

# Acupuncture for Generalized Anxiety Disorder: A Systematic Review

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## Abstract

**Objective:** Generalized Anxiety Disorder (GAD) is the most common anxiety disorder in primary care. The clinical studies on anxiety disorders have been commonly conducted; however the efficacy of acupuncture in treating GAD is uncertain. We therefore performed a systematic review to evaluate the evidence regarding acupuncture for GAD.

**Data sources:** CBM, CAJ, CSJD, CNKI, Wan Fang, EMBASE, Pubmed/MEDLINE, OVID EBM Reviewers, Cochrane Library, Up-to-date, ACP journal club were searched through July 2013. Search terms included Condition = (Generalized Anxiety Disorder or Generalized Anxiety or GAD) And Intervention = (acupuncture\* or acupressure or acupoint\* or electro acupuncture\* or electro-acupuncture\*).

**Study selection:** Included in this study were randomized controlled trials of participants have GAD diagnosed by operational criteria.

**Data extraction:** Two review authors extracted data from each study independently. Information relating to study population, sample size, interventions, comparators, potential biases in the conduct of the trial, outcomes including adverse events, follow-up and methods of statistical analysis were abstracted from the original reports.

**Data synthesis:** 3 RCTs (443 patients) were included. Overall the risk of bias in included studies was high. The included trials were extremely heterogeneous regarding acupuncture and control interventions. Therefore, pooling of data was not performed. We found equal benefits of acupuncture and medications for HAMA or SAS in 2 trials. In another trial no difference was found in the baseline analysis with HAMA and SAS measurement between groups at the 2nd, 4th week time-point. Adverse events associated with acupuncture are rarely reported.

**Conclusion:** Even though some methodological shortcomings influence the quality of the included studies, this review still suggests that acupuncture was an effective alternative therapy for generalized anxiety is safe.

**Keywords:** Acupuncture; GAD; Systematic review

## Introduction

Generalized Anxiety Disorder (GAD) is an anxiety disorder that is characterized by excessive, uncontrollable, unexplained and often irrational worry about everyday things that is disproportionate to the actual source of worry [1]. It is characterized by persistent anxiety and worry that are difficult to control and are associated with somatic symptoms like restlessness, fatigue, muscle tension, and psychological symptoms such as difficulty concentrating and irritability [2]. GAD is the most common anxiety disorder in primary care. The 12-month prevalence of GAD is 3.1 percent in population-based surveys [3]. GAD is also frequently found in conjunction with other psychiatric conditions, including depression, panic disorder, posttraumatic stress disorder, and social phobia [4].

Acupuncture, known as one of the complementary and alternative medicine, has gained popularity and greater acceptance as a medical therapy. It is a characteristic component of traditional Chinese medicine (TCM). In recent years, several western countries have seen a sharp increase in the number of people using acupuncture to treat common ailments.

According to traditional Chinese medicine, classical acupuncture practice is based on the concept of a vital force or energy called "Qi", flowing around the body through channels known as meridians [5], stimulation of acupuncture points located along meridians is considered to balance the opposing forces (Yin and Yang) ensuring energy flow and thus maintenance or restoration of health. Emerging research implies acupuncture is effective for some but not all conditions. Some animal studies suggest that, in an animal model, both behavioral and biochemical marker changes occur

to reduce anxiety by statistically significant levels [6,7]. Some researches suggested that it may be effective in treating depression and anxiety, several studies suggest that the emotional well-being of humans may be affected through the release of neurotransmitters such as serotonin [8,9], but not all professors agreed with that.

