# Does the outcome of acupuncture differ according to the location of sham needling point in acupuncture trials of migraine: a systematic review and network meta-analysis

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**Abstract**

**Background**: In acupuncture clinical trials, sham acupuncture was sometimes performed on the same acupuncture points as the verum acupuncture group to evaluate the efficacy of acupuncture, despite the evidence of acupuncture points specificity. We aimed to assess whether the outcome of acupuncture was different according to needling point of sham acupuncture for migraine for which acupuncture has been actively used in clinical settings and research.

**Methods**: Four databases were searched for sham acupuncture or waiting list-controlled acupuncture clinical trials for migraine on December 25, 2023. Sham acupuncture was classified according to needling point: needling at the same acupuncture point with verum acupuncture group (SATV) or at non-indicated sham point (SATS). Network meta-analysis was performed based on the frequentist framework for headache pain intensity and response rate (at least 50% reduction of migraine frequency).

**Results**: Eighteen studies involving 1936 participants were analyzed. Compared with SATS, headache pain intensity significantly improved and the response rate was significantly higher in verum acupuncture group. However, there was no significant difference between SATV and verum acupuncture. When comparing SATS and SATV, there was no significant difference in headache pain intensity and response rate, however the results were in favor of SATV. The impact of the risk of bias on the comparison between verum and sham acupunctures was judged to be generally low.

**Conclusion:** In the acupuncture clinical trial for migraine, the outcome of verum and sham acupunctures was different depending on the needling point of sham acupuncture. Sham acupuncture method should be established according to the research hypothesis, and SATV should not be misused as a placebo control to evaluate the efficacy of acupuncture.

**Keywords:** Acupuncture therapy, migraine, migraine disorders, sham acupuncture, placebo

## 1. Introduction

Clinical trials evaluating the efficacy of acupuncture have used sham acupuncture as a control group. However, because the factors inducing the effects of acupuncture are diverse and complex, controversy has continued to arise as to whether a physiologically inert placebo that can control all of these is possible (1, 2). The types of sham acupuncture that have been used can be largely divided into using a non-penetrating sham acupuncture device (3, 4) and superficial needling depending on whether it penetrates the skin (5, 6). In addition, depending on the needling point of sham acupuncture, it can be divided into using acupuncture points and non-acupuncture points (5, 6). The technical procedures of sham acupuncture, such as skin penetration or needling point, should be established and interpreted according to the research hypothesis, however it has often been misused and interpreted as a placebo control to evaluate the efficacy of acupuncture. Furthermore, although evidence for the specificity of acupuncture points has been suggested (7-9), sham acupuncture has been sometimes performed on the same acupuncture points as the verum acupuncture group to evaluate the efficacy of acupuncture (5, 6). These might have led to inconsistent conclusions about the effectiveness of acupuncture in clinical practice guidelines (10-12).

In our previous network meta-analysis (NMA), we confirmed that acupuncture clinical trials targeting chronic nonspecific low back pain (13), cancer-related pain (14), and knee osteoarthritis (15) showed different results depending on whether the needling point used in sham acupuncture was the same in the verum acupuncture group. Even in NMA for chronic nonspecific low back pain, sham acupuncture needling at the same acupuncture point as verum acupuncture significantly increased pain intensity and function compared to needling at the non-indicated sham point. Based on these results, we hypothesized that similar results could be obtained in sham acupuncture controlled acupuncture clinical trials for other conditions.

Migraine is one of the neurological diseases with a high prevalence worldwide and a large socioeconomic burden (16, 17). Several medications are used for acute relief and prevention of migraine, however due to the risk of overuse of acute medications and adverse effects such as gastrointestinal or cardiovascular symptoms (18, 19), acupuncture, one of the non-pharmacological interventions, has been recommended due to its safety and low risk of side effects (18, 20). Many clinical trials have been conducted to date to evaluate the effect of acupuncture on migraine, however the conclusions are still controversial especially when compared to sham acupuncture (20-22). Therefore, the purpose of this review was to assess whether the outcome of acupuncture was different according to whether it was conducted at the same acupuncture point with verum acupuncture group or at non-indicated sham point, using sham-controlled trials of acupuncture for migraine in which acupuncture has been actively used in clinical settings and a significant number of acupuncture studies have been conducted.

## 2. Methods

The protocol of this systematic review was registered in PROSPERO (CRD0000).

## 2.1. Eligibility criteria

(1) Population: Trials involving adults diagnosed with migraine without restrictions on age, sex, race, or nationality were included.

(2) Intervention and comparator: Verum acupuncture, sham acupuncture, and waiting list (blank control) were included. Verum acupuncture included only manual acupuncture that penetrates the skin without additional stimulation such as electrical stimulation. Sham acupuncture was classified into two groups according to the needling point: either sham acupuncture needling at the same point as verum acupuncture (SATV) or needling at non-indicated sham point (SATS). Studies that could not be classified as SATV or SATS due to ambiguous information on the needling point of sham acupuncture were excluded. The waiting list (blank control) group was included for the connected loop on the network map, and only the use of rescue medication was allowed.

(3) Outcome measure: The primary outcome was headache pain intensity measured by Visual Analog Scale (VAS), Numerical Rating Scale (NRS), or other validated outcome measures. If multiple pain scales were used, priorities were determined by comparing baseline scores between groups through agreement between the authors. Secondary outcomes included response rate (responder: at least 50% reduction of migraine frequency) and the frequency of migraine attacks.

As a unit of analysis, the earliest results after full-treatment sessions were used. If there was no presented value after treatment, the value assessed at the time closest to the end of treatment was used. Additionally, data from eligible studies were not presented in a format suitable for meta-analysis, and if these could not be obtained even after contacting the corresponding authors, they were excluded.

(4) Study design: Randomized controlled clinical trials (RCTs) were eligible.

(5) Others: There were no restriction imposed on publication year and language. In addition, not only articles published in journals but also gray literature such as conference proceedings were included.

## 2.2. Information sources and search strategy

We searched MEDLINE via Pubmed, Embase via Elsevier, Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane library, and Allied and Complementary Medicine Database (AMED) via ovid to find eligible studies on December 25, 2023. The reference lists of eligible studies and relevant review articles, and International Clinical Trials Registry Platform were hand-searched to find additional studies. The search terms were determined through consensus by systematic review experts, and the detailed search terms and results for all databases are described in **Supplement 1**.

## 2.3. Study selection and data extraction

Bibliographic information of studies obtained through database searches and other sources was imported into Endnote 20 (Clarivate Analytics, Philadelphia, PA, USA), and after removing duplicates, titles and abstracts were reviewed, and full-texts were reviewed for eligible studies to confirm the final included studies.

The following data were extracted from the included studies using a standardized and pilot-tested Excel form: basic study characteristics (publication year, country, and sample size), details of populations, interventions, and comparators, the outcomes of interest, and the results. If the relevant information was ambiguous or the result data was not presented in a format suitable for meta-analysis, the corresponding author was contacted by email to request additional information. Two researchers (BL and CYK) conducted study selection and data extraction independently, and any disagreement was resolved by discussion between them.

### 2.4. Risk of bias assessment

The risk of bias for the included studies was assessed using Cochrane risk of bias tool (23). The following items were evaluated in individual studies with low, unclear, and high risk of bias: random sequence generation, allocation concealment, blinding of participants, acupuncturists, and outcome assessors, completeness of outcome data, selective reporting, and other bias. The other bias item was evaluated, especially based on the statistical and clinical similarity of the baseline data between the groups. One researcher (BL) evaluated the risk of bias, and another researcher (CYK) reviewed the results independently. Any disagreement was resolved through discussion between them.

### 2.5. Data analysis and synthesis

NMA based on the frequentist framework was carried out for our outcomes of interest using network packages in Stata/MP 16.1 (StataCorp LLC, College Station, TX, USA). NMA was performed only if statistical consistency assumption was satisfied, and it was tested through the node-splitting method (local approach) and design-by-treatment interaction model (global approach). Pairwise meta-analysis on direct evidence was performed using Review Manager 5.4.1 (Cochrane, London, UK) to confirm consistency in statistical significance with NMA results. Since the headache pain intensity and the frequency of migraine attacks, which are continuous variables, were evaluated using different questionnaires and units in individual studies, they were pooled using standardized mean differences (SMDs) and 95% confidence intervals (CIs). The response rate, a dichotomous variable, was pooled using risk ratio (RR) and 95% CI. A random-effects model was selected in both NMA and pairwise meta-analysis considering unavoidable clinical heterogeneity between the included studies. The number of participants and direct trials included in the NMA were shown through the network map, and the results of the NMA and pairwise meta-analysis were shown in the interval plot and league table.

If sufficient studies ($n \geq 10$) were included in the analysis, potential publication bias was assessed using a funnel plot and Egger's test for asymmetry. In addition, to identify the best treatment, the surface under the cumulative ranking curve (SUCRA) statistic was examined. The certainty of evidence for effect estimates was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (24).

## 3. Results

### 3.1. Study selection and characteristics

A total of 3542 studies were searched in the database, and no studies were added from other sources. After using Endnote's duplicate removal function, the titles and abstracts of the remaining 2406 studies were reviewed. Since then, full-texts of retrieved 71 studies were reviewed, and 53 studies were excluded for the following reasons: not RCTs (n = 16), not about only manual acupuncture (n = 6), not sham acupuncture or waiting list-controlled trials (n = 11), not reporting outcomes of interest appropriately (n = 17), only abstract available (n = 1), and using duplicated data (n = 2) (**Supplement 2**). Finally, 18 studies involving 1936 participants were included in the analysis (25-42) (**Figure 1**).

