Journal of Pain Research

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REVIEW

# Effectiveness of Acupuncture for Neck Pain: Systematic Review and Meta-analysis with Trial Sequential Analysis

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**Purpose and Objectives:** Acupuncture is widely utilized intervention for neck pain. Previous research has indicated that acupuncture effectively reduces pain intensity of neck pain. However, its validity remains inconclusive due to repeated significance testing. We aimed to examine the efficacy and safety of acupuncture for neck pain through meta-analysis and trial sequential analysis (TSA).

**Methods:** We searched the OVID Medline, Embase, and Cochrane Library from inception to October 30, 2024. Randomized controlled trials (RCTs) comparing acupuncture with inert treatment, manual therapy, or other active treatments for neck pain in adults were included.

**Results:** Twenty-six trials involving 3520 participants were included. Thirteen (50%) trials were at a low risk of bias. Acupuncture treatment demonstrated significantly greater reductions in pain intensity (mean difference [MD] –1.26, 95% confidence interval [CI] –1.77 to –0.75, $P < 0.001$) and pain perception (MD –3.46, 95% CI –5.71 to –1.21, $P = 0.003$) compared with inert treatment. The TSA revealed that the cumulative Z-curves for both analyses intersected the TSA cut-off in favor of acupuncture, with the total sample size exceeding the required information size (RIS). Additionally, acupuncture was superior to inert treatment in reducing functional disability after treatment (MD –6.52, 95% CI –9.8 to –3.2, $P < 0.001$), with cumulative sample size reaching RIS. Acupuncture also showed significant improvements in quality of life. The cumulative z-curve intersects with the TSA cut-off, which is beneficial to acupuncture.

**Conclusion:** In conclusion, despite the very low to moderate quality of evidence and high heterogeneity that weaken the pooled estimates, our analysis suggests acupuncture might be a safe and effectiveness therapy for neck pain, a finding corroborated by TSA. These results position acupuncture as a potential treatment option, particularly for patients with an inadequate response to conventional therapies. Future high-quality trials are unequivocally needed to strengthen this evidence.

**Keywords:** acupuncture, neck pain, meta-analysis, trial sequential analysis, systematic review

## Introduction

Neck pain is a common cause of pain and disability worldwide, often accompanied by symptoms such as limited movement and muscle stiffness.[1,2] According to the course of the disease, it can be divided into acute (< 4 weeks), subacute (4–12 weeks) and chronic (> 12 weeks). It is estimated that the global prevalence is 223 million people and 22 million people have disabilities.[3] Neck pain seriously affects the quality of life of patients, and about 30–50% of patients suffer from reduced work efficiency or even inability to work due to pain, resulting in significant socio-economic burden.[4–7] Low back and neck pain is

Received: 5 August 2025
Accepted: 4 November 2025
Published: 25 November 2025

one of the leading causes of healthcare spending, estimated at $134.5 billion in the United States in 2016, while Belgium accounts for an average 3 billion € in medical expenses and 2 billion € in indirect costs per year.[8,9]

Pharmacological treatments for neck pain, such as non-steroidal anti-inflammatory drugs and muscle relaxants can relieve pain, but long-term use may trigger adverse reactions and have limited efficacy for chronic neck pain.[10–12] Current evidence also emphasizes that the treatment of neck pain should focus on non-drug therapy, drugs as an adjuvant, and avoid long-term use of opioids.[13,14] As an important part of non-pharmacological therapy, acupuncture has been widely used to treat pain diseases.[15] Furthermore, accumulating evidence demonstrates its efficacy for a spectrum of non-pain conditions, such as constipation in cancer patients,[16] irritable bowel syndrome,[17] and urticaria,[18] broadening its recognized therapeutic scope. Distinguishing its specific physiological effects from non-specific placebo effects is a challenge in evaluating the clinical value of acupuncture. Whereas comparisons with sham controls are necessary to establish effect specificity, direct comparisons against active treatments (eg, physiotherapy, manual therapy) are essential to determine its position as an alternative or adjunctive therapy.

Existing RCTs show that acupuncture can reduce the intensity of neck pain, improve neck dysfunction, improve patients' quality of life, and have fewer adverse reactions.[19–21] However, previous meta-analyses on acupuncture for neck pain have several limitations. Their methodology is often constrained by the small sample sizes, high heterogeneity, and bias risks of the included trials, leading to inconsistencies in the pooled effect sizes and conclusions.[22–25] Furthermore, when updated periodically with data from small sample size trials, repeated significance testing increases the likelihood of type I errors, consequently overestimating the therapeutic efficacy of acupuncture.[26,27] Therefore, although the current published trial design is of sufficient quality, the research efficacy of the current meta-analysis is still questioned, the evidence strength of acupuncture for neck pain is not quantified, and clinical practice and follow-up studies lack more reliable evidence-based evidence.

Trial sequential analysis (TSA) integrates cumulative meta-analysis with sequential hypothesis testing to reduce type I errors (false positives) by adjusting the significance threshold and calculating the required information size (RIS).[28–30] TSA corrects the meta-analysis results by establishing a test sequential monitoring boundary (TSMB), which comprises both the statistical significance boundary and the invalidity boundary of the intervention effect.[29,30] When the cumulative sample size exceeds the RIS or the Z curve crosses the TSMB, it suggests that the existing evidence is sufficient and no repeatability test is required. Conversely, further research is needed to verify the intervention's effect.

Based on the aforementioned facts, we conducted a systematic review with meta-analysis and a TSA to compare the efficacy of acupuncture with inert treatment, manual therapy, and other active treatments for neck pain. To examine whether acupuncture is effective for neck pain after adjustment for significance levels and to explore whether new trials are warranted for specific outcomes (ie pain intensity, functional disability, pressure pain threshold, and pain perception).

# Methods

Our systematic review and meta-analysis were designed and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and meta-Analyses (PRISMA) guidelines.[31] Our study had registered at Open Science Framework (https://doi.org/10.17605/OSF.IO/ZH8RE).

## Search Strategy

We searched the OVID Medline, Embase, and Cochrane Library from inception to October 30, 2024, with the publication language limited to English. The details of the retrieval strategy are provided in eTables 1–3. The clinical registry (clinicaltrials.gov) was also searched for randomized controlled trials (RCTs) that were completed but unpublished. We also searched previously published systematic reviews and read their reference lists to search for any missing RCT.

## Eligibility Criteria

The study eligibility criteria were defined according to the PICOS (Population, Intervention, Comparison, Outcomes, Study Design) framework.

### Population

Eligible participants were adults (≥ 18 years) diagnosed with neck pain, classified as follows: (1) Neck pain, including non-specific, mechanical or simple neck pain of unknown etiology; myofascial pain syndrome in the upper trapezius region; neck pain associated with degenerative changes; and whiplash-related disorder (WAD) classes I and II; (2) Neck diseases with nerve root manifestations, including degenerative joint or intervertebral disc diseases with spinal stenosis, spondylolisthesis or discogenic radiculopathy; and WAD class III; (3) Neck pain related to cervicogenic headache.[32,33]

We excluded participants with the following characteristics: (1) Clear or possible signs of long bundles involvement (eg, myelopathy); (2) Neck pain due to other pathological entities (eg, head and neck cancer, fibromyalgia and rheumatoid arthritis); (3) Headaches not caused by neck issues but associated with neck pain; (4) Coexisting headaches where neck pain was not the primary issue or where headaches were not triggered by neck movement or sustained neck posture; (5) "Mixed" headache subtypes (eg, migraine and cervicogenic headache); (6) Myofascial pain confined to the lower trapezius region (shoulder pain).[32,33]

For studies that included participants with pain at multiple anatomical sites (eg, back, neck, shoulders, legs), we included only those studies that presented subgroup outcomes specifically for neck pain.

### Intervention

Trials were eligible if they included at least one group receiving any form of acupuncture therapy.