Some kind of interventions used for anxiety, pharmacologic interventions such as anxiolytics and antidepressants, and psychological preparation programs, are effective in anxiety symptoms, however, that be considered time consuming, cause undesirable side effects, and increase health care costs [10]. The clinical studies on anxiety disorders have been commonly conducted, however the acupuncture interventions applied in them vary so as do the controlled methods. Moreover, the accuracy and extrapolation of many trials was challenged for their small sample sizes. The lacking of evidence also limits the accurate access to the effectiveness of acupuncture or the comparison of the effectiveness with different treatment regimens. Therefore, a systematic review on anxiety may hopefully lead to the

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correct assessment of the effectiveness and safety of acupuncture in the treatment for anxiety.

## Methods

### Study criteria

**Types of studies:** Randomized controlled trials comparing acupuncture with a control (sham or placebo acupuncture), no treatment, pharmacological treatment, other structured psychotherapies (psychotherapy or counseling), or standard care. Parallel and crossover were included; dissertations and abstracts were also included. We excluded studies testing acupuncture as part of more complex interventions in which acupuncture was the only one of several treatments and causal inferences were thus limited.

**Types of participants:** Participants were include men and women aged 18-75 with a diagnosis of an anxiety disorder, as defined by the Diagnostic and Statistical Manual (DSM-IV), Research Diagnostic Criteria (RDC), International Classification of Disease (ICD) or the Criteria for Classification and Diagnosis of Mental Diseases (CCMD-3).

**Types of interventions:** Acupuncture was defined as the stimulation of acupuncture points or trigger points by needles that pierce the skin, by heating of the mug wort herb (moxibustion) in combination with needles, or by electrical stimulation [11]. Methods of stimulating acupuncture points that non-needle insertion (e.g. laser, pressure) were also included. Controls included no treatment, sham acupuncture and pharmacological treatment or physical therapy. Comparisons with other acupuncture groups do not (for the purposes of this review) constitute an eligible control group.

**Types of outcome measures:** The outcomes of interest include reduction of anxiety, improvement of quality of life, adverse effects, and participant perception of acupuncture.

### Search methods for identification of studies

**Electronic searches:** The CCDANCTR-Studies Register was searched using the following terms:

Condition = (Generalized Anxiety or Generalized Anxiety or GAD)

And

Intervention = (acupuncture\* or acupressure or acupoint\* or electro acupuncture\* or electro-acupuncture\*)

The author team conducted complementary searches on the following Chinese biomedical databases: Chinese Biomedical Literature Database (CBM); China Academic Journals (CAJ); Chinese Scientific Journals Database (CSJD); China National Knowledge Infrastructure (CNKI); Wan Fang Data.

And the following biomedical databases: EMBASE, Pubmed/MEDLINE, OVID EBM Reviewers, Cochrane Library, Up-to-date, ACP journal club.

**Searching other resources:** Ongoing trials: The WHO International Clinical Trials Registry Platform (ICTRP) and the Chinese Clinical Trial Registry were searched for ongoing (and unpublished) trials.

### Selection of studies

Two review authors examined the abstracts of all publications obtained through the search strategy. Full articles of all the studies identified by either of the review authors were then obtained and

inspected by the same two review authors for trials meeting the following criteria:

1. Randomized controlled trial;
2. Participants have GAD diagnosed by operational criteria;
3. Any acupuncture therapy approach, compared with no treatment, sham acupuncture and pharmacological treatment or physical therapy approach.

Conflicts of opinion regarding eligibility of a study were discussed with a third review author, having retrieved the full paper and consulted the authors if necessary, until consensus was reached. External subject or methodological experts were consulted if necessary. Reasons for excluding trials were stated.

### Data extraction and management

Two review authors extracted data from each study independently. Any disagreement was discussed with an additional review author and where necessary, the authors of the studies were contacted for further information. Information relating to study population, sample size, interventions, comparators, potential biases in the conduct of the trial, outcomes including adverse events, follow-up and methods of statistical analysis were abstracted from the original reports into specially designed paper forms then entered into a spreadsheet. Missing data or clarification on the study were sought from the respective authors by telephone, mail or email.

### Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions [12].