The countries where the research were conducted were China (32, 33, 37, 38, 40, 42), Germany (27, 28, 34, 36), Iran (29-31), Austrailia (39), Canada (41), Sweden (35), Brazil (25), and Italy (26), and two studies targeted menstrual migraine patients (35, 41), and only female patients were included in three studies (26, 35, 41). Four studies (32-34, 40) compared verum acupuncture, sham acupuncture, and waiting list, and the remaining studies compared verum acupuncture and sham acupuncture. The needling point of sham acupuncture group was SATV in one study (35), and all of the rest of the studies were SATS. The primary outcome, headache pain intensity, was evaluated in 13 studies (26, 28, 29, 31-35, 37-39, 41, 42), response rate was evaluated in 8 studies (25, 27, 28, 34, 35, 39-41), and the frequency of migraine attacks was evaluated in 12 studies (27, 30-37, 39, 41, 42) (**Table 1** and **Supplement 3**). In one study (39), the 6-point Likert scale and VAS were used to evaluate headache pain intensity, and after discussion by the researchers, the 6-point Likert scale, which had a smaller difference in baseline scores between groups, was adopted as the target of analysis.

Four-node network maps were constructed (**Figure 2**). In the global approach for statistical consistency testing, the p-values for headache pain intensity, response rate, and frequency of migraine attacks were 0.4348, 0.9749, and 0.0154, respectively. In addition, only headache pain intensity and response rate satisfied the statistical consistency test according to the local approach (**Supplement 4**). Therefore, NMA was performed only on headache pain intensity and response rate. The contribution matrix of the direct comparison to the NMA estimate is presented in **Supplement 5**.

### 3.2. Risk of bias assessment

Thirteen studies (25-29, 32, 34, 35, 37-40, 42) appropriately generated random sequences using methods such as statistical software, and 8 studies (25, 28, 34, 37-40, 42) concealed allocation appropriately by using opaque sealed envelopes or central telephone or fax procedures. However, 3 studies (33, 36, 41) and 8 studies (26, 27, 29, 32, 33, 35, 36, 41) were evaluated as unclear risk of bias because they did not report information about the random sequence generation and allocation concealment, respectively. In addition, two studies (30, 31) in which dropped-

out patients were withdrawn and replaced with new recruits were judged to have a high risk of bias in random sequence generation and allocation concealment. In the four studies including waiting list control (32-34, 40), blinding of participants was not possible, and blinding of outcome assessors was also not possible because the outcome evaluation was based on patient-reported scales. However, the remaining studies comparing only acupuncture and sham acupuncture were judged to have appropriately blinded participants and outcome assessors. In addition, although blinding of acupuncturists was not possible in all studies, it was judged that this would not affect the study results. Seven studies (26, 27, 32, 33, 36, 37, 41) that only performed per-protocol analysis and one study (36) that did not report pain intensity results were assessed as having a high risk of attrition and reporting bias, respectively. Two studies (25, 29) with significant differences in baseline clinical data between groups and three studies (26, 27, 41) with insufficient relevant information were evaluated as having a high or unclear risk of other bias, respectively (**Supplement 6**).

### 3.3. Headache pain intensity

In NMA, compared to waiting list, verum acupuncture (SMD -1.43, 95% CI -1.98 to -0.88), SATS (SMD -1.00, 95% CI -1.55 to -0.45), and SATV (SMD -1.97, 95% CI -3.21 to -0.74) all significantly reduced headache pain intensity. Verum acupuncture significantly improved pain intensity compared to SATS (SMD 0.43, 95% CI 0.15 to 0.71), however there was no significant difference between SATV and AT (SMD -0.54, 95% CI -1.65 to 0.56). The effect estimate between SATV and SATS was in favor of SATV, but there was no statistically significant difference (SMD -0.97, 95% CI -2.12 to 0.17) (**Figure 3(a)**). Pairwise meta-analysis and NMA were consistent in terms of statistical significance and direction of effect (**Table 2**). The analysis results showed asymmetry in the funnel plot, and the p-value in Egger's test was 0.032, suggesting publication bias (**Supplement 7**). In the SUCRA test, SATV ranked first in improving headache pain intensity (92.8%), followed by verum acupuncture (72.2%), SATS (35%), and waiting list (0%) (**Supplement 8**). The certainty of evidence of the estimates was generally moderate to very low, and the reason for downgrade was risk of bias, inconsistency, publication bias, or imprecision (**Supplement 9**).

### 3.4. Response rate

In NMA, verum acupuncture (RR 3.95, 95% CI 2.26 to 6.92), SATS (RR 2.98, 95% CI 1.70 to 5.24), and SATV (RR 6.84, 95% CI 1.15 to 40.71) all showed high response rates compared to waiting list control. Verum acupuncture significantly improved the response rate compared to SATS (RR 0.75, 95% CI 0.59 to 0.97), however there was no significant difference between SATV and AT (RR 1.73, 95% CI 0.32 to 9.41). The comparative estimate between SATV and SATS was in favor of SATV, although there was no statistical significance between the two groups (RR 2.30, 95% CI 0.41 to 12.72) (**Figure 3(b)**). Pairwise meta-analysis was consistent with NMA in terms of statistical consistency and direction of effect (**Table 3**). Because 8 studies were included in the analysis, publication bias testing was not possible, and according to the SUCRA test, SATV ranked first (84.8%), followed

by verum acupuncture (74.9%), SATS (39.6%), and waiting list (0.6%) (**Supplement 8**). The certainty of evidence in the analysis results was high or moderate, and the reason for the downgrade was risk of bias or imprecision (**Supplement 9**).

## 4. Discussion

Due to the adverse effects of conventional medications (18-20), acupuncture, a non-pharmacological intervention, has been actively used to treat migraine, and clinical trials evaluating its effects have been actively performed. Accordingly, many systematic reviews have been conducted to date to summarize the effects of acupuncture on migraine (20-22), however, to the best of our knowledge, no study has been conducted focusing on the needling point of sham acupuncture.

As a result of analyzing 18 acupuncture clinical trials including 1936 migraine participants, when SATS was used as the control group, headache pain intensity significantly improved and the response rate was significantly higher in the acupuncture group. However, when SATV was used as a control group, there was no significant difference between the two groups. These results are consistent with our previous studies in which NMA was performed on acupuncture clinical trials in patients with chronic nonspecific low back pain (13), cancer pain (14), and knee osteoarthritis (15). When comparing SATS and SATV, there was no significant difference in headache pain intensity and response rate between the two groups, however the results were in favor of SATV. In the previous study involving 4379 patients with chronic nonspecific low back pain (13), SATV significantly improved pain and function compared to SATS. This study, which included 1,936 migraine patients, did not show statistically significant results between them due to imprecision such as relatively small sample size and wide confidence intervals, causing downgrade of the certainty of evidence of the NMA estimate. However, the result showed similar trends with previous studies (13-15) and may show statistical significance when sham acupuncture-controlled acupuncture trials are additionally conducted in the future. There were four studies (32-34, 40) in which blinding of participants and outcome assessors was not possible because they included a waiting list control and evaluated outcomes by patient self-assessment. However, because blinding between the acupuncture and sham acupuncture groups was maintained in these studies (32-34, 40), the impact of the risk of bias on the comparison between these groups was judged to be low.

Sham acupuncture has been used differently in several studies depending on techniques such as skin penetration and needling points, and examples can be divided into using sham acupuncture device or superficial needling on acupuncture points or non-acupuncture points (5, 6). Transparent reporting on sham acupuncture is important to understand the purpose and implications of the research. In particular, this may affect understanding the effects of acupuncture. However, the reporting quality of sham acupuncture in acupuncture clinical trials was generally poor (43), and therefore, sham acupuncture reporting guidelines were recently developed to improve this (44-47). According to them (44-47), the rationale for setting the chosen sham acupuncture should be reported. This should be clearly reported according to the research hypothesis and design. If the same acupuncture points as the verum

acupuncture group are used as the needling point for sham acupuncture, this is not evaluating the efficacy of acupuncture, but rather examining the effect due to differences in needling methods such as skin penetration, use of a sham acupuncture device, and needling depth. In addition, since questions have continued to be raised about whether sham acupuncture is a physiologically inert placebo, it should not be misused as a placebo control until mechanism studies on its activity are conducted. Recently, mechanism research on sham acupuncture has not made much progress (48). Such research can help understand not only the physiological activity of sham acupuncture, but also the effectiveness of acupuncture in previous acupuncture clinical trials (49, 50).

The limitation of this study is that only English databases were searched. Although a comprehensive search strategy was used as much as possible and other sources such as reference lists and clinical trial registries were also searched, there might be missing studies that were not listed in them. Additionally, our study examined the outcomes according to needling points among various sham acupuncture procedures, and could not examine the effects of other techniques, such as the use of sham acupuncture devices. Previous NMA studies showed that the outcome of verum acupuncture in acupuncture trials using a sham acupuncture device was inferior to verum acupuncture in acupuncture trials without a sham device for hot flashes and knee osteoarthritis (51, 52). In our study, there was only one study using SATV, so we were unable to examine the influence of variables other than needling points, which may also have influenced the results.

In conclusion, in the acupuncture clinical trials for migraine, the outcome of acupuncture was different depending on the needling point of sham acupuncture, and there was no significant difference between SATV and acupuncture. The sham acupuncture method should be established according to the research hypothesis, and SATV should not be misused as a placebo control to evaluate the efficacy of acupuncture.

**Conflicts of interest**

The authors have no conflicts of interest to declare.

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**Role of the funder/sponsor**

The funders had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, the preparation, review, and approval of the manuscript, or the decision to submit the manuscript for publication.

**Authors' contributions**

Conceptualization: BL and MSL; Methodology: BL, CYK, and MSL; Writing – original draft: BL; Writing – review & editing: CYK, HWL, AN, LSW, THK, SB, TA, and MSL; Supervision: MSL.

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290 **Data sharing statement**

291 The authors confirm that the data supporting the findings of this study are available within the article and its
292 supplementary materials.