### Comparison

Eligible control groups included: (1) Inert treatment: any type of intervention described as no intervention, placebo acupuncture, sham acupuncture, or waiting list treatment; (2) Manual therapy: including high-velocity low-amplitude /thrust manipulation; mobilization, such as passive mobilization, mobilization -with-movement; soft tissue techniques such as massage, myofascial techniques, trigger point manual treatment, and tuina; and manual traction; (3) Other active therapies: including usual care, physical agents, traction and non-steroidal anti-inflammatory drugs (NSAIDs).[22]

## Outcomes

We included RCTs evaluating any of the following outcomes: pain intensity, functional disability, pressure pain threshold, pain perception, quality of life, and adverse events. The primary outcome was pain intensity, measured using the visual analog scale and the numerical pain rating scale. Secondary outcomes included: (1) Functional disability, assessed via the neck disability index and the Northwick Park neck pain questionnaire; (2) Pressure pain threshold; (3) Pain perception, evaluated using the McGill pain questionnaire and the simplified McGill pain questionnaire; (4) Quality of life, including short form 36 (SF-36) and short form 12 (SF-12); (5) Adverse events, if no adverse events are mentioned in the study, it is assumed that no adverse events are measured. Outcomes were categorized into two periods: post-treatment and follow-up. The length of follow-up in this study was not limited. For the primary outcome measured at multiple follow-up time points, the data closest to the end of treatment were utilized.

## Study Design

RCTs with the parallel design and crossover design RCTs reporting the first period data separately (prior to treatment group crossover) were included.

## Data Extraction

Two reviewers (C-RX and Z-YZ) independently screened the titles and abstracts of the identified studies and reviewed the full texts to determine the eligibility of RCTs. Any disagreements regarding RCT eligibility were resolved through panel discussion, with arbitration by a third evaluator (LZ). Two evaluators (C-RX and Q-FT) extracted data from included RCTs using standardized extraction forms. Including: (1) Name of the first author, year of publication, country, study design, neck pain classification, sample size, average age of participants, and proportion of women; (2) Detailed information on the intervention and control group, including names of interventions and treatment durations. (3) Results

data, including outcome names, number of participants in each treatment group, means, and criteria for continuous data. Disagreements in data extraction were also resolved through panel discussion and arbitrated by a third examiner (LZ).

## Risk of Bias Assessment

The risk of bias (RoB) in the included trials was evaluated using the second version of the Cochrane Risk of Bias Tool.[34] Each study was assessed across five domains to determine the overall RoB level: (1) Randomization process; (2) Deviations from intended interventions; (3) Missing outcome data; (4) Measurement of the outcome; (5) Selection of the reported result. Studies were ultimately classified as low RoB, some concern RoB, or high RoB. The RoB assessment was conducted using an Excel template by two independent reviewers, with discrepancies resolved through discussion.

## Statistical Analysis

Conventional meta-analysis was performed using the meta package (R 4.4.3, www.r-project.org). Effect sizes for all outcomes were calculated as mean differences (MD) with corresponding 95% confidence intervals (CIs). Heterogeneity among RCTs was assessed using the $I^2$ statistic.[35] When $I^2 < 50\%$, results were summarized using a fixed-effects model (inverse variance method); When $I^2 \geq 50$, indicating significant heterogeneity, a random effects model (DerSimon Laird method) was employed. To test the robustness of the study results, a leave-one-out sensitivity analysis was conducted, evaluating the impact of removing one study at a time from the meta-analysis.

TSA was performed to calculate the RIS and TSMB using TSA 0.9. 5.10 beta (https://www.ctu.dk/tsa/). A type I error rate of 0.05 and a type II error rate of 0.2 were allowed in the TSA analysis when estimating the RIS. Significance boundaries were calculated using the O'Brien-Fleming alpha spending function to ensure that the overall risk of type I error remained within 5%. The "sample size" was set as the "information axis", with the MD and variance estimated based on software-generated empirical assumptions. The correction for heterogeneity was based on "Model Variance".

### The Certainty of the Evidence

The certainty of the evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Evidence levels were categorized as high, moderate, low, or very low based on five criteria: risk of bias, inconsistency, indirectness, imprecision, and additional considerations.

# Result

## Characteristics of the Included RCTs

The search process yielded 1220 records, and after screening, we finally included 26 RCTs involving 3520 participants.[19–21,36–58] Figure 1 shows the screening process of the systematic review, and the main characteristics of the included RCTs are shown in Table 1. The studies were conducted across twelve countries. Fifteen RCTs recruited participants with chronic neck pain, nine involved unclassified neck pain (including neck pain, myofascial pain syndrome and whiplash), one focused on acute neck pain, and one included both subacute and chronic whiplash.

The proportion of female participants was 71.1%, with a mean age of 40.7 years. Seventeen studies compared acupuncture to inert treatments; six studies compared acupuncture with manual therapy, and three studies compared acupuncture with other active treatments (including NSAIDs, physical agent, and usual care). The RoB assessment for the included RCTs is presented in eFigure 1. Thirteen RCTs were classified as low risk, ten as some concerns, and three as high risk.

## Pain Intensity

### Acupuncture vs Inert Treatment

Seventeen studies (n = 1916, $I^2 = 89.9\%$) were included to compare the effects of acupuncture versus inert treatment on pain intensity. Acupuncture demonstrated superiority over inert treatment in reducing neck pain intensity both after treatment (MD –1.26, 95% CI –1.77 to –0.75, $P < 0.001$, Figure 2A) and at follow-up (13 trials, n=1814; $I^2$ =74.8%; MD –0.88, 95% CI –1.23 to –0.53, $P < 0.001$, eFigure 3A). Sensitivity analyses confirmed the robustness of these findings (eFigures 2A and 3B), but the GRADE evidence was very low (eTables 4 and 5).

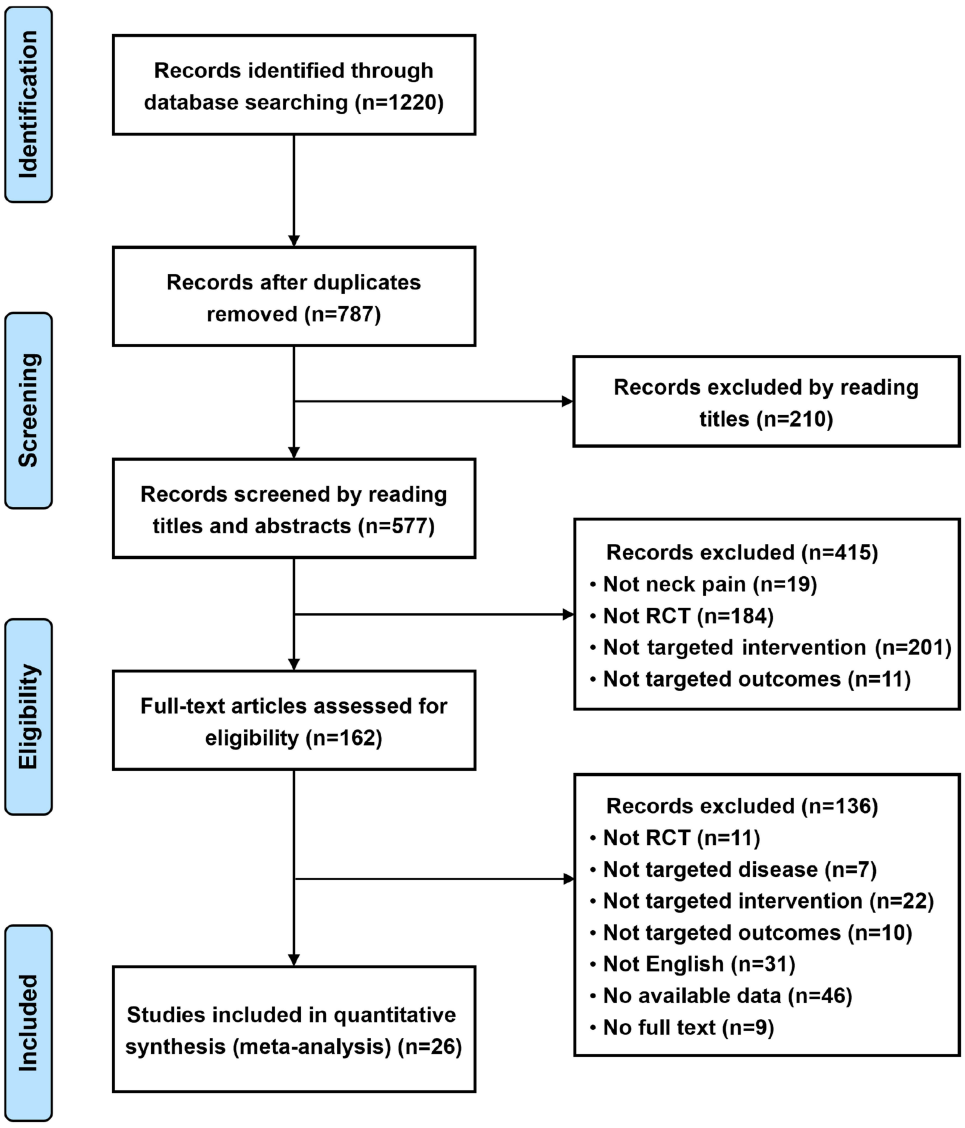


**Figure 1** PRISMA flow diagram of literature search and study selection.

TSA showed that the cumulative Z-curves crossing both traditional level of statistical significance and TSMB (after treatment, Figure 2B; follow-up, eFigure 3C). The accrued sample sizes (after treatment, n=649; follow-up, n=586) exceeded the RIS, providing conclusive evidence for acupuncture's effectiveness over inert treatment.

