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# Efficacy and safety of acupuncture with moxibustion for knee osteoarthritis: a meta-analysis of randomized controlled trials

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## Abstract

**Background** Osteoarthritis (OA) is prevalent, yet its management remains challenging. This meta-analysis aims to evaluate the efficacy of acupuncture combined with moxibustion versus other standard treatments in patients with knee osteoarthritis (KOA) based on randomized controlled trials (RCTs).

**Methods** Searches were conducted in Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials to retrieve relevant RCTs. Data on baseline characteristics, treatment efficacy, and adverse events were extracted. The analysis utilized pooled weighted mean differences (WMD) and risk ratios (RR) with 95% confidence intervals (CIs) to assess the superior treatment modality.

**Results** A total of 18 RCTs were included. Acupuncture combined with moxibustion demonstrated significant improvement in the visual analog scale (VAS) for pain and the long-term (> 60 weeks) Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores for pain, stiffness, and physical function compared to other treatments. In contrast, short- (< 4 weeks) and mid-term (6–60 weeks) WOMAC outcomes for pain, stiffness, and physical function indicated varied results. The overall efficacy rate also favored the combined therapy significantly in the short- and mid-term evaluations. Notably, this therapy was associated with fewer adverse events.

**Conclusion** The meta-analysis reveals that acupuncture combined with moxibustion is notably more effective and safer than other treatment modalities for KOA, particularly during mid- and long-term follow-up periods.

**Keywords** Acupuncture, Moxibustion, Knee osteoarthritis, Meta-analysis, Treatment, Adverse events

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## Background

Osteoarthritis (OA) is a prevalent and progressive disorder characterized by pain and dysfunction in the affected joint [1]. It impacts approximately 10% of men and 18% of women over 60 [2]. OA can involve multiple peripheral joints, both small (such as those in the hands) and large (including the knee and hip joints), which may be affected either simultaneously or asynchronously [1]. The treatment of OA remains challenging as understanding its classifications, risk factors, and pathophysiology continues evolving [3]. Symptoms such as pain, transient morning stiffness, and crepitus during joint movement—a grating sound or sensation—indicate a severe condition



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that can deteriorate quality of life (QOL) and lead to joint instability [4].

OA is treated with pharmacotherapy, physical therapy, rehabilitation therapy, acupuncture, and massage [5–7]. However, long-term use of pharmacotherapy has a risk of several negative consequences, such as hypertension, kidney damage, gastrointestinal problems, congestive heart failure, and heart attacks [8]. Moreover, surgery is not necessary for early-stage OA, and physical therapy is not appropriate for end-stage OA. Therefore, exploring a well-tolerated treatment modality is essential for OA patients.

According to traditional Chinese medicine's (TCM) holistic theory, an organism can only remain vibrant and vigorous when there is harmony between its body and soul. With the integration of ancient Chinese philosophy, TCM has progressively developed into a unique method that blends movement and quiet, dredges meridians, controls qi and blood, and focuses on strengthening, feeding, and managing the body to avoid illnesses [9]. Among all the TCM modalities, acupuncture and moxibustion have demonstrated substantial efficacy with minimal adverse reactions [10]. Often used in conjunction with acupuncture to treat musculoskeletal issues, moxibustion is a TCM technique that increases blood circulation by burning wormwood at acupuncture sites [11, 12], and the evidence about acupuncture combined with moxibustion in treating OA was almost all reported in knee OA (KOA). Moreover, there are various acupuncture techniques for treating OA. However, systematic evidence comparing the efficacy of various acupuncture techniques combined with moxibustion in terms of recovery or pain reduction in the treatment of KOA is lacking.

Hence, this meta-analysis aims to compare the efficacy of acupuncture combined with moxibustion with other standard treatment modalities in enhancing recovery and reducing pain among KOA patients with randomized controlled trial (RCT) studies included.

## Methods

### Search strategy

This meta-analysis aligned with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Searches were performed on Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from the inception of each database until June 30, 2024. Reference lists from relevant articles were scrutinized to assess eligibility. The detailed search strategy employed for MEDLINE is documented in Appendix Material 1. Our study protocol was also registered on the PROSPERO website under the registration number CRD42024562008.

### Selection criteria and data extraction

#### Inclusion criteria

RCTs focusing on OA affecting any peripheral or extremity joints, with no restrictions regarding the duration or severity of OA, included any acupuncture techniques combined with moxibustion, as were studies comparing these techniques to other interventions. Articles in all languages were considered.

#### Exclusion criteria

Studies were excluded if they involved animal or laboratory research, had unclear outcomes, or involved OA that did not affect the extremities (e.g., the neck or lumbar spine). Studies employing the small needle knife technique as the intervention were also excluded.

Working in pairs, two reviewers independently conducted titles and abstracts screening, full-text screening, data extraction, and risk of bias (RoB) assessment for included studies using a piloted electronic data extraction form (the Excel sheet). Reviewers resolved disagreement by discussion and, when necessary, consulting a third reviewer and clinical experts. Data extracted include the author's name, year of publication, countries, study registry ID, patient characteristics (age, sex, location of OA, severity of condition, and length of disease, etc.), intervention information (type of acupuncture and moxibustion, length of treatment, and co-intervention, etc.), and efficacy and safety outcomes (measure name, type of data, timepoint of follow-up, and outcome values, etc.). The RoB of the included studies will be assessed using the Cochrane RoB 2.0 tool for RCTs [13]. The combination of acupuncture and moxibustion group was considered the experimental group for all the included studies. When a study had more than three arms, the patients in the group without any intervention were excluded from the meta-analysis.