### Data synthesis and statistics

We carried out statistical analysis using the Review Manager software (Rev Man 5.0.24). Mean difference (MD) was calculated along with its 95% Confidence Intervals (CI) for continuous outcomes. A random effects model was selected to account for the large amount of anticipated heterogeneity among the primary trials. In the event of substantial heterogeneity, trial results were not pooled, but were presented with forest plots.

## Results

### Literature search results

The search period ranged from the inception of the databases to the end of July 2013. The initial electronic searching revealed 26 studies. After reading the text titles and abstracts, we excluded 7 citations, which are non-randomized controlled trials, duplicate publications, and non-clinical research literatures. We have read these 19 entire studies and contacted 10 trial authors by telephone or e-mail for confirmation of the method of random sequence generation. 16 documents were excluded for not meeting the inclusion criteria. Finally, a total of 3 papers were included with 443 patients.

### Description of studies

Three studies were conducted in the China, which were single-center study. All studies were published in Chinese. The key data from all of the included studies are listed in Table 1 [11-13].

### Participants

443 participants were involved. All included participants were diagnosed GAD based on the CCMD-3-R diagnostic criteria.

**Sample size:** All included studies didn't clearly explain their sample size calculation. The sample size ranged from 26 participants to 186 per arm.

**Interventions and comparators:** We found 2 RCTs comparing acupuncture to medications and 1 RCT comparing acupuncture plus acupoint injection. The 3 trials used a fixed needling program, and the electrical stimulation of the needles was not used. Two studies of which used the experiential treatment options. 1 trial used Dong's extra acupoint acupuncture, another used Jin's three-needle acupuncture therapy.

**Outcomes:** Main outcome measurement tools are SAS (Self-Rating Anxiety Scale) and HAMA Hamilton Anxiety Scale. 1 trial reported the 2 domains of HAMA (mental anxiety factors, physical anxiety factors), and 2 trials used TESS as adverse effects measurement tools.

### Risk of bias in included studies

Overall the risk of bias in included studies was high.

All three trials perform randomization; two trials reported the method of random sequence generation. The details of randomization of another trial were confirmed from researcher's email. Only one trial reported adequate details on allocation concealment. Blinding was not performed to the participants or physicians or treatment evaluator, no sham treatment was used in the trials. Follow-up was not performed in all 3 trials; there was no statement on dropouts or withdrawals. For 2 trials, it appears that all data were reported for every outcome assessed. In another trial, the outcomes assessed were not introduced before the data were reported in the results section (Figure 1).

### Effects of interventions

The included trials were extremely heterogeneous regarding acupuncture and control interventions. Therefore, pooling of data was not performed.

First author (year)	Sample size	Intervention group	Control group	Main outcomes
Zhang(2010)[13]	325 participants in total; 186 participants in the intervention group and 139 participants in the control group	Dong's extra acupoint acupuncture plus acupoint injection once daily for 30 days	Buspirone 5 mg three times per day for 30 days	HAMA SAS TESS
Luo(2007)[14]	58 participants in total; 29 participants in the intervention group and 29 participants in the control group	Jin's three-needle acupuncture once daily for six weeks	Fluoxetine or Paroxetine 20mg per day for six weeks	HAMA TESS
Wang(2005)[15]	65 participants in total; 35 participants in the intervention group and 30 participants in the control group	acupuncture once daily for 30 days	Lorazepam 0.5-2mg two or three times per day for 30 days; Plus with oryzanol 20mg or propranolol 10-20mg three times per day for 30 days;	SAS

Table 1: Summary of included studies.