## Acupuncture vs Manual Therapy

Six studies (n = 329, $I^2$ = 52.9%) compared acupuncture with manual therapy. Acupuncture showed superior pain reduction after treatment (MD –0.66, 95% CI –0.96 to –0.37, $P < 0.001$, eFigure 4A), with stable results in sensitivity analysis (eFigure 4B). However, three studies (n = 219, $I^2$ = 74.9%) showed no significant between-group difference at follow-up (MD –0.87, 95% CI –1.85 to 0.11, $P = 0.083$, eFigure 5A), and sensitivity analysis showed stable results (eFigure 5B). The GRADE showed the quality-evidence was low (eTables 6 and 7).

TSA showed that the cumulative Z-curve crossing both traditional level of statistical significance and TSMB after treatment (after treatment, n = 342, eFigure 4C; follow-up, n = 575, eFigure 5C). This provides definitive evidence for the short-term analgesic advantage of acupuncture over manual therapy.


https://doi.org/10.2147/JPR.S558059

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**Table 1** Characteristics of the Included Trials

| Study | Country | Sample Size | Mean Ages | Female (%) | Participants | Diagnostic Criteria/Scale | Interventions | Treatment (Weeks) | Follow-up (Weeks) |
|---|---|---|---|---|---|---|---|---|---|
| Aki 2020[36] | Turkey | 40 | 37.4 | 57.5 | Chronic mechanical neck pain | NDI score ≥ 5 | Acupuncture vs manual therapy | 4 | 0 |
| Cameron 2011[37] | Australia | 124 | 41.8 | 55 | Subacute and chronic whiplash | Quebec Task Force Classification for WAD (Grade I or II) | Acupuncture vs Inert treatment | 6 | 24 |
| Chen 2020[20] | China | 896 | 42.1 | 66 | Neck pain | ICD-10-defined cervical spondylosis-related neck pain | Acupuncture vs Inert treatment | 4 | 12 |
| Cho 2014[38] | Korean | 45 | 38.8 | 64.4 | Chronic neck pain | VAS score ≥ 5 | Acupuncture vs NSAIDs | 3 | 4 |
| Fu 2009[39] | China | 117 | 40.6 | 72.6 | Neck pain | "Standard for Diagnosis and Efficacy Evaluation of TCM Syndromes and Diseases" (1994)-Cervical/Nerve Root | Acupuncture vs Inert treatment | 3 | 12 |
| Ho 2017[40] | China | 154 | 45 | 81.2 | Neck pain | Criteria for degenerative joint disease or cervical spondylosis, VAS score ≥ 3 | Acupuncture vs Inert treatment | 2 | 4 |
| ILBULDU 2004[41] | Turkey | 60 | 33.8 | 100 | Myofascial pain syndrome | Local/referred pain, taut band, point tenderness, restricted movement | Acupuncture vs Inert treatment | 4 | 24 |
| Irnich 2001[42] | Germany | 177 | 52.4 | 66.1 | Chronic neck pain | The Schöps and Senn diagnostic system | Acupuncture vs manual therapy | 3 | 12 |
| Itoh 2007[43] | Japan | 40 | 63.2 | 72.5 | Chronic neck pain | Non-radiating neck pain | Acupuncture vs Inert treatment | 8 | 3 |
| Kwak 2011[44] | Korean | 40 | 45.2 | 60 | Whiplash-associated disorder | Cervical and related symptoms following a car accident, VAS score 2-7 | Acupuncture vs Inert treatment | 2 | 0 |
| Llamas-Ramos 2014[45] | Spain | 94 | 31 | 66 | Chronic mechanical neck pain | Taut band hypersensitive spot, local twitch response, and referred pain reproduction | Acupuncture vs manual therapy | 1 | 2 |
| Mejuto-Vázquez 2014[46] | Spain | 17 | 24.5 | 52.9 | Acute mechanical Neck Pain | Neck-shoulder pain provoked by posture, movement, or palpation; characteristic signs of upper trapezius trigger points | Acupuncture vs manual therapy | 1 | 1 |
| Nabeta 2002[47] | Japan | 34 | 32.5 | 55.8 | Chronic neck pain | Chronic dull pain and stiffness of the neck and shoulder without any arm symptoms | Acupuncture vs Inert treatment | 3 | 0 |
| Petrie 1986[48] | UK | 27 | 50.5 | 64 | Chronic neck pain | Pain arising from neck, with or without radiation to shoulders/occiput | Acupuncture vs Inert treatment | 4 | 4 |
| Rayegani 2013[49] | Iran | 37 | 35.3 | NA | Myofascial pain syndrome | Radiating shoulder pain, palpable taut bands/trigger points, compression reproduces familiar pain | Acupuncture vs Physical agents | 1 | 4 |
| Sahin 2010[50] | USA | 31 | 36.9 | 89.7 | Chronic neck pain | Chronic mechanical neck pain, VAS score ≥ 3 | Acupuncture vs Inert treatment | 4 | 12 |
| Segura-Ortí 2016[51] | USA | 34 | 32.3 | 73.5 | Neck pain | Active MTPs in upper trapezius (referred pain, palpation, and contraction/stretch) | Acupuncture vs Inert treatment | 3 | 0 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Teixeira 2019[52] | Portugal | 31 | 40.9 | 58.1 | Neck pain | Nonspecific cervical pain with mechanical characteristics and mobility deficits | Acupuncture vs Inert treatment | 1 | 0 |
| Valiente-Castrillo 2020[53] | Spain | 62 | 41 | 85 | Chronic myofascial neck pain | Active MTrP criteria (taut band, tenderness, referred pain), NDI score ≥ 5, VAS score ≥ 3 | Acupuncture vs usual care | 2 | 12 |
| Vas 2006[54] | Spain | 123 | 46.7 | 82.1 | Chronic neck pain | VAS score ≥ 3 | Acupuncture vs Inert treatment | 3 | 24 |
| Voulgarakis 2021[55] | Greece | 45 | 41.7 | 66.7 | Chronic Neck Pain | Medical report with neck pain diagnosis | Acupuncture vs manual therapy | 8 | 0 |
| White 2004[21] | UK | 135 | 53.4 | 64.4 | Chronic mechanical neck pain | VAS score ≥ 3 | Acupuncture vs Inert treatment | 4 | 48 |
| Yeganeh Lari 2015[56] | Iran | 60 | 25 | 100 | Myofascial pain syndrome | Latent MTrP in upper trapezius (palpable taut band, nodule, and tender spot at 25N) | Acupuncture vs manual therapy | 1 | 0 |
| Zeng 2021[57] | China | 175 | 39.8 | 82.9 | Neck pain | VAS score ≥ 3 | Acupuncture vs Inert treatment | 3 | 12 |
| Zhang 2013[58] | China | 206 | 45.8 | 70 | Chronic neck pain | Chronic mechanical neck pain | Acupuncture vs Inert treatment | 3 | 24 |
| Zhao 2024[19] | China | 716 | 39.4 | 72.2 | Chronic neck pain | APTA Clinical Practice Guidelines (orthopedic section), VAS score ≥ 3 | Acupuncture vs Inert treatment | 4 | 24 |

**Abbreviations**: APTA, American Physical Therapy Association; ICD-10, International Classification of Diseases, 10th edition; MTPs/ MTrP, Myofascial Trigger Points; NDI, neck disability index; NPQ, Northwick Park Neck Pain Questionnaire; TCM, Traditional Chinese Medicine; VAS, visual analogue scale; WAD, whiplash-associated disorders.