#### Statistical analysis

Information regarding the characteristics of included studies, patients, and interventions was comprehensively summarized. For each direct comparison, the risk ratio (RR) and associated 95% CIs were calculated for dichotomous outcomes, while weighted mean differences (WMDs) and corresponding 95% CIs were determined for continuous outcomes. The random-effects model was used to conduct statistical analysis due to the high heterogeneity in our study.

Prior to pooling, scales for continuous outcomes were standardized. For instance, most studies employed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) to assess treatment efficacy. The WOMAC subscales include pain

(score range: 0–20), stiffness (0–8), and physical function (0–68). Conversely, some studies utilized a 0–100 scoring system for these subscales, which required mathematical conversion to WOMAC scales. A pairwise meta-analysis using a random-effects model was conducted. The certainty of the evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. Sensitivity analyses were performed to evaluate the stability of the results by systematically excluding studies and observing any significant alterations in the outcomes, as well as a funnel plot to examine the possibility of publication bias.

## Results

### Study selection

The PRISMA flowchart of study selection is presented in Fig. 1 [14]. In total, 4565 studies (Medline = 1259, Embase = 3339, and CENTRAL = 67) were identified. After the duplicate and abstract screening, 85 studies were included in the full-text screening. Eventually, 18 papers satisfied the inclusion criteria and were included in the meta-analysis [15–32].

### Study characteristics

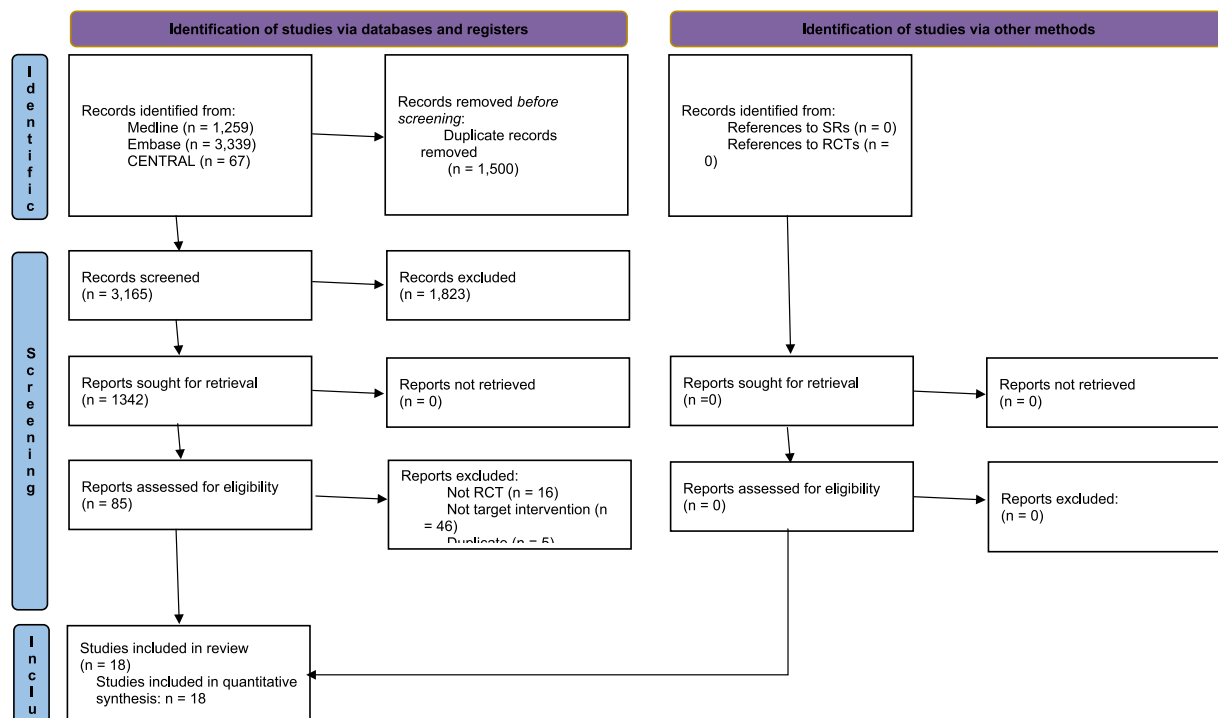
All the RCT studies were conducted in China to evaluate the treatment efficacy for KOA. Among them, 18 studies were published, 2 in English, and 16 in Chinese. No studies were registered on National ClinicalTrials.gov.

Among the 18 studies, 15 were identified as having a high risk of bias, and the other 3 were identified as having a medium risk of bias (Fig. 2). The summary of blinding in the included studies is summarized in Appendix Material 2.

In total, 736 patients were enrolled in the experimental group, and 696 patients were enrolled in the control group. The study characteristics for the included patients were presented in Table 1, and the intervention details for the enrolled patients were summarized in Appendix Material 3.

