Updated systematic review and meta-analysis of acupuncture for chronic knee pain

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ABSTRACT

Objective To assess the effectiveness and safety of acupuncture for the treatment of chronic knee pain (CKP).

Methods We searched the MEDLINE, EMBASE, Cochrane CENTERAL, CINAHL and four Chinese medical databases from their inception to June 2017. We included randomised controlled trials of acupuncture as the sole treatment or as an adjunctive treatment for CKP. The primary outcome was pain intensity measured by visual analogue scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale and 11-point numeric rating scale. Secondary outcome measurements included the 36-Item Short Form Health Survey and adverse events. The quality of all included studies was evaluated using the Cochrane risk-of-bias criteria and the STRICTA (Standards for Reporting Interventions in Controlled Trials of Acupuncture) checklist.

Results Nineteen trials were included in this systematic review. Of these, data from 17 studies were available for analysis. Regarding the effectiveness of acupuncture alone or combined with other treatment, the results of the meta-analysis showed that acupuncture was associated with significantly reduced CKP at 12 weeks on WOMAC pain subscale (mean difference (MD) −1.12, 95% confidence interval (CI) −1.98 to −0.26, I^2=62%, 3 trials, 608 participants) and VAS (MD −10.56, 95% CI −17.69 to −3.44, I^2=0%, 2 trials, 145 patients). As for safety, no difference was found between the acupuncture and control groups (risk ratio 1.08, 95% CI 0.54 to 2.17, I^2=29%).

Conclusion From this systematic review, we conclude that acupuncture may be effective at relieving CKP 12 weeks after acupuncture administration, based on the current evidence and our protocol. However, given the heterogeneity and methodological limitations of the included trials, we are currently unable to draw any strong conclusions regarding the effectiveness of acupuncture for chronic knee pain. In addition, we found that acupuncture appears to have a satisfactory safety profile, although further studies with larger numbers of participants are needed to confirm the safety of this technique.

Strengths Systematic review without language restrictions.

Limitations Only a few high-quality and consistent trials could be included in this review.

INTRODUCTION

Chronic knee pain is a common complaint in elderly patients with knee osteoarthritis, particularly aged 50–69 years.[1 2] It is often accompanied by disability,[3 4] reduced quality of life[5–8] and high healthcare expenditures.[9–11] The prevalence of knee pain in adults over 45 years of age is estimated at 25% and increases with age.[12–14] For example, 9.5% of participants aged 63–93 had symptomatic knee osteoarthritis and 33% had radiographic evidence of knee osteoarthritis.[14] Other studies report that the rates of osteoarthritis in patients over 60 and 65 years are 33% and 38%, respectively.[15 16]

Pharmacological treatments available for osteoarthritis include anti-inflammatory drugs (cyclooxygenase (COX) I and COX II inhibitors). These agents may not be adequately effective, and are often associated with various side effects.[17] Joint replacement surgery is sometimes recommended.[18] Complementary and alternative therapies, including acupuncture and moxibustion, may be employed as adjuvant treatments.[19–24]

It has been reported that acupuncture is effective for knee pain management, especially for chronic knee pain and knee pain after total knee arthroplasty.[25–27] The potential mechanisms of acupuncture underlying its beneficial effects on knee pain may include prevention of further cartilage erosion as well as more conventional analgesic mechanisms.[28] Although previous systematic reviews of acupuncture for chronic knee pain have been published,[27 29 30] in the past 5 years only one review specifically focused on acupuncture for knee pain.[27] The authors of that study concluded that acupuncture could significantly reduce pain intensity[27]; however, this conclusion was based in part

on pain intensity data that were incorrectly pooled from four studies, and the heterogeneity of the pooled data for functional mobility was very high. In addition, a recent study[31] in the *Journal of the American Medical Association* (*JAMA*) concluded that acupuncture negatively affected chronic knee pain, though the study had several shortcomings in its clinical design.[32–37] The purpose of this systematic review was to provide an updated overview of the literature in this area and to further critically assess the effectiveness and safety of acupuncture for chronic knee pain with the inclusion of additional studies to assist with informed clinical decision-making.

METHODS

This review is reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement guidelines.[38] The review was registered in the PROSPERO 2014 (registration number: CRD42014015514).[39]

Literature search

Studies were identified via the following databases from their inception through 20 June 2017: MEDLINE, EMBASE, CENTRAL, CINAHL, the Chinese Biomedical Literature Database (CBM), the China National Knowledge Infrastructure (CNKI), VIP Information and Wanfang. Furthermore, ClinicalTrials.gov and the reference lists of previously published reviews related to chronic knee pain and acupuncture were also screened for eligible clinical trials.

Inclusion criteria

Inclusion criteria were randomised controlled trials (RCT) of chronic knee pain (defined as more than 3 months prior to study randomisation) examining the effectiveness, comparative effectiveness and safety of acupuncture relative to a non-acupuncture intervention or usual care. Participants in the control group had to have received the same baseline interventions as the acupuncture group for those trials in which acupuncture was being evaluated as an adjunctive therapy. The included trials had to report pain outcomes in at least one of the following forms: visual analogue scale (VAS) (0–100), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) index score pain subscale, or an 11-point numeric rating scale (NRS).

