0.84	0.75	0.93	−0.63	−0.76	−0.5	Park needle	Consumption of type of antiemetics
2013, Cho, Y J [37]	130	0.07	−0.1	0.24	−0.23	−0.39	−0.08	Blunt needle	Visual analog scale (VAS)

Table 1 (continued)

Year, name	Sample size	BI of acupuncture	95%CI		BI of Sham acupuncture	95%CI		Sham treatment	Primary outcome
			Lower	Upper		Lower	Upper		
2013, Choi, S M [38]	188	0.21	0.1	0.32	−0.11	−0.23	0	Disposable needle	Total Nasal Symptom Score (TNSS)
2014, Itoh, K [39]	16	0.5	0	1	−0.5	−1	0	Blunt needle	The pain intensity
2014, Mao, J J [40]	41	0.43	0.17	0.69	0.15	−0.14	0.44	Streitberger needle	Pain score
2015, Chen, X Y [41]	30	0.7	0.44	0.96	−1	0	0	Streitberger needle	Knee Injury and Osteoarthritis Outcome Score (KOOS)
2015, Chung, K F [42]	90	0.1	0.01	0.19	−0.03	−0.16	0.09	Streitberger needle	Insomnia Severity Index score
2015, Gamermann, P W [43]	58	1	0	0	−1	0	0	Disposable needle	Visual analog scale (VAS)
2016, Greenlee, H [44]	63	0.67	0.42	0.92	−0.82	−1.02	−0.62	Park needle	Brief Pain Inventory-Short Form (BPI-SF)
2016, Liu, Z S [45]	1072	0.8	0.68	0.92	−0.78	−0.91	−0.66	Disposable needle	Complete Spontaneous Bowel Movements (CSBMs)
2018, Deng, G [46]	60	0.17	−0.13	0.47	−0.1	−0.38	0.19	Disposable needle	MD Anderson Symptom Inventory (MDASI)
2018, Liu, Z S [47]	360	0.89	0.83	0.94	−0.9	−0.95	−0.84	Blunt needle	Menopause Rating Scale (MRS)
2018, Qin, Z S [48]	68	0.76	0.6	0.93	−0.53	−0.75	−0.31	Pragmatic placebo needles	National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI)
2018, Smith, C A [49]	848	0.18	0.12	0.25	0.06	−0.01	0.13	Park needle	Pregnancy rate
2019, Huang, Z L [50]	46	0.74	0.53	0.95	−0.67	−0.9	−0.44	Blunt needle	Visual analog scale (VAS)
2019, Kargozar, R [51]	72	0.94	0.84	1.03	−1	0	0	Disposable needle	Hot flashes and the change in the quality of life (MENQOL)
2019, Zheng, Z [52]	77	0.3	0.1	0.52	−0.11	−0.4	0.14	Disposable needle	The dosage of opioid medicine (OM)
2020, Kong, J T [53]	121	0.5	0.31	0.68	0.2	−0.07	0.5	Streiberger needle	Pain score
2020, Lee, B [54]	150	0.65	0.5	0.83	−0.26	−0.52	0.01	Park needle	Insomnia Severity Index (ISI) score
2020, Li, S S [55]	84	0.38	0.21	0.55	−0.14	−0.36	0.08	Streiberger needle	Pittsburgh Sleep Quality Index (PSQI)
2020, Lin, Z X [56]	99	0.96	0.87	1.04	−0.59	−0.82	−0.36	Blunt needle	Frequency of urgency urinary incontinence (UUI)
2020, Qin, Z S [57]	80	0.39	0.25	0.54	−0.31	−0.48	−0.14	Disposable needle	The Modified Roland-Morris Disability Questionnaire (RMDQ)
2020, Xu, S B [58]	120	0.74	0.62	0.85	−0.68	−0.81	−0.56	Streiberger needle	Change of migraine days
2020, Yang, J W [59]	278	0.51	0.38	0.64	−0.55	−0.68	−0.42	Disposable needle	Response rate
2020, Zhang, L X [60]	96	0.54	0.37	0.72	−0.44	−0.63	−0.24	Park needle	Pittsburgh Sleep Quality Index (PSQI)
2021, Kim, K W [61]	120	0.19	0.03	0.41	0.25	0.16	0.34	Park needle	High-density lipoprotein (HDL)
2021, Kim, M [62]	30	0.64	0.26	1.02	−0.77	−1.08	−0.46	Park needle	17-items HRDS

Table 1 (continued)

Year, name	Sample size	BI of acupuncture	95%CI		BI of Sham acupuncture	95%CI		Sham treatment	Primary outcome
			Lower	Upper		Lower	Upper		
2021, Li, H [63]	120	0.66	0.5	0.81	−0.36	−0.56	−0.16	Blunt needle	Montreal Cognitive Assessment(MoCA)
2021, Lynning, M [64]	44	0.33	0.03	0.63	0.22	−0.05	0.5	Streiberger needle	Functional Assessment of Multiple Sclerosis (FAMS)
2021, Park, J G [65]	32	0.5	0.14	0.86	0.12	−0.28	0.53	Park needle	SCORing Atopic Dermatitis index score (SCORAD)
2021, Rona, M R [66]	28	1	0	0	0.12	−0.41	0.66	Disposable needle	Visual analog scale (VAS)
2021, Tu, J F [67]	442	0.63	0.57	0.69	−0.45	−0.55	−0.35	Disposable needle	The Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index-Function
2021, Yeung, W F [68]	140	0.34	0.21	0.48	−0.13	−0.27	0.01	Streitberger needle	Hospital Anxiety and Depression Scale (HADS)
2021, Zheng, Y J [69]	130	0.49	0.32	0.67	0.33	0.14	0.53	Disposable needle	Spontaneous Bowel Movements (SBMs)
2022, Fan, J Q [70]	60	−0.13	−0.43	0.16	0.2	−0.1	0.49	Disposable needle	Hamilton Anxiety Rating Scale (HAM-A)
2022, Qi, L Y [71]	90	−0.27	−0.49	−0.06	0.19	−0.03	0.5	Blunt needle	Response rate
2022, Taras, I U [72]	120	0.27	0.11	0.42	0.1	−0.04	0.24	Self-adhesive tape	Pain score
2022, Tu, J F [73]	80	0.15	0.06	0.24	0.08	0	0.14	Disposable needle	Visual analog scale (VAS)
2022, Wang, Y [74]	249	0.33	0.2	0.47	−0.17	−0.32	−0.02	Disposable needle	The time to first defecation
2022, Yin, X [75]	180	0.5	0.4	0.7	−0.4	−0.6	−0.3	Streitberger needle	Pittsburgh Sleep Quality Index (PSQI)
2022, Zeng, D [76]	169	0.53	0.38	0.68	0.02	−0.12	0.16	Disposable needle	Northwick Park Neck Pain Questionnaire (NPQ)

points may influence the success of blinding in acupuncture clinical trials.