### Treatment efficacy

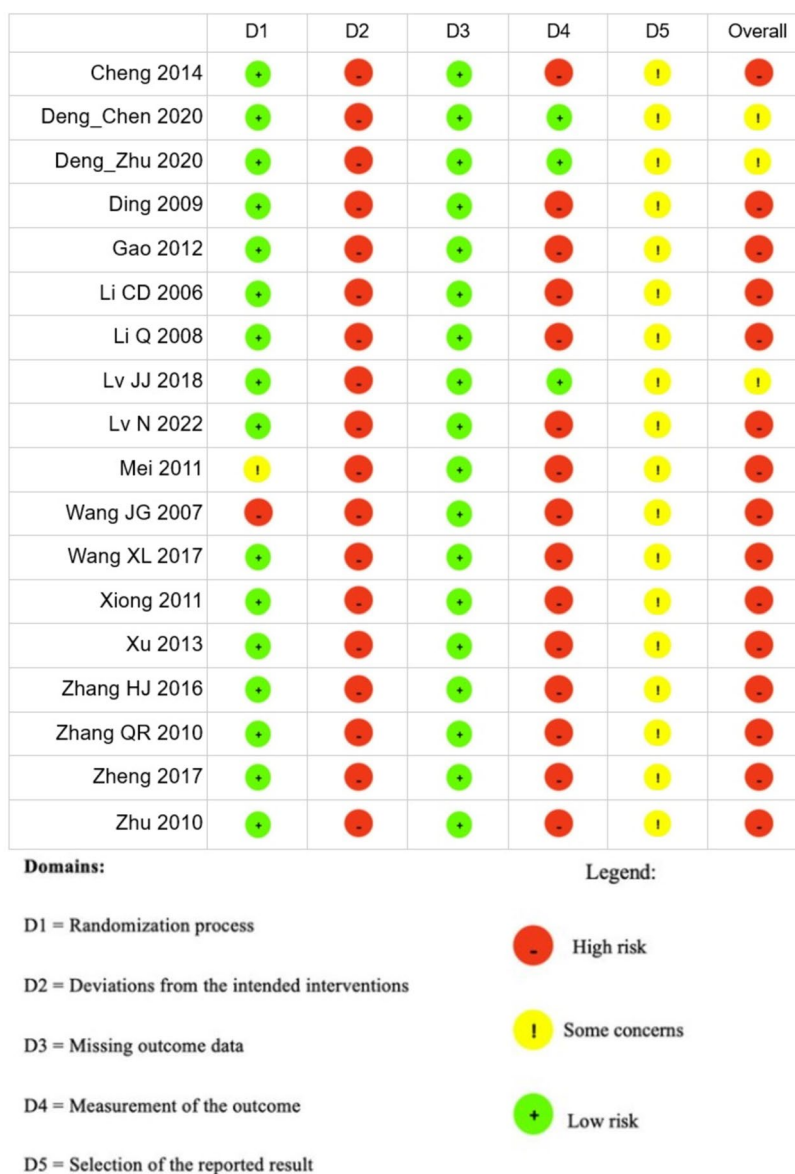
Regarding pain scores evaluated by visual analog scales (VAS), ten studies reported short-term (< 4 w) outcomes; the pooled WMD was -1.00 (95% CI: -1.35 to -0.65;  $I^2=84.0\%$ ,  $p=0.00001$ ). Seven studies reported middle-term (6–60w) outcomes; the pooled SMD was -1.28 (95% CI: 1.91 to -0.65;  $I^2=90.0\%$ ,  $p=0.0001$ ) (Fig. 3). These results indicated that the patients undergoing



Abbreviations: RCT = randomized controlled trial.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>

**Fig. 1** PRISMA flowchart of literature selection



**Fig. 2** Risk of bias based on Cochrane 2.0 tool for each study

acupuncture combined with moxibustion treatment significantly reduced the VAS pain score compared to patients undergoing other treatments.

Regarding WOMAC, eight studies reported short-term treatment (2–6w) outcomes, seven studies reported middle-term (7w–5 months) treatment outcomes, and one study reported long-term (>7 months) treatment outcomes. For pain score, the WMD was -1.00 (95% CI: -2.80 to 0.8;  $I^2=97.0\%$ ,  $p=0.28$ ) for short-term outcomes, the WMD was -2.37 (95% CI: -5.15 to 0.41;  $I^2=99.0\%$ ,  $p=0.09$ ) for middle-term treatment outcomes, and the WMD was -3.49 (95% CI: -4.32 to -2.66;  $p=0.0001$ ) for long-term treatment outcomes (Fig. 4A).

For stiffness, the WMD was -0.62 (95% CI: -1.26 to 0.02;  $I^2=88.0\%$ ,  $p=0.06$ ) for short-term outcomes, the WMD was -0.08 (95% CI: -1.26 to -0.34;  $I^2=73.0\%$ ,  $p=0.0007$ ) for middle-term treatment outcomes, and the WMD was -1.97 (95% CI: -2.45 to -1.49;  $p=0.0001$ ) for long-term treatment outcomes (Fig. 4B).