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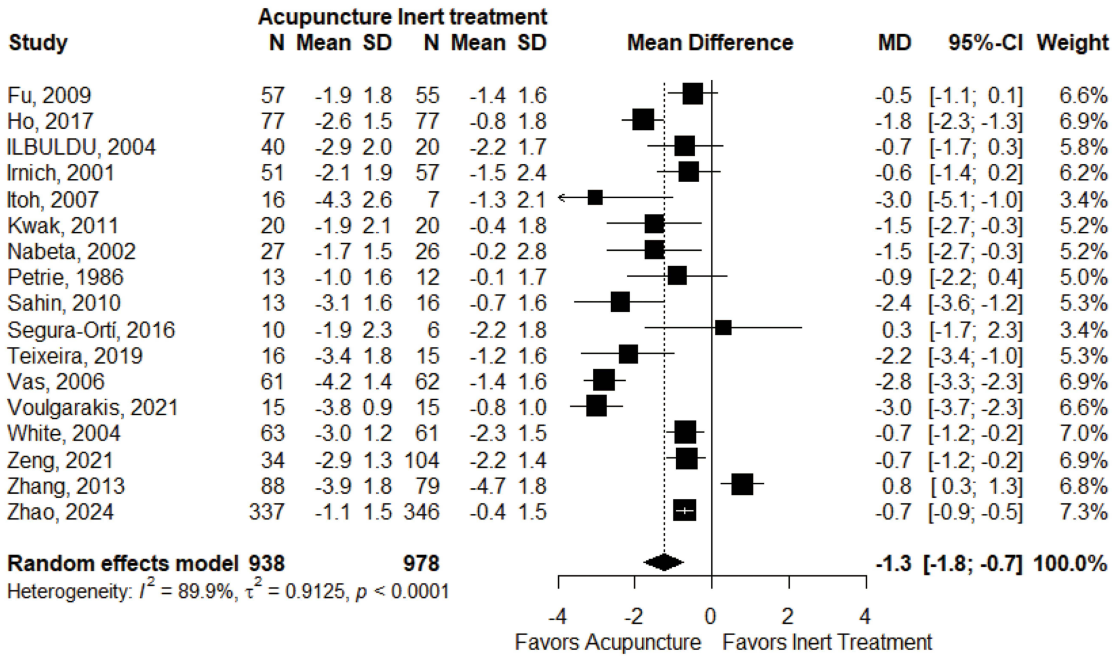
**A**




**B**

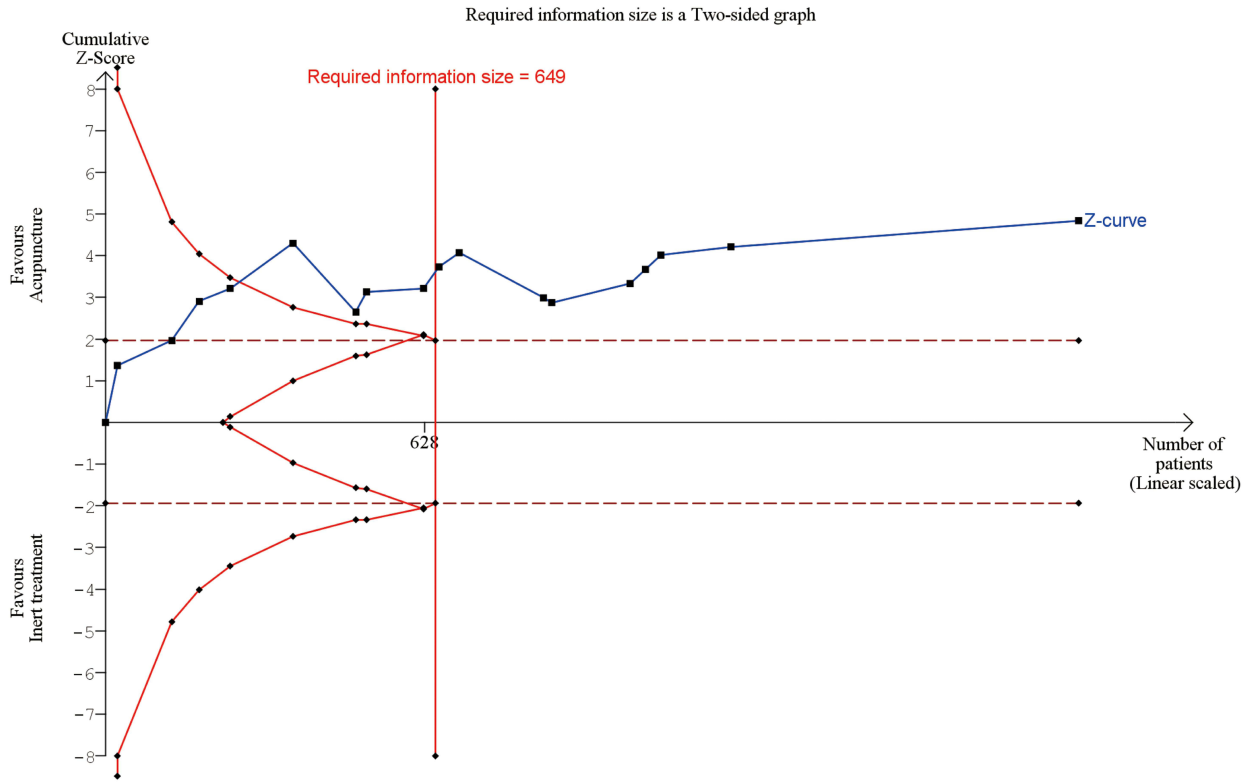



**Figure 2** Meta-analysis (**A**) and TSA (**B**) of acupuncture vs inert treatment in the pain intensity after treatment.

**Notes**: TSA, trial sequential analysis. The blue curve represents the Z-curve, the red curves above and below represent trial sequential monitoring boundaries, the dashed red line represents the traditional level of statistical significance, and the red vertical line represents required information size value, the red lines on the sides closest to the horizontal line are boundaries for futility.

**Abbreviations**: CI, confidence interval; MD, mean difference; N, number; SD, standard deviation.

### Acupuncture vs Other Active Treatments

One study each found that acupuncture led to greater pain reductions than NSAIDs or usual care, both after treatment (eFigure 6A and B) and at follow-up (eFigure 6E and F). However, there were no significant differences between acupuncture and physical therapy (eFigure 6C and G) or traction (eFigure 6D).

## Functional Disability

### Acupuncture vs Inert Treatment

Twelve RCTs (n = 2166, $I^2$ = 91.3%) were compared. The results revealed that acupuncture was significantly more effective in reducing functional disability compared to inert treatment both after treatment (MD –6.52, 95% CI –9.83 to –3.20, $P < 0.001$, Figure 3A) and at follow-up (10 trials, n = 2102, $I^2$ = 87.9%; MD –4.74, 95% CI –7.72 to –1.76, $P = 0.002$, eFigure 7A). Sensitivity analyses confirmed the robustness of these findings (eFigures 2B and 7B), but the GRADE evidence was very low (eTables 4 and 5).

TSA showed that the cumulative Z-curve crossed the traditional level of statistical significance and the sample sizes exceeding the RIS (after treatment, Figure 3B, n = 1139; follow-up, eFigure 7C, n = 1693), and the cumulative Z-curve of follow-up crossed the TSMB. These results provide definitive evidence that acupuncture significantly reduces functional disability compared to inert treatment.

### Acupuncture vs Manual Therapy

The study found no significant difference between acupuncture and manual therapy in functional disability improvement after treatment (2 trials, n = 70, $I^2$ = 28%; MD –1.85, 95% CI –4.26 to 0.56, $P = 0.133$, eFigure 8A) and at follow-up (1 trial: MD –0.90, 95% CI –3.72 to 1.92, $P = 0.532$, eFigure 8B). This finding remained consistent in sensitivity analysis (eFigure 8C), but the GRADE evidence was low (eTable 6) or very low (eTable 7).

TSA indicated insufficient evidence, with the cumulative Z-curve failing to cross the traditional cutoff value and the TSMB, and the cumulative sample size not reaching the RIS (eFigure 8D, n = 338). These findings suggest that current evidence is inadequate to establish comparative effectiveness between acupuncture and manual therapy for functional disability.

### Acupuncture vs Other Active Treatments

One study showed that acupuncture was superior to usual care at both after treatment and at follow-up (eFigure 9A and D). However, the other two studies showed no significant differences between acupuncture and NSAIDs (eFigure 9B and E) or traction (eFigure 9C).