Endpoints

The primary endpoint was chronic knee pain intensity, measured by the VAS, WOMAC and NRS scales. Secondary endpoints were quality of life, measured on the 36-Item Short Form Health Survey (SF-36) scale and adverse events.

Study selection

Eligible RCTs were those in which patients with chronic knee pain treated with acupuncture were compared with a non-acupuncture intervention were included. Two authors (JHY and QHZ) independently screened articles for inclusion. A third review author (ZRS) helped resolve any discrepancies. A flow chart detailing study selection is presented in figure 1.

Data extraction

Data were extracted independently by two review authors (JHY and QHZ) using a specifically designed data extraction form. For each study, study characteristics (author, title, publication year, journal, country, sample size, risk of bias), patient characteristics (duration of the complaint, inclusion/exclusion criteria), details of treatment and control procedures (including the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) checklist), duration of follow-up, main outcomes (primary and secondary outcomes), withdrawals and conflicts of interest were recorded. Differences encountered during this process were settled by a third author (YL) through discussion.

Quality assessment

Two authors (YJH and ZQH) independently evaluated the methodological quality of the included studies using the Cochrane risk-of-bias tool[40] and the completeness of the STRICTA checklist. Disagreements were resolved by the third author (YL) through discussion.

Measures of treatment effect

Continuous outcomes, such as pain (measured by VAS, WOMAC pain subscale or NRS scales) and quality of life (measured by SF-36 scale), were expressed as mean difference (MD) with a 95% confidence interval (CI). Other forms of continuous data were converted into MD values. Dichotomous data, such as adverse events, were expressed as risk ratio (RR) with a 95% CI. Other binary data were converted into an RR value.

Unit of analysis concerns

Cluster-randomised trials and crossover studies were excluded in this study.

Missing data

Missing data were acquired by contacting the original study authors. If the missing data were not able to be obtained, we analysed the available data.

Data synthesis

We used RevMan V.5.3 software (The Cochrane Collaboration, Oxford, England, available online at www.cochrane.org) to perform a meta-analysis of the outcome data.[41] For dichotomous data, RR and 95% CIs were reported. For continuous data, MD and 95% CIs were reported. A fixed effects models was used if I^2 was less than 50%, otherwise, a random effects model was used. If heterogeneity was too great to conduct