For physical function, the WMD was -3.41 (95% CI: -6.71 to -0.11;  $I^2=92.0\%$ ,  $p=0.04$ ) for short-term outcomes, -4.39 (95% CI: -8.94 to 0.17;  $I^2=93.0\%$ ,  $p=0.06$ ) for middle-term treatment outcomes, and -6.03 (95% CI: -9.71 to -2.35;  $p=0.001$ ) for long-term treatment outcomes (Fig. 4C). Moreover, four studies reported short-term (2–4w) changes in WOMAC total scores;

**Table 1** The characteristics of included studies

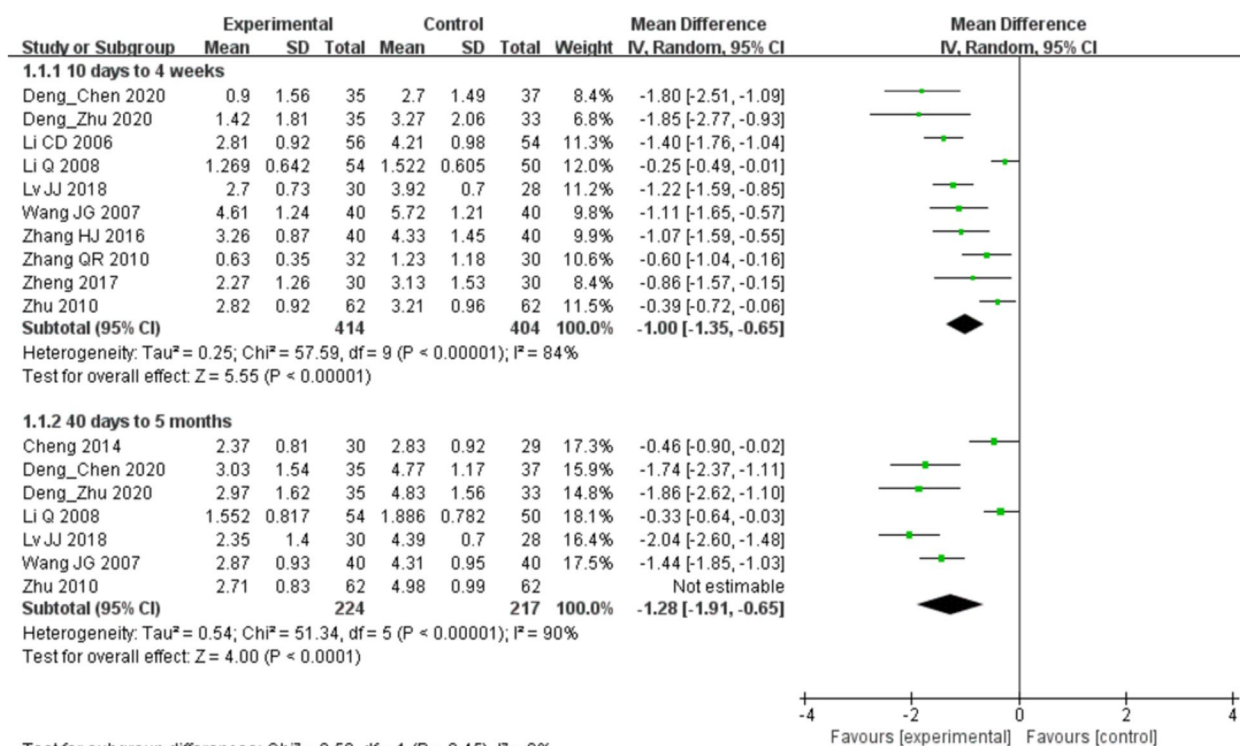
Study	N (intervention/ control)	Indication	Age, mean (SD), years	Sex (Male/Female)	Disease duration, mean (SD), months	Severity	Treatment duration	Follow-up
Cheng 2014	30/29	KOA	60.0 (5.0)	28/31	50.5 (11.7)	NR	44d (30d + two 1w rest in between 3 treatment cycles)	1w
Deng_Chen 2020	35/37 for efficacy outcomes, 38/38 for safety outcome	KOA of cold-dampness type	60.1 (7.7)	30/42 (sex information was missing for 4 patients)	58.8 (17.2)	Kellgren-Lawrence grade 0-III	30d (28d + 2d of rest in between)	1 m
Deng_Sheng 2020	35/33 for efficacy outcomes, 36/36 for safety outcome	KOA of cold-damp type	52.9 (8.5)	35/37	49.2 (17.4)	NR	30d (28d + 2d of rest in between)	4 m
Ding 2009	30/30	KOA	55.7 (14.6)	17/43	56.2 (46.6)	VAS score of 7 cm or lower	2w	10w
Gao 2012	35/34	KOA of kidney deficiency and marrow insufficiency pattern/syndrome	58.2 (8.8)	28/41	38.1 (11.4)	NR	4w, 8w	NA
Li CD 2006	56/54	KOA of kidney-yang deficiency and cold syndrome	59.4 (5.2)	65/55	NR	VAS pain score 4 or greater, Lequesne Index of 6 or higher	7d, 15d (14d + 1d of rest in between 2 cycles)	NA
Li Q 2008	30/30 (54/50 knees)	KOA of Yang-deficiency pattern	64.1 (5.6)	16/44	105.6 (86.4)	Kellgren-Lawrence grade II-IV	10d	1 m
Lü JJ 2018	30/28	KOA of Yang-deficiency pattern	53.0 (8.5)	33/25	18.9 (5.0)	NR	22d (20d + 2d of rest in between)	1 m
Lü N 2022	48/48	KOA	63.9 (11.0)	40/56	79.2 (21.8)	Kellgren-Lawrence grade III	4w	NA
Mei 2011	68/69	KOA	60.9 (6.9)	48/89	20.5 (5.3)	NR	42d (20*2 + 2; once every other day 10 times, over 2 courses of treatment with a 2-day interval between courses)	2w
Wang JG 2007	40/40	KOA	59.4 (5.3)	37/43	Value NR, shorter than 120 months as one of the inclusion criteria	NR	20d, 43d (40d + 3d of rest in between of 2 cycles)	NA
Wang XL 2017	25/21	KOA	59.6 (6.6)	10/36	range, 24 to 360 months	Kellgren-Lawrence grade II or greater, and VAS score of 3 cm or greater	3w	NA
Xiong 2011	30/30	KOA	55.3 (8.6)	13/47	0.9 (0.4)	NR	20d	NA