## Pressure Pain Threshold

### Acupuncture vs Inert Treatment

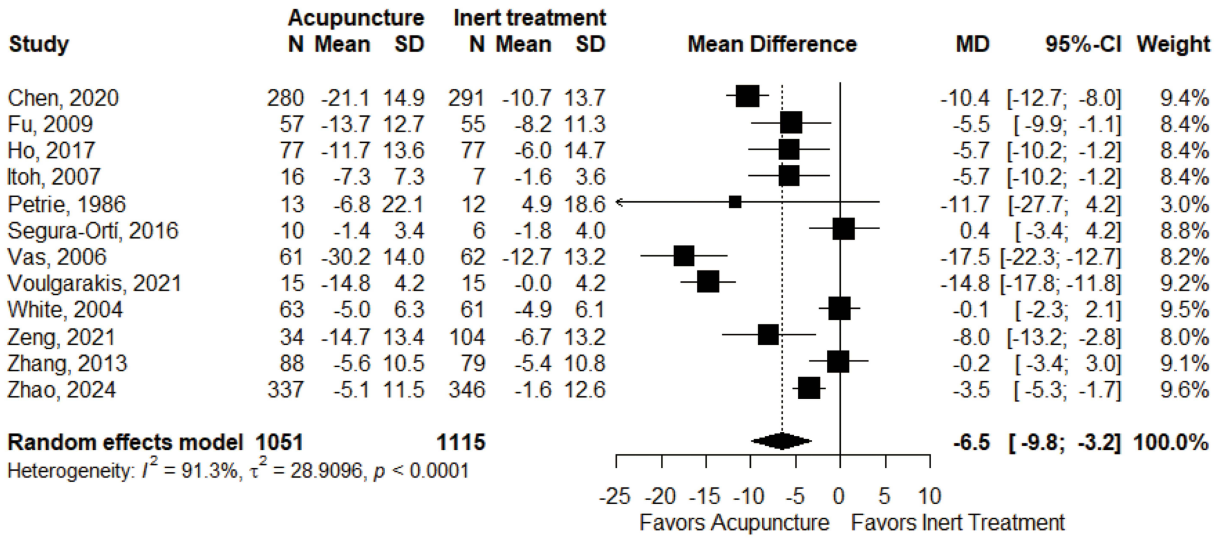
Four studies were included (n = 211, $I^2$ = 86.9%). The results showed no significant difference between acupuncture and inert treatment in raising the pressure pain threshold both after treatment (MD 0.52, 95% CI –0.03 to 1.07, $P = 0.063$, Figure 4A) and at follow-up (2 trials, n = 168, $I^2$ = 0%; MD –0.18, 95% CI 0.002 to 0.36, $P = 0.047$, eFigure 10A). Sensitivity analysis verified that these results were robust (eFigures 2C and 10B), and GRADE evidence was low (eTable 4) or moderate (eTable 5).

TSA showed that after treatment and during follow-up, the cumulative Z-curve did not cross the TSMB and the cumulative sample size did not exceed the RIS (after treatment, n = 469, Figure 4B; follow-up, n = 388, eFigure 10C), indicating the lack of conclusive evidence supporting a significant difference in pressure pain threshold between acupuncture and inert treatment, which still needs more trials to demonstrate.

### Acupuncture vs Manual Therapy

We compared 4 studies (n = 259, $I^2$ = 87.6%), and found that acupuncture improved the pressure pain threshold better than manual therapy both after treatment (MD 0.59, 95% CI 0.04 to 1.14, $P = 0.035$, eFigure 11A) and at follow-up (3 trials, n=219; $I^2$ = 88.0%; MD 0.56, 95% CI 0.06 to 1.06, $P = 0.027$, eFigure 12A). Sensitivity analysis verified that the results were robust (eFigures 11B and 12B). The GRADE showed the quality-evidence was low (eTables 6 and 7).

**A**

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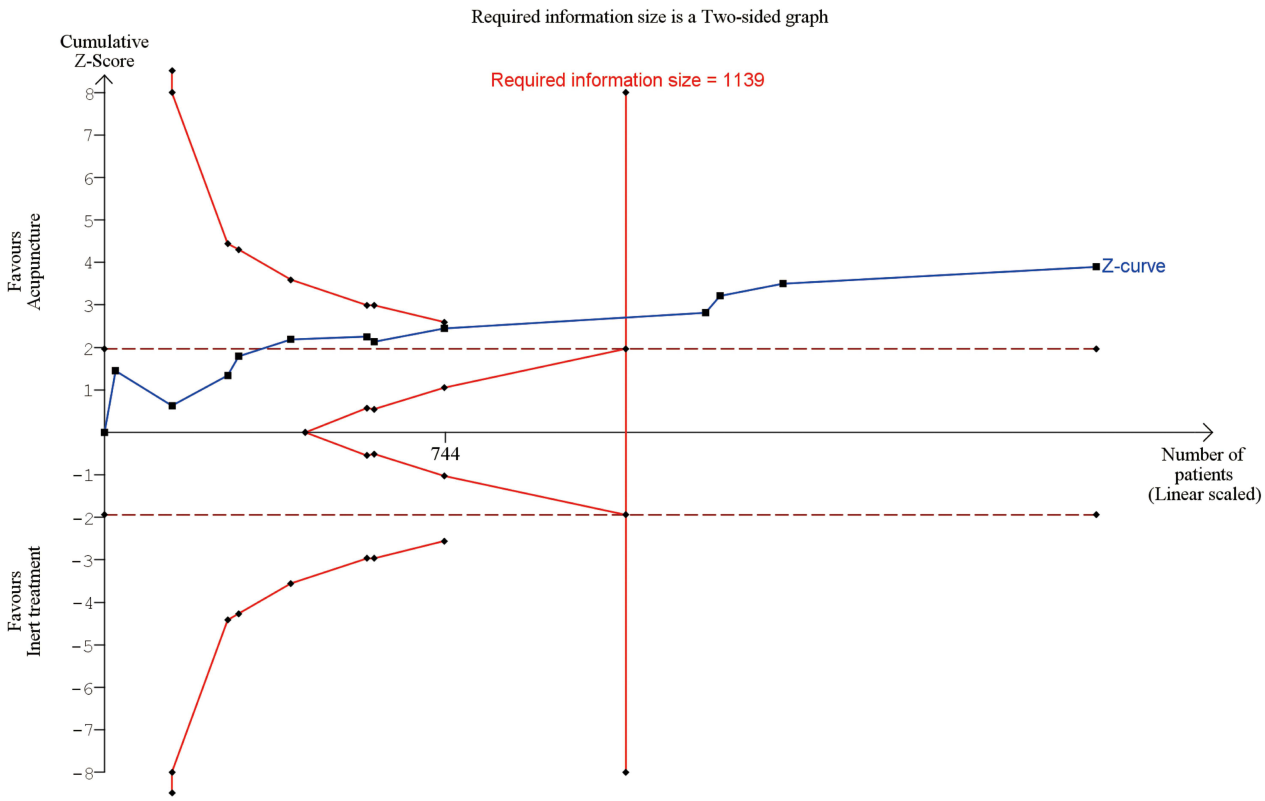


**Figure 3** Meta-analysis (**A**) and TSA (**B**) of acupuncture vs inert treatment in the functional disability after treatment.

**Notes**: TSA, trial sequential analysis. The blue curve represents the Z-curve, the red curves above and below represent trial sequential monitoring boundaries, the dashed red line represents the traditional level of statistical significance, and the red vertical line represents required information size value, the red lines on the sides closest to the horizontal line are boundaries for futility.