The distribution of Bang's BI in both the verum and sham acupuncture group was consistent with the previous studies [78, 79]. This was determined by the characteristics of acupuncture. In acupuncture trials, achieving effective blinding is primarily achieved through simulating needle penetration and other manipulations crucially linked to participant perception. Consequently, participants receiving sham acupuncture often believe they are receiving real acupuncture, known as "wishful thinking" [11]. This is also considered a successful blinding and further supported by the negative Bang's BI of the sham acupuncture group observed in our study.

In contrast, pharmacological trials typically achieve blinding through identical appearances and tastes of active drugs and placebos [80]. This uniformity allows for random assignment guessing, in contrast to acupuncture trials where participants' experiences during needling make random guessing highly improbable. Therefore, blinding scenarios in acupuncture trials differ significantly. There are two primary blinding scenarios in acupuncture: scenario 1, where Bang's BI > 0 for verum acupuncture and < 0 for sham acupuncture (indicating wishful thinking), is generally considered successful blinding in acupuncture trials but suggestive of response bias in pharmacological studies [81]. Another scenario, where both verum and sham acupuncture have BI > 0, suggests potential unblinding risks requiring closer attention. Despite the overall negative BI for sham acupuncture in our study, indicating successful blinding in most cases, some trials still pose unblinding risks. We recommend discussing and reporting detailed findings, particularly when Bang's BI > 0, to provide a comprehensive assessment of blinding effectiveness. Additionally, a cutoff − 0.2 to 0.2 was used and the assignment was

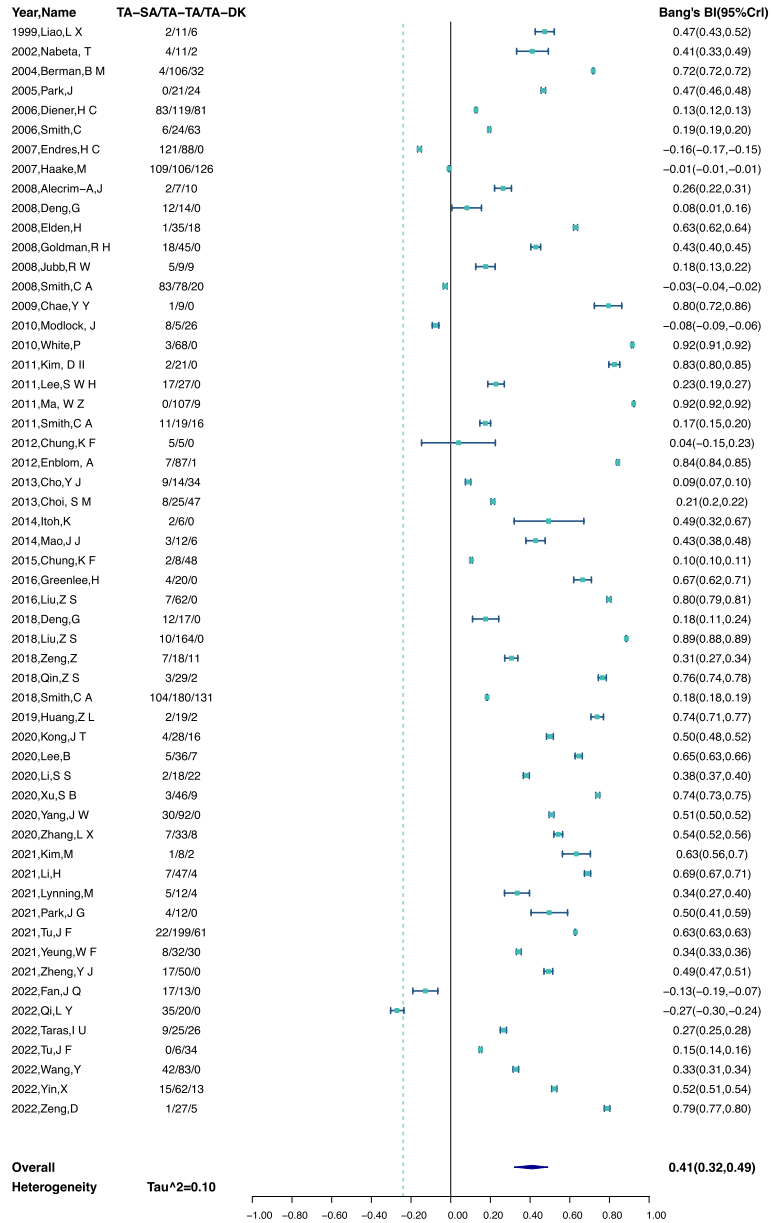

Fig. 2 Effect size forest plot of Bang index in verum group. TA, treatment acupuncture; SA, sham acupuncture; DK, don't know. We used the study which reported the number of participants' guesses to calculate the posterior index of Bang's BI

randomly guessed, which is generally suitable for pharmacological trials. Its application to acupuncture trials is less straightforward due to the inherent difficulty in achieving random guessing [82]. Therefore, we advocate against adopting this cutoff for sham acupuncture trials and instead propose that the blinding of verum and sham acupuncture should be separately assessed. Regarding the cutoff for Bang's BI in sham acupuncture, it should ideally be equal or less than 0, and we recommend judging blinding status using a one-sided 95% CI or a one-sided test. For verum acupuncture, Bang's BI should be greater than 0.