**Table 1** (continued)

Study	N (intervention/ control)	Indication	Age, mean (SD), years	Sex (Male/Female)	Disease duration, mean (SD), months	Severity	Treatment duration	Follow-up
Xu 2013	80/80	KOA	58.0 (13.8)	82/78	56.5 (44.6)	Kellgren-Lawrence grade II, and VAS score of 70 mm or lower	5w	3 m, 6 m
Zhang HJ 2016	40/10	KOA with cold-damp stagnation	50.5 (10.5)	47/33	27.6 (15.8)	NR	20d	6 m but only for recurrence rate
Zhang QR 2010	32/30	KOA	59.7 (6.9)	31/31	54.0 (42.7)	NR	22d (20d + 2d of rest in between)	NA
Zheng 2017	30/30	KOA with yang-deficiency and cold-stagnation syndrome	53.0 (10.5)	31/29	14.3 (5.7)	NR	22d (20d + 2d of rest in between)	NA
Zhu 2010	62/62	KOA of cold-damp type	53.4 (2.8)	48/76	66.0 (45.5)	NR	4w	10w

SD standard deviation, EA electroacupuncture, KOA knee osteoarthritis, NA not applicable, NR not reported, OA osteoarthritis, d day, m month, w week





**Fig. 3** Forest plot showing the difference in visual analog scale pain scores between moxibustion combined with acupuncture and other treatments for osteoarthritis knee

the WMD was  $-3.58$  (95% CI:  $-6.36$  to  $-0.80$ ;  $I^2 = 1.0\%$ ,  $p = 0.01$ ). Three studies reported middle-term (2–4w) change in WOMAC total scores; the WMD was  $-5.64$  (95% CI:  $-9.15$  to  $-2.14$ ;  $I^2 = 32.0\%$ ,  $p = 0.002$ ) (Fig. 4D). These results indicated the heterogeneity advantages of acupuncture combined with moxibustion over other treatments in improving WOMAC.

Finally, the overall efficacy rate was analyzed. Eleven studies reported short-term treatment (2–6w) outcomes; the RR was 1.05 (95% CI: 0.99 to 1.12;  $I^2 = 62.0\%$ ,  $p = 0.10$ ). In 9 studies of middle-term treatment (7w–5 m) outcomes, the RR was 1.15 (95% CI: 1.05 to 1.25;  $I^2 = 62.0\%$ ,  $p = 0.002$ ). One study reported long-term (>7 months) treatment outcome; the RR was 1.26 (95% CI: 1.11 to 1.42,  $p = 0.0003$ ) (Fig. 5). These results indicated that the advantages of acupuncture combined with moxibustion over other treatments were evident in middle and long-term periods.

**Treatment-related adverse events**

Seven studies reported treatment-related AEs. In total, thirteen adverse events were reported in the acupuncture combined with the moxibustion group. Among them, ten cases developed redness and pain in the local skin, two cases developed faintness, and one developed scald during treatments. All the AEs were mild and resolved

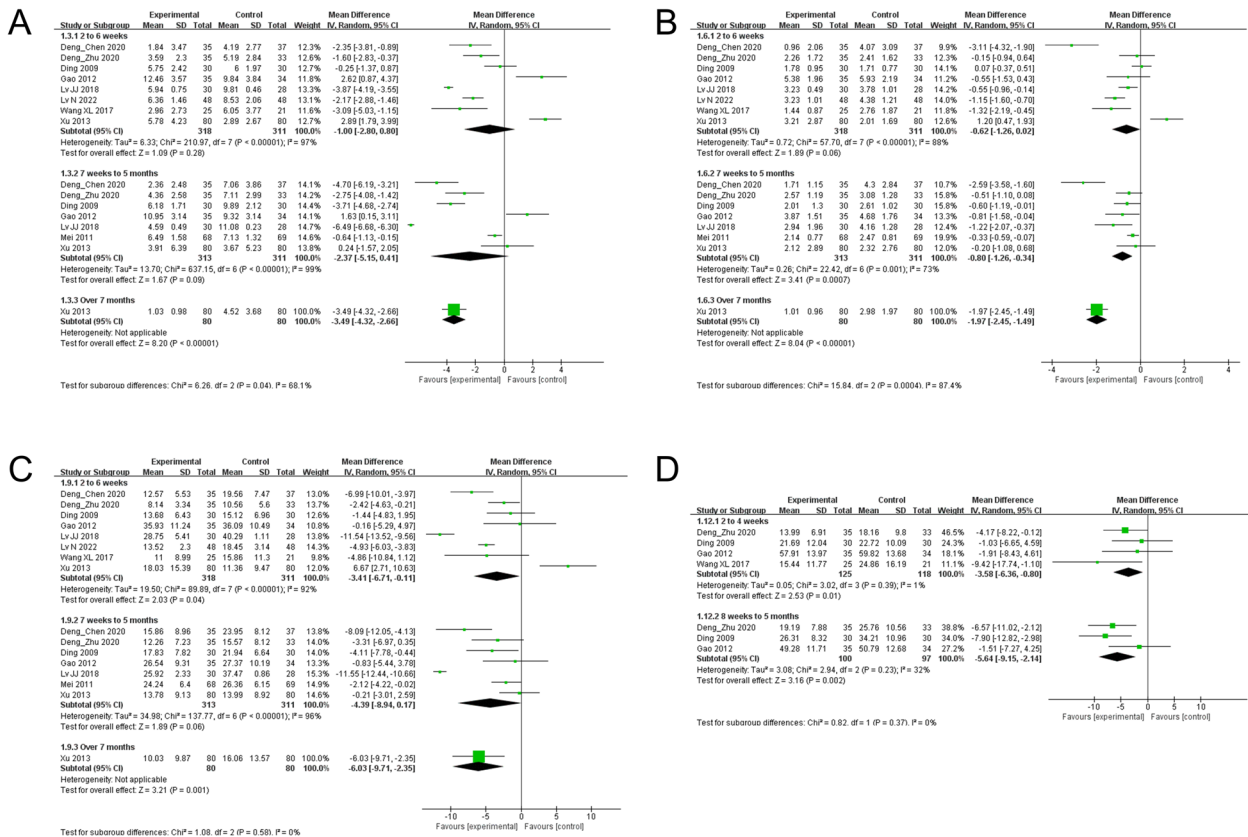
with proper treatments. No severe AEs were reported in any studies. Meanwhile, 38 AEs were reported in other treatment groups. The RR was 0.28 (95% CI: 0.15 to 0.54;  $I^2 = 0\%$ ,  $p = 0.001$ ). The result indicated that acupuncture combined with moxibustion was safer than other treatments (Fig. 6).