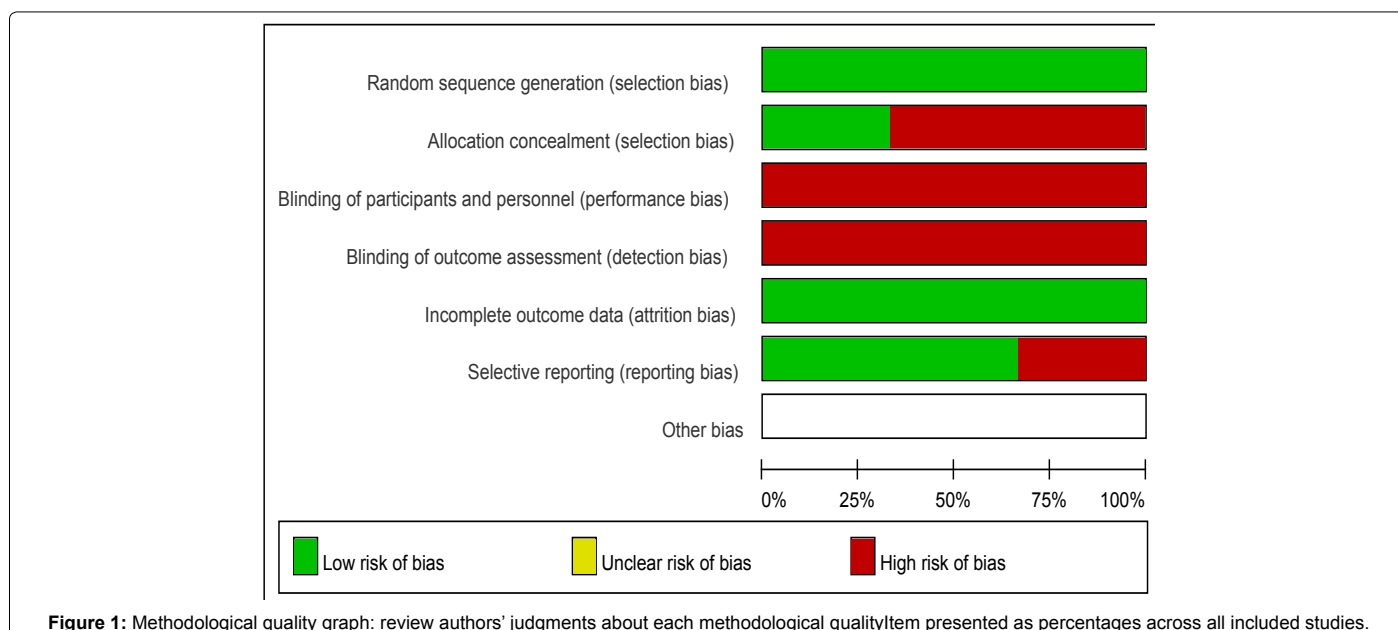


Figure 1: Methodological quality graph: review authors' judgments about each methodological quality item presented as percentages across all included studies.

### Acupuncture versus medications

The efficacy evaluation was measured with HAMA and SAS at the 2nd, 4th and 6th week after the first treatment. We found equal benefits of acupuncture and medications evaluated with the HAMA, SAS (Figure 2) at the 3 observation time-points. In this study, serious adverse events were evaluated with TESS. We found that serious adverse events associated with acupuncture are rare.

Another study evaluated with SAS at the 4 weeks after the first treatment, and no statistical difference was found between two groups (Figure 3). This study did not report the presence of harmful side effects.

### Acupuncture plus injection versus medications

The study evaluated with HAMA and SAS at the 1st, 2nd and 4th week after the first treatment.

Medication was statistically superior to acupuncture group at 1st week time-point (Figure 4). No difference was found in the baseline analysis with HAMA and SAS measurement between groups at the 2nd, 4th week time-point (Figure 5). And the following side effects happened in the medication group: dizziness, thirst, headache, nausea, constipation, insomnia, difficulty urinating. But no adverse events of acupuncture were reported.