There are some factors that may be associated to the blinding outcomes [83–85]. Our study found study site, study area, treatment sessions, and acupoints number, and the number of evaluations and evaluation time points were related to the blinding of sham acupuncture. Non-Asian populations tend to be more effectively blinded, likely due to differences in cultural backgrounds, acceptance and popularity of acupuncture treatment

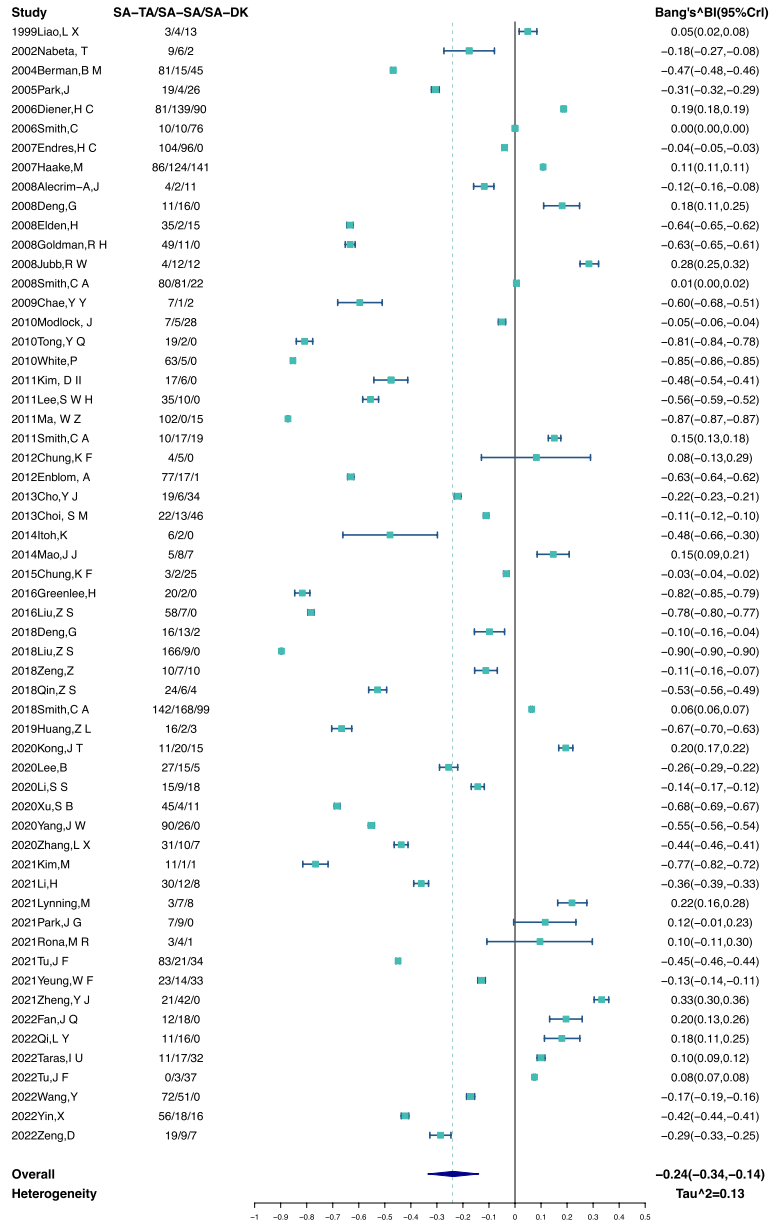

Fig. 3 Effect size forest plot of Bang index in the sham group. TA, treatment acupuncture; SA, sham acupuncture; DK, don't know. We used the study which reported the number of participants' guesses to calculate the posterior index of Bang's BI

Table 2 Number of studies with different blinding scenarios in acupuncture clinical trials

		Verum acupuncture		*N* (%)
		Bang's BI > 0	Bang's BI < 0	
Sham acupuncture	Bang's BI < 0	*Scenario 1* 40 (62.50%)	*Scenario 2* 2 (3.13%)	42 (65.60%)
	Bang's BI > 0	*Scenario 3* 18 (28.13%)	*Scenario 4* 4 (6.25%)	22 (34.40%)
N (%)		58 (90.63%)	6 (9.47%)	64 (100.00%)

should be a main contribution to this difference [70]. If the participants have prior knowledge or experience with these practices, it may be more difficult to maintain blinding because they may be more likely to guess the treatment they are receiving [86]. Another significant factor influencing participant blinding is whether the sham acupuncture actually penetrates the skin. Due to its closer resemblance to the sensation of a real acupuncture, makes it more difficult for patients to guess their true group, thus facilitating random guessing.

Penetrating sham needling generally achieves better blinding, although some researchers caution against its use due to potential physiological effects that could diminish the specific effect of acupuncture [58]. Therefore, a balance between blinding and the effect of sham acupuncture needs to be achieved in acupuncture clinical trial design [87]. In sham acupuncture design, treatment sessions and acupoints number can influence the blinding. More treatment sessions will offer participants greater opportunities to discern the differences between verum acupuncture and sham acupuncture, thereby heightening the risk of unblinding. Additionally, participants may deduce their true group assignment based on their treatment effects, particularly those in the sham acupuncture group. Regarding assessment timing, it is methodologically crucial to select the time point when Bang's BI is most likely to reveal broken blinding. Currently, there are no definitive criteria for determining these time points. Berman and Freed suggest evaluating blinding at multiple time points, but excessive assessments may lead to heightened attention and speculation about group assignments [2, 83]. Based on our findings, we recommend assessing blinding status at the end of treatment. Additionally, the number of treatment sessions and acupuncture points may influence blinding outcomes. Longer treatment durations or more acupuncture points inserted increase the likelihood of participants correctly guessing their group assignment, potentially compromising blinding.

For Bang's BI and treatment effect association, our study did not find a clear link, suggesting the need for further investigation. Participants' perceptions of efficacy often influence their guesses about group assignments, particularly in studies utilizing placebo or sham control [84, 85]. Many studies indicate that sham acupuncture exerts certain physiological effects, even without skin penetration [88]. The effects might weaken the association between efficacy and blinding. Our study provides valuable insights for designing sham acupuncture controls in acupuncture trials.

