Author's response to reviews

Title: Acupuncture for ankle sprain: systematic review and meta-analysis

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Author's response to reviews: see over
Dear Dr. Tom Rowl es,

We are pleased to submit the revised manuscript entitled “Acupuncture for ankle sprain: Systematic review and meta-analysis” for consideration for publication in BMC Complement Altern Med. (Manuscript no. 162010349801865). We greatly appreciate the associate editor’s critical comments and have tried our best to incorporate his suggestions and recommendations into the revised manuscript. Attached are point-by-point detailed responses to the comments from the associate editor and a tracked copy of the 2nd revision. We also used the English language editing service from Edanz to improve the style of written English as recommended (Manuscript no. G1302-3029-Lee).

We thank you in advance for your consideration of this revised manuscript.

Yours faithfully,

Hyangsook Lee, KMD, PhD, associate professor
(1) Background:
(a) p.5 first paragraph second sentence. "It has been estimated..." Why only cited the incidence in US? Seems insufficient as your data were drawn from studies in different countries. Could add a little more background information (at least the prevalence or incidence info in Korea). And move this sentence to p.6 before discussing acupuncture for a better flow.

ANSWER: Currently, we are afraid that we have no official statistics on incidence or prevalence of ankle sprain in Korean population. However, we did our best to provide detailed background information, so we added detailed Korean information (based on the national health insurance statistical yearbook published in 2010) in the manuscript as the editor suggested. Korean information was put before acupuncture part as the editor suggested.

We revised this part and introduction as a whole with a help from English language editing service and hope that the revised introduction would satisfy the editor.

(b) p.6, before discussing acupuncture, you may want to add some transition discussion from the conventional three treatment options to CAM treatments to make the article flow better.

ANSWER: Yes, we revised this paragraph to put additional information on treatment options available in complementary and alternative medicine and their evidence. Then we put acupuncture’s increasing popularity especially in painful conditions, survey data on physicians’ use of acupuncture for ankle sprain, Korean information on acupuncture’s use for ankle sprain, followed by research examples. As mentioned above, we revised this part and introduction as a whole with a help from English language editing service and hope that the revised introduction would satisfy the editor.

(2) Methods:
(a) p. 13-14 although I understand why you chose to use RR of non-responders based on the correspondence between the authors and reviewers, it would be
helpful to elaborate a little more why you use non-responder and how to interpret the results. Lower RR of non-responders doesn’t translate to global symptom improvement intuitively.

**ANSWER**

We revised the statistical analyses part accordingly and added a sentence explaining how to interpret the RR of non-responders. Please see statistical analyses in the methods section.

(b) p. 14 and p. 20. It seemed that the definition of non-responders are not consistent.

**ANSWER**

We corrected and harmonized them. Please see page 24 in the tracked manuscript.

(3) Results:

(a) p.27. 2 sample size. "resulted in significant difference" of WHAT? Need to clarify.

**ANSWER**

We revised the sentence as follows: When 4 studies which had ≥40 participants per group [24, 26, 33, 40] were pooled, there was no significant difference in the risk of symptoms persisting or getting worse between acupuncture and control group (RR 0.50, 95% CI 0.24 to 1.05, $I^2 = 55\%$). Please see page 31 in the tracked manuscript.

(b) p.23. 2. Ankle instability & swelling. If No study reported as a separated outcomes measures, why did you use this measure?

**ANSWER**

When we prepared a protocol of this review, we referred to some relevant guidelines (KNGF guideline & AHRQ guideline) \(^1\) for ankle sprains. We discussed together and judged that ankle instability and swelling are important factors in assessing the treatment effect. So we decided to include them in our secondary outcome measures, but there was no study reporting this outcome and we reported as such.


(4) Discussion: Implications for practice section didn’t add much new information and can be combined with “Applicability of evidence”.

ANSWER> As you recommended, we combined two sections into one, “Implications for practice”. Please see pages 38-41 in the tracked manuscript.

(5) Overall writing: Although a review article requires more description, this paper reads a little redundant and needs to be more precise. Some paragraphs are choppy. The heading and subheading are confusing, please refer to BMCCAM published articles to see how to better organize the content.

ANSWER> We referred to other reviews published in BMC CAM and tried to reorganize the contents, and rename headings and subheadings to minimize redundancy and ensure readers’ clear understanding of our manuscript. We also used a professional language editing service (Edanz) as recommended so that our manuscript reads well (Manuscript no. G1302-3029-Lee).

We sincerely thank the associate editor for his valuable comments which we believe have improved the revised manuscript.
Acupuncture for ankle sprains: systematic review and meta-analysis

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Abstract

Background: Ankle sprain is one of the most frequently encountered musculoskeletal injuries. However, the efficacy of acupuncture for treating ankle sprains remains uncertain. Therefore, we performed a systematic review to evaluate the evidence on acupuncture for ankle sprains.

Methods: We searched 15 data sources and two trial registries up to February 2012. Randomized controlled trials of acupuncture were included if they involved patients with ankle sprains and reported outcomes of symptom improvement including pain. A Cochrane risk of bias assessment tool was used. Relative risk (RR) or mean difference (MD) were calculated with 95% confidence intervals (CI) in a random effects model. Subgroup analyses were performed based on acupuncture type, grades of sprain, and control types. Sensitivity analyses were also performed with respect to risk of bias, sample size, and outcomes reported.

Results: Seventeen trials involving 1820 participants were included. Trial quality was generally poor, with three reporting adequate methods of randomization and only one a method of allocation concealment. Significantly more
participants in the acupuncture group reported global symptom improvement

compared with no acupuncture group (RR of non-responder symptoms persisting with acupuncture = 0.56, 95% CI 0.42 to 0.77). However, this is probably an overestimate due to heterogeneity ($I^2 = 51\%$) and high risk of bias of the included studies. Acupuncture as an add-on treatment also improved global symptoms compared with other treatment only without significant variability (RR 0.61, 95% CI 0.51 to 0.73, $I^2 = 1\%$). Acupuncture’s benefit remained significant when the analysis was limited to two studies with a low risk of bias. Acupuncture was more effective than various controls in relieving pain, facilitating return to normal activity, and promoting quality of life, but these analyses were based on only a small number of studies. Acupuncture does not appear to be associated with adverse events.

**Conclusion:** Given methodological shortcomings and the small number of high-quality primary studies, the available evidence is insufficient to recommend acupuncture as an evidence-based treatment option, calling for further rigorous investigations.
**Key words:** acupuncture; ankle sprain; systematic review; randomized controlled trial; meta-analysis.
Background

Description of the condition

An acute ankle sprain is an acute injury of one or more of the ligaments of the ankle. Among the tendon and ligament injuries presenting to physicians, acute ankle sprain is one of the most commonly encountered musculoskeletal injuries in athletes and sedentary people. Ankle sprains result in high costs to society due to increased healthcare resource use and work absence. It has been estimated that ankle sprain occurs at a rate of one injury per 10,000 people every day in the US, accounting for an estimated 2 million injuries per year and 20% of all sports injuries [1, 2]. In Korea, ankle injury is the 3rd most common disease and about two million patients visit oriental medical clinic per day, with an incidence of ... patients per year [7].