**Sensitivity analyses**

Sensitivity analyses covered all evaluated outcomes except the WOMAC total scores and adverse events, as detailed in Supplementary Tables 1–4. The analysis revealed no single study that markedly affected the direction or magnitude of the outcomes. The  $I^2$  statistic for these outcomes consistently remained above 50%, indicating a moderate to high level of heterogeneity.

**Publication bias**

We used a funnel plot to examine the possibility of publication bias. The short-term and middle-term VAS score (Supplementary Fig. 1), WOMAC pain score (Supplementary Fig. 2), WOMAC stiffness (Supplementary Fig. 3), and physical function (Supplementary Fig. 4). The overall efficacy rate (Supplementary Fig. 5) had no publication bias.



**Fig. 4** Forest plot showing the difference in Western Ontario McMasters University Osteoarthritis Index between moxibustion combined with acupuncture and other treatments for osteoarthritis knee. **A** pain; **B** stiffness; **C** physical function; **D** total score

**Discussion**

Two of the most widely utilized TCM modalities in China are moxibustion and acupuncture [32, 33]. They are commonly applied in clinical settings, with an expanding evidence base, including case reports, longitudinal studies, and randomized controlled trials, supporting their use in OA treatment. However, evidence was previously insufficient for the efficacy of combining moxibustion with acupuncture in managing KOA. Our meta-analysis is the first to demonstrate that the combination of moxibustion and acupuncture is superior to other treatments (acupuncture alone, moxibustion alone, or pharmaceuticals), particularly showing more pronounced benefits during middle-term and long-term follow-ups.

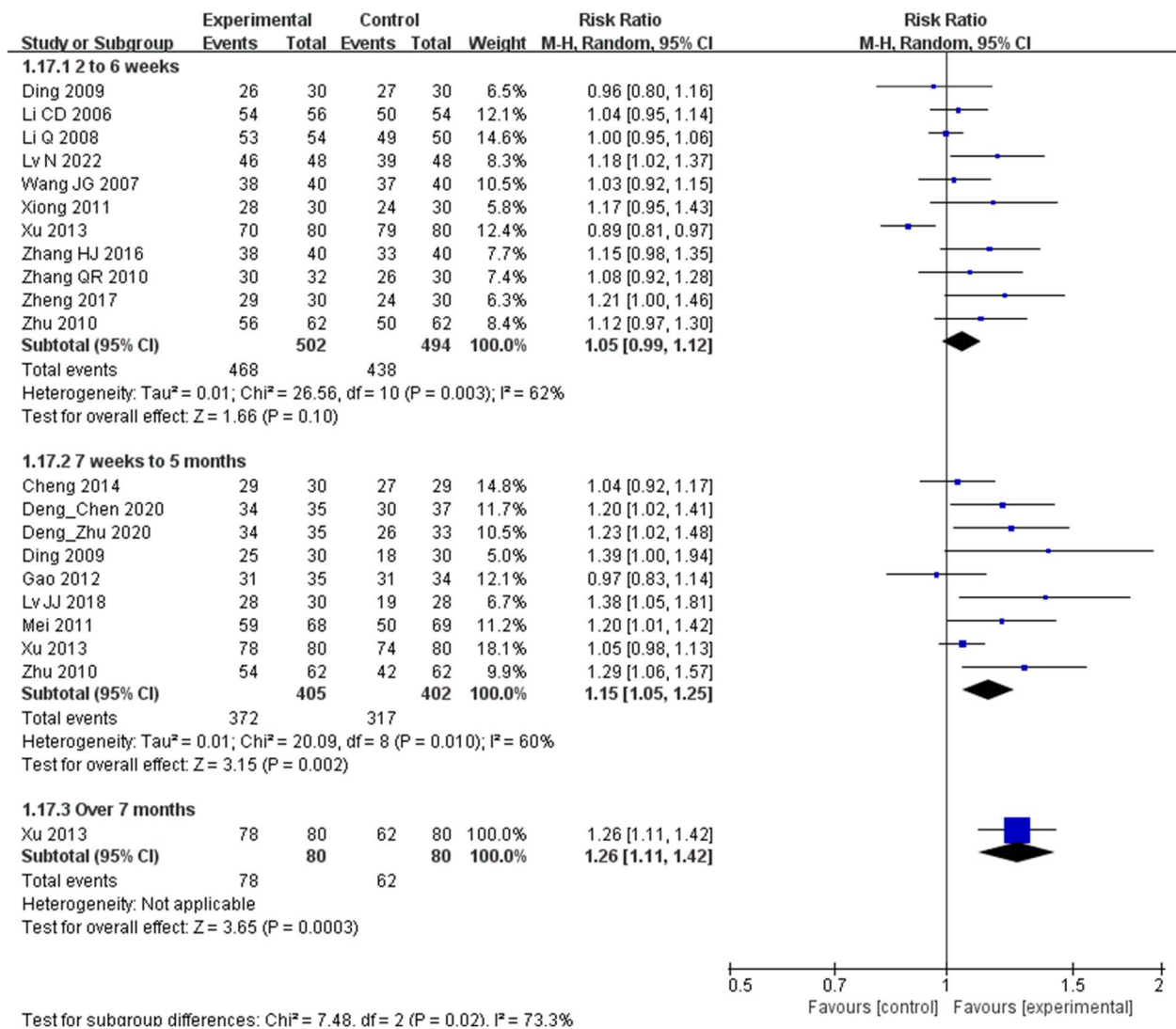
Moxibustion enhances blood circulation at the knee joint, reduces cartilage degradation, and decreases macrophage infiltration. It also inhibits the production of inflammatory mediators such as interleukin-6, mast cell cyclooxygenase, and tumor necrosis factor, contributing to the restoration of articular chondrocytes [34, 35]. Additionally, moxibustion has been shown to regulate insulin-like and transforming growth factors, strengthening the knee joint's limb pedal strength [36]. The efficacy