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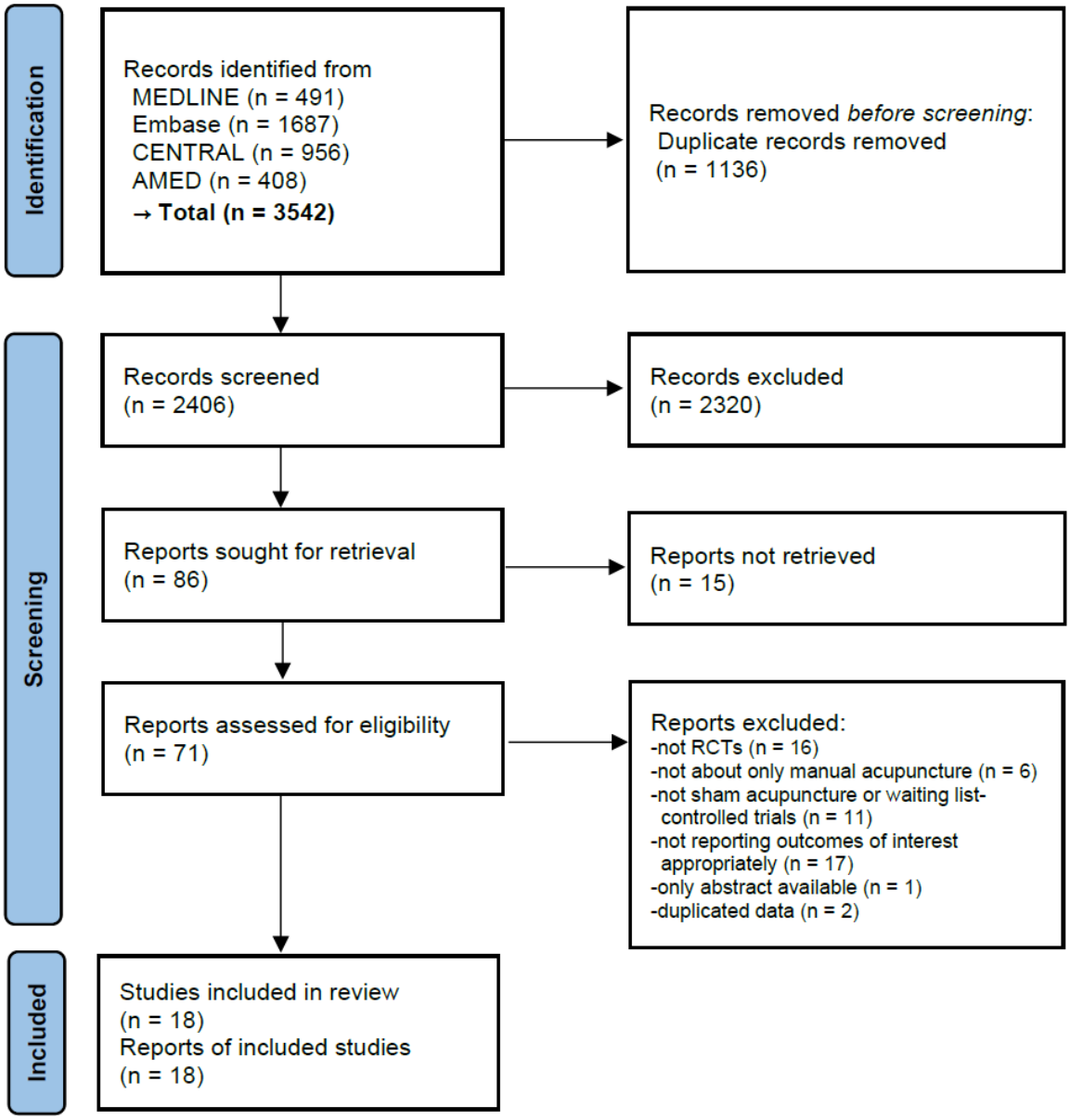
**Figure legends**

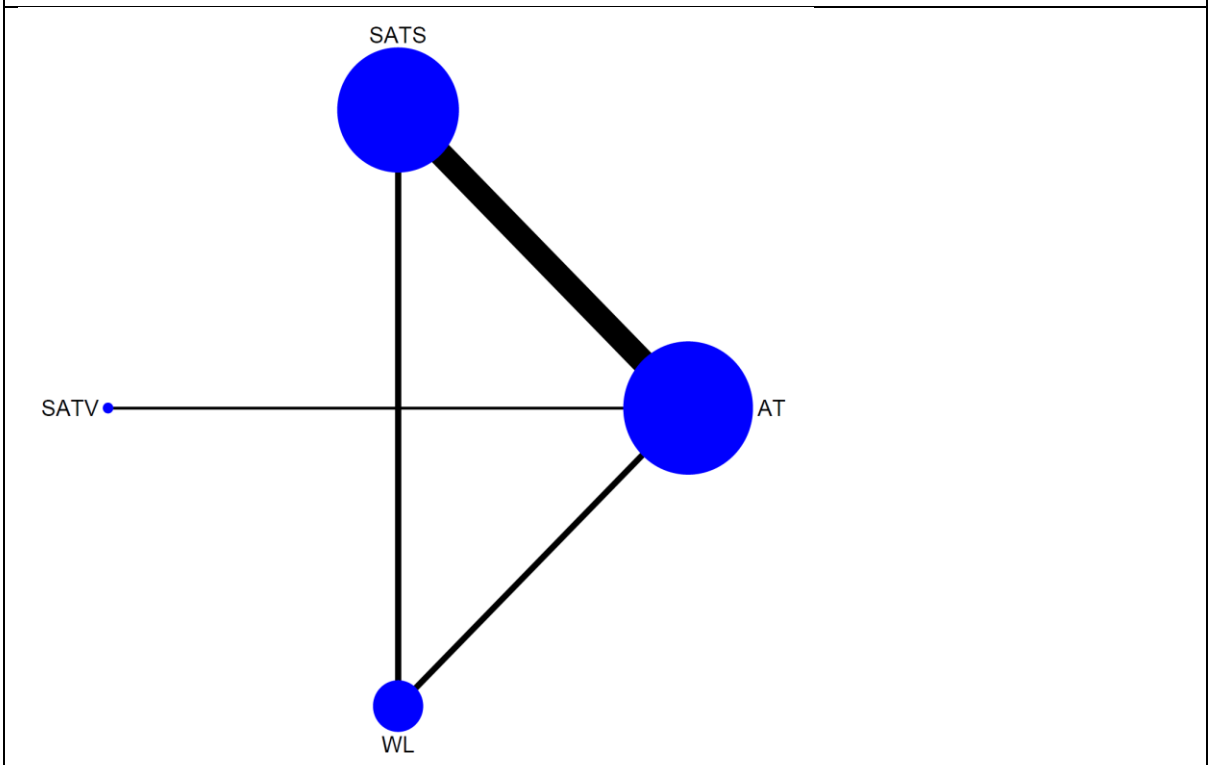
**Figure 1**. Flow diagram of the study screening and selection processes



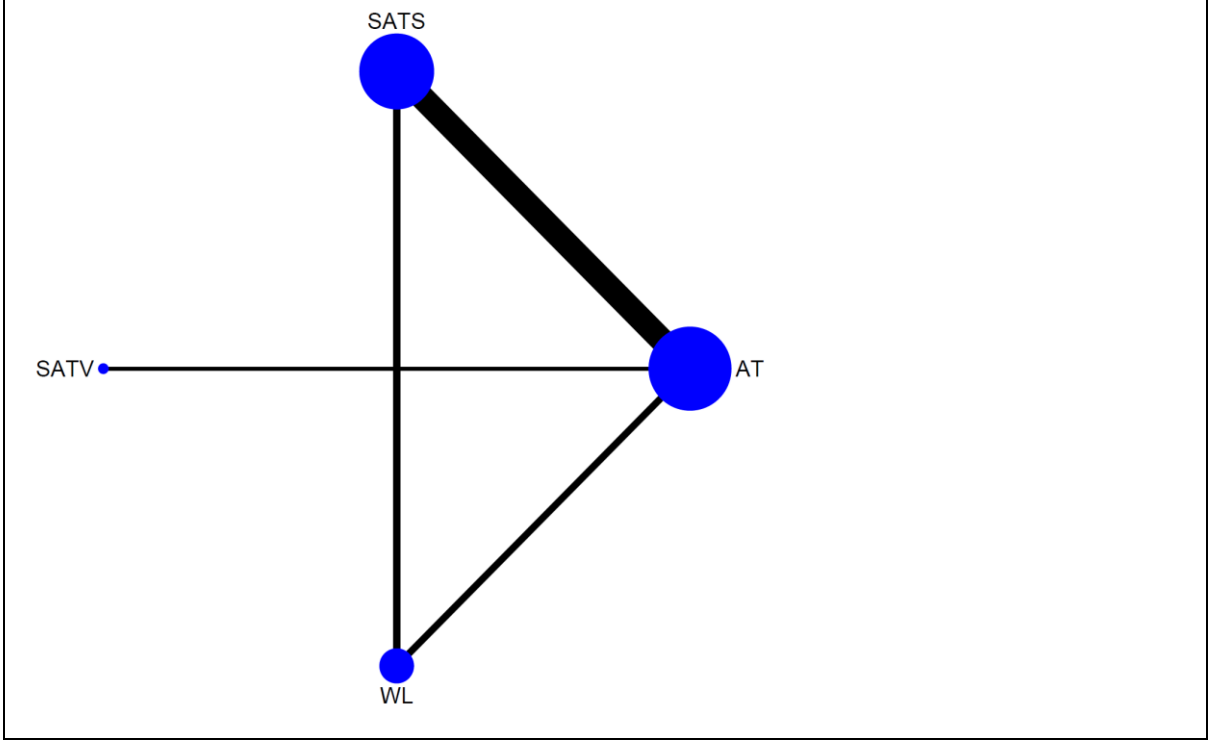

RCT, randomized controlled clinical trial.