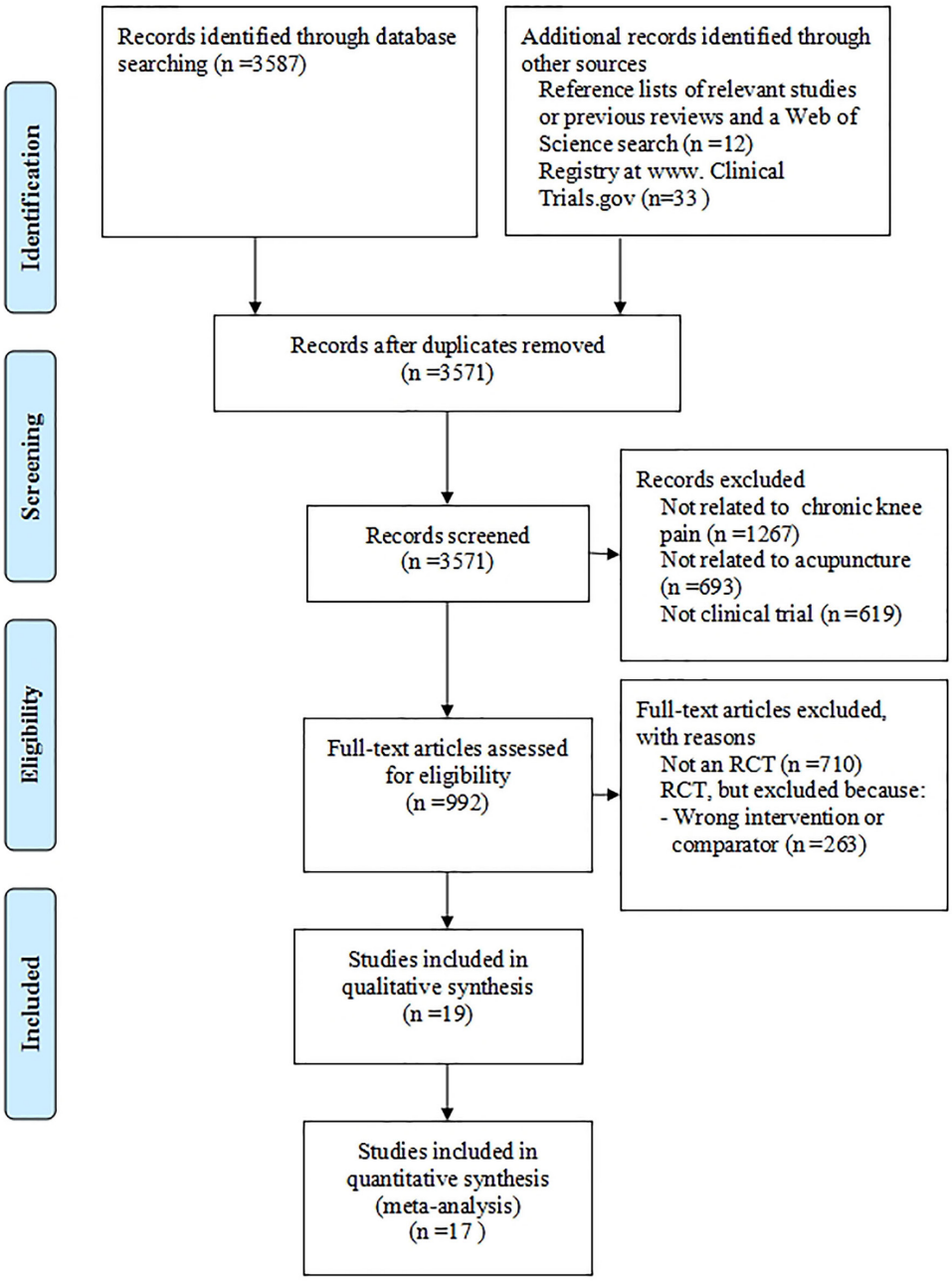

Figure 1 Flow diagram of the trial selection process. RCT, randomised controlled trial.

a meta-analysis ($I^2 \geq 75\%$), then narrative description was used to report the data.

Assessment of heterogeneity

It was planned that I^2 and χ^2 tests would be used to estimate heterogeneity of both the MD and RR. Where heterogeneity was not statistically significant, the fixed effects model was used to interpret the results; otherwise the random effects model was used, and subgroup analysis was added to explore its possible causes.

Subgroup analysis

Where the data allowed, we planned to conduct a subgroup analysis on outcomes according to type of acupuncture intervention, type of control, the country where the study was conducted, and different outcomes measured.

Sensitivity analysis

It was planned that any sources of heterogeneity would be explored using sensitivity analysis. Where heterogeneity was significant, the lower quality studies were removed. We repeated the meta-analysis, excluding the poor-quality studies. We then compared the results and discussed the causes of heterogeneity.

Assessment of reporting bias

We planned to screen for publication bias using a funnel plot if enough primary studies were available.[42]

RESULTS

Study selection

A total of 3571 studies were searched initially, of which 3552 studies were excluded. The reasons for study exclusion are described in the flow diagram of the trial selection process in figure 1. Nineteen remaining studies were included for systematic review, of which two studies had incomplete outcome data, which the authors were unable to provide (figure 1). Thus, 17 studies were included in the meta-analysis (figure 1).

Study characteristics

Characteristics of all included trials are presented in table 1. These 19 studies were published between 1992 and 2014.[43–61] The number of participants in the studies varied from 20 to 712. Two studies were conducted in the USA,[43–45] three in Germany,[46 58 59] four in China,[47–49 61] three in the UK,[52 56 57] and one each in Australia,[50] Japan,[51] Greece,[53] Iran,[54] Thailand[55] and Denmark.[60] Thirteen studies compared acupuncture as a primary treatment against different types of control intervention,[43–45 47 48 50–52 56–60] of which two consisted of no treatment,[50 56] three used allocation to a waiting list,[58–60] two used pharmaceutical interventions (namely sodium hyaluronate[47] and glucosamine hydrochloride capsules[48]), and one each used standard care (oral therapy),[43] usual care (medications and interventions),[52] education,[44 45] topical poultices,[51] isometric exercises[54] and home exercises.[57] Three studies tested electroacupuncture (EA) alone compared with ibuprofen,[49] etoricoxib[55] and transcutaneous electrical nerve stimulation.[61] One study used auricular electroacupuncture alone compared with autogenic training alone.[46] Two studies evaluated acupuncture as an adjunctive treatment compared with usual care[52] and etoricoxib.[53] Overall, between 4 and 23 sessions of acupuncture were administered over a period of 2–26 weeks.

Study quality

The risk of bias of each included study as a marker of quality is presented in figure 2. Fifteen trials specified the method of randomisation, while the remaining four studies stated that participants were randomised to groups[46 47 54 55] but failed to provide a more detailed description. Nine studies did not report allocation concealment.[46–49 51 53–55 61] As these were effectiveness trials (as opposed to sham-controlled efficacy trials), it was not feasible to blind the participant or the therapist and therefore this domain was considered to be non-applicable. However, nine studies failed to provide information about the blinding of outcome assessors[43 46–51 53 61] and three trials revealed that they did not perform any blinding of the outcome assessors.[52 57 59] Twelve studies had a high risk of bias due to incomplete outcome data,[43 46 47 49 51–54 56 57 60 61] because of high withdrawals, dropouts[43 46 51 52 57] and incomplete reporting.[47 49 53 54 56 60 61] Seven studies did not report any kind of safety information,[47 49 51 53 54 60 61] and one study failed to report WOMAC score data.[56] Regarding other potential sources of bias (including lack of intention-to-treat analysis, information about cointerventions, compliance, acceptability and baseline comparisons), 16 studies were found to demonstrate an unclear risk of bias due to the lack of intention-to-treat analysis, insufficient information about cointerventions, compliance and acceptability.[45–61] Additionally, one of these trials failed to report baseline WOMAC and VAS information.[56]