Additionally, there is few studies assessing and reporting on blinding outcomes in sham-controlled trials. Given the unique nature of acupuncture, adequate reporting of sham acupuncture control details and the blinding assessment is crucial for accurately evaluating the effect of acupuncture [89]. Guidelines for reporting sham acupuncture controls have been published and recommend reporting the details of blinding assessment, including the blinding index [8]. However, these guidelines lack specific guidance on conducting blinding assessments. It is advisable for researchers to establish consensus guidelines on blinding assessments in acupuncture clinical trials to enhance reporting quality, thereby improving our understanding of acupuncture's effects. Key aspects to report include (1) the objects blinded—participants, operators, data collectors, outcome assessors, or statisticians—rather than merely indicating single- or double-blinding; (2) the timing of blinding assessments, such as immediately after the first treatment or post-final treatment, or multiple assessments to monitor blinding status [87]; and (3) transparent and comprehensive reporting of blinding assessment results.

Our study has several strengths. Firstly, this is the first to comprehensively assess the overall blinding status of sham acupuncture in acupuncture randomized control trials, especially the scenarios and influencing factors. Utilizing data from the most comprehensive English-language sham acupuncture-controlled RCTs, our study offers reliable evidence regarding the blinding status in acupuncture RCTs. Secondly, the identified factors influencing the blinding of sham acupuncture provide valuable guidance for designing future sham acupuncture studies. Lastly, we offer recommendations to improve the blinding assessment of sham acupuncture in clinical acupuncture trials.

Our study also has several limitations. Firstly, this study only assessed the Bang index and did not include other relevant indexes, such as the James index, which provides a comprehensive assessment of the overall blinding effectiveness rather than assessing each group separately. Considering to the characteristics of acupuncture clinical trials and the different directions of blinding between the verum and sham acupuncture, the Bang's index was chosen in our study. Secondly, due to limited reporting in the literature, we were unable to evaluate the blinding of other parties besides participants. In acupuncture trials, acupuncturists typically cannot be blinded due to the nature of their role in therapy administration [77]. While a few studies attempted blinding for acupuncturists, this was rarely reported. Thirdly, most included studies were rated as having a "high" or "some concern" bias risk according to the RoB2 assessment, largely due to the inability to blind acupuncturists—a characteristic rather than a methodological flaw of acupuncture as a non-pharmacological therapy [90]. Fourth, our study only included English-language articles. Future research should update these findings with new literature as it becomes available. Finally, the heterogeneity among studies remains high and does not decrease even after conducting a subgroup analysis. These findings suggest that the factors influencing blinding in acupuncture trials may be multifaceted. Furthermore, the blinding index appears to be associated with specific research details,

such as the type of disease and the intervention methods used. Although we performed subgroup analyses based on many factors, detailed information regarding them was unavailable.

Conclusion

The overall blinding status in current acupuncture clinical trials shows successful blinding, with a majority correctly guessing the verum group and the opposite guessing for the sham group. However, in some acupuncture trials, the blinding of sham acupuncture might be compromised. Factors such as the Asian population, penetrating sham needling, and querying participants about their group assignment during the study increase the risk of unblinding and warrant careful consideration in sham acupuncture control design. Furthermore, researchers should closely monitor the blinding status of sham acupuncture and transparently report details of blinding assessments.

Abbreviations

RCTs	Randomized controlled trials
Bang's BI	Bang's Blinding Index
CrI	Credibility interval
SHARE	SHam acupuncture REporting guidelines and a checklist in clinical trials
TIDieR-Placebo	TIDieR-Placebo: A guide and checklist for reporting placebo and sham controls
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses

Supplementary Information

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Supplementary Material 1: eTable 1.PRISMA 2020, 27-item checklist. eTable 2. Subgroup analysis in sham acupuncture group. eTable 3. Risk of bias of all included trials. eFigure 1. Forest plot of priori Bang's BI in verum group. eFigure 2. Forest plot of priori Bang's BI in sham group. eFigure 3. Histogram of Bang's BI for sham group. eFigure 4. Histogram of Bang's BI for verum group. eFigure 5. Risk of bias summary. eFigure 6. Risk of bias. eFigure 7. Funnel plot of sham group.

Authors' contributions

All authors revised the manuscript critically and gave the final approval of the manuscript submitted. Shiyan Yan, Tinglan Liu, Haoran Zhang, and Baoyan Liu formulated and designed the review. Zhiyi Xiong, Chongyang Sun, and Rong Zhuang did the literature search and extracted data. Tinglan Liu, Shuangjing Li, and Shuyang Cheng analyzed and interpreted the results. Rong Zhuang and Lijiao Jiang verified the reproducibility of the results. Tinglan Liu and Shiyan Yan drafted the manuscript.

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Availability of data and materials