**Figure 2**. Network map for (a) headache pain intensity, (b) response rate, and (c) the frequency of migraine attacks

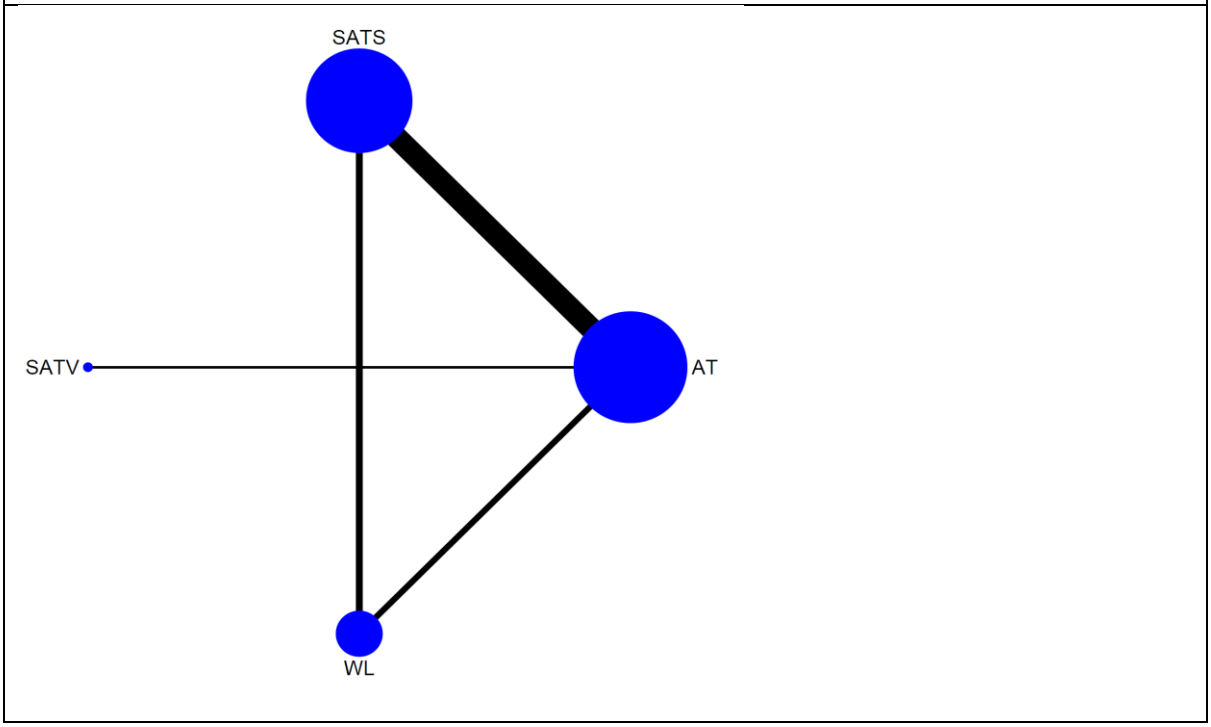
(a) headache pain intensity




(b) response rate

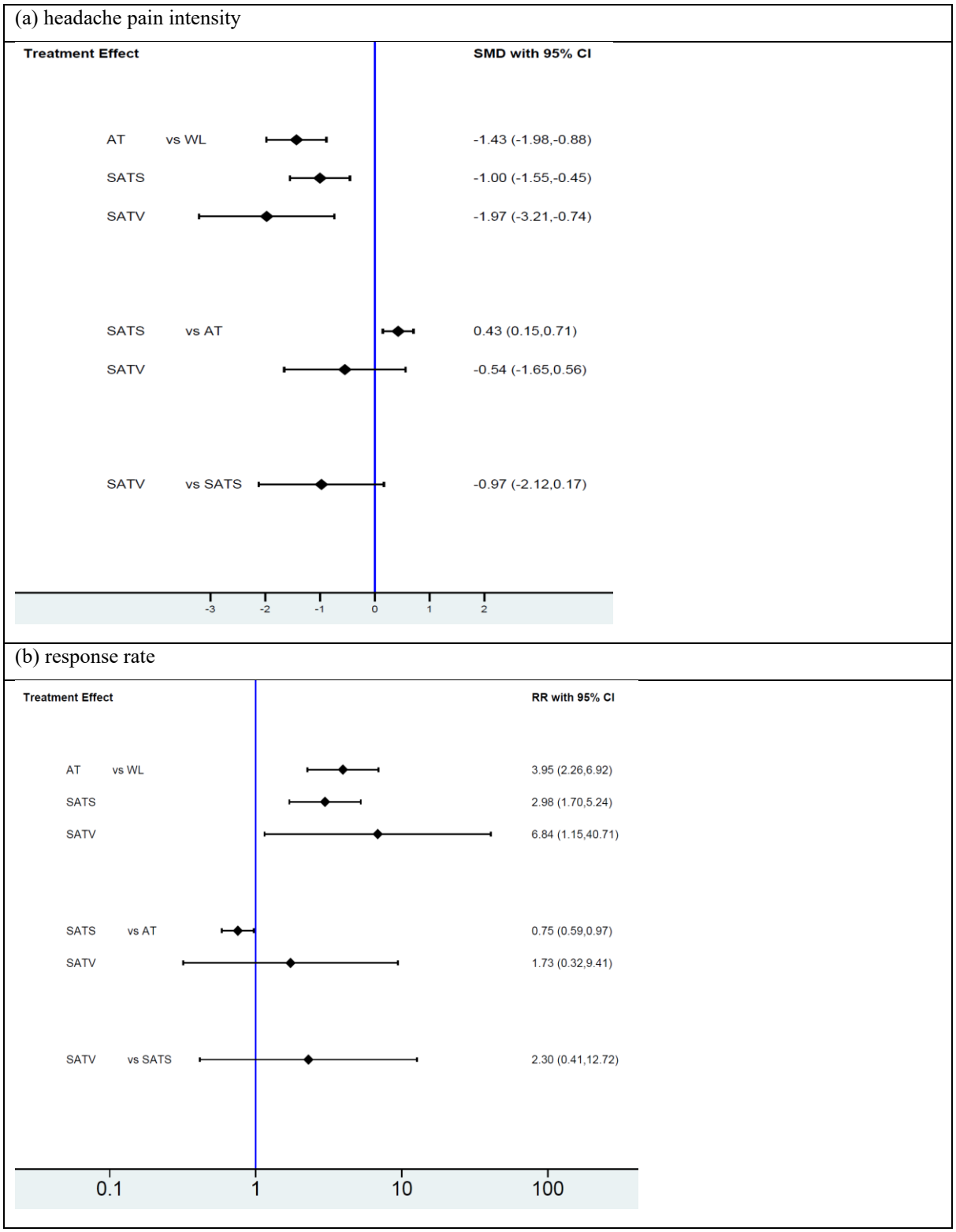


(c) the frequency of migraine attacks




AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; WL, waiting list.

**Figure 3**. Interval plots for (a) headache pain intensity and (b) response rate




AT, acupuncture therapy; CI, confidence interval; RR, risk ratio; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; SMD, Standardized mean difference WL, waiting list.

**Table 1. Characteristics of the included studies**

| Study ID (Country) | Sample size (AT/SAT/WL) | Age (year) mean ± SD | SAT protocol | Outcomes of interest | Treatment duration | Time point for analysis |
|---|---|---|---|---|---|---|
| Alecrim 2008 (Brazil) | 36 (19/17/-) | AT: 36.7 ± 9.2, SAT: 33.2 ± 9.2 | SATS, superficial needling at non-indicated acupuncture points | response rate | 12 weeks | 12 weeks |
| Allais 2011 (Italy) | 89 (43/46/-) | AT: 35.93, SAT: 33.2 | SATS, a semi-permanent needle at non-indicated acupuncture point (sciatic nerve) | headache pain intensity (0-10 VAS) | one session (1 day) | 1 day |
| Backer 2008 (Germany) | 19 (9/10/-) | 43.5 ± 8.5 | SATS, superficial needling at non-acupuncture points | response rate, migraine frequency | 8 weeks | 12 weeks |
| Diener 2006 (Germany) | 607 (290/317/-) | AT: 37.1 ± 10.5, SAT: 38.3 ± 10.4 | SATS, superficial needling at non-acupuncture points | headache pain intensity (Von Korff Chronic Pain Grade Questionnaire), response rate | 6 weeks | 6 weeks (response rate), 13 weeks (headache pain intensity) |
| Farahmand 2018 (Iran) | 60 (30/30/-) | 31.4 ± 7.6 | SATS, needling at non-indicated acupuncture points (stomach, spleen, etc) | headache pain intensity (0-10 VAS) | 4 hours | 4 hours |
| Foroughipour 2014 (Iran) | 100 (50/50/-) | AT: 35.8 ± 10.9, SAT: 37.2 ± 11.2 | SATS, superficial needling at non-acupuncture points | migraine frequency | 1 month | 1 month |
| Habibabadi 2021 (Iran) | 80 (40/40/-) | AT: 37.1 ± 9.33, SAT: 36.65 ± 8.86 | SATS, a piece of adhesive paper without a needle at the inactive points | headache pain intensity (0-10 VAS), migraine frequency | 2 weeks | 2 weeks |
| Li 2017 (China) | 62 (35/11/16) | 21.29 | SATS, needling at non-acupuncture points | headache pain intensity (0-10 VAS), migraine frequency | 4 weeks | 4 weeks |
| Li 2023 (China) | 38 (12/13/13) | AT: 36.1 ± 10.5, SAT: 38.0 ± 10.4, WL: 38.5 ± 8.6 | SATS, superficial needling at non-acupuncture points | headache pain intensity (0-10 VAS), migraine frequency | 10 days | 10 days |
| Linde 2004 (Sweden) | 28 (14/14/-) | AT: 35.2 ± 7.5, SAT: 37.4 ± 8.6 | SATV, non-penetrating Streitberger needles at same acupuncture points | headache pain intensity (0-10 VAS), response rate, migraine frequency | 3 months | 3 months |
| Linde 2005 (Germany) | 302 (145/81/76) | 42.6 ± 11.4 | SATS, superficial needling at non-acupuncture points | headache pain intensity (0-10 NRS), response rate, migraine frequency | 8 weeks | 9-12 weeks |