The completeness of the STRICTA checklist for each study is detailed in table 2. All 19 studies reported the acupuncture rationale very well, except for that fact that eight studies did not cite literature sources to justify the treatment rationale[46–50 54 57 59]. Regarding needling details, 2 studies did not report the acupuncture points used[52 59]; only 6 studies reported the number of needles used[43 44 55 58 60 61]; 9 studies reported depths of insertion[43 44 51 54–56 60 61]; 12 studies reported the responses elicited [43 44 48 49 51 53 55–58 60 61] and degree of needle stimulation[43–46 48 49 51 53 55–58 60 61]; 17 studies reported needle retention time[43–51 53–58 60 61]; and 15 studies reported the needle type used.[43–53 55–58] All studies reported the treatment regimen very well.[43–61] Only two trials applied cointerventions.[52 53] As for practitioner background, five studies reported the duration of relevant training[46 51 52 58 59]; six studies the length of clinical experience[44–46 50–52]; and only one study reported the therapists' expertise in the specific condition.[57] All studies except one reported the intended effect of the control intervention and its appropriateness to the research question.[60] Nine studies provided the explanations given to patients regarding the treatment and control interventions, and details of the control intervention.[44–46 53–55 58 59 61] Seven studies reported sources that justifed the choice of control.[46 53–55 58 59 61]

Outcome measurements

Acupuncture versus no treatment

Acupuncture therapy was compared with no treatment in five studies,[50 51 58–60] of which two compared acupuncture with no treatment,[50 51] while the other three used waiting list control[58–60] (online supplementary table 1). One study had incomplete data, which could not be combined with the data from the other studies.[60] The outcome data from the remaining studies mentioned above, when examined individually, showed improvement in the WOMAC pain subscale at the time point closest to 8 weeks post-randomisation (MD −2.05, 95% CI −2.55 to −1.55)[58] with no significant effects at 4 weeks (MD −0.78, 95% CI −1.71 to 0.15)[51] and an apparent worsening of scores at 1 year (MD 2.10, 95% CI 0.89 to 3.31).[50] The equivalent data for VAS at the 4-week and 1-year time points also showed no significant difference (MD −3.70, 95% CI −18.82 to 11.42[51] and MD −6.00, 95% CI −15.45 to 3.45,[50] respectively).

Table 1 Characteristics of the included RCTs

Study	Location	Age (years)	Number of patients (acupuncture/control)	Treatment group	Control group	Total acupuncture sessions	Main outcome measures	Duration of intervention (weeks)
Berman *et al*[43]	USA	T: 65.7 (8.0) C: 65.5 (9.1)	73 (37/36)	Acupuncture	Standard care (oral therapy)	16	WOMAC pain scale AEs	12
Berman *et al*[44]	USA	T: 65.2 (8.4) C: 65.1 (8.8)	379 (190/189)	Acupuncture	Education	23	WOMAC pain scale SF-36 PCS AEs	26
Manheimer *et al*[45]								
Bernateck *et al*[46]	Germany	T: 51.1 (13.2) C: 52.2 (11.2)	37 (19/18)	Auricular EA	Autogenic training	6	VAS AEs	6
Dong *et al*[47]	China	T: 58.3 (7.2) C: 57.8 (7.2)	200 (100/100)	Acupuncture + sodium hyaluronate	Sodium hyaluronate	4	VAS	4
Fu and Zhang[48]	China	T: 59.3 (12.3) C: 58.0 (11.6)	120 (60/60)	Acupuncture	Glucosamine hydrochloride capsules	20	WOMAC pain scale SF-36 PCS SF-36 MCS AEs	4
Fu and Li[49]	China	T: 85 (4) C: 85 (5)	60 (30/30)	EA	Ibuprofen	20	VAS	3
Hinman *et al*[50]	Australia	T: 64.3 (8.6) C: 62.7 (8.7)	141 (70/71)	Acupuncture	No treatment	8–12	WOMAC pain scale NRS SF-12 PCS SF-12 MCS AEs	12
Itoh *et al*[51]	Japan	62–83	16 (8/8)	Acupuncture	No treatment	5	VAS	5
Lansdown *et al*[52]	UK	T: 62.9 (8.0) C: 64.2 (8.5)	30 (15/15)	Acupuncture + usual care	Usual care (medications and interventions)	10	WOMAC pain scale SF-36 PCS AEs	10
Mavrommatis *et al*[53]	Greece	T: 62.3 (9.9) C: 63.0 (10.6)	80 (40/40)	Acupuncture + etoricoxib	Etoricoxib	4	WOMAC pain scale VAS	8
Saleki *et al*[54]	Iran	40–65	40 (20/20)	Acupuncture	Isometric exercises	12	VAS	4
Sangdee *et al*[55]	Thailand	T: 65.1 (3.4) C: 62.1 (7.5)	97 (48/49)	EA	Etoricoxib)	12	WOMAC pain scale VAS AEs	4
Tukmachi *et al*[56]	UK	T: 61 C: 61	20 (10/10)	Acupuncture	No treatment	10	WOMAC pain scale VAS	5
Williamson *et al*[57]	UK	T: 72.4 (7.7) C: 69.6 (10.0)	121 (60/61)	Acupuncture	Home exercises	6	VAS AEs	6
Witt *et al*[58]	Germany	T: 64.5 (6.4) C: 63.4 (6.6)	219 (149/70)	Acupuncture	Waiting list	12	WOMAC pain scale SF-36 PCS SF-36 MCS AEs	12