Depending on the severity of injuries, ankle sprains are classified into three grades: grade I indicates mild stretching or partial tear of the anterior talofibular and/or calcaneofibular ligaments accompanied by mild tenderness and swelling but with slight or no functional loss; grade II is incomplete tear of ligaments with moderate pain, swelling and functional loss; and grade III is...
characterized by complete tear of ligaments that results in severe swelling, pain
and loss of function and motion [3].

The main goals of treatment are to relieve pain, maintain range of motion
(ROM), return to pre-injury level, and prevent recurrence of injury. Among
many different treatment options used for ankle sprains, the three major
treatments are conservative treatment, functional treatment and surgical
treatment. Conservative treatment means plaster cast immobilization and
functional treatment indicates early mobilization with using external supports
(e.g. elastic bandage, tape or orthotic support), plus coordination training [4].

For patients with grade I or II, early use of PRICE (protection, rest, ice,
compression and elevation), ankle support and keeping of ROM are necessary.

For patients with grade III, surgical treatment is recommended [3]. In addition
to these treatments, analgesics such as acetaminophen and non-steroidal anti-
-inflammatory drugs (NSAIDs) are commonly used as an adjunct. Therapeutic
ultrasonography and short-wave diathermy are also commonly used, but there

is little evidence to promote their use in terms of symptom relief [5, 6].

**Description of the intervention**
In addition to conventional treatments for ankle sprains, complementary and alternative therapies such as herbs and homeopathy have been thought to relieve pain, reduce swelling, and help the body restore damaged tissue, but the evidence is sparse and limited [7, 8]. Acupuncture, one of the most commonly used therapeutic modalities in complementary and alternative medicine, has been extensively applied for painful conditions [9, 10]. One survey reported that 76% of responding American physicians used acupuncture for ankle sprain and 90% of them assessed its efficacy as very/somewhat effective [11]. In 2009, approximately 2.8 million Korean people were diagnosed as ankle injury. Among them, 1.2 million patients sought acupuncture treatment, with an ankle injury being the 5th most common disease for visiting Korean Medicine clinics [12]. Acupuncture is one of the most frequently used complementary and alternative medicine modalities in Asian countries including Korea, ankle injury being the 3rd most common disease for patients to seek acupuncture treatment from Korean Medicine Doctors [7]. In 2009, approximately 2.8 million people were diagnosed as ankle injury. Among them, 1.2 million patients sought Korean Medicine
treatment, with an ankle injury being the 5th most common disease for visiting Korean Medicine clinics [7]. Clinical experience and some animal studies have also reported that ankle sprain responds rapidly to acupuncture, which achieves alleviation in pain intensity and duration, and also contributes to the prompt return to their pre-injury activity [13, 14][8, 9]. Given its popular use and claimed effectiveness, however, the efficacy evidence of acupuncture for treating ankle sprain remains unclear.

**Objective**

As there is no concluded convincing information on the efficacy of acupuncture for ankle sprains, therefore, we decided to critically evaluate the evidence for or against acupuncture for ankle sprains.
Methods

--- Data sources

We searched the Cochrane Central Register of Controlled Trials, Pubmed (1975 to February 2012), Ovid EMBASE (1980 to February 2012), the Cumulative Index to Nursing and Allied Health Literature (CINAHL, 1996 to February 2012), SPORTDiscus (1982 to February 2012), the Allied and Complementary Medicine Database (AMED, 1990 to February 2012), Rehabilitation and Sports Medicine Source (2007 to February 2012) and China National Knowledge Infrastructure databases (CNKI, 1979 to February 2012). We also searched Korean databases including Oriental Medicine Advanced Searching Integrated System, Korean Studies Information Service System, RISS4U, Korea Institute of Science and Technology Information, KOREAMED, DBPIA, and Korea National Assembly Library. Ongoing trials were searched in trial registries of www.controlled-trials.com and www.clinicaltrials.gov. Reference lists of reviews and relevant articles were screened for additional studies.

Search terms used for Cochrane Central Register of Controlled Trials were as follows: (“ankle injuries”[MeSH] OR “sprains and strains”[MeSH] OR “sprain”)[ti,ab]
ab, kw] OR “strain*”[ti, ab, kw] OR “injur*”[ti, ab, kw] OR “ankle*”[ti, ab, kw]) AND
(“acupuncture”[MeSH] OR “acupuncture therapy”[MeSH] OR “acupunc*”[ti, ab, kw] OR “electroacupunc*”[ti, ab, kw] OR “meridian*”[ti, ab, kw] OR “acupoint*”[ti, ab, kw] OR “moxibustion*”[ti, ab, kw] OR “moxa*”[ti, ab, kw]). These search terms were slightly modified for other databases. Trials published in English, Korean and Chinese were sought.

Study selection

Eligibility criteria

Types of studies:

All randomized controlled trials (RCTs) evaluating acupuncture treatment for ankle sprains were considered.

Types of participants:

Studies enrolling patients who reported an ankle sprain regardless of duration were eligible for inclusion. The diagnosis could be based on any methods, e.g. physical examination (positive anterior drawer test, pain and swelling), an arthrogram or a stress radiograph of the injured ankle. Trials including patients with congenital deformities, degenerative conditions, or fractures were excluded. Mixed population studies including adults and children were included.
Types of intervention:

Acupuncture included needle acupuncture, ear acupuncture, electroacupuncture, pharmacopuncture (injection of herbal medicine into acupuncture points), bee-venom acupuncture, scalp acupuncture, warm acupuncture and moxibustion.

Studies which assessed the combined effect of acupuncture plus other related treatments (e.g. acupuncture plus moxibustion) were also considered. We did not include trials testing non-penetrating acupuncture point stimulation (e.g. acupressure, transcutaneous electrical nerve stimulation (TENS), or magnets).

Trials comparing different forms of acupuncture were excluded, because the efficacy of control intervention could not be determined. Details of acupuncture interventions were extracted and tabulated based on the revised STAndards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [15][10].

Types of control:

For control groups, we considered placebo, usual care and no interventions.

Sham or placebo acupuncture interventions mean non-penetrating sham needle or superficial needling at non-acupuncture points. Usual care includes PRICE technique, analgesic drugs, functional exercise, and/or electrotherapy such as
ultrasound or short-wave. When acupuncture was given with other usual
treatment, we only included trials where the identical usual treatment was
administered both to the acupuncture group and the control group.

*Types of outcome measures:*

The primary outcome of this systematic review was patient-reported global
symptom improvement at the end of treatment. Pain intensity data were
included in the review if data for global symptoms were not provided.