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

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Boutron I, Estellat C, Guittet L, et al. Methods of Blinding in Reports of Randomized Controlled Trials Assessing Pharmacologic Treatments: A Systematic Review. Vallance P, ed. *PLoS Med*. 2006;3(10):e425. https://doi.org/10.1371/journal.pmed.0030425
2. Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AMK, Hochberg MC. Effectiveness of Acupuncture as Adjunctive Therapy in Osteoarthritis of the Knee: A Randomized, Controlled Trial. Ann Intern Med. 2004;141(12):901. https://doi.org/10.7326/0003-4819-141-12-200412210-00006.
3. Hróbjartsson A, Emanuelsson F, Skou Thomsen AS, Hilden J, Brorson S. Bias due to lack of patient blinding in clinical trials. A systematic review of trials randomizing patients to blind and nonblind sub-studies. *Int J Epidemiol*. 2014;43(4):1272–1283. https://doi.org/10.1093/ije/dyu115
4. Savović J, Turner RM, Mawdsley D, et al. Association Between Risk-of-Bias Assessments and Results of Randomized Trials in Cochrane Reviews: The ROBES Meta-Epidemiologic Study. Am J Epidemiol. 2018;187(5):1113–22. https://doi.org/10.1093/aje/kwx344.
5. Wood L, Egger M, Gluud LL, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ. 2008;336(7644):601–5. https://doi.org/10.1136/bmj.39465.451748.AD.
6. Lee YS, Kim SY, Kim M, et al. Reporting quality of sham needles used as controls in acupuncture trials: a methodological evaluation. Chin Med. 2022;17(1):64. https://doi.org/10.1186/s13020-022-00608-5.
7. Lee Y, Kim S, Lee H, Chae Y, Lee MS. ACURATE: A guide for reporting sham controls in trials using acupuncture. J Evid-Based Med. 2023;16(1):82–90. https://doi.org/10.1111/jebm.12524.
8. Ma P, Liu X, Liu Z, et al. The SHARE: SHam acupuncture REporting guidelines and a checklist in clinical trials. J Evid-Based Med. Published online October 31, 2023:jebm.12560. https://doi.org/10.1111/jebm.12560
9. Howick J, Webster RK, Rees JL, et al. TIDieR-Placebo: A guide and checklist for reporting placebo and sham controls. PLOS Med. 2020;17(9):e1003294. https://doi.org/10.1371/journal.pmed.1003294.
10. Lavazza C, Galli M, Abenavoli A, Maggiani A. Sham treatment effects in manual therapy trials on back pain patients: A systematic review and pairwise meta-analysis. BMJ Open. 2021;11(5): e045106. https://doi.org/10.1136/bmjopen-2020-045106.
11. Bang H, Ni L, Davis CE. Assessment of blinding in clinical trials. Control Clin Trials. 2004;25(2):143–56. https://doi.org/10.1016/j.cct.2003.10.016.
12. James KE, Bloch DA, Lee KK, Kraemer HC, Fuller RK. An index for assessing blindness in a multi-centre clinical trial: disulfiram for alcohol cessation—a va cooperative study. Stat Med. 1996;15(13):1421–34. https://doi.org/