**Abbreviations**: CI, confidence interval; MD, mean difference; N, number; SD, standard deviation.

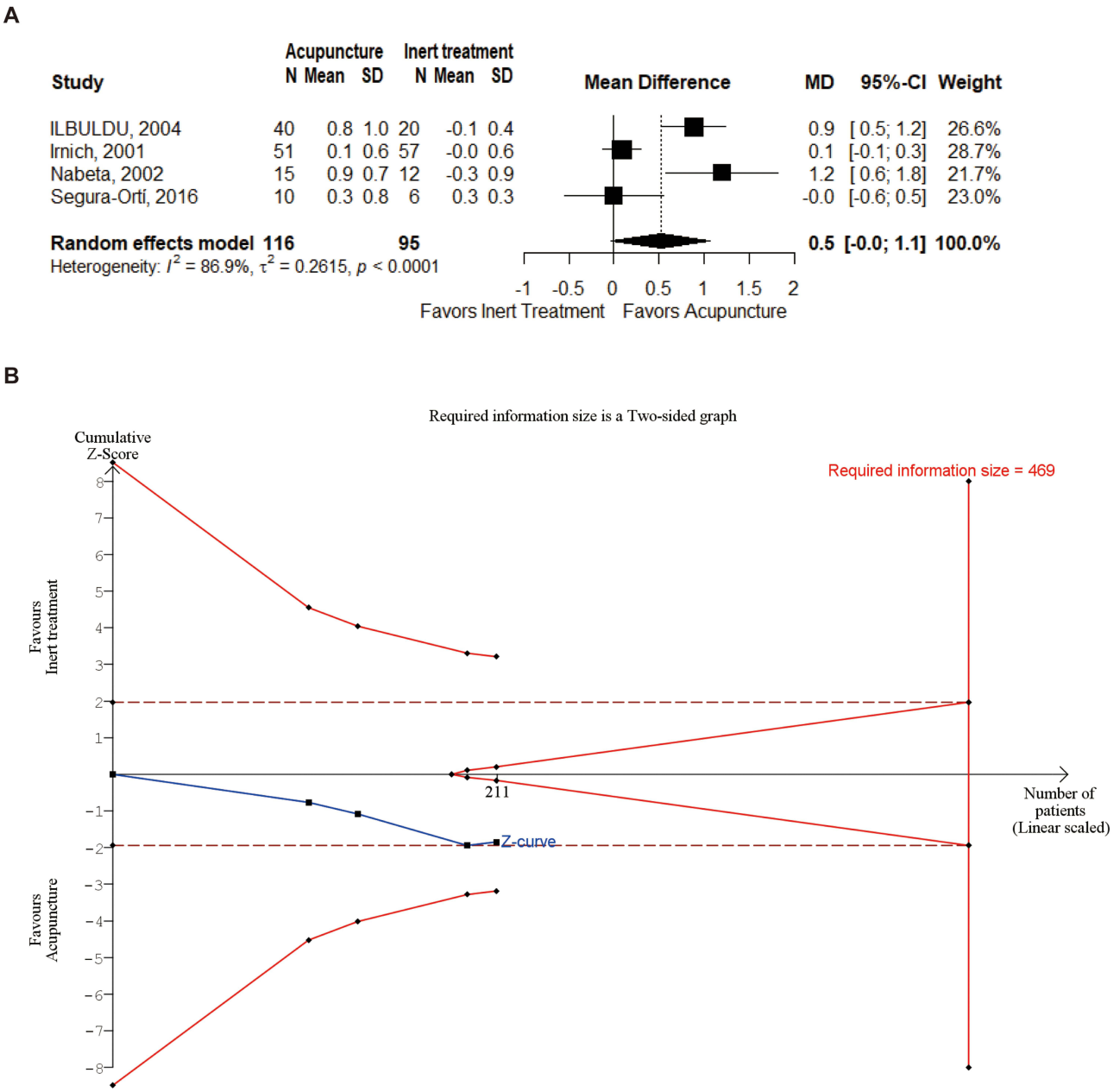


**Figure 4** Meta-analysis (**A**) and TSA (**B**) of acupuncture vs inert treatment in the pressure pain threshold after treatment.
**Notes**: TSA, trial sequential analysis. The blue curve represents the Z-curve, the red curves above and below represent trial sequential monitoring boundaries, the dashed red line represents the traditional level of statistical significance, and the red vertical line represents required information size value, the red lines on the sides closest to the horizontal line are boundaries for futility.
**Abbreviations**: CI, confidence interval; MD, mean difference; N, number; SD, standard deviation.

The TSA showed that the cumulative Z-curve did not cross the TSMB after treatment and during follow-up, and the cumulative sample size did not exceed the RIS (after treatment, n = 451, eFigure 11C; follow-up, n = 358, eFigure 12C), indicating the lack of conclusive evidence supporting a significant difference between acupuncture and manual therapy in terms of pressure pain threshold, which still needs to be demonstrated by more trials.

## Acupuncture vs Other Active Treatments

One study each found no significant differences between acupuncture and physical therapy (eFigure 13A and C) or traction (eFigure 13B).


https://doi.org/10.2147/JPR.S558059

# Pain Perception

## Acupuncture vs Inert Treatment

Four studies (n = 1417, $I^2$ = 82.3%) were included in this comparison. The results showed that acupuncture was superior to inert treatment in improving pain perception both after treatment (–3.46, 95% CI –5.71 to –1.21, $P$ = 0.003, Figure 5A) and at follow-up (5 trials, n = 1533, $I^2$ = 84.5%; MD –2.37, 95% CI –4.72 to –0.02, $P$ = 0.048, eFigure 14A). Sensitivity analysis showed stable results (eFigures 2D and 14B), and the GRADE evidence was low (eTables 4 and 5).

TSA showed that the cumulative Z-curve crossed the traditional level of statistical significance and TSMB after treatment, and the sample size exceeded the RIS (after treatment, n = 1238, Figure 5B; follow-up, n = 3377, eFigure 14C). Suggesting

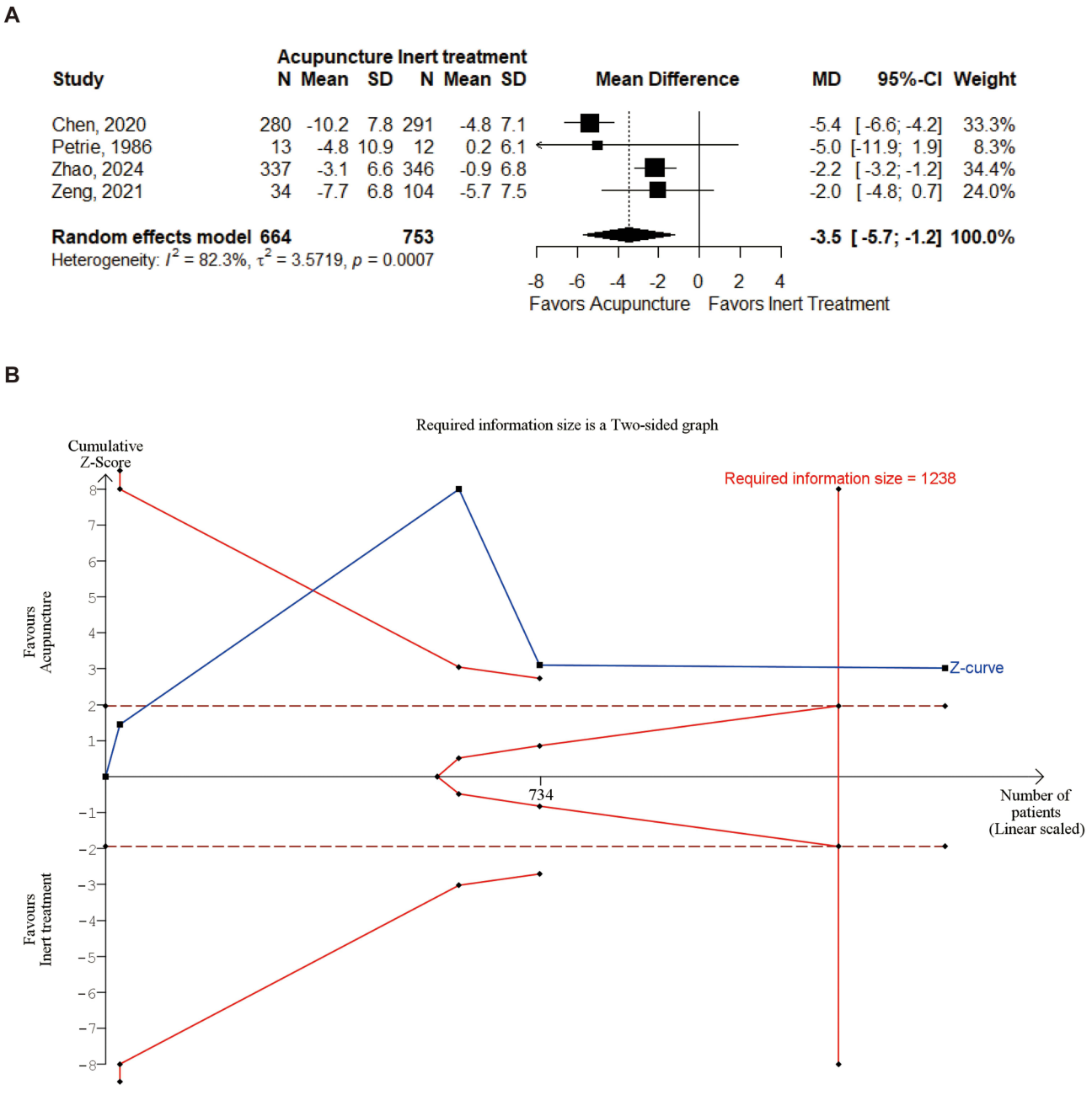


**Figure 5** Meta-analysis (**A**) and TSA (**B**) of acupuncture vs inert treatment in the pain perception after treatment.