Secondary outcomes included time to achieve pre-injury level of work or sports,
both subjective (e.g. giving way) and objective (e.g. inversion stress test, talar
tilt, anterior drawer test, postural sway analysis) evaluations of ankle instability,
dichotomous (e.g. yes or no) and continuous data (e.g. visual analog scale,
VAS) of swelling, recurrence of ankle sprain, subsequent surgery or long-term
treatment, health-related quality of life (e.g. SF-36), and adverse events related
to acupuncture treatment.

**Literature search**

We searched the Cochrane Central Register of Controlled Trials, Pubmed (1975
to February 2012), Ovid EMBASE (1980 to February 2012), the Cumulative Index
to Nursing and Allied Health Literature (CINAHL, 1996 to February 2012),
SPORTDiscus (1982 to February 2012), the Allied and Complementary Medicine Database (AMED, 1990 to February 2012), Rehabilitation and Sports Medicine Source (2007 to February 2012) and China National Knowledge Infrastructure databases (CNKI, 1979 to February 2012). We also searched Korean databases including Oriental Medicine Advanced Searching Integrated System, Korean Studies Information Service System, RISS4U, Korea Institute of Science and Technology Information, KOREAMED, DBPIA, and Korea National Assembly Library. Ongoing trials were searched in trial registries of www.controlled-trials.com and www.clinicaltrials.gov. Reference lists of reviews and relevant articles were screened for additional studies.

Search terms used for Cochrane Central Register of Controlled Trials were as follows: (“ankle injuries”[MeSH] OR “sprains and strains”[MeSH] OR “sprain*”[ti, ab, kw] OR “strain*”[ti, ab, kw] OR “injur*”[ti, ab, kw] OR “ankle*”[ti, ab, kw]) AND (“acupuncture”[MeSH] OR “acupuncture therapy”[MeSH] OR “acupunc*”[ti, ab, kw] OR “electroacupunc*”[ti, ab, kw] OR “meridian*”[ti, ab, kw] OR “acupoint*”[ti, ab, kw] OR “moxibustion*”[ti, ab, kw] OR “moxa*”[ti, ab, kw]). These search terms
were slightly modified for other databases. Trials published in English, Korean and Chinese were sought.

**Study selection and data extraction and risk of bias assessment**

**Data extraction:** Two reviewers (Jimin Park & Ji-Yeun Park) independently reviewed all searched articles to evaluate suitability for inclusion. If there was disagreement, it was resolved by discussion among reviewers and further information was sought from the original authors if necessary.

After selection of studies, the aforementioned two reviewers extracted data from the selected articles independently: author, year of publication, country, study design, participants (age, gender), duration of disease, acupuncture intervention, control intervention, outcome measures, main results and adverse events.

**Risk of bias assessment**

**Risk of bias assessment:** Two reviewers (Jimin Park & Ji-Yeun Park) independently evaluated risk of bias for the included studies according to the Cochrane Collaboration’s risk of bias assessment tool [16][14]. The evaluated items for risk of bias were as follows:
(1) Was the method of randomization sequence generation adequate?

(2) Was the treatment allocation adequately concealed?

(3) Was the patient blinded to the intervention?

(4) Was the outcome assessor blinded to the intervention?

(5) Were incomplete outcome data adequately addressed?

(6) Are reports of the study free of suggestion of selective outcome reporting?

Reviewers rated risk of bias for each item using ‘Yes, Unclear, or No’ as keys of judgments; the answer ‘Yes’ meant a low risk of bias (Y), ‘Unclear’ meant uncertain or unknown risk of bias (U), and ‘No’ meant a high risk of bias (N). If there were disagreements, it was resolved by discussion among reviewers.

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**Statistical Analyses**

Statistical analysis: Review Manager software (version 5.1 for Windows; The Nordic Cochrane Centre, Copenhagen, Denmark) was used to perform statistical analysis. Studies were classified and combined in the main analysis according to the purpose of acupuncture intervention, i.e. acupuncture as an alternative or as an add-on treatment. Data were pooled using a random effects model. The impacts of acupuncture on dichotomous data were
expressed as a risk ratio (RR) of non-responders of global symptoms improvement persisting with acupuncture compared with control with 95 % confidence intervals (CIs), i.e. RR of non-responders. To define non-responders, patient-reported global symptoms in ordinal assessments were divided into two groups (e.g. ‘poor or good’ as non-responder vs. ‘very good or excellent’ as responder). If different strata were used to define improvement, the cut-off point with the least improvement was taken (e.g. if the ordinal assessment was poor, good, and excellent, we utilized a poor vs. good or excellent comparison).

Taken together, an RR value of less than 1 indicates a lower risk of symptoms persisting or getting worse with acupuncture compared with control group. For continuous outcomes, the mean difference (MD) with a 95 % CI was calculated.

Visual inspection of the forest plots and a $\chi^2$ test with a significance level of $p < 0.1$ was used to assess heterogeneity among studies. To quantify inconsistencies among the included studies, the $I^2$ test was used and the $I^2$ value of 50 % or more was considered to be indicators of a substantial level of heterogeneity [17][42]. Subgroup analyses were conducted in terms of different acupuncture interventions (e.g. manual acupuncture, electroacupuncture), different grades of
ankle sprain, and control types (e.g. usual care, sham acupuncture). Sensitivity analyses were also planned by including studies with low risk of bias only, or by including studies with sample size ≥ 40 per arm, and by differently grouping the outcome measures. We analyzed the trials with a low risk of bias for randomization and/or allocation concealment only [18, 19][13, 14] and examined if the estimate of the intervention effect was affected. Studies with ≥ 40 participants per arm were analyzed separately to see whether there emerges any difference in the estimate [20][45]. For outcome measures, as it is common for Chinese trials to report outcomes based on an ordinal assessment (e.g. ‘excellent’, ‘very good’, ‘good’, ‘poor’), we also performed a sensitivity analysis by re-analyzing the dichotomous outcomes; we compared the ‘excellent, very good vs. good, poor’ scenario which was our original analysis to the ‘excellent, (very) good vs. poor’ scenario to ascertain any discrepancies.
Results

Selection of eligible Description of studies

Our search terms yielded 387 records: 5 in the Cochrane Central Register of Controlled Trials, 21 in the EMBASE, 42 in the CINAHL, 10 in the SPORTDiscus, 10 in the AMED, 2 in the Rehabilitation and Sports Medicine Source, 175 in the CNKI, 90 in the Pubmed, and 32 in the relevant Korean journals. After duplicate studies were removed, 380 records were screened. Based on the title and abstract, 322 records were excluded; 162 articles were not specific to the topic of this review and 160 were not clinical studies or were non-randomized trials.

Out of the remaining 58 studies, (1) 37 studies did not satisfy the inclusion criteria for acupuncture or control intervention; comparison of different acupuncture styles (n = 9), acupuncture vs. Chinese herbal medicine or bee venom of which the efficacy has not been established (n = 8), trials where acupuncture was given with other therapies so that the effect of acupuncture per se cannot be isolated (n = 9), and trials comparing the effect of other therapy given with acupuncture to acupuncture alone (n = 11). (2) One study published in French was excluded; (3) we failed to obtain full texts of three...
studies. Finally 17 studies were included in our review and 16 studies reporting patient-reported global assessment outcome were pooled in the main analysis.