10.1002/(SICI)1097-0258(19960715)15:13%3c1421::AID-SIM266%3e3.0.CO;2-H.
13. Gelman A, Rubin DB. Inference from iterative simulation using multiple sequences. Stat Sci. 1992;7(4). https://doi.org/10.1214/ss/1177011136
14. Lao L, Bergman S, Hamilton GR, Langenberg P, Berman B. Evaluation of acupuncture for pain control after oral surgery: A placebo-controlled trial. Arch Otolaryngol Neck Surg. 1999;125(5):567. https://doi.org/10.1001/archotol.125.5.567.
15. Nabeta T, Kawakita K. Relief of chronic neck and shoulder pain by manual acupuncture to tender points—a sham-controlled randomized trial. Complement Ther Med. 2002;10(4):217–22. https://doi.org/10.1016/S0965-2299(02)00082-1.
16. Park J, White AR, James MA, et al. Acupuncture for subacute stroke rehabilitation: A sham-controlled, subject- and assessor-blind, randomized trial. Arch Intern Med. 2005;165(17):2026. https://doi.org/10.1001/archinte.165.17.2026.
17. Diener HC, Kronfeld K, Boewing G, et al. Efficacy of acupuncture for the prophylaxis of migraine: A multicentre randomised controlled clinical trial. Lancet Neurol. 2006;5(4):310–6. https://doi.org/10.1016/S1474-4422(06)70382-9.
18. Smith C, Coyle M, Norman RJ. Influence of acupuncture stimulation on pregnancy rates for women undergoing embryo transfer. Fertil Steril. 2006;85(5):1352–8. https://doi.org/10.1016/j.fertnstert.2005.12.015.
19. Endres HG, Böwing G, Diener HC, et al. Acupuncture for tension-type headache: A multicentre, sham-controlled, patient-and observer-blinded, randomised trial. J Headache Pain. 2007;8(5):306–14. https://doi.org/10.1007/s10194-007-0416-5.
20. Haake M. German acupuncture trials (gerac) for chronic low back Pain-Randomized, multicenter, blinded, parallel-group trial with 3 groups. Arch Intern Med. 2007;167(17):1892. https://doi.org/10.1001/Archinte.167.17.1892.
21. Alecrim-Andrade J, Maciel-Júnior JA, Carnè X, Severino Vasconcelos GM, Correa-Filho HR. Acupuncture in migraine prevention: A randomized sham controlled study with 6-months posttreatment follow-up. Clin J Pain. 2008;24(2):98–105. https://doi.org/10.1097/AJP.0b013e3181590d66.
22. Deng G, Rusch V, Vickers A, et al. Randomized controlled trial of a special acupuncture technique for pain after thoracotomy. J Thorac Cardiovasc Surg. 2008;136(6):1464–9. https://doi.org/10.1016/j.jtcvs.2008.07.053.
23. Elden H, Fagevik-Olsen M, Ostgaard H, Stener-Victorin E, Hagberg H. Acupuncture as an adjunct to standard treatment for pelvic girdle pain in pregnant women: Randomised double-blinded controlled trial comparing acupuncture with non-penetrating sham acupuncture. BJOG Int J Obstet Gynaecol. 2008;115(13):1655–68. https://doi.org/10.1111/j.1471-0528.2008.01904.x.
24. Goldman RH, Stason WB, Park SK, et al. Acupuncture for treatment of persistent arm pain due to repetitive use: A randomized controlled clinical trial. Clin J Pain. 2008;24(3):211–8. https://doi.org/10.1097/AJP.0b013e31815ec20f.
25. Jubb RW, Tukmachi ES, Jones PW, Dempsey E, Waterhouse L, Brailsford S. A blinded randomised trial of acupuncture (manual and electroacupuncture) compared with a non-penetrating sham for the symptoms of osteoarthritis of the knee. Acupunct Med. 2008;26(2):69–78. https://doi.org/10.1136/aim.26.2.69.
26. Smith CA, Crowther CA, Collins CT, Coyle ME. Acupuncture to induce labor: A randomized controlled trial. Obstet Gynecol. 2008;112(5):1067–74. https://doi.org/10.1097/AOG.0b013e31818b46bb.
27. Chae Y, Lee H, Kim H, et al. Parsing brain activity associated with acupuncture treatment in parkinson's diseases. Mov Disord. 2009;24(12):1794–802. https://doi.org/10.1002/mds.22673.
28. Modlock J, Nielsen B, Uldbjerg N. Acupuncture for the induction of labour: A double-blind randomised controlled study. BJOG Int J Obstet Gynaecol. 2010;117(10):1255–61. https://doi.org/10.1111/j.1471-0528.2010.02647.x.
29. Tong Y, Guo H, Han B. Fifteen-day acupuncture treatment relieves diabetic peripheral neuropathy. J Acupunct Meridian Stud. 2010;3(2):95–103. https://doi.org/10.1016/S2005-2901(10)60018-0.
30. White P, Prescott P, Lewith G. Does needling sensation (*de qi*) affect treatment outcome in pain? analysis of data from a larger single-blind, randomised controlled trial. Acupunct Med. 2010;28(3):120–5. https://doi.org/10.1136/aim.2009.001768.
31. Kim DI, Jeong JC, Kim KH, et al. Acupuncture for hot flushes in perimenopausal and postmenopausal women: A randomised, sham-controlled trial. Acupunct Med. 2011;29(4):249–56. https://doi.org/10.1136/aim.2011.004085.
32. Lee SWH, Liong ML, Yuen KH, Leong WS, Khan NK, Krieger JN. Validation of a sham acupuncture procedure in a randomised, controlled clinical trial of chronic pelvic pain treatment. Acupunct Med. 2011;29(1):40–6. https://doi.org/10.1136/aim.2010.003137.
33. Ma W, Bai W, Lin C, et al. Effects of sanyinjiao (SP6) with electroacupuncture on labour pain in women during labour. Complement Ther Med. 2011;19:S13–8. https://doi.org/10.1016/j.ctim.2010.09.001.
34. Smith CA, Crowther CA, Petrucco O, Beilby J, Dent H. Acupuncture to treat primary dysmenorrhea in women: A randomized controlled trial. Evid Based Complement Alternat Med. 2011;2011:1–11. https://doi.org/10.1093/ecam/nep239.
35. Chung KF, Yeung WF, Zhang ZJ, et al. Randomized non-invasive sham-controlled pilot trial of electroacupuncture for postpartum depression. J Affect Disord. 2012;142(1–3):115–21. https://doi.org/10.1016/j.jad.2012.04.008.
36. Enblom A, Johnsson A, Hammar M, Onelöv E, Steineck G, Börjeson S. Acupuncture compared with placebo acupuncture in radiotherapy-induced nausea—a randomized controlled study. Ann Oncol. 2012;23(5):1353–61. https://doi.org/10.1093/annonc/mdr402.
37. Cho YJ, Song YK, Cha YY, et al. Acupuncture for chronic low back pain: A multicenter, randomized, patient-assessor blind, sham-controlled clinical trial. Spine. 2013;38(7):549–57. https://doi.org/10.1097/BRS.0b013e318275e601.
38. Choi SM, Park J-E, Li S-S, et al. A multicenter, randomized, controlled trial testing the effects of acupuncture on allergic rhinitis. Allergy. 2013;68(3):365–74. https://doi.org/10.1111/all.12053.
39. Itoh K, Saito S, Sahara S, Naitoh Y, Imai K, Kitakoji H. Randomized trial of trigger point acupuncture treatment for chronic shoulder pain: A preliminary study. J Acupunct Meridian Stud. 2014;7(2):59–64. https://doi.org/10.1016/j.jams.2013.02.002.
40. Mao JJ, Xie SX, Farrar JT, et al. A randomised trial of electro-acupuncture for arthralgia related to aromatase inhibitor use. Eur J Cancer. 2014;50(2):267–76. https://doi.org/10.1016/j.ejca.2013.09.022.
41. Chen X, Spaeth RB, Freeman SG, et al. The modulation effect of longitudinal acupuncture on resting state functional connectivity in knee osteoarthritis patients. Mol Pain. 2015;11:s12990–015–0071. https://doi.org/10.1186/s12990-015-0071-9
42. Chung KF, Yeung WF, Yu YM, et al. Acupuncture for residual insomnia associated with major depressive disorder: A placebo- and sham-controlled, subject- and assessor-blind, randomized trial. J Clin Psychiatry. 2015;76(06):e752–60. https://doi.org/10.4088/JCP.14m09124.
43. Gamermann PW, Martins ALC, Rosa L, et al. Acupuncture as a complement to the pharmacological management of pain, nausea and vomiting after cesarean section: A randomized clinical trial. Acupunct Relat Ther. 2015;3(1):11–4. https://doi.org/10.1016/j.arthe.2014.12.002.
44. Greenlee H, Crew KD, Capodice J, et al. Randomized sham-controlled pilot trial of weekly electro-acupuncture for the prevention of taxane-induced peripheral neuropathy in women with early stage breast cancer. Breast Cancer Res Treat. 2016;156(3):453–64. https://doi.org/10.1007/s10549-016-3759-2.
45. Liu Z, Yan S, Wu J, et al. Acupuncture for chronic severe functional constipation: A randomized, controlled trial. *Ann Intern Med*. Published online September 13, 2016. https://doi.org/10.7326/M15-3118
46. Deng G, Giralt S, Chung DJ, et al. Acupuncture for reduction of symptom burden in multiple myeloma patients undergoing autologous hematopoietic stem cell transplantation: A randomized sham-controlled trial. Support Care Cancer. 2018;26(2):657–65. https://doi.org/10.1007/s00520-017-3881-7.
47. Liu Z, Ai Y, Wang W, et al. Acupuncture for symptoms in menopause transition: A randomized controlled trial. Am J Obstet Gynecol. 2018;219(4):373.e1–373.e10. https://doi.org/10.1016/j.ajog.2018.08.019.
48. Qin Z, Zang Z, Zhou K, et al. Acupuncture for chronic prostatitis/chronic pelvic pain syndrome: A randomized, sham acupuncture controlled trial. J Urol. 2018;200(4):815–22. https://doi.org/10.1016/j.juro.2018.05.001.
49. Smith CA, De Lacey S, Chapman M, et al. Effect of acupuncture vs sham acupuncture on live births among women undergoing