**Notes**: TSA, trial sequential analysis. The blue curve represents the Z-curve, the red curves above and below represent trial sequential monitoring boundaries, the dashed red line represents the traditional level of statistical significance, and the red vertical line represents required information size value, the red lines on the sides closest to the horizontal line are boundaries for futility.

**Abbreviations**: CI, confidence interval; MD, mean difference; N, number; SD, standard deviation.

that there is conclusive evidence to confirm the significant difference between acupuncture and inert treatment in improving pain perception.

## Quality of Life

### Acupuncture vs Inert Treatment

A total of 6 studies assessed health-related quality of life (eFigure 15A–J and eFigure 16A–J). Compared with inert treatment, acupuncture showed significant improvements in the three dimensions of physical functioning (PF), general health (GH), and mental component summary (MCS) both after treatment (eFigure 15A, D and J) and at follow-up (eFigure 16A, D and J). Additionally, acupuncture showed benefits in the vitality domain after treatment (eFigure 15F) and the mental health domain at follow-up (eFigure 15I). Among these domains where acupuncture showed benefits, except for the MCS domain where GRADE evidence is low, the remaining 4 domains showed high evidence (eTables 4 and 5). No significant between-group differences were observed in the remaining domains. Sensitivity analyses confirmed the robustness of these findings (eFigure 17A–J and eFigure 18A–J).

The TSA (eFigure 19A–J and eFigure 20A–J) showed that the cumulative z-curves for the PF dimension (post-treatment and follow-up, eFigures 19A and 20A) and the MCS dimension (follow-up, eFigure 20J) crossed the traditional level of statistical significance and TSMB. These findings provide strong evidence that acupuncture is significantly superior to inert treatment in improving the PF domain and the MCS domain of quality of life.

## Adverse Events

### Acupuncture vs Inert Treatment

A total of 12 studies (n = 2272, $I^2$ =4.4%) were included to compare the safety of acupuncture and inert treatment after treatment. There was no significant difference between the two groups (RR 1.45, 95% CI 0.10 to 2.10; $P$ = 0.052, Figure 6A), which was stable in a sensitivity analysis (eFigure 2E). The GRADE showed low evidence of quality (eTable 4).

TSA showed that after treatment, the cumulative Z-curve did not cross the TSMB and the cumulative sample size did not exceed the RIS (n = 4426, Figure 6B), which indicates that there is no conclusive evidence to support a statistical difference in safety between acupuncture and sham acupuncture.

### Subgroup Analysis

Subgroup analysis by acupuncture classifications revealed that manual acupuncture (11 trials, n = 1398, $I^2$ = 90.2%; MD –1.63, 95% CI –2.25 to –1.01, $P$ < 0.001, eFigure 21A–C) was associated with greater reductions in neck pain intensity after treatment compared to electroacupuncture and dry needling. At follow-up, both manual acupuncture (7 trials, n = 1200, $I^2$ = 74.5%; MD –1.02, 95% CI –1.47 to –0.58, $P$ < 0.001, eFigure 22A) and electroacupuncture (4 trials, n = 446, $I^2$ = 85%; MD –0.96, 95% CI –1.87 to –0.04, $P$ = 0.040, eFigure 22B) demonstrated superior effectiveness over dry needling (eFigure 22C). Sensitivity analysis showed robust results (eFigures 23A–C and 24A and B).

The subgroup analysis including participants with chronic neck pain only showed results consistent with the main analysis. Acupuncture was significantly more effective than inert treatment in reducing pain sensation intensity both after treatment (11 trials, n = 1503, $I^2$ = 92,8%; –1.32, 95% CI –2.01 to –0.64, $P$ < 0.001, eFigure 25A) and at follow-up (9 trials, n = 1372, $I^2$ = 73.3%; –0.92, 95% CI –1.32 to –0.51, $P$ < 0.001, eFigure 25C), with stable results in sensitivity analysis (eFigure 25B and D).

# Discussion

## Summary of Evidence

Our meta-analysis suggests that acupuncture is an effective and safe intervention for neck pain management, despite very low to moderate evidence quality and high heterogeneity. Compared with inert treatment, acupuncture significantly reduces pain intensity, enhances functional ability, and improves pressure pain thresholds, pain perception, and quality of life (mental component summary, physical function). Additionally, acupuncture is superior to manual therapy in reducing pain intensity and improving pressure pain thresholds. When compared to usual care, NSAIDs, and physical therapy,

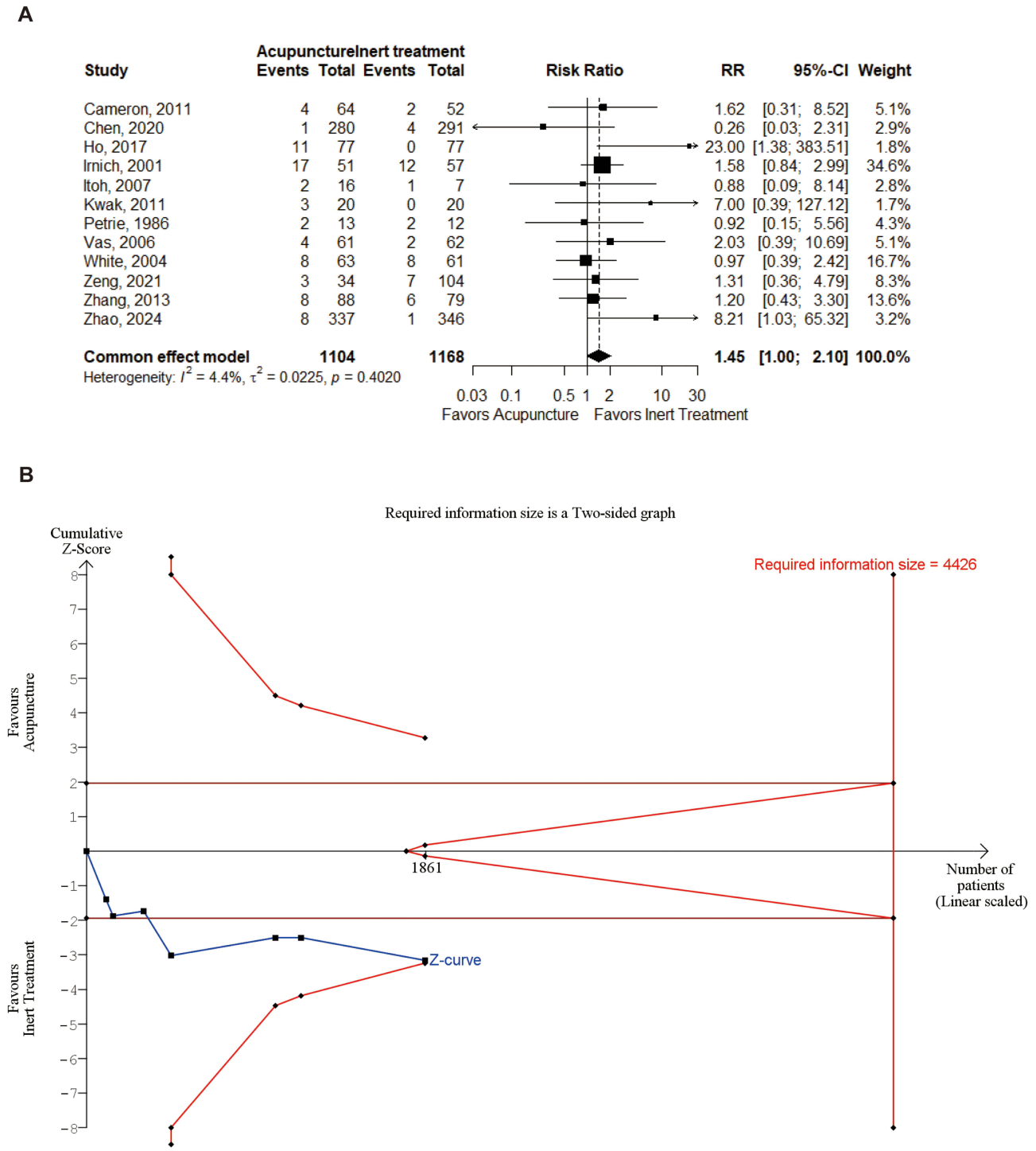


**Figure 6** Meta-analysis (**A**) and TSA (**B**) of acupuncture vs inert treatment in the adverse events.
**Notes**: TSA, trial sequential analysis. The blue curve represents the Z-curve, the red curves above and below represent trial sequential monitoring boundaries, the dashed red line represents the traditional level of statistical significance, and the red vertical line represents required information size value, the red lines on the sides closest to the horizontal line are boundaries for futility.
**Abbreviations**: CI, confidence interval; RR, risk ratio.