| | | | | | | |
|---|---|---|---|---|---|---|
| Wallasch 2012 (Germany) | 35 (18/17/-) | AT: 37.2 ± 9.6, SAT: 39.3 ± 11.7 | SATS, superficial needling at non-acupuncture points | migraine frequency | 8 weeks | 8 weeks |
| Wang 2012 (China) | 150 (75/75/-) | AT: 37.8 ± 10.6, SAT: 38.6 ± 12.6 | SATS, needling at non-acupuncture points | headache pain intensity (0-10 VAS) | one session (30 minutes) | 1 day |
| Wang 2015 (Austrailia) | 50 (26/24/-) | AT: 41.6 ± 14.9, SAT: 43.8 ± 13.4 | SATS, non-penetrating blunted cocktail stick tapped at non-acupuncture points on scalp, face and neck and superficial needling at non-acupuncture points on four extremities | headache pain intensity (6-point Likert scale, 0-10 VAS), response rate, migraine frequency | 20 weeks | 20 weeks |
| Wang 2017 (China) | 38 (19/19/-) | AT: 30 ± 6, SAT: 31 ± 7 | SATS, needling at non-acupuncture points | headache pain intensity (0-10 VAS), migraine frequency | 4 weeks | 4 weeks |
| Xu 2020 (China) | 150 (60/60/30) | AT: 36.6 ± 12.0, SAT: 36.0 ± 10.9, WL: 37.3± 11.7 | SATS, non-penetrating Streitberger needles at non-acupuncture points | response rate | 8 weeks | 17-20 weeks |
| Yu 2018 (Canada) | 12 (7/5/-) | range 22-52 | SATS, superficial needling at non-indicated acupuncture points | headache pain intensity (0-10 NRS), response rate, migraine frequency | 3 months | 4-6 months |
| Zhao 2014 (China) | 80 (40/40/-) | AT: 33.35 ± 11.69, SAT: 33.23 ± 9.73 | SATS, needling at non-indicated acupuncture points | headache pain intensity (0-10 VAS), migraine frequency | 8 weeks | 5-8 weeks |

AT, acupuncture therapy; NRS, numeric rating scale; SAT, sham acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; SD, standard deviation; VAS, visual analog scale; WL, waiting list.

**Table 2. League table for pairwise meta-analysis (right upper part) and network meta-analysis (left lower part) effect estimates: Headache pain intensity**

| | | | |
|---|---|---|---|
| **WL** | **-1.38 [-2.05, -0.72]** | **-0.99 [-1.29, -0.70]** | - |
| **-1.43 [-1.98, -0.88]** | **AT** | **0.49 [0.20, 0.79]** | -0.54 [-1.30, 0.21] |
| **-1.00 [-1.55, -0.45]** | **0.43 [0.15, 0.71]** | **SATS** | - |
| **-1.97 [-3.21, -0.74]** | -0.54 [-1.65, 0.56] | -0.97 [-2.12, 0.17] | **SATV** |

Results are presented as the standardized mean difference [95% confidence interval]. Comparison must be read from left to right. A standardized mean difference greater than zero indicates that the treatment on the left is favored in both pairwise and network meta-analyses. The values in bold text indicate statistical significance.

AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; SD, standard deviation; WL, waiting list.

**Table 3. League table for pairwise meta-analysis (right upper part) and network meta-analysis (left lower part) effect estimates: Response rate**

| | | | |
|---|---|---|---|
| **WL** | **3.76 [2.18, 6.49]** | **3.11 [1.95, 4.97]** | - |
| **3.95 [2.26, 6.92]** | **AT** | **0.76 [0.59, 0.96]** | 1.73 [0.34, 8.81] |
| **2.98 [1.70, 5.24]** | **0.75 [0.59, 0.97]** | **SATS** | - |
| **6.84 [1.15, 40.71]** | 1.73 [0.32, 9.41] | 2.30 [0.41, 12.72] | **SATV** |

Results are presented as the risk ratio (95% confidence interval). Comparison must be read from left to right. A risk ratio greater than one indicates that the treatment on the right is favored in both pairwise and network meta-analyses. The values in bold text indicate statistical significance.

AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; SD, standard deviation; WL, waiting list.

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**Supplement 1. The search strategy used in each database**

**MEDLINE via PubMed**

| | Searches | Results |
|---|---|---|
| #1 | Headache[MH] OR "Headache Disorders"[MH] OR headach*[TIAB] OR migrain*[TIAB] OR cephalgi*[TIAB] OR cephalalgi*[TIAB] | 139,657 |
| #2 | Acupuncture[MH] OR “Acupuncture Therapy”[MH] OR “Acupuncture Points”[MH] OR acupunct*[TIAB] OR acupoint*[TIAB] OR “Dry Needling”[MH] OR “dry needling”[TIAB] OR "filiform needle"[TIAB] | 39,702 |
| #3 | “Randomized Controlled Trial”[PT] OR “Controlled Clinical Trial”[PT] OR randomized[TIAB] OR placebo[TIAB] OR “Clinical Trials as Topic”[Mesh:noexp] OR randomly[TIAB] OR trial[TI] | 1,582,690 |
| #4 | animals[MH] NOT humans[MH] | 5,179,719 |
| #5 | (#1 AND #2 AND #3) NOT #4 | **491** |

**Embase via Elsevier**

| | Searches | Results |
|---|---|---|
| #1 | headache/exp OR 'headache and facial pain'/exp OR headach*:ab,ti OR migrain*:ab,ti OR cephalgi*:ab,ti OR cephalalgi*:ab,ti | 427,544 |
| #2 | acupuncture/exp OR acupuncture*:ab,ti OR ‘acupuncture point’/exp OR ‘body meridian’/exp OR ‘body meridian’:ab,ti OR acupoint*:ab,ti OR 'dry needling'/exp OR 'dry needling':ab,ti OR ‘filiform needle’:ab,ti | 64,595 |
| #3 | 'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer*):de,ab,ti | 3,253,041 |
| #4 | #1 AND #2 AND #3 | **1,687** |

**CENTRAL**

| | Searches | Results |
|---|---|---|
| #1 | MeSH descriptor: [Headache] explode all trees | 5,947 |
| #2 | MeSH descriptor: [Headache Disorders] explode all trees | 4,545 |
| #3 | (headach* OR migrain* OR cephalgi* OR cephalalgi*):ti,ab,kw | 41,853 |
| #4 | #1 OR #2 OR #3 | 41,853 |
| #5 | MeSH descriptor: [Acupuncture] explode all trees | 713 |

| | | |
|---|---|---|
| #6 | MeSH descriptor: [Acupuncture Therapy] explode all trees | 6,525 |
| #7 | MeSH descriptor: [Acupuncture Points] explode all trees | 2,539 |
| #8 | MeSH descriptor: [Dry Needling] explode all trees | 166 |
| #9 | (acupunct* OR acupoint* OR “dry needling” OR "filiform needle"):ti,ab,kw | 22,387 |
| #10 | #5 OR #6 OR #7 OR #8 OR #9 | 22,737 |
| #11 | (#4 AND #10) in Trials | **956** |

**AMED via EBSCO**

| | Searches | Results |
|---|---|---|
| #1 | SU Headache OR SU “Tension Type Headache” OR SU “Tension Headache” OR SU Migraine OR TX headach* OR TX migrain* OR TX cephalgi* OR TX cephalalgi* | 2,455 |
| #2 | SU Acupuncture OR SU “Acupuncture Therapy” OR SU "Acupuncture Analgesia" OR SU Acupoints OR SU Needles OR SU Needling OR SU "Dry needling" OR TX acupuncture* OR TX acupoint* OR TX needl* | 12,850 |
| #3 | #1 AND #2 | **408** |

**Supplement 2. Excluded studies after full-text review**

**- Not randomized controlled clinical trials: 16**


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**- Not sham acupuncture or waiting list-controlled trials: 11**

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**- Not reporting outcomes of interest appropriately: 17**

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**- Duplicated data: 2**

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**Supplement 3. Details of acupuncture treatment method**