in vitro fertilization: A randomized clinical trial. Obstet Gynecol Surv. 2018;73(8):466–7. https://doi.org/10.1097/01.ogx.0000544552.75306.7c.
50. Huang Z, Liu S, Zhou J, Yao Q, Liu Z. Efficacy and safety of acupuncture for chronic discogenic sciatica, a randomized controlled sham acupuncture trial. Pain Med. 2019;20(11):2303–10. https://doi.org/10.1093/pm/pnz167.
51. Kargozar R, Salari R, Jarahi L, et al. Urtica dioica in comparison with placebo and acupuncture: A new possibility for menopausal hot flashes: a randomized clinical trial. Complement Ther Med. 2019;44:166–73. https://doi.org/10.1016/j.ctim.2019.04.003.
52. Zheng Z, Gibson S, Helme RD, et al. Effects of electroacupuncture on opioid consumption in patients with chronic musculoskeletal pain: A multicenter randomized controlled trial. Pain Med. 2019;20(2):397–410. https://doi.org/10.1093/pm/pny113.
53. Kong JT, Puetz C, Tian L, et al. Effect of electroacupuncture vs sham treatment on change in pain severity among adults with chronic low back pain: A randomized clinical trial. JAMA Netw Open. 2020;3(10): e2022787. https://doi.org/10.1001/jamanetworkopen.2020.22787.
54. Lee B, Kim BK, Kim HJ, et al. Efficacy and safety of electroacupuncture for insomnia disorder: A multicenter, randomized, assessor-blinded, controlled trial. Nat Sci Sleep. 2020;12:1145–59. https://doi.org/10.2147/NSS.S281231.
55. Li S, Wang Z, Wu H, et al. Electroacupuncture versus sham acupuncture for perimenopausal insomnia: A randomized controlled clinical trial. Nat Sci Sleep. 2020;12:1201–13. https://doi.org/10.2147/NSS.S282315.
56. Lin Z xiu, Chan NHT, Kwan Y keung, et al. A randomized controlled trial to assess the effectiveness and safety of acupuncture for overactive bladder: A study in hong kong population. Chin Med. 2020;15(1):108. https://doi.org/10.1186/s13020-020-00388-w
57. Qin Z, Ding Y, Xu C, et al. Acupuncture vs noninsertive sham acupuncture in aging patients with degenerative lumbar spinal stenosis: A randomized controlled trial. Am J Med. 2020;133(4):500–507.e20. https://doi.org/10.1016/j.amjmed.2019.08.038.
58. Xu S, Yu L, Luo X, et al. Manual acupuncture versus sham acupuncture and usual care for prophylaxis of episodic migraine without aura: Multicentre, randomised clinical trial. BMJ. Published online March 25, 2020:m697. https://doi.org/10.1136/bmj.m697
59. Yang JW, Wang LQ, Zou X, et al. Effect of acupuncture for postprandial distress syndrome: A randomized clinical trial. Ann Intern Med. 2020;172(12):777–85. https://doi.org/10.7326/M19-2880.
60. Zhang L, Tang Y, Hui R, et al. The effects of active acupuncture and placebo acupuncture on insomnia patients: A randomized controlled trial. Psychol Health Med. 2020;25(10):1201–15. https://doi.org/10.1080/13548506.2020.1738015.
61. Kim KW, Shin WC, Choi MS, et al. Effects of acupuncture on anthropometric and serum metabolic parameters in premenopausal overweight and obese women: A randomized, patient- and assessor-blind, sham-controlled clinical trial. Acupunct Med. 2021;39(1):30–40. https://doi.org/10.1177/0964528420912259.
62. Kim M, Choi EJ, Kwon OJ, et al. Electroacupuncture plus moxibustion for major depressive disorder: A randomized, sham-controlled, pilot clinical trial. Integr Med Res. 2021;10(3): 100727. https://doi.org/10.1016/j.imr.2021.100727.
63. Huang L, Yin X, Li W, et al. Effects of Acupuncture on Vascular Cognitive Impairment with No Dementia: A Randomized Controlled Trial. Khalsa D, ed. J Alzheimers Dis. 2021;81(4):1391–1401. https://doi.org/10.3233/JAD-201353
64. Lynning M, Hanehøj K, Westergaard K, et al. Effect of acupuncture on cytokine levels in persons with multiple sclerosis: A randomized controlled trial. J Altern Complement Med. 2021;27(10):832–40. https://doi.org/10.1089/acm.2020.0510.
65. Park JG, Lee H, Yeom M, Chae Y, Park HJ, Kim K. Effect of acupuncture treatment in patients with mild to moderate atopic dermatitis: A randomized, participant- and assessor-blind sham-controlled trial. BMC Complement Med Ther. 2021;21(1):132. https://doi.org/10.1186/s12906-021-03306-1.
66. Abad-Constantino RMR, Caro-Chang LM, Gatmaitan-Dumlao JKG, Abalos-Babaran S, Tan-Gatue PN, Dofitas BL. Acupuncture as an adjunct to standard therapy for pruritus in patients with atopic dermatitis: A patient- and assessor-blinded, randomized, placebo-controlled trial. Acta Med Philipp. 2021;55(5). https://doi.org/10.47895/amp.v55i5.3226
67. Tu J, Yang J, Shi G, et al. Efficacy of intensive acupuncture versus sham acupuncture in knee osteoarthritis: A randomized controlled trial. Arthritis Rheumatol. 2021;73(3):448–58. https://doi.org/10.1002/art.41584.
68. Yeung WF, Yu BYM, Yuen JWM, et al. Semi-individualized acupuncture for insomnia disorder and oxidative stress: A randomized, double-blind, sham-controlled trial. Nat Sci Sleep. 2021;13:1195–207. https://doi.org/10.2147/NSS.S318874.
69. Zheng Y, Jiang X, Gao Y, et al. Microbial profiles of patients with antipsychotic-related constipation treated with electroacupuncture. Front Med. 2021;8: 737713. https://doi.org/10.3389/fmed.2021.737713.
70. Fan J qi, Lu W jing, Tan W qiang, et al. Effectiveness of Acupuncture for Anxiety Among Patients With Parkinson Disease: A Randomized Clinical Trial. JAMA Netw Open. 2022;5(9):e2232133. https://doi.org/10.1001/jamanetworkopen.2022.32133
71. Qi LY, Yang JW, Yan SY, et al. Acupuncture for the treatment of diarrhea-predominant irritable bowel syndrome: A pilot randomized clinical trial. JAMA Netw Open. 2022;5(12): e2248817. https://doi.org/10.1001/jamanetworkopen.2022.48817.
72. Usichenko TI, Henkel BJ, Klausenitz C, et al. Effectiveness of acupuncture for pain control after cesarean delivery: A randomized clinical trial. JAMA Netw Open. 2022;5(2): e220517. https://doi.org/10.1001/jamanetworkopen.2022.0517.
73. Tu JF, Cao Y, Wang LQ, et al. Effect of adjunctive acupuncture on pain relief among emergency department patients with acute renal colic due to urolithiasis: A randomized clinical trial. JAMA Netw Open. 2022;5(8): e2225735. https://doi.org/10.1001/jamanetworkopen.2022.25735.
74. Wang Y, Yang JW, Yan SY, et al. Electroacupuncture vs sham electroacupuncture in the treatment of postoperative ileus after laparoscopic surgery for colorectal cancer: A multicenter, randomized clinical trial. JAMA Surg. 2023;158(1):20. https://doi.org/10.1001/jamasurg.2022.5674.
75. Yin X, Li W, Liang T, et al. Effect of electroacupuncture on insomnia in patients with depression: A randomized clinical trial. JAMA Netw Open. 2022;5(7): e2220563. https://doi.org/10.1001/jamanetworkopen.2022.20563.
76. Zeng D, Yan X, Deng H, et al. Placebo response varies between different types of sham acupuncture: A randomized double-blind trial in neck pain patients. Eur J Pain. 2022;26(5):1006–20. https://doi.org/10.1002/ejp.1924.
77. Boutron I, Tubach F, Giraudeau B, Ravaud P. Blinding was judged more difficult to achieve and maintain in nonpharmacologic than pharmacologic trials. J Clin Epidemiol. 2004;57(6):543–50. https://doi.org/10.1016/j.jclinepi.2003.12.010.
78. Lin YH, Sahker E, Shinohara K, et al. Assessment of blinding in randomized controlled trials of antidepressants for depressive disorders 2000–2020: A systematic review and meta-analysis. eClinicalMedicine. 2022;50:101505. https://doi.org/10.1016/j.eclinm.2022.101505
79. Mavrommatis CI, Argyra E, Vadalouka A, Vasilakos DG. Acupuncture as an adjunctive therapy to pharmacological treatment in patients with chronic pain due to osteoarthritis of the knee: A 3-armed, randomized, placebo-controlled trial. Pain. 2012;153(8):1720–6. https://doi.org/10.1016/j.pain.2012.05.005.
80. Naudet F, Millet B, Reymann JM, Falissard B. Improving study design for antidepressant effectiveness assessment: Improving Antidepressant Effectiveness Assessment. Int J Methods Psychiatr Res. Published online August 2013:n/a-n/a. https://doi.org/10.1002/mpr.1391
81. Bang H, Flaherty SP, Kolahi J, Park J. Blinding assessment in clinical trials: A review of statistical methods and a proposal of blinding assessment protocol. Clin Res Regul Aff. 2010;27(2):42–51. https://doi.org/10.3109/10601331003777444.
82. Braithwaite FA, Walters JL, Li LSK, Moseley GL, Williams MT, McEvoy MP. Blinding Strategies in Dry Needling Trials: Systematic Review and Meta-Analysis. Phys Ther. 2019;99(11):1461–80. https://doi.org/10.1093/ptj/pzz111.
83. Moroz A, Freed B, Tiedemann L, Bang H, Howell M, Park JJ. Blinding Measured: A Systematic Review of Randomized Controlled Trials of Acupuncture. Evid Based Complement Alternat Med. 2013;2013:1–12. https://doi.org/10.1155/2013/708251.
84. Freed B, Williams B, Situ X, et al. Blinding, sham, and treatment effects in randomized controlled trials for back pain in 2000–2019: A review and meta-analytic approach. Clin Trials. 2021;18(3):361–70. https://doi.org/10.1177/1740774520984870.