Figure 1 shows a flow diagram of literature searching as recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Characteristics of the included studies

Details of the included studies are summarized in Tables 1, 2 and supplementary table 1.

Participants:

Seventeen studies involving 1,820 participants were included in our review. All of them were conducted in China and they were published in Chinese. When divided into acute, chronic and mixed ankle sprains based on 6 months after onset cutoff [22, 23][17–18], 12 studies [24-35][19-30] involved participants with acute ankle sprains, three studies [36-38][31-33] involved mixed participants, no study involved participants with chronic ankle sprains only, and one study [39][34] did not report disease duration but it was assumed that the participants had acute ankle sprain. Another study [40][35] mentioned ‘acute’ in the title but
326 participants had sprained ankles for less than two days while the other 12 did so for more than three days. Regarding the severity of the sprain, only 4 trials clearly reported that the participants had grade I or II injuries [24, 28, 31, 39] [19, 23, 26, 34].

**Acupuncture intervention:**

Highly variable acupuncture interventions were given either alone or as an add-on treatment to control intervention. Out of the included 17 studies, 9 [24-26, 31-35, 40] [19-21, 26-30, 35] tested manual acupuncture, 4 [27, 30, 38, 39] [22, 25, 33, 34] used electroacupuncture, three [28, 36, 37] [23, 31, 32] used warm acupuncture and one [29] [24] used warm acupuncture in addition to manual acupuncture. Among 5 trials that assessed the effect of acupuncture alone, three studies evaluated electroacupuncture [27, 30, 39] [22, 25, 34]; one each evaluated warm acupuncture [28] [23] and manual acupuncture [26] [24]. Fixed (i.e. all participants received the same treatment), partially individualized (using a fixed set of points to be given with a set of points flexibly to be used) and individualized acupuncture treatment (each participant received a tailored treatment) were given; out of the 17 studies, 7 used fixed [24, 25, 29, 30, 33-35].
6 used partially individualized [26, 27, 31, 38-40][21, 22, 26, 33-35] and 4 used individualized acupuncture treatment [28, 32, 36, 37][23, 27, 31, 32]. The number of acupuncture sessions ranged from three to 15 over three days to 4 weeks. De-qi, acupuncture-evoked specific sensations such as numbness, heaviness, soreness, or distention, was sought in 11 studies [24-27, 29-31, 36-39][19-22, 24-26, 31-34]. Regarding acupuncture points used in the studies, 14 studies [24-27, 29-31, 33-35, 37-40][19-22, 24-26, 28-30, 32-35] used 12 meridian points and/or extra points while the other two studies [28, 36][23, 31] used tender points and one study [32][27] did not report acupuncture points. Details of acupuncture interventions are summarized in Table 2 based on the revised STRICTA [15][10].

Control intervention:

A range of control interventions were used including ice pack, exercise, bandage, analgesic drugs, herbal medicine, infrared radiation, tuina massage, hot pack or TENS. No study adopted sham acupuncture as a control group (Table 1). More than one comparison groups were used in 5 trials [33-36, 40][28-31, 35]. For 9 trials evaluating the effect of acupuncture alone, usual care [26, 27, 30, 33-
or infrared radiation [26, 28, 39][21, 23, 34] were used as a control. Two studies adopted hot pack [26, 30][21, 25] or herbal medicine [26, 35][21, 30] as a control treatment, respectively. Only one study [40][35] adopted tuina massage. Among the other 12 trials testing acupuncture as an add-on treatment, 7 trials [24, 25, 29, 33-36][19, 20, 24, 28-31] used usual care, three trials used herbal medicine [31, 32, 35][26, 27, 30] or tuina massage [37, 38, 40][32, 33, 35], respectively. One each adopted infrared radiation [38][33] or TENS [37][32].

**Outcome measures:**

Outcome measures reported in the included studies were patient-reported global assessment (in 16 trials) [24-27, 29-35, 37-40][19-22, 24-30, 32-35], pain (one trial) [36][34], time to return to pre-injury level of work or sports (4 trials) [24-26, 29][19-21, 24], recurrence rate (one trial) [38][33], health-related quality of life (one trial) [36][31] and adverse events (two trials) [34, 35][29, 30]. For patient-reported global assessment outcomes, a range of definitions were used to assess efficacy. We thus used the proportion of participants who had less
than 50% symptom poor or good improvement, i.e. non-responders, in the main analysis.

Risk of bias in the included studies

The majority of the included trials were assessed as having a high risk of bias.

Three out of the 17 studies reported adequate method of sequence generation such as using a random number table or coin tossing [24, 31, 36][19, 26, 34], and among them, group assignment was adequately concealed using sealed opaque envelopes in only one trial [24][19]. For participant and personnel blinding, not a single trial was rated as having a low risk of bias because there was no sham-controlled trial. Except three studies where outcome measure was assessed by non-blinded participants [24, 27, 33], the other 14 studies were rated as having an unclear risk of bias as we could not completely exclude the possibility that the blinded 3rd party assessor might have evaluated global symptom improvement. Regarding incomplete outcome data addressing, all but one trial were assessed as having a low risk of bias as they had no missing outcome data; one study [24][19] did not report the number of participants analyzed in the outcome measure. As to selective outcome reporting, we could
not locate and compare the protocol of any included studies, hence we judged a risk of bias based on the described methods in each study. Six studies had a high risk of bias for selective outcome reporting because they were reporting unplanned outcome measurements [24-26, 29, 37, 38][19-21, 24, 32, 33] (Table 3).

**Effects of acupuncture on primary outcome**

The key outcomes from the included studies are provided in Table 1 and Figure 2. We evaluated primary outcomes of patient-reported global assessment. Pain was considered if global assessment was not available.

1. Effects of acupuncture as an alternative treatment

Nine trials with 797 participants [26-28, 30, 33-35, 39, 40][21-23, 25, 28-30, 34, 35] reported global symptom improvement as a dichotomous outcome. Approximately 9 sessions of acupuncture were given over 11.5 days of period. Acupuncture had a statistically significant effect in reducing global symptoms of ankle sprain (RR of non-responders symptoms persisting with acupuncture = 0.56; 95 % CI 0.42 to 0.77, Figure 2 (A)). However, there was substantial heterogeneity among trials ($\chi^2 = 16.38$, degrees of freedom (df) = 8, $p = 0.04$, $I^2 = 51\%$).
2. Effects of acupuncture as an add-on treatment

Eleven trials with 926 participants reported the add-on effect of acupuncture [24, 25, 29, 31-35, 37, 38, 40][19, 20, 24, 26-30, 32, 33, 35]. Median 10 sessions of acupuncture over 9 days of period was provided. When added to other treatment, acupuncture statistically significantly improved global symptoms compared with other treatment only (RR of non-responder symptoms persisting with acupuncture = 0.61; 95 % CI 0.51 to 0.73, Figure 2 (B)). There was no significant heterogeneity among studies ($\chi^2 = 10.08, \text{df} = 10, p = 0.43, I^2 = 1\%$).