| Study ID | Acupuncture protocol | Number of needle | Treatment points | Depth of insertion | Needle stimulation | Needle retention time | Needle type | Number of treatment session | Frequency | Other interventions | Qualification or experiences on acupuncture |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Alecrim 2008 | Individualized | a maximum of 20 needles | individualized (bilateral) | NR | De qi, manipulation by rotation | 30 min | Sterile disposable and steel needles (0.25 × 40 mm) | 16 | twice a week for first 4 weeks, then once a week for 8 weeks* | Rescue medication as needed | experienced physicians specialized in acupuncture for more than 11 years |
| Allais 2011 | Individualized | mean number 3.2 ± 0.23 | Antero-internal part of the antitragus on the same side of pain (positive to needle contact test) (unilateral) | NR | NR | 1 day | auricular semi-permanent needles | 1 | one session | NR | an experienced acupuncturist |
| Backer 2008 | Semi-standardized | NR | GV20, GB20, EX-HN5, TE23, TE5, LR3, GB41 (bilateral) | NR | De qi, manipulation by rotation (a frequency of 2 to 4 Hz and an amplitude of approximately 90 to 120 degrees) | 30 min | Sterile disposable and steel needles (0.25 × 40 mm) | 12 | NR | NR | 2 experienced acupuncturists |
| Diener 2006 | Semi-standardized | mean 15.4 ± 4.6 (10-25) | depending on TCM diagnosis predefined collections of obligatory and flexible points (bilateral) | 2-20 mm | De qi | 30 min | Sterile disposable and steel needles (0.25-0.30 × 25-40 mm) | 10 (if moderate response further 5 sessions possible) | twice a week | NR | 149 physicians with at least 140 hours' acupuncture training and 2 years' professional experience |
| Farahmand 2018 | Standardized | NR | Shenmen, Autonomic, Thalamus, Frontal, Temple | NR | NR | 4 hours | sterile metallic needles (0.25 x 13 mm) | 1 | one session | Rescue medication as needed | one operator who had been trained during 1 month course prior to sampling |
| Foroughipour 2014 | Individualized | NR | according to involved meridians (Shaoyang, Yangming, Taiyang or Jueyin) and their pattern identification, thus adding individualized acupuncture | NR | De qi | 30 min | Sterile disposable and steel needles (0.25 x 40 mm, 0.18 x 25 mm) | 12 | three times a week | continue prophylactic treatment | acupuncturist in Imam Reza hospital Chinese medicine and acupuncture clinic |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Habibabadi 2021 | Semi-standardized | maximum of 4 needles in the most active points in each ear | Sympathetic, Gallbladder, GB3, GB40, Lesser occipital nerve, Thalamus, Ear apex, Forehead, Zero, Shenmen, Prostaglandin 1, Prostaglandin 2, Liver, Hypothalamus, Frustration, Temple, Occiput, local cervical point (back), local cervical point (front), worry point | NR | NR | NR | auricular semi-permanent needles | 2 | once every two weeks | propranolol 20 mg every 12 hours | an anesthesiologist and pain medicine specialist who had an auricular medicine certificate along with 15 years of experience |
| Li 2017 | Standardized | 6 | AT1: GB34, GB40, TE5,<br>AT2: GB33, GB42, TE8,<br>AT3: ST36, ST42, LI6<br>(bilateral) | 5-15 mm | De qi | 30 min | Sterile disposable and steel needles | 202 | 5 sessions for week | Rescue medication (ibuprofen) as needed | two licensed acupuncturists |
| Li 2023 | Standardized | NR | GB20, LR3, EX-HN5, GV20, EX-HN1 | NR | De qi, amplitude of lifting-thrusting: 0.3–0.5 cm; frequency: 60–90 times/min; twirling angle: 90°–180° | 30 min | Sterile disposable and steel needles (0.30 x 40 mm) | 10 | once a day | Rescue medication as needed | NR |
| Linde 2004 | Semi-standardized | 12 | GB8, GB20, LI4, LR3, SP6 (bilateral)<br>*depending on the site of usual maximum headache<br>-frontal pain: GB14<br>-temporal pain: EX-HN5<br>-occipital pain: BL10 | 10-30 mm | De qi, rotated manually every 10 min | 30 min | Sterile disposable filiform needles (0.25 x 15 mm or 0.30 x 30 mm) | 9 | three times a month (8, 5, and 3 days before expected date of menstruation in three cycles) | Rescue medication as needed | experienced physiotherapists |
| Linde 2005 | Semi-standardized | limited to 25 | GB20, GB40, GB41, GB42, GV20, LR3, TE3, TE5, EX-HN5 (bilateral)<br>*additional points according to individual symptoms | NR | De qi, stimulated manually at least once during each session | 30 min | Sterile disposable and steel needles, physicians could choose needle length and diameter. | 12 | twice a week for first 4 weeks, then once a week for 4 weeks | Rescue medication as needed | physicians trained (at least 140 hours, median 500 hours) and experienced (median 10 years) in acupuncture |
| Wallasch 2012 | Semi-standardized | 6-10 | LI4, ST36, TE5, GB41, SI3, BL62, GV20, GB20, EX-HN5, TE23, LR3, KI3 (bilateral) | NR | De qi, manually rotated to achieve a needle sensation | 30 min | Sterile disposable and steel needles (0.30 x 35 mm) | 8 | once a week | NR | licensed, with long experience in TCM and history of practicing acupuncture methodology in China |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Wang 2012 | Semi-standardized | 10-12 | GV20, GV24, ST8, GB8, GB20<br>*according to different syndromes<br>-Shaoyang headache: TE5, GB34<br>-Yangming headache: LI4, ST44<br>-Taiyang headache: BL60, SI3<br>-Jueyin headache: LR3, GB40<br>-nausea and vomiting: PC6<br>-dysphoria and susceptibility to rage: LR3 | 10-15 mm | De qi, stimulated manually by twirling and lifting–thrusting | 30 min | Sterile disposable and steel needles (1.5-in. filiform needle, 0.32 x 40 mm) | 1 | one session | Rescue medication (Aspirin) as needed | acupuncturists with at least 20 years of clinical experience |
| Wang 2015 | Semi-standardized | 9-12 | GB20 (bilateral), EX-HN5, GB8, LI4 (unilateral)<br>*according to pattern identification<br>-ascending hyperactivity of liver yang: GV20, LR2, LR3, KI3, GB39, SP6<br>-deficiency of both qi and blood: GV20, GV23, ST36, SP6<br>-wind phlegm blocking the meridians: ST40, CV12, SP9<br>-blood stasis: SP6, SP10, ashi point | 10-30 mm | De qi, stimulation every 10 minutes | 25 min | Sterile disposable and steel needles (0.25 x 30 or 40 mm) | 16 | twice a week for 4 weeks, once a week for next 4 weeks, once every two weeks for next 4 weeks, once a month for 2 months | Rescue medication as needed | one registered acupuncturist, with a 5-year bachelor degree and 3 years of clinical experience in acupuncture |
| Wang 2017 | Standardized | NR | headache point (midpoint of the hollow in front of the juncture of the 1st and 2nd metatarsal bones on the dorsum of the foot) | 25-40 mm | De qi, lifting-thrusting | no retention | Sterile disposable and steel needles (0.35 x 75 mm) | 20 | once a week, 5 times a week | Rescue medication (ibuprofen) as needed | NR |
| Xu 2020 | Semi-standardized | NR | LI4, LR3, EX-HN5, GB20, GB8 (bilateral)<br>*according to meridian diagnosis and the patient's symptoms<br>-Yangming headache: ST8 (bilateral)<br>-Taiyang headache: BL10<br>-Jueying headache: GV20 | 0.3-1.2 cun | De qi, manual manipulation for each acupoint lasted 10 seconds and was repeated four times with intervals of 10 minutes | 30 min | Streitberger acupuncture needles (0.30 x 30 mm) | 20 | once every other day | usual care (lifestyle changes and migraine self-management), and rescue medication (diclofenac sodium) as needed | 14 licensed acupuncturists with more than 5 years of clinical experience |
| Yu 2018 | Semi-standardized | NR | LR3, LI4, SP6, GB20<br>*according to pattern identification<br>-qi and blood deficiency: ST36<br>-qi stagnation and blood stasis: SP10<br>-liver and kidney yin deficiency: KI3<br>-liver fire: LR2 | 15-20 mm | De qi, manual rotation of approximately four times per second and an amplitude of approximately 1-2 full rotations at a 10-min interval | 20 min | Sterile disposable and steel needles (0.18 x 30 mm) | 9 | three times a month | Rescue medication as needed | acupuncturist licensed by the college of TCM practitioners and acupuncturists of Ontario |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Zhao 2014 | Standardized | 8 | TE5, GB20, GB34, GB40 (bilateral) | 2.5-3.5 cm | De qi, twisted with rotation (90°<amplitude<180°) at a frequency of 1–2 Hz | 30 min | Sterile disposable and steel filiform needles (0.25-0.30 x 25-40 mm) | 32 | 4 times a week | NR | two specialized acupuncturists with at least 5 years of training and 3 years of experience |

NR, not recorded; TCM, traditional Chinese medicine.
*information from *Linde K, Allais G, Brinkhaus B, Fei Y, Mehring M, Vertosick EA, Vickers A, White AR. Acupuncture for the prevention of episodic migraine. Cochrane Database Syst Rev. 2016;2016(6):CD001218.*

**Supplement 4. Results of testing inconsistency at the local level through the node splitting method.**

(a) Headache pain intensity

| Side | Direct comparison | | Indirect comparison | | Difference | | p value |
|---|---|---|---|---|---|---|---|
| | Coefficient | SE | Coefficient | SE | Coefficient | SE | |
| AT WL | 1.333515 | 0.3084614 | 1.866674 | 0.6233917 | -0.5331587 | 0.6827231 | 0.435 |
| AT SATS | 0.4287293 | 0.1433069 | -2.933106 | 551.2447 | 3.361835 | 551.2447 | 0.995 |
| AT SATV | -0.5442294 | 0.5649827 | 2.818541 | 629.4517 | -3.36277 | 629.452 | 0.996 |
| SATS WL | 1.109116 | 0.3129665 | 0.5758676 | 0.614562 | 0.5332481 | 0.682721 | 0.435 |

(b) Response rate

| Side | Direct comparison | | Indirect comparison | | Difference | | p value |
|---|---|---|---|---|---|---|---|
| | Coefficient | SE | Coefficient | SE | Coefficient | SE | |
| AT WL | -1.385841 | 0.3113524 | -1.367913 | 0.5779875 | -0.017928 | 0.5690105 | 0.975 |
| AT SATS | -0.2824249 | 0.128896 | 3.216478 | 946.2885 | -3.498903 | 946.2886 | 0.997 |
| AT SATV | 0.548566 | 0.8638623 | -2.78497 | 1344.814 | 3.333536 | 1344.814 | 0.998 |
| SATS WL | -1.088902 | 0.3177867 | -1.106791 | 0.5631636 | 0.0178883 | 0.5690171 | 0.975 |