Continued

Table 1 Continued

Study	Location	Age (years)	Number of patients (acupuncture/control)	Treatment group	Control group	Total acupuncture sessions	Main outcome measures	Duration of intervention (weeks)
Witt *et al*[59]	Germany	T: 60.6 (10.2) C: 61.9 (10.6)	463 (235/228)	Acupuncture	Waiting list	15	WOMAC pain scale SF-36 PCS SF-36 MCS AEs	12
Christensen *et al*[60]	Denmark	69.2 (48–75)	29 (14/15)	Acupuncture	Waiting list	6	VAS	9
Ng *et al*[61]	China (Hong Kong)	T: 84.4 (6.5) C: 85.0 (6.9)	24 (8/8)	EA	TENS	8	NRS	2

AE, adverse event; C, control group; EA, electroacupuncture; MCS, Mental Component Summary; NR, not reported; NRS, 11-point numeric rating scale; PCS, Physical Component Summary; SF-12, 12-Item Short Form Health Survey; SF-36, 36-Item Short Form Health Survey; T, treatment group; TENS, transcutaneous electrical nerve stimulation; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

However, meta-analysis of three studies showed that acupuncture was associated with significantly reduced chronic knee pain at 12 weeks on the WOMAC pain subscale (MD −1.12, 95% CI −1.98 to −0.26, I^2=62%) (figure 3) and VAS (MD −10.56, 95% CI −17.69 to −3.44, I^2=0%) (figure 3). A sensitivity analysis of WOMAC pain subscale at 12 weeks was conducted

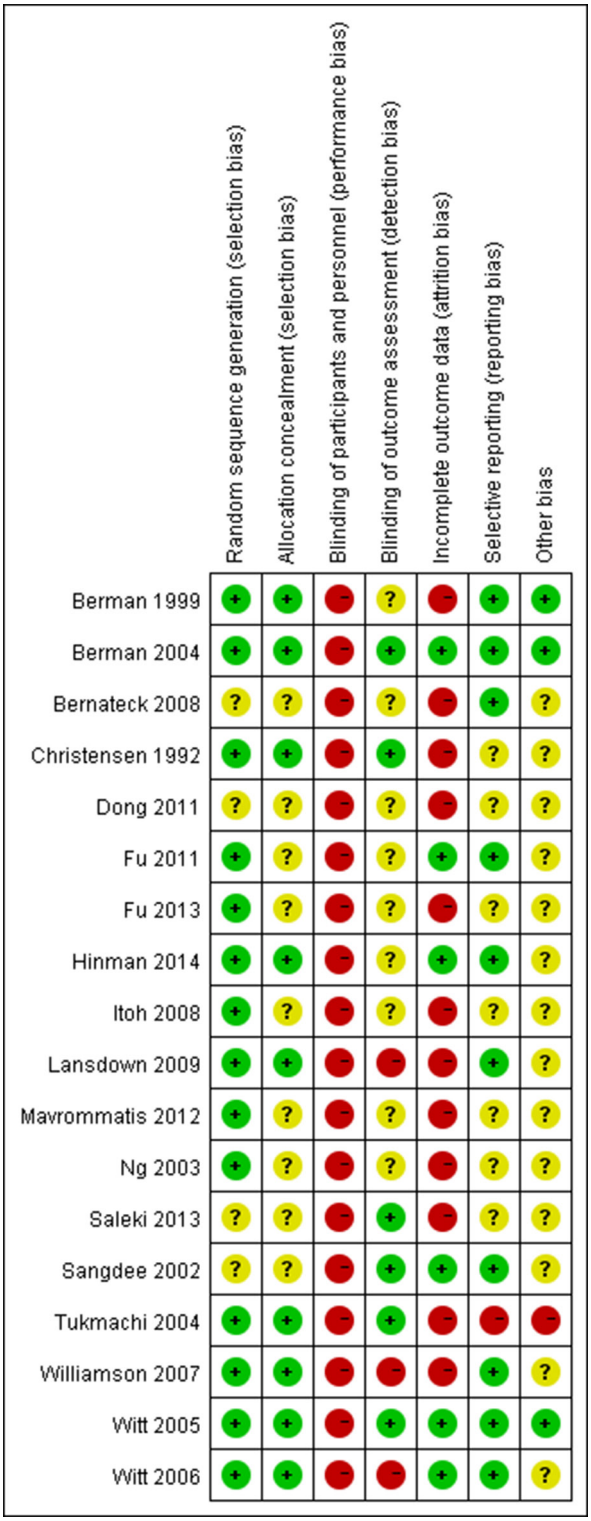

Figure 2 Risk of bias summary.