3. Effects of acupuncture for pain intensity

One study reported pain intensity on VAS immediately and over two years after treatment [36][34]. At immediately after treatment, warm needling significantly alleviated pain compared with the control group (1.32 ± 0.42 vs. 6.55 ± 1.76, MD -5.23, 95 % CI -5.61 to -4.85). At the long-term follow up of 28.8 months on average, the analgesic effect was maintained (1.01 ± 0.15 vs. 5.89 ± 1.93, MD -4.88, 95 % CI -5.29 to -4.47).

Effects of acupuncture on secondary outcomes

1. Time to achieve pre-injury level of work or sports
Four studies reported time to cure [24-26, 29][19-21, 24]. Of them, one study [24][49] reported that acupuncture in addition to functional exercise shortened the time to return to normal activity by 3.4 days than the functional exercise only group (5.2 ± 0.7 vs. 8.6 ± 1.4, MD -3.40, 95 % CI -3.88 to -2.92). In the other three studies [25, 26, 29][20, 21, 24], participants were not more likely to have recovered within a week than those in the control group whether they were given acupuncture as an add-on (two trials, RR 2.49, 95 % CI 0.60 to 10.29, I² = 0 %) or alternative treatment (one trial, RR 1.21, 95 % CI 0.99 to 1.47).

2. Ankle instability & swelling

No study reported on ankle instability and/or swelling as a separate outcome measure because the majority of the included studies reported a composite measure of patient-reported global symptom assessment.

3. Recurrence of ankle sprain

One study [38][39] reported that one participant in the acupuncture group had a re-injury while 5 in the control group did so at 6-month follow-up (RR 0.17, 95 % CI 0.02 to 1.33).
4. Health-related quality of life

One study [36][31] reported quality of life using SF-36 at immediately and over two years after treatment. At immediately after treatment, the acupuncture group reported significantly better quality of life than the control group (91.25 ± 10.16 vs. 76.53 ± 5.24, MD 14.72, 95 % CI 12.32 to 17.12). At 2-year follow up, the effect remained significant (93.62 ± 9.05 vs. 62.31 ± 6.67, MD 31.31, 95 % CI 28.95 to 33.67).

5. Adverse events

Two studies [34, 35][29, 30] reported mild adverse events such as mild allergic response to drug which was recovered at stopping (three participants).

Subgroup analyses

We conducted subgroup analyses based on the pre-defined characteristics, i.e., types of acupuncture interventions, different grades of ankle sprain, and control types.

1. Acupuncture types

Manual acupuncture [24, 25, 31-35, 40][19, 20, 26-30, 35] has an additional effect on symptom improvement compared with control groups (8 trials, RR
When given as an alternative [26][24], the RR of non-responders symptoms persisting with acupuncture was 0.20 (95 % CI 0.06 to 0.65). Electroacupuncture as a sole treatment [27, 30, 39][22, 25, 34] had no significant benefit compared with oral/topical NSAIDs or infrared radiation (three trials, RR 0.50, 95 % CI 0.20 to 1.22, $\text{I}^2 = 76 \%$). When added to massage and infrared radiation [38][33], the effect of electroacupuncture was statistically significantly better than the massage and infrared radiation only (one trial, RR 0.11, 95 % CI 0.01 to 0.82).

2. Grades of ankle sprain

There were insufficient data for subgroup analyses on the severity of the sprain; only 4 trials [24, 28, 31, 39][19, 23, 26, 34] clearly reported that the participants had grade I or II injuries and the RR of non-responders symptoms persisting with acupuncture was 0.39 (two trials, 95 % CI 0.18 to 0.88, $\text{I}^2 = 0 \%$) when acupuncture was given as an add-on treatment and 0.35 (two trials, 95 % CI 0.17 to 0.71, $\text{I}^2 = 0 \%$) when it was an alternative treatment.

3. Control types

1) Acupuncture vs. oral/topical NSAIDs
(1) Acupuncture vs. NSAIDs

Two trials with 122 participants tested the effect of acupuncture on global symptom improvement against oral/topical NSAIDs [27, 30][22, 25]. There was no statistical difference between groups (Figure 3 (A1), RR 0.64, 95 % CI 0.29 to 1.39, $I^2 = 67 \%$).

(2) Acupuncture plus NSAIDs vs. NSAIDs

Acupuncture had no additional effects on global symptom improvement compared with oral/topical NSAIDs only [33, 34][28, 29] (Figure 3 (A2), RR 0.72, 95 % CI 0.50 to 1.05, $I^2 = 22 \%$).

2) Acupuncture plus herbal medicine vs. herbal medicine

When added to oral/topical herbal medicine [31, 32, 35][26, 27, 30], significantly less participants remained with symptoms in the acupuncture group (Figure 3 (B), RR 0.56, 95 % CI 0.40 to 0.78, $I^2 = 0 \%$).

Sensitivity analyses

We also performed sensitivity analyses by excluding studies with pre-defined less desirable characteristics;

1. Risk of bias
When the analysis was limited to two studies with a low risk of bias for random sequence generation and/or allocation concealment [24, 31][19, 26], the add-on effect of acupuncture on patient-reported global assessment remained significant (RR 0.39, 95 % CI 0.18 to 0.88, I² = 0 %).

2. Sample size

When combining 4 studies which had ≥ 40 participants per group [24, 26, 33, 40][19, 21, 28, 35] were pooled, resulted in there was no significant difference in symptom improvement the risk of symptoms persisting or getting worse between acupuncture and control group (RR 0.50, 95 % CI 0.24 to 1.05, I² = 55 %).

3. Outcome measures

For 16 studies reporting the dichotomous outcome based on the ordinal assessment, we compared ‘excellent, very good’ vs. ‘good, poor’ scenario (16 trials, RR 0.55, 95% CI 0.45 to 0.69, I² = 40 %) with ‘excellent, (very) good vs. poor’ scenario (RR 0.26, 95 % CI 0.18 to 0.38, I² =0 %); the estimate remained significant without variability.
Discussion

Summary of main finding evidence

This systematic review aimed at establishing the evidence of acupuncture treatment for ankle sprains. There were a total of 17 RCTs included in this review. They investigated the effect of acupuncture as an alternative or as an add-on to other treatment on global symptom improvement of ankle sprain.

When evaluating acupuncture compared with other treatment, acupuncture has a therapeutic benefit in improving global symptoms of ankle sprain (RR of non-responders symptoms persisting with acupuncture = 0.56, 95% CI 0.42 to 0.77).

However, this is probably an overestimate due to heterogeneity ($I^2 = 51\%$) and high risk of bias of the included studies.

Compared with other treatment alone, acupuncture as an adjunct to other treatment significantly alleviated global symptoms of ankle sprain without significant variability (RR of non-responders symptoms persisting with acupuncture = 0.61, 95% CI 0.51 to 0.73).