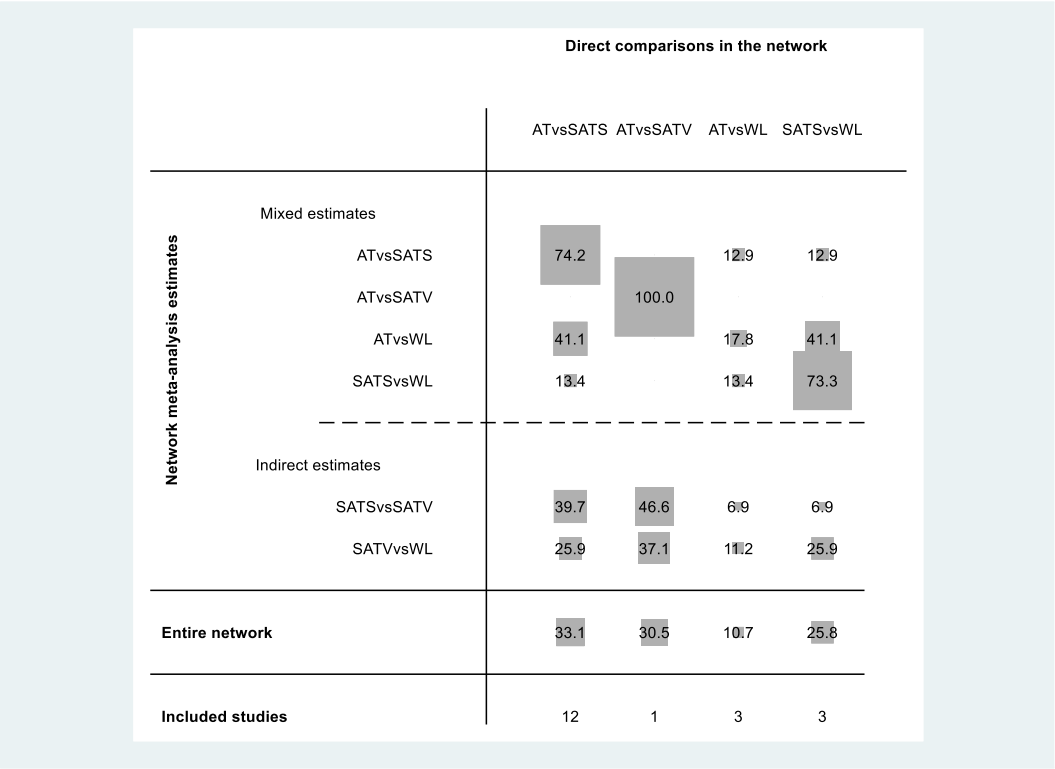
(c) Frequency of migraine attacks

| Side | Direct comparison | | Indirect comparison | | Difference | | p value |
|---|---|---|---|---|---|---|---|
| | Coefficient | SE | Coefficient | SE | Coefficient | SE | |
| AT WL | 0.6973213 | 0.1721473 | 1.721596 | 0.3981054 | -1.024275 | 0.4226712 | 0.015 |
| AT SATS | 0.4958241 | 0.1220656 | -1.59058 | 625.5491 | 2.086404 | 625.5491 | 0.997 |
| AT SATV | -0.4060445 | 0.4626638 | 1.681852 | 626.0662 | -2.087896 | 626.0664 | 0.997 |
| SATS WL | 0.5662731 | 0.1863988 | -0.4580195 | 0.3786898 | 1.024293 | 0.4226715 | 0.015 |

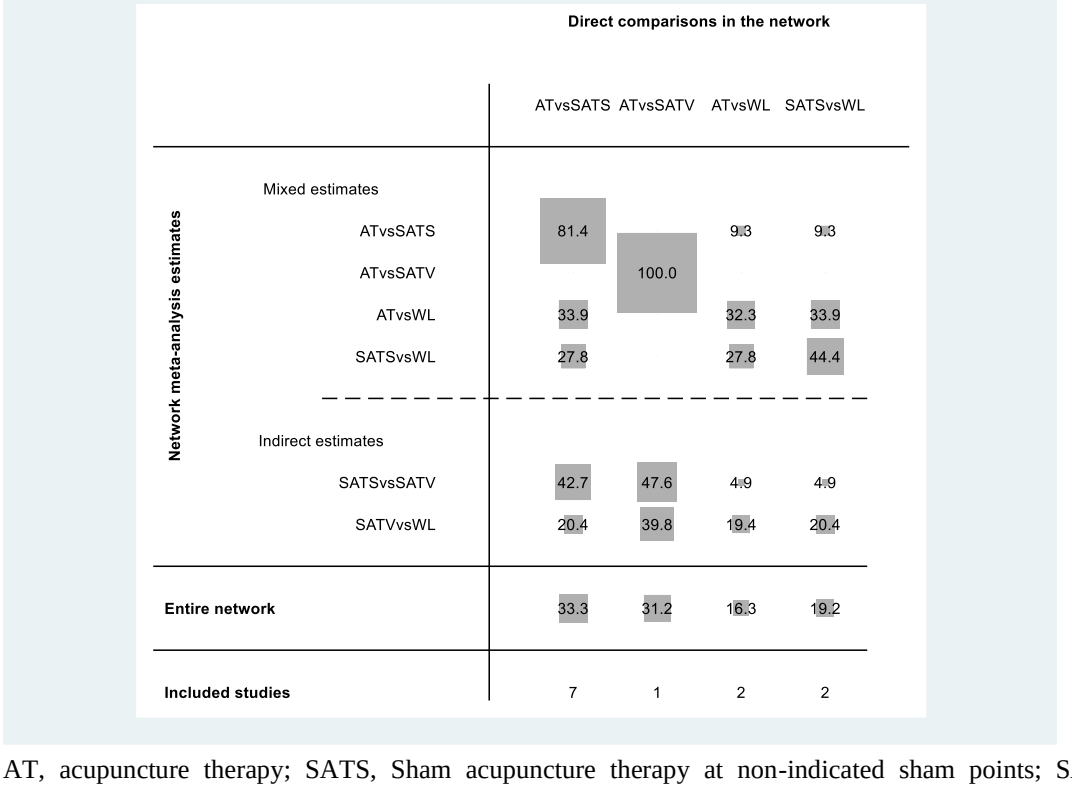
Note. All the evidence about these contrasts comes from the trials which directly compare them.
AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; SD, standard deviation; WL, waiting list.