Table 2 Completeness of the STRICTA checklist for the included trials

Study	Acupuncture rationale			Needling details							Treatment regimen		Cointerventions	Practitioner background			Control intervention		
Items	1a	1b	1c	2a	2b	2c	2d	2e	2f	2g	3a	3b	4a	5a	5b	5c	6a	6b	6c
Berman *et al*[43]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Berman *et al*[44]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	No
Manheimer *et al*[45]																			
Bernateck *et al*[46]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
Dong *et al*[47]	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Fu and Zhang[48]	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Fu and Li[49]	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Hinman *et al*[50]	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	No	No
Itoh *et al*[51]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	No
Lansdown *et al*[52]	Yes	Yes	Yes	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No
Mavrommatis *et al*[53]	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes
Saleki *et al*[54]	Yes	Yes	No	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes
Sangdee *et al*[55]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes	Yes
Tukmachi *et al*[56]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No
Williamson *et al*[57]	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	No	No
Witt *et al*[58]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
Witt *et al*[59]	Yes	Yes	No	No	No	No	No	No	No	No	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
Christensen *et al*[60]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	No	No	No	No	No	No	No
Ng *et al*[61]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes	Yes

1a, style of acupuncture; 1b, rationale for treatment (eg, syndrome patterns, segmental levels, trigger points) and individualisation if used; 1c, literature sources to justify rationale; 2a, points used (unilateral/bilateral); 2b, numbers of needles inserted; 2c, depths of insertion (eg, cun or tissue level); 2d, responses elicited (eg, de qi or twitch response); 2e, needle stimulation (eg, manual or electrical); 2f, needle retention time; 2g, needle type (gauge, length, and manufacturer or material); 3a, number of treatment sessions; 3b, frequency of treatment; 4a, other interventions (eg, moxibustion, cupping, herbs, exercises, lifestyle advice); 4b, setting and context of treatment, including instructions to practitioners, and information and explanations to patients; 5a, duration of relevant training; 5b, length of clinical experience; 5c, expertise in specific condition; 6a, intended effect of control intervention and its appropriateness to research question and, if appropriate, blinding of participants (eg, active comparison, minimally active penetrating or non-penetrating sham, inert); 6b, explanations given to patients of treatment and control interventions, details of control intervention (precise description, as for item 2 above, and other items if different); 6c, sources that justify choice of control; No, no details report; STRICTA, Standards for Reporting Interventions in Controlled Trials of Acupuncture; Yes, details reported.

after removing one study with a very small sample size and incomplete outcome data[51]; the pooled results similarly showed that acupuncture decreased chronic knee pain (MD −1.33, 95%CI −2.31 to −0.35, I^2=59%) (figure 3).

Quality of life, measured using the SF-36 Physical Component Summary (PCS) was significantly improved at 8 weeks (MD 4.40, 95% CI 2.28 to 6.52[58]) and 12 weeks (MD 5.40, 95% CI 4.01 to 6.79[50,59]) but not at 1 year (MD 5.40, 95% 4.01 to 6.79[50 59]) post-randomisation. SF-36 Mental Component Summary (MCS) scores were improved at 8 weeks (MD 2.90, 95% CI 0.51 to 5.29[59]) but not at 12 weeks (MD −1.10, 95% CI −6.97 to 4.76) or 1 year (MD −3.30, 95% CI −7.08 to 0.48[50]) post-randomisation.

Acupuncture versus standard care (oral therapy)

One trial compared the effectiveness of acupuncture on pain (measured by WOMAC pain subscale) with standard care (online supplementary table 1). WOMAC scores, expressed as MD (95%CI), were significantly improved at all time points studied: −3.21 (−4.81 to −1.61), −4.12 (−5.77 to −2.47) and −3.95 (−5.43 to −2.47) at 4, 8 and 12 weeks, respectively.

Acupuncture plus usual care versus usual care (medications and interventions)

One study[52] evaluated pain by WOMAC pain subscale and found a significant reduction at 12 weeks (MD −2.97, 95% CI −5.70 to −0.24) but not 1 year (MD −0.60, 95% CI −2.89 to 1.69). There was also no significant difference in quality of life, expressed as MD (95% CI), when measured by SF-36 PCS or MCS at 12 weeks and 1 year: 12.71 (−1.60 to 27.02) and 5.30 (−4.40 to 15.00) for PCS; and 5.00 (−8.37 to 18.37) and 8.10 (−4.85 to 21.05) for MCS, respectively.