A sensitivity analysis of the trials with a low risk for selection bias suggested that the beneficial effect of acupuncture was maintained while the effect of

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Acupuncture was not any more significant when the analysis was limited to studies with adequate sample size. Acupuncture was more effective than various controls in relieving pain, facilitating return to normal activity, and promoting quality of life, but these analyses were based on only a small number of studies. Acupuncture does not appear to be associated with serious adverse events but the evidence is limited.

**Applicability of evidence**

This systematic review suggests that there is insufficient high-quality evidence supporting the use of acupuncture to improve global symptoms of ankle sprain when it is given as an alternative treatment. Although the benefit of acupuncture as an add-on treatment for global symptom improvement in ankle sprain is significant and a sensitivity analysis of high-quality trials supports this finding, the number of studies is too small to strongly recommend it.

Although this systematic review seems to show that acupuncture may be effective in symptom improvement in ankle sprain, the true intervention effects estimated are likely to be inflated due to poor methodological design and conduct.
There are several issues worth considering before we make any judgements on acupuncture for ankle sprain in practice. First of all, tested acupuncture interventions were diverse across trials in terms of acupuncture types, acupuncture points, number of sessions, and duration of treatment. So it is difficult to determine adequate or optimal acupuncture intervention.

Secondly, control interventions used in the included studies also varied. They included usual care (e.g. ice pack, exercise, bandage, or analgesics), herbal medicine, infrared radiation, tuina massage, hot pack or TENS. Recently, studies about the efficacy of topical NSAIDs for acute pain compared with oral NSAIDs were conducted actively due to the adverse events of oral NSAIDs such as gastrointestinal complications or cardiovascular toxicities. In a recent review on topical NSAIDs for musculoskeletal pain [36], topical NSAIDs demonstrated comparable efficacy and better safety compared with oral NSAIDs for acute pain including sprains and strains and the effect of topical NSAIDs was 1.6 times better than placebo at 7 days. In our review, acupuncture as an add-on or alternative treatment demonstrated no better effect than oral/topical NSAIDs.
but it was associated with few side effects. Acupuncture was only significantly effective for symptom improvement when added to oral/topical herbal medicine. Thirdly, outcome measures of the included studies were not consistent. The clinical relevance of acupuncture's benefit shown is not obvious [37]. As there are no dependable data on the minimal clinically important difference (MCID) in patient-reported global symptom improvement of ankle sprains, we may only infer that the effect of acupuncture, is small [37]. Fourthly, all trials included in this review were conducted in China. Acupuncture may be highly culture-specific and further research is necessary to investigate the reported interventions are applicable and acceptable in other countries. Receiving acupuncture everyday may not be a generalizable treatment schedule outside China. Lastly, clinically meaningful information on severity of injury or follow-up data was sparse in the included trials. So the available evidence prevents us from determining if acupuncture exerts different effects at different injury level or how long its benefit is maintained.

Risk of bias
The majority of the included studies suffered from a serious risk of bias. Only three studies had a low risk of bias for adequate randomization and/or allocation concealment. It is well known that inadequate allocation concealment/random sequence generation leads to overestimation of treatment effect [18, 19][13–14]. Although the included studies uniformly reported no difference in baseline characteristics between groups, we cannot exclude possibility that selection bias may have played a role under such circumstances. However, when we limited our main analysis to the studies rated as having a low risk of bias for randomization/allocation concealment, acupuncture’s benefit remained significant.

Although we could not formally test for the funnel plot asymmetry to detect small-study effects – a tendency for the intervention effects estimated in smaller studies to differ from those estimated in larger studies [41][38] – due to a small number of studies, Chinese studies may have been more likely to publish positive outcomes [42, 43][39–40]; but more importantly, the effect size of small studies in this review may have been inflated due to poor methodological design and conduct [44][41]. As it is well-known that small,
poor-quality studies tend to spuriously inflate the intervention’s effect, we need
to be more conservative in interpretation of the results.

**Limitations of this review**

Although we made every endeavor to search all the relevant trials in a range of
databases and related journals, comprehensive searches do not necessarily
remove publication bias or language bias. All trials were conducted in China
and published in Chinese journals in Chinese language. Egger et al. [43][40]
reported that studies published in non-English languages or studies published
in journals that are not indexed in Medline are likely to increase the degree of
asymmetry in the funnel plot in a systematic review and this may have a
relevance to this review.

The included trials were mostly of poor quality thus reported data are likely to
be overestimated. In addition, the small sample size of the studies may have
resulted in heterogeneity of the effect size. Moore et al. [20][15] reported in the
simulation study that at least 40 participants per arm are required to get
clinically relevant results in trials of pain. Our sensitivity analysis on sample size,
i.e. trials ≥ 40 per group only [24, 26, 33, 36][19, 21, 28, 31], produced no significant benefit from acupuncture.

Finally, as is usual with other Chinese acupuncture trials, most studies in our review used various subjective outcomes. As no study compared acupuncture with sham acupuncture, this makes outcome assessment blinding even more critical. Failure in outcome assessment blinding may have influenced the results.

**Implications for practice**

This systematic review suggests that there is insufficient high-quality evidence supporting the use of acupuncture to improve global symptoms of ankle sprain when it is given as an alternative treatment. Although the benefit of acupuncture as an add-on treatment for global symptom improvement in ankle sprain is significant and a sensitivity analysis of high-quality trials supports this finding, the number of studies is too small to strongly recommend it.

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To sum up, currently we have inconclusive evidence supporting the use of acupuncture for patients with ankle sprain.

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acupuncture as an add-on treatment for global symptom improvement in ankle sprain is significant and a sensitivity analysis of high-quality trials supports this finding. The number of studies is too small to strongly recommend it. Acupuncture was more effective than various controls in relieving pain, facilitating return to normal activity, and promoting quality of life, but these analyses were based on only a small number of studies. We have no convincing evidence supporting acupuncture compared with NSAIDs whether given as an alternative or add-on treatment. Acupuncture does not appear to be associated with adverse events but the evidence is limited. To sum up, currently we have inconclusive evidence supporting the use of acupuncture for patients with ankle sprain.

Implications for research

To give a more definite answer to the efficacy of acupuncture for ankle sprain, we need more carefully designed and conducted trials. Researchers should use adequate randomization methods and make sure that group assignment is adequately concealed as these two are critical in avoiding systematic differences between baseline characteristics of the groups that are compared, i.e. selection
bias. As it is virtually impossible for the therapist to be blinded to the acupuncture intervention that they provide, it may be more important to blind participants and outcome assessor. However, there was no study with sham control in this review, so performance bias is likely to play a part in our findings. In the future, sham-controlled trial would be needed to avoid performance bias.