acupuncture also resulted in lower pain intensity. The incidence of adverse reactions in the acupuncture group was 6.4%, with slight side effects and no serious adverse reactions. These findings corroborate previous research supporting acupuncture as an effective and safe preventive treatment for neck pain.[22–24,59]

To strengthen the robustness of our conclusions, we conducted TSA, a methodological advancement not employed in prior studies. While existing meta-analyses have reported acupuncture's superiority over sham interventions,[22–25] none have addressed sample size adequacy. Our TSA results provide compelling evidence. The available sample size is sufficient to confirm that acupuncture has significant benefits in pain intensity, functional disability, quality of life, and pain perception, with a very low to moderate level of quality of evidence. Furthermore, TSA validated acupuncture's superiority to manual therapy in pain intensity reduction and pressure pain threshold elevation. However, additional studies are needed to draw definitive conclusions regarding functional disability and pain perception outcomes in this comparison.

The results of our analysis highlight the potential benefits of acupuncture for neck pain management, despite the well-established efficacy of conventional therapies including manual therapy, physiotherapy, usual care, and NSAIDs.[60–63] Our findings indicate that acupuncture provides significantly greater pain reduction both after treatment and during follow-up compared to usual care and NSAIDs. This indicates poor and non-sustained analgesia with conventional drugs. Compared with physiotherapy and manual therapy, acupuncture showed superior results after treatment, but this advantage appears to diminish during follow-up. These findings underscore the importance of acupuncture as an effective treatment option, particularly where conventional treatments fail to adequately relieve pain in neck pain. However, it is worth noting that these comparative results are limited by the small number of existing studies, necessitating caution in our conclusions. Systematic reviews have indicated that multimodal non-pharmacological interventions are more effective than inert treatment for reducing both pain and disability outcomes, with possible to define clinical importance.[19] Therefore, more high-quality pragmatic clinical trials are needed to comprehensively evaluate the effectiveness of acupuncture combined with other active treatments for neck pain.

While our findings suggest a potential benefit of acupuncture for neck pain, several methodological limitations warrant consideration. Some observed treatment effects may be partly due to non-specific effects,[57,64,65] such as patient expectations, placebo effects, and physician-patient communication during treatment. Furthermore, the comparison with active treatments is limited by the variability of different interventions in treatment frequency, treatment cycle, quality of implementation and protocol standardization, thus affecting the robustness of clinical comparison results.

## Implication for Practice

Our TSA-validated results provide robust evidence that acupuncture significantly reduces pain intensity and functional disability, improve pain experience and quality of life, and is safe. This provides additional evidence suggesting that these effects are unlikely to represent type I errors,[66] though the relative contributions of specific and non-specific (including placebo) effects remain to be fully elucidated. In clinical practice, acupuncture should be included in the treatment plan of neck pain. For patients requiring long-term analgesia, acupuncture can be combined with conventional treatments to reduce opioid dosages. Additionally, acupuncture serves as an alternative therapy for patients with poor drug tolerance or inadequate responses to standard treatments. According to international cost-effectiveness threshold values,[67–70] acupuncture is a cost-effective treatment strategy in patients with chronic neck pain, either alone or in combination with conventional treatment.

Several studies have confirmed the significant analgesic effect of acupuncture[71–75] and investigated the underlying mechanisms. Acupuncture stimulates the release of various neurotransmitters, endogenous opioid-like substances, and cytokines, while simultaneously inhibiting glial cell activation, regulating cellular signaling pathways, and modulating nociceptors to alleviate pain.[76–79] The inactivation of spinal microglia and astrocytes mediates the immediate and long-term analgesic effects of acupuncture, respectively.[77] Additionally, acupuncture modulates complex networks involving the pain inhibitory system, limbic system, and multiple brain regions to exert its analgesic effects.[76,80] Similarly, manual therapy has been demonstrated to alleviate pain by regulating cortical activity, functional connectivity, and neuroplasticity within the central nervous system.[81] Importantly, placebo analgesia has been shown to involve comparable central networks and to influence pain perception through descending regulatory pathways.[82,83] The phenomenon of overlapping central mechanisms across different interventions complicates the interpretation of acupuncture's specificity. The observed neurophysiological changes may reflect both shared mechanisms and certain distinct components, a distinction that requires further investigation to elucidate.

The effective rate of acupuncture for acute pain is as high as 77–92%,[84,85] and the efficacy rate of chronic pain is 65%–80%.[86–88] Currently, the evidence supporting acupuncture for acute or subacute neck pain remains unclear and requires further investigation. Our observations revealed that acupuncture still had advantages in pain intensity, functional disability, pressure pain threshold and quality of life during follow-up. This may be attributed to our selection of data closest to the end of treatment over a shorter time frame, which warrants further exploration. Additionally, our subgroup analysis identified differences in effectiveness among various acupuncture methods (eg, manual acupuncture, electroacupuncture, and dry needling), suggesting that clinical outcomes may be influenced by the intervention method. At present, there is a lack of standardized treatment protocols based on evidence-based medicine, which limits the standardized application of acupuncture therapy to some extent.

## Limitations

Our study has some limitations. First, the TSA results depend on predefined model parameters (eg, effect size); variations in these estimates would alter the RIS and TSMB, thus the robustness of our conclusions is contingent upon the accuracy of these assumptions. Second, TSA cannot overcome inherent methodological flaws (eg, high risk of bias) or outcome reporting biases in the original trials. Third, 10 of the included RCTS did not distinguish between subtypes of neck pain, which, while enhancing generalizability, complicates the interpretation of the results. Fourth, considerable heterogeneity existed across studies in treatment duration, session frequency, and acupoint selection protocols; insufficient reporting precluded subgroup analyses to assess these factors. Finally, the overall quality of evidence (rated as low to very low by GRADE), combined with heterogeneity and risk of bias in primary studies, constrains the strength of conclusions. Additionally, the assumption that unreported adverse events equated to none occurring in safety assessments may have led to an underestimation of the true incidence.

## Conclusion

Our study indicates that acupuncture can reduce pain intensity, functional disability, and pain perception, while also improving pressure pain threshold and quality of life in neck pain patients, with TSA confirming the robustness of these findings. However, the very low to moderate evidence quality, combined with substantial heterogeneity that weakens the precision of pooled estimates, necessitates caution in interpretation. We therefore propose acupuncture as a potential treatment candidate and emphasize the critical need for future high-quality studies to validate these results and elucidate underlying mechanisms.

## Highlights

1. This study is the first to confirm the effectiveness of acupuncture for neck pain through trial sequential analysis (TSA), addressing the false-positive risk in traditional meta-analyses.
2. Acupuncture offers comprehensive benefits across pain, function, and quality of life domains with a favorable safety profile, though evidence quality remains limited.
3. Acupuncture is positioned as a viable alternative when conventional treatments fail, and provide TSA evidence for guideline updates while emphasizing the need for definitive trials.

## Data Sharing Statement

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

## Ethical Approval

This systematic review and meta-analysis utilized exclusively data from previously published studies, which constitutes research involving legally obtained publicly available data. In accordance with China's *Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects* (effective February 18, 2023), Article 32, Items 1 and 2, which state that ethical review is exempt for "research using legally obtained publicly available data" and "research using anonymized information data", this study was exempt from ethical approval by an institutional review board.

## Acknowledgments

We thank the researchers and the study participants for their contributions.

## Author Contributions

Chao-rong Xie, Zhi-yang Zhang and Qing-feng Tao contributed equally. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This work was supported by the Major and Stubborn Disease Project of National Administration of Traditional Chinese Medicine Interdisciplinary (ZDYN-2024-A-094) and the Chengdu University of Traditional Chinese Medicine Talent Training Fund (No. JQRC20210001).

## Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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