Acupuncture versus exercise

Two studies examined the effectiveness of acupuncture at relieving pain, measured by VAS, relative to exercise at three different time points.[54 57] One study found acupuncture to be inferior to exercise at 4 weeks (MD 8.03, 95% CI 2.46 to 13.60).[54] The other study found no significant difference in VAS scores between the groups at 8 and 12 weeks (MD −5.60, 95% CI

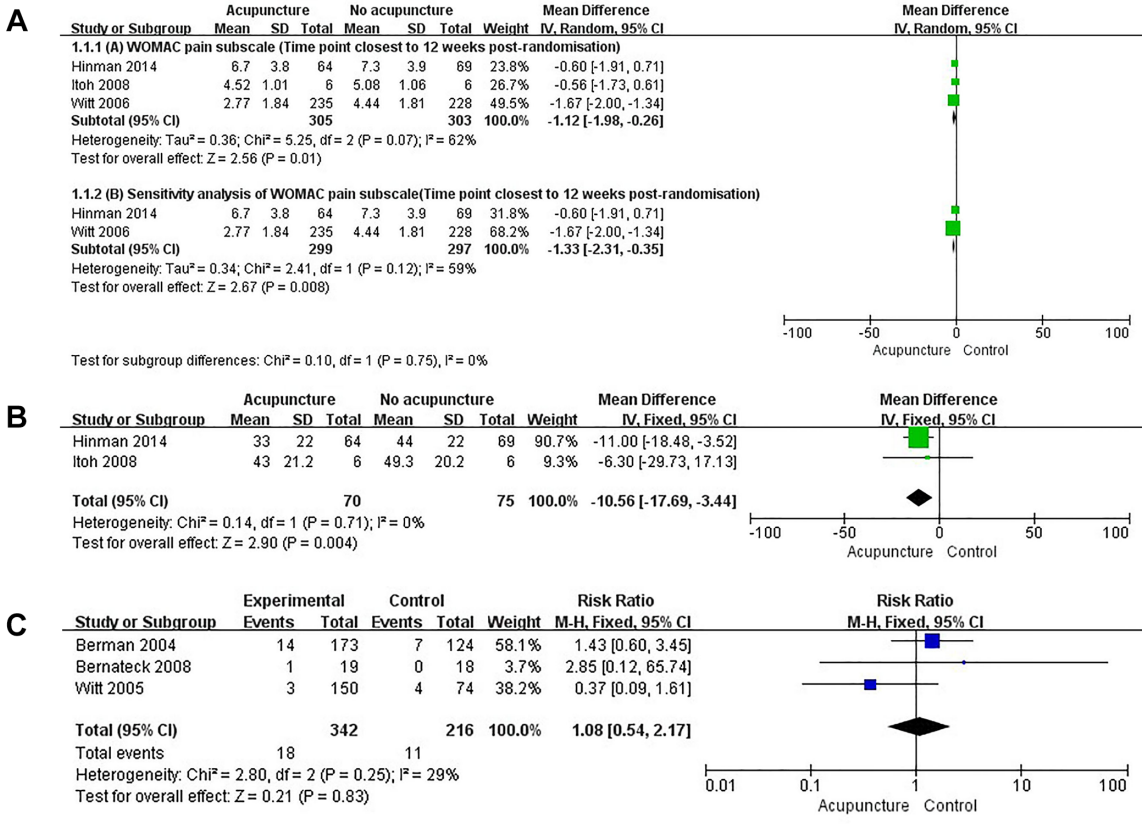

Figure 3 Meta-analyses of trials examining the effectiveness/safety of acupuncture for chronic knee pain measured by the following parameters: (A) Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale; (B) visual analogue scale (VAS); and (C) adverse events.

−14.14 to 2.94, and MD −6.60, 95% CI −14.38 to 1.18, respectively).[57]

Auricular electroacupuncture versus autogenic training

One study demonstrated a reduction in VAS scores following auricular EA at 4 weeks (MD −11.30, 95% CI −21.70 to −0.90).[46]

Acupuncture versus education

One study reported a significant reduction in pain intensity, measured using the WOMAC pain subscale, at 4, 8, 12 and 26 weeks. The MDs (95%CI) were −1.38 (−2.07 to −0.69), −1.90 (−2.72 to −1.08), −2.09 (−3.01 to −1.17) and −2.10 (−3.01 to −1.19) at the four different time points, respectively.[44 45] Quality of life was also evaluated using SF-36 PCS scores at 8 and 26 weeks and found to be increased: MDs (95% CI) were 4.90 (1.16 to 8.64) and 6.70 (2.40 to 11.00) at the two different time points.[44 45]

Electroacupuncture versus etoricoxib

One study reported on the effectiveness of acupuncture at treating chronic knee pain compared to etoricoxib using two different outcome measurements (WOMAC pain subscale and VAS, respectively) at 4 weeks and found no significant differences between groups (MD −0.75, 95% CI−2.30 to 0.80, and MD −15.25, 95% CI−25.70 to −4.80, respectively).[55]

Electroacupuncture versus ibuprofen

One study assessed chronic knee pain in EA- versus ibuprofen-treated groups using the VAS scale at 4 weeks and found a significant reduction in pain scores associated with EA (MD −3.70, 95% CI −6.08 to −1.32).[49]

Acupuncture plus etoricoxib versus etoricoxib

One study reported the effects of acupuncture as an adjunct to etoricoxib on chronic knee pain assessed by WOMAC pain subscale and VAS scale at 4, 8 and 12 weeks.[53] The MDs (95%CI) were −4.01 (−5.76 to −2.26), −7.08 (−8.53 to −5.63) and −7.59 (−9.22 to −5.96); and −16.30 (−21.65 to −10.95), −24.30 (−28.19 to −20.41), −25.90 (−30.39 to −21.41) at the three time points, respectively. When quality of life was assessed at 8 weeks, there was a significant improvement in SF-36 PCS scores (MD 10.50, 95% CI 7.95 to 13.05) but not SF-36 MCS scores (MD 1.50, 95% CI −1.88 to 4.88)[53] (online supplementary table 1).