To maintain outcome assessor blinding, validated assessment tools are required. Recent studies have tested validity, reliability and responsiveness of relevant scales [47, 48][42, 43]. For example, the validity and responsiveness of ankle functional score (AFS) based on fundamental functional outcomes such as pain, swelling, weight bearing, stability and gait, was tested and the study concluded that AFS was easy-to-use and might be used alongside subjective clinical assessment to evaluate recovery after acute ankle sprain [48][43]. Using not only subjective patient-reported symptom improvement but also validated outcome measures, and ensuring outcome assessment blinding should be considered for future trials.
Conclusions

Given methodological flaws of the included studies, the available evidence is insufficient to recommend acupuncture as an evidence-based treatment option for ankle sprain. Further well-designed and conducted trials are needed to draw a definitive conclusion.

Additional materials file

Additional file Supplementary table 1: Characteristics of the included studies

Competing interests

The authors declare that they have no conflicts of interest.

Authors’ contributions

HSL and JMP designed this review, searched databases, and screened trials for inclusion. JMP and JYP extracted data, evaluated studies and it was checked by HSL. HSL and JMP performed analyses and discussed with HJP and SKH. All authors read and approved the final manuscript.
Authors’ information

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<table>
<thead>
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<th>Author (year)</th>
<th>Treatment (no. of participants analyzed/randomized)</th>
<th>Outcome measures</th>
<th>Results</th>
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<tr>
<td>Sun (2011) [24][49]</td>
<td>(A) MA + functional exercise (41/41)</td>
<td>1) PRGA* at 14 d</td>
<td>1) NS</td>
</tr>
<tr>
<td></td>
<td>(B) Functional exercise (41/41)</td>
<td>2) Time to cure (d)</td>
<td>2) (A) significantly better than (B)</td>
</tr>
<tr>
<td>Zheng (2010) [25][20]</td>
<td>(A) MA + PRICE (≤ 24 h), MA + EA (≥ 24 h) (40/40†; 27/40‡)</td>
<td>1) PRGA* at 15 d</td>
<td>1) (A) significantly better than (B)</td>
</tr>
<tr>
<td></td>
<td>(B) PRICE (≤ 24 h), EA (≥ 24 h) (33/33†; 12/33‡)</td>
<td>2) Time to cure</td>
<td>2) NS</td>
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<td>Wei (2010) [37][32]</td>
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<td>PRGA§ at 10 d</td>
<td>NS</td>
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<tr>
<td></td>
<td>(B) TENS + massage (30/30)</td>
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<tr>
<td>Tang (2010) [38][33]</td>
<td>(A) EA + massage + IR (30/30)</td>
<td>1) PRGA* at 10 d</td>
<td>1) (A) significantly better than (B)</td>
</tr>
<tr>
<td></td>
<td>(B) Massage + IR (30/30†; 25/30‡)</td>
<td>2) Recurrence rate at 6 month follow-up (%)</td>
<td>2) NS</td>
</tr>
<tr>
<td>He (2010) [36][34]</td>
<td>(A) WA + small needle-knife therapy + drug injection + rehabilitation (87/87)</td>
<td>1) Pain (VAS) at immediately and two yrs after treatment</td>
<td>1) (A) significantly better than (B)</td>
</tr>
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<td></td>
<td>(B) Small needle-knife therapy + drug injection + rehabilitation (87/87)</td>
<td>2) QOL (SF-36) at immediately and two yrs after treatment</td>
<td>2) (A) significantly better than (B)</td>
</tr>
<tr>
<td></td>
<td>(C) WA + rehabilitation (87/87)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>He (2006) [29][24]</td>
<td>(A) MA + PRICE (≤ 24 h), EA + WA (≥ 24 h) (46/46†; 31/46‡)</td>
<td>1) PRGA* at 15 d</td>
<td>1) (A) significantly better than (B)</td>
</tr>
<tr>
<td></td>
<td>(B) PRICE (≤ 24 h), EA (≥ 24 h) (33/33†; 12/33‡)</td>
<td>2) Time to cure</td>
<td>2) NS</td>
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<tr>
<td>Li (2002) [31][26]</td>
<td>(A) MA + oral/topical HM (23/23)</td>
<td>PRGA§ at 8 d</td>
<td>(A) significantly better than (B)</td>
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<td></td>
<td>(B) Oral/topical HM (23/23)</td>
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<tr>
<td>Ge (2000) [32][27]</td>
<td>(A) MA + oral HM (50/50)</td>
<td>PRGA§ at 10 d</td>
<td>NS</td>
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<td>(B) Oral HM (30/30)</td>
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<tr>
<td>Yu (1999) [33][28]</td>
<td>(A) MA + topical NSAIDs (50/50)</td>
<td>PRGA‡‡ at 7 d</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(B) Topical NSAIDs (50/50)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(C) MA (50/50)</td>
<td></td>
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</tbody>
</table>
Yu (20199) (A) MA + topical NSAIDs + ice pack (30/30) PRGA †† at 7 d (A) significantly better than (B), (C), or (D)

Yu (1996) (A) MA + topical HM + ice pack (30/30) PRGA § at 7 d (A) significantly better than (B)

Ruan (1995) (A) MA + massage (116/116)

Acupuncture alone vs. other therapy

Ni (2010) (A) MA (64/64 †; 61/64 ‡) 1) PRGA * at 3 d 1) (A) significantly better than (B)

Luo (2009) (A) EA (23/23)

Zhou (2008) (A) WA (26/26)

Zhao (2005) (A) EA (43/43)

Wang (2005) (A) EA (27/27)

* cured/significantly improved/improved/failed; †, for outcome measure 1); ‡, for outcome measure 2); §,
cured/improved/failed **, decrease rate ≥ 5 / decrease rate ≤ 5 (mean score of pain and swelling)
††, significantly improved/improved/failed
‡‡, cured/significantly improved/improved

There were 4 trials which reported acupuncture alone vs. other treatment and acupuncture plus other treatment vs. other treatment [33-35, 40][28-30, 35]. They were put as acupuncture as an add-on treatment trials in this table.