**Supplement 5. Contribution matrix**

(a) Headache pain intensity

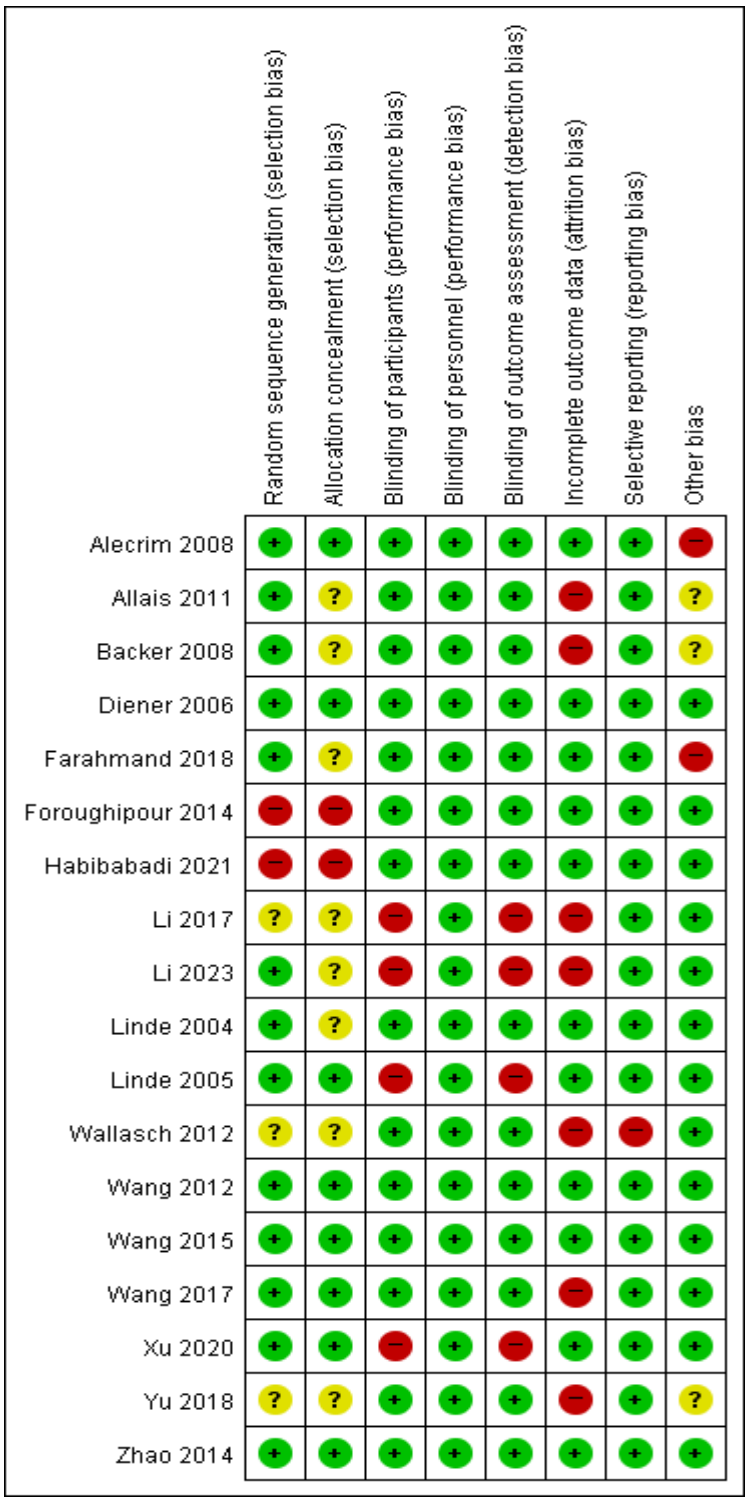



(b) Response rate



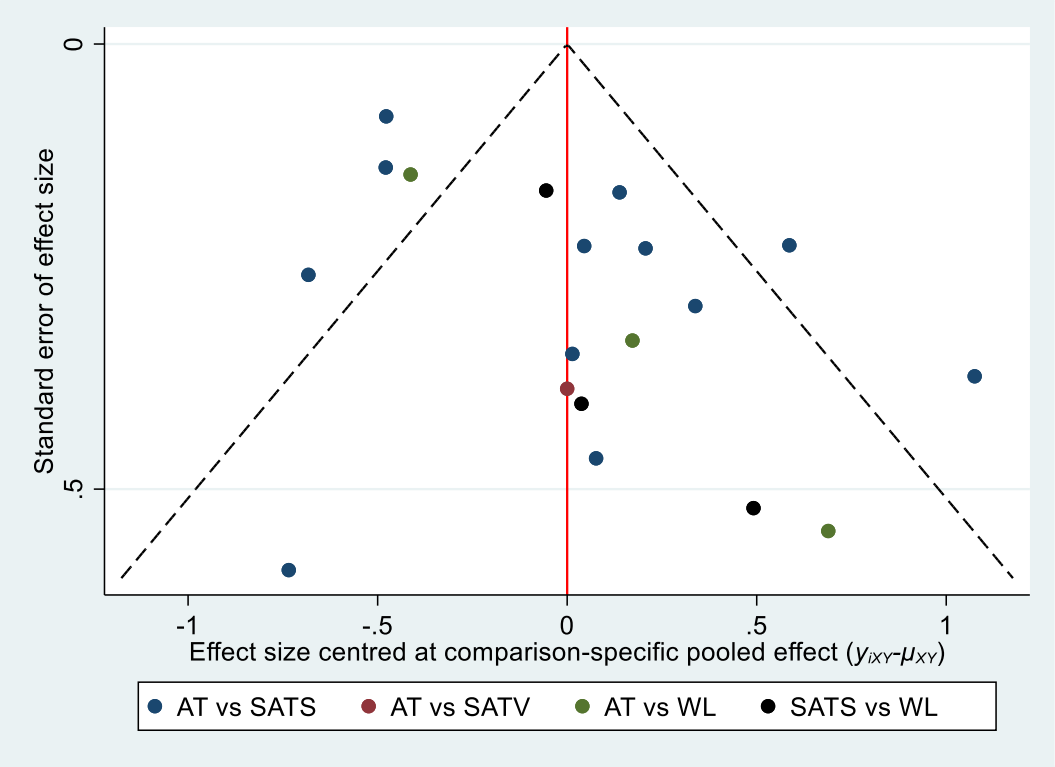

AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; WL, waiting list.

**Supplement 6. Risk of bias summary for all included studies**




Low, unclear, and high risk, respectively, are represented with the following symbols: “+”, “?”, and ″-″.

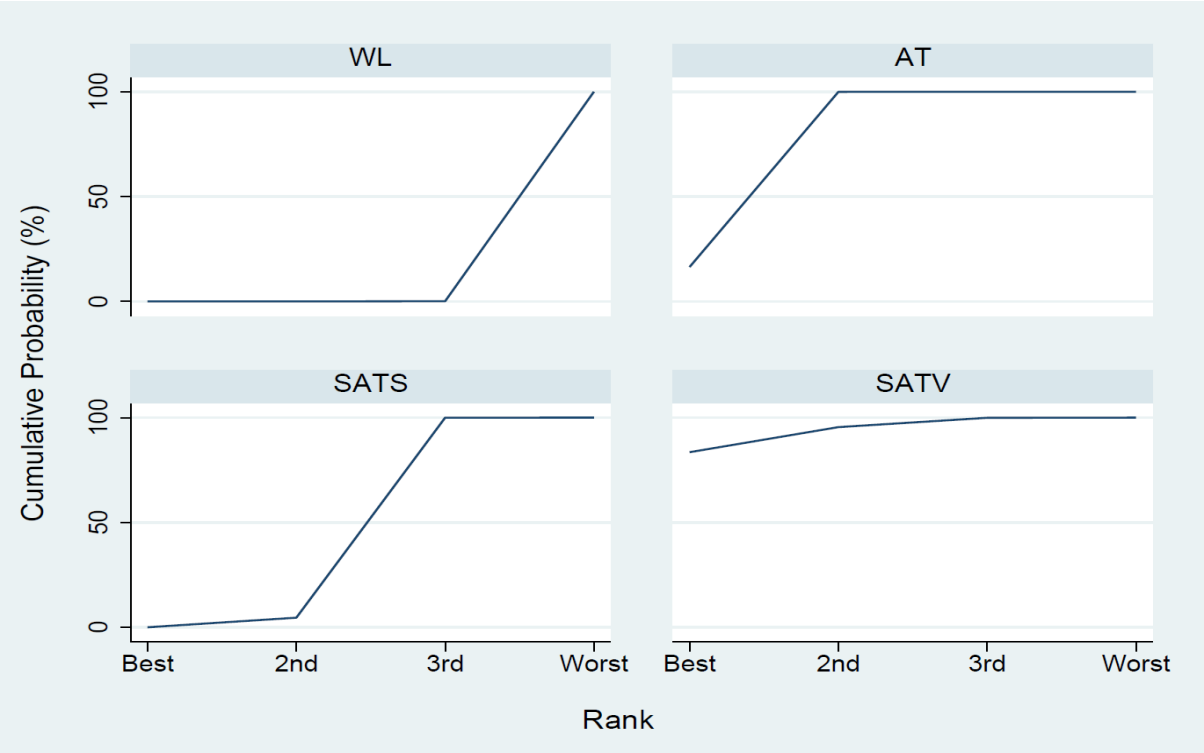
**Supplement 7. Funnel plot for headache pain intensity**



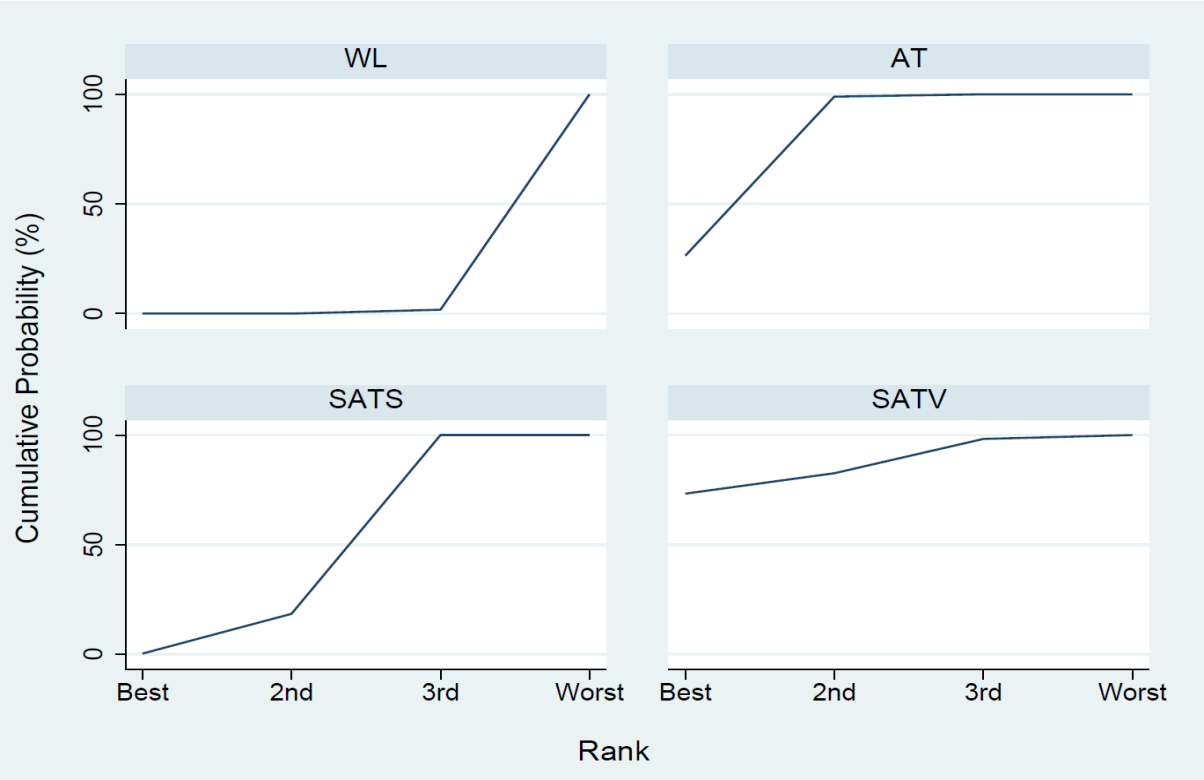

AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; WL, waiting list.

**Supplement 8. SUCRA plots**

(a) Headache pain intensity




(b) Response rate




AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; WL, waiting list.

**Supplement 9. The certainty of the evidence**

| Comparison | | Direct evidence | Indirect evidence | Network meta-analysis |
|---|---|---|---|---|
| **Headache pain intensity** | | | | |
| AT | SATS | Low<br>Inconsistency (-1)<br>Publication bias (-1) | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) |
| AT | SATV | High | - | Moderate<br>Imprecision (-1) |
| AT | WL | Moderate<br>Risk of bias (-1) | Low<br>Inconsistency (-1)<br>Publication bias (-1) | Moderate<br>Risk of bias (-1) |
| SATS | SATV | - | Low<br>Inconsistency (-1)<br>Publication bias (-1) | Very Low<br>Inconsistency (-1)<br>Publication bias (-1)<br>Imprecision (-1) |
| SATS | WL | Moderate<br>Risk of bias (-1) | Low<br>Inconsistency (-1)<br>Publication bias (-1) | Moderate<br>Risk of bias (-1) |
| SATV | WL | - | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) |
| **Response rate** | | | | |
| AT | SATS | High | Moderate<br>Risk of bias (-1) | High |
| AT | SATV | High | - | Moderate<br>Imprecision (-1) |
| AT | WL | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) |
| SATS | SATV | - | High | Moderate<br>Imprecision (-1) |
| SATS | WL | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) |
| SATV | WL | - | Moderate<br>Risk of bias (-1) | Moderate<br>Risk of bias (-1) |

AT, acupuncture therapy; SATS, Sham acupuncture therapy at non-indicated sham points; SATV, Sham acupuncture therapy at the same acupuncture points as the verum acupuncture group; WL, waiting list.