Acupuncture versus glucosamine hydrochloride capsules

Two studies compared the effects of an acupuncture intervention alone for the treatment of chronic knee pain using the WOMAC pain subscale at 4[48 56] and 8[48] weeks as well as the VAS scale at 4 weeks.[47 56] There was no significant change in either parameter when examined at 4 weeks (MD −3.13, 95% CI −9.50 to 3.25, for WOMAC score, and MD −13.32, −58.49 to 31.85, for VAS score, respectively; random effects model). However, the WOMAC pain subscale scores were significantly lower (MD −1.87, 95% −2.19 to −1.56; fixed effects model).

One study reported the quality of life with SF-36 PCS and MCS at 4 and 8 weeks.[48] A significant improvement in both parameters was seen at 8 weeks (MD 4.99, 95% CI 1.83 to 8.15, for PCS; MD 6.22, 95% CI 3.33 to 9.11, for MCS, respectively) but not at 4 weeks (MD 1.83, 95% CI −0.86 to 4.52, for PCS; and MD 2.88, 95% CI −0.90 to 6.66, for MCS, respectively).

Safety

Four studies reported adverse events associated with acupuncture treatment of chronic knee pain. One study examining the use of acupuncture as adjunctive therapy reported that seven minor adverse events occured in the acupuncture group. The other three trials compared the safety of acupuncture with other interventions. The results of our meta-analysis showed that there was no significant difference in the rate of adverse events between acupuncture and control groups (RR 1.08, 95%CI 0.54 to 2.17, I^2=29%) (figure 3).

DISCUSSION

In this systematic review, RCTS of acupuncture therapy, administered as an isolated or adjunctive intervention, were identified and evaluated to assess the effectiveness and safety of this technique for the treatment of chronic knee pain. We were only able to conduct two meta-analyses due to the fact that studies employed different intervention comparisons and outcome measurements. One meta-analysis combined the data from three studies using the WOMAC pain subscale (time point closest to 12 weeks post-randomisation)[50 51 59] and data of two studies using VAS (time point closest to 12 weeks post-randomisation) as outcome measures.[50 51] The second meta-analysis combined the data from three studies relating to adverse events.[44 46 58]

Limited data resulted in an inability to pool the results of most of the included studies. Fortunately, the data from several studies were available for synthesis.[44 46 50 56 58 59] However, due to high heterogeneity, only one meta-analysis could be conducted to evaluate effectiveness in this study. As for safety, only three studies reported adverse events for acupuncture alone. The analysis showed no difference between the acupuncture intervention and control therapies.

Several limitations were identified in this study. First, several sham control acupuncture studies were excluded because they did not meet our inclusion criteria according to our previously published protocol.[62] Therefore, it was not possible to reach a global and comprehensive summary of all the evidence. For example, we excluded 11 studies based on design limitations.

Secondly, the time points at which outcomes were reported and measured in many of the studies varied significantly, which frequently resulted in insufficient data for a given outcome measurement being available to pool at a given time point. Thus, we were unable to synthesise the outcome data measured at several different time points into one meta-analysis.

Thirdly, the overall methodological quality of the included trials was not satisfactory. Some studies provided insufficient information to be able to evaluate the risk of bias. For instance, four studies did not clearly describe the specifics of randomisation,.[44 47 54 55] and allocation concealment was not mentioned in nine studies.[44 47–49 51 53–55 61] Furthermore, many studies did not provide a published protocol or register it prior to execution.

There are several important implications from this review that can be applied to the design of future clinical studies. Firstly, all clinical trials should be prospectively registered in an openly-accessible national or international trial registry, such as ClinicalTrials.gov, which is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.[63] In this way, researchers can easily identify whether a trial is affected by selective reporting, incomplete outcome reporting or other limitations. While an appropriate control group is crucial for the design of future clinical acupuncture studies (including sham acupuncture, waiting list or control treatments), it would be helpful for comparison in systematic reviews for researchers to increase the homogeneity of control interventions and standardisation of time points measured. Finally, the outcome measurement tools should also be clinically validated in future studies.

CONCLUSION

In this systematic review, based on the current available evidence, we can draw the conclusion that acupuncture only or as an adjunctive intervention may be effective for treating chronic knee pain at 12 weeks after acupuncture administration. In addition, the safety record is satisfactory for acupuncture intervention based on the analysed trials. However, given the heterogeneity and methodological limitations of the included trials, we are currently unable to draw any strong conclusions regarding the effectiveness and safety of acupuncture for chronic knee pain.

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Updated systematic review and meta-analysis of acupuncture for chronic knee pain

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