d indicates days; EA, electroacupuncture; h, hours; HM, herbal medicine; IR, infrared radiation; MA, manual acupuncture; no., number; NS, no significant difference between groups; NSAIDs, non-steroidal anti-inflammatory drugs; PRGA, patient-reported global assessment; PRICE, protection, rest, ice,
compression and elevation; QOL, quality of life; TENS, transcutaneous electrical nerve stimulation; VAS, visual analog scale; WA, warm acupuncture; wks, weeks; yrs, years
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Acupuncture method (Fixed/ partially individualized/ individuallyized)*</th>
<th>Treatment rationale</th>
<th>Regimen</th>
<th>Acupuncture points**</th>
<th>Response sought</th>
<th>Co-interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sun (2011)[24]</td>
<td>MA, fixed</td>
<td>Modern acupuncture (hand acupuncture)</td>
<td>14 sessions (once daily for 14 d)</td>
<td>Ex-UE205</td>
<td>De-qi***</td>
<td>Functional exercise</td>
</tr>
<tr>
<td>Zheng (2010)[25]</td>
<td>MA, fixed</td>
<td>Clinical experience</td>
<td>15 sessions (once daily for 5 d X 3)</td>
<td>LI15</td>
<td>De-qi</td>
<td>PRICE + EA</td>
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<td>He (2010)[36]</td>
<td>WA, individualized</td>
<td>TCM theory</td>
<td>n.r</td>
<td>Tender points</td>
<td>De-qi</td>
<td>Small needle-knife therapy + drug injection + rehabilitation Massage</td>
</tr>
<tr>
<td>Wei (2010)[37]</td>
<td>WA, individualized</td>
<td>TCM theory</td>
<td>10 sessions (once daily for 10 d)</td>
<td>Selected points from ST36, KI13, BL60, GB40, GB39, ST41, LR3 etc.</td>
<td>De-qi</td>
<td>None</td>
</tr>
<tr>
<td>Ni (2010)[26]</td>
<td>MA, partially individualized</td>
<td>TCM theory</td>
<td>3 sessions (once daily for 3 d)</td>
<td>Ex-UE140 + additional points (pain sensitive points on the contralateral wrist joint)</td>
<td>De-qi</td>
<td>None</td>
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<tr>
<td>Tang (2010)[38]</td>
<td>EA, partially individualized</td>
<td>TCM theory</td>
<td>10 sessions (once daily for 5 d X 2)</td>
<td>Ashi points(GB40, BL60, BL62, KI6) + additional points(ST41, GB39, GB34, ST36)</td>
<td>De-qi</td>
<td>Massage + IR</td>
</tr>
<tr>
<td>Luo (2009)[27]</td>
<td>EA, partially individualized</td>
<td>TCM theory</td>
<td>12 sessions (six times per 2 wks X 2)</td>
<td>ST41, BL60, GB40 + ashi points</td>
<td>De-qi</td>
<td>None</td>
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<tr>
<td>Zhou (2008)[28]</td>
<td>WA, individualized</td>
<td>TCM theory</td>
<td>5 sessions (once daily for 5 d)</td>
<td>Tender points</td>
<td>n.r.</td>
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<td>He (2006)[29]</td>
<td>MA+WA, fixed</td>
<td>TCM theory clinical experience</td>
<td>15 sessions (once daily for 5 d X 3)</td>
<td>MA, WA : GB34</td>
<td>De-qi</td>
<td>PRICE + EA</td>
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<tr>
<td>Zhao (2005)[30]</td>
<td>EA, fixed</td>
<td>TCM theory</td>
<td>14 sessions (once per 2 days for 2 wks X 2)</td>
<td>Penetrating needling (GB40 and KI6)</td>
<td>De-qi</td>
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<td>Wang (2005)[39]</td>
<td>EA, partially individualized</td>
<td>Modern experimental study</td>
<td>5 sessions (once daily for 5 d)</td>
<td>ST41, GB40, BL62, BL60, GB39, ashi points</td>
<td>De-qi</td>
<td>None</td>
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<tr>
<td>Li (2002)[31]</td>
<td>MA, partially individualized</td>
<td>n.r.</td>
<td>8 sessions (once daily for 8 d)</td>
<td>ST36, GB39, BL60, additional points (pain sensitive points on the</td>
<td>De-qi</td>
<td>Oral &amp; topical HM</td>
</tr>
<tr>
<td>Ref</td>
<td>First Author</td>
<td>Type of Treatment</td>
<td>Number of Sessions</td>
<td>Points Used</td>
<td>Type of Medicine</td>
<td>Comments</td>
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<td>[26]</td>
<td>Ge (2000) MA, individualized</td>
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<td>10 sessions</td>
<td>n.r</td>
<td>n.r</td>
<td>oral HM</td>
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<td>[27]</td>
<td>Yu (1999) MA, fixed</td>
<td>TCM Theory</td>
<td>14 sessions (twice daily for 7 d)</td>
<td>ST36, GB39, KI3, BL60</td>
<td>n.r</td>
<td>Topical NSAIDs</td>
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<tr>
<td>[28]</td>
<td>Yu (1999) MA, fixed</td>
<td>n.r</td>
<td>14 sessions (twice daily for 7 d)</td>
<td>ST36, GB39, KI3, BL60</td>
<td>n.r</td>
<td>Topical NSAIDs + ice pack</td>
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<td>[29]</td>
<td>Yu (1996) MA, fixed</td>
<td>n.r</td>
<td>7 sessions (once daily for 7 d)</td>
<td>ST36, GB39, KI3, BL60</td>
<td>n.r</td>
<td>Topical HM + ice pack</td>
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<tr>
<td>[30]</td>
<td>Ruan (1995) MA, partially individualized</td>
<td>n.r</td>
<td>Once daily</td>
<td>Ex-LE222, Ex-LE226, BL62, GB39, GB40, BL60, KI6, SP6, KI2, ST41, ST36, GB34, SP9, ashi points</td>
<td>n.r</td>
<td>Massage</td>
</tr>
</tbody>
</table>

*, Acupuncture method was classified into three categories based on the levels of individualization: ‘fixed’ means all patients receive the same treatment at all sessions, ‘partially individualized’ means using a fixed set of points to be combined with a set of points to be used flexibly, and ‘individualized’ means each patient receives a unique and evolving diagnosis and treatment; **, Acupuncture point LI5 refers to 5th point of large intestine meridian and extra points have different nomenclature (e.g., Ex-UE3 means 3rd extra point in upper extremity). Ashi points mean local pain points; ***, De-qi means acupuncture-evoked specific sensations such as soreness, numbness, heaviness, and distention at the site of needle placement and these sensations may spread to other parts of the body; d indicates days; EA, electroacupuncture; HM, herbal medicine; IR, infrared radiation; MA, manual acupuncture; n.r., not reported; NSAIDs, non-steroidal anti-inflammatory drugs; PRICE, protection, rest, ice, compression and elevation; TCM, traditional Chinese medicine; WA, warm acupuncture; wks, weeks.
| 1. Was the method of randomization adequate? | Y | U | Y | U | U | U | U | U | Y | U | U | U | U | U | U | U |
| 2. Was the treatment allocation concealed? | Y | U | U | U | U | N | N | U | U | U | N | U | U | U | U | U |
| 3. Was the patient blinded to the intervention? | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| 4. Was the outcome assessor blinded to the intervention? | U | U | N | U | U | U | U | N | U | U | U | U | U | U | U | U |
| 5. Were incomplete outcome data adequately | N | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
6. Are reports of the study free of suggestion of selective outcome reporting?

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*Based on the risk of bias assessment tool from the Cochrane Handbook for Systematic Reviews of Interventions [16][11]; ‘Y’ indicates “Yes (low risk of bias)”; ‘U’, “Unclear”; ‘N’, “No (high risk of bias)”; A study with a low risk of bias (in bold) was defined as a study receiving ‘Y’ for randomisation and/or allocation concealment.


27. Luo W, He SW, Chen YQ: Clinical observation of electroacupuncture in treating chronic


40. Ruan ZQ: Comparative observation of therapeutic effect of acupuncture plus massage


20. Zheng Q, Wang L: Therapeutic effects of puncturing Jianyu (LI 15) on sprain of


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