of various moxibustion techniques has been explored, with fire needle moxibustion potentially showing the most remarkable efficacy [37]. Future research is needed to ascertain the most effective moxibustion technique.

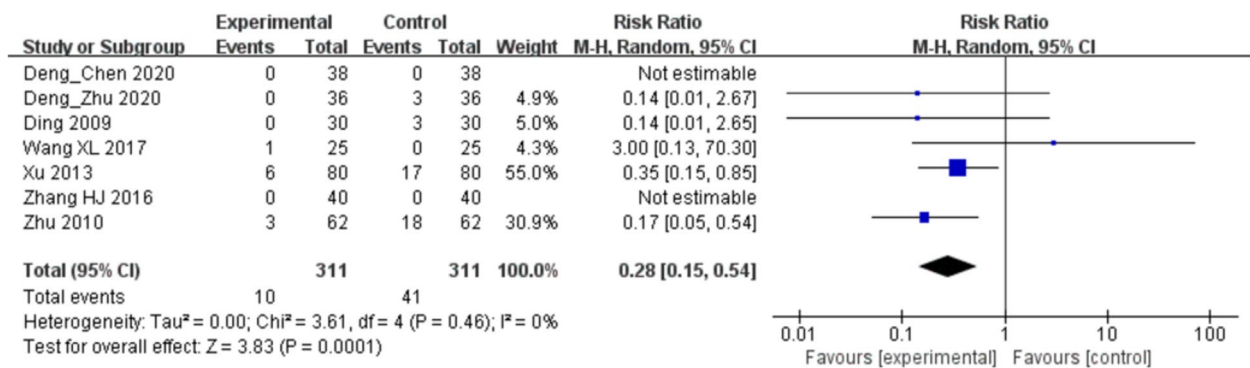
Acupuncture, another fundamental component of TCM, operates on the principle of enhancing qi flow through specific acupoints and meridians. Selecting acupoints is critical for effective treatment [38, 39]. In KOA model rabbits, acupuncture has been shown to decrease the anaerobic glycolytic metabolism rate and levels of metabolites, potentially protecting the cartilage [40]. It may also alleviate cartilage hypoxia and improve oxygen levels through enhanced synovial microcirculation and fluid PO<sub>2</sub>. Furthermore, He et al. [41] revealed significant upregulation of miR-214 and its targets, TRPV4 and BAX, in damaged articular cartilage following acupuncture, suggesting a therapeutic mechanism for KOA recovery. Research into various acupuncture modalities is encouraged to further understand their specific effects on KOA [42].

Although the individual benefits of moxibustion and acupuncture are well-documented, comprehensive reviews comparing these combined therapies to other





**Fig. 5** Forest plot showing the difference in the overall efficacy rate between moxibustion combined with acupuncture and other treatments for osteoarthritis knee



**Fig. 6** Forest plot showing the difference in adverse events between moxibustion combined with acupuncture and other treatments for osteoarthritis knee

treatments are scarce. Qu et al.'s meta-analysis, which included 10 RCTs, found that combining acupotomy, acupuncture, and moxibustion offers superior therapeutic benefits for KOA, reducing postoperative pain and enhancing clinical efficacy [43]. Similarly, Park et al. reported significant pain reduction in KOA patients treated with single or integrated oriental medicine modalities (acupuncture, herbal medicine, pharmacopuncture, and moxibustion) [44]. These findings align with our results, suggesting that combined TCM modalities may offer enhanced treatment efficacy.