85. Vase L, Baram S, Takakura N, et al. Specifying the nonspecific components of acupuncture analgesia. Pain. 2013;154(9):1659–67. https://doi.org/10.1016/j.pain.2013.05.008.
86. White P, Bishop FL, Prescott P, Scott C, Little P, Lewith G. Practice, practitioner, or placebo? A multifactorial, mixed-methods randomized controlled trial of acupuncture. Pain. 2012;153(2):455–62. https://doi.org/10.1016/j.pain.2011.11.007.
87. Moustgaard H, Clayton GL, Jones HE, et al. Impact of blinding on estimated treatment effects in randomised clinical trials: meta-epidemiological study. BMJ. 2020;368: l6802. https://doi.org/10.1136/bmj.l6802.
88. Lee B, Kwon CY, Lee HW, et al. Needling point location used in sham acupuncture for chronic nonspecific low back pain: A systematic review and network meta-analysis. JAMA Netw Open. 2023;6(9): e2332452. https://doi.org/10.1001/jamanetworkopen.2023.32452.
89. Webster RK, Bishop F, Collins GS, et al. Measuring the success of blinding in placebo-controlled trials: Should we be so quick to dismiss it? J Clin Epidemiol. 2021;135:176–81. https://doi.org/10.1016/j.jclinepi.2021.02.022.
90. Long Y, Luo S, Chen R, et al. Agreement of risk-of -bias varied in systematic reviews on acupuncture and was associated with methodological quality. J Clin Epidemiol. 2021;129:12–20. https://doi.org/10.1016/j.jclinepi.2020.08.017.

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