However, significant heterogeneities were identified in most results. The reason was complicated. First, the disease condition of KOA was challenging to balance among all the studies. Different doctors judged the severity of KOA, and the standard may be inconsistent among different studies. Second, the improvements in KOA after treatments were measured using subjective evaluation tools. Potential biases may exist among different studies. Third, the follow-up period was varied. The short-term, middle-term, and long-term results were analyzed from different studies. Therefore, the interpretations of the results in our study should be cautious due to the high heterogeneity.

In our study, using different evaluation tools resulted in different outcomes. It suggested that the assessment tool selected may impact how well moxibustion and acupuncture are considered to work together. While WOMAC did not reveal a significant difference in short-term or middle-term outcomes, other evaluation tools identified better treatment outcomes with the combination approach. A plausible rationale for these disparities might be the variation of pain measures. It is also essential to consider the pain score as a proportion of the overall score. For instance, the VAS offers a more comprehensive evaluation of pain, whereas the WOMAC scale emphasizes on physical functions more. The difference in measurement tools could explain some of the heterogeneity in our study.

Moreover, the results of the GRADE analysis, which revealed highly low-quality evidence, underscore the necessity for more rigorous and standardized research in this field. The significant risk of bias and inconsistency among studies cannot be overlooked despite including RCTs, which are considered the gold standard for evaluating therapy efficacy. The variability in treatment modalities in the control groups, the differing durations of therapy, and the diverse techniques of moxibustion combined with acupuncture contribute to an elevated risk of publication bias. Future research should focus on designing RCTs with robust methodologies to minimize bias and ensure consistency across studies. Additionally, establishing standardized treatment guidelines in

this field and using advanced techniques, such as artificial intelligence systems [45], to help select the preferred treatment modality for KOA are essential.

The strength of this meta-analysis lies in its aggregation of a significant number of RCTs, each with considerable sample sizes (18 studies involving over 1400 participants). However, our review has notable limitations. Firstly, the quality of most included studies was low. Significant publication bias and heterogeneity among the studies were observed, which could influence the interpretation of results. Secondly, implementing blinding methods was challenging, and subjective assessments might have increased the risk of bias, potentially leading to overestimating the efficacy of combined therapy. Thirdly, the follow-up periods were generally short, making it difficult to assess long-term treatment efficacy. Future studies should aim to conduct well-designed, blinded trials with extended follow-up periods to more accurately determine the outcomes of our findings.

## Conclusion

A meta-analysis of RCT studies found that combining acupuncture and moxibustion treatment was significantly more effective and safer than other treatments. The benefits were particularly pronounced during the middle-term and long-term follow-up periods.

## Abbreviations

OA	Osteoarthritis
QOL	Quality of life
TCM	Traditional Chinese medicine
KOA	Knee osteoarthritis
RCT	Randomized controlled trial
RR	Risk ratio
WMDs	Weighted mean differences
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13643-025-02762-x>.

Supplementary Material 1. Appendix 1. The detailed search strategy.

Supplementary Material 2. Appendix 2. Summary of Blinding in the Included Studies

Supplementary Material 3. Appendix 3. Intervention details for the experimental and control groups.

Supplementary Material 4. Figure S1. Funnel plot for visual analog scale pain outcome.

Supplementary Material 5. Figure S2. Funnel plot for Western Ontario McMasters University Osteoarthritis Index pain outcome.

Supplementary Material 6. Figure S3. Funnel plot for Western Ontario McMasters University Osteoarthritis Index stiffness outcome.

Supplementary Material 7. Figure S4. Funnel plot for Western Ontario McMasters University Osteoarthritis Index physical function outcome.

Supplementary Material 8. Figure S5. Funnel plot for overall efficacy rate outcome.

Supplementary Material 9.

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### Authors' contributions

Conceptualization: Xing Li, Wei Zhai, Cheng Chen, Mi Liu, Ge-Shu Du. Data curation: Zhao-Bo Yan, Cheng Chen, Wei Zhai. Formal analysis: Rui-Xin Zhu, Xing Li. Funding acquisition: Xing Li, Wei Zhai, Cheng Chen, Mi Liu, Ge-Shu Du. Investigation: Heng-Cai Zhang, Wen-Juan Ma, Kun-Fu Wang. Methodology: Zhao-Bo Yan, Cheng Chen, Wei Zhai, Heng-Cai Zhang, Wen-Juan Ma, Fu-Kun Wang. Project administration: Mi Liu, Ge-Shu Du. Resources: Heng-Cai Zhang, Wen-Juan Ma, Fu-Kun Wang. Software: Zhao-Bo Yan, Heng-Cai Zhang, Wen-Juan Ma, Fu-Kun Wang. Supervision: Mi Liu, Ge-Shu Du. Validation: Mi Liu, Ge-Shu Du. Visualization: Mi Liu, Ge-Shu Du. Writing - original draft: Rui-Xin Zhu, Xing Li. Writing - review & editing: Mi Liu, Ge-Shu Du

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### Data availability

The authors confirm that the data supporting the findings of this study are available within the article. Further inquiries can be directed to the corresponding author.

### Declarations

#### Ethics approval and consent to participate

Institutional Review Board approval was not required because this is a meta-analysis.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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