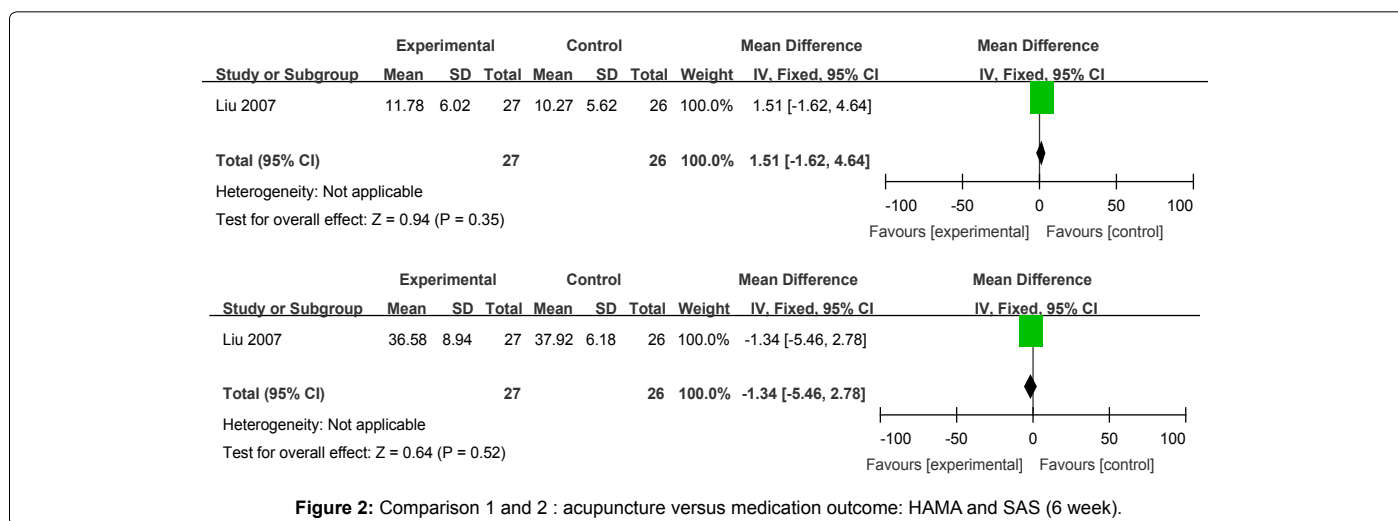


Figure 2: Comparison 1 and 2 : acupuncture versus medication outcome: HAMA and SAS (6 week).

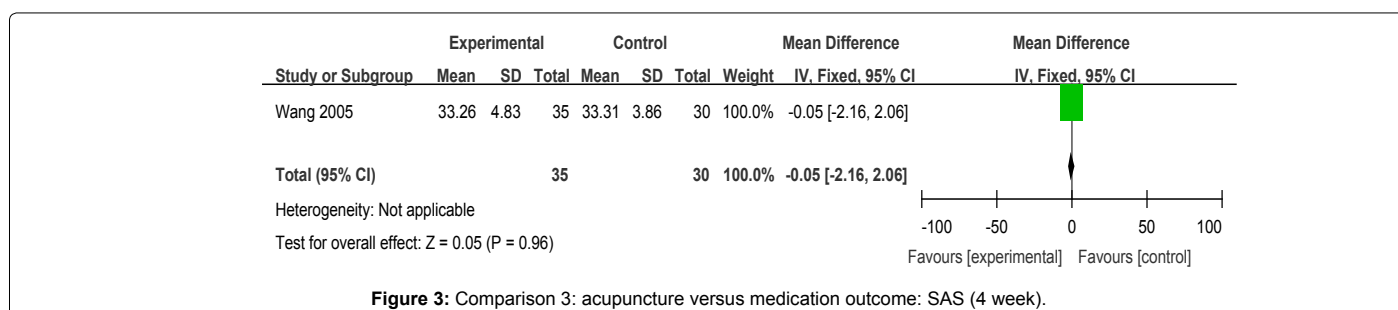


Figure 3: Comparison 3: acupuncture versus medication outcome: SAS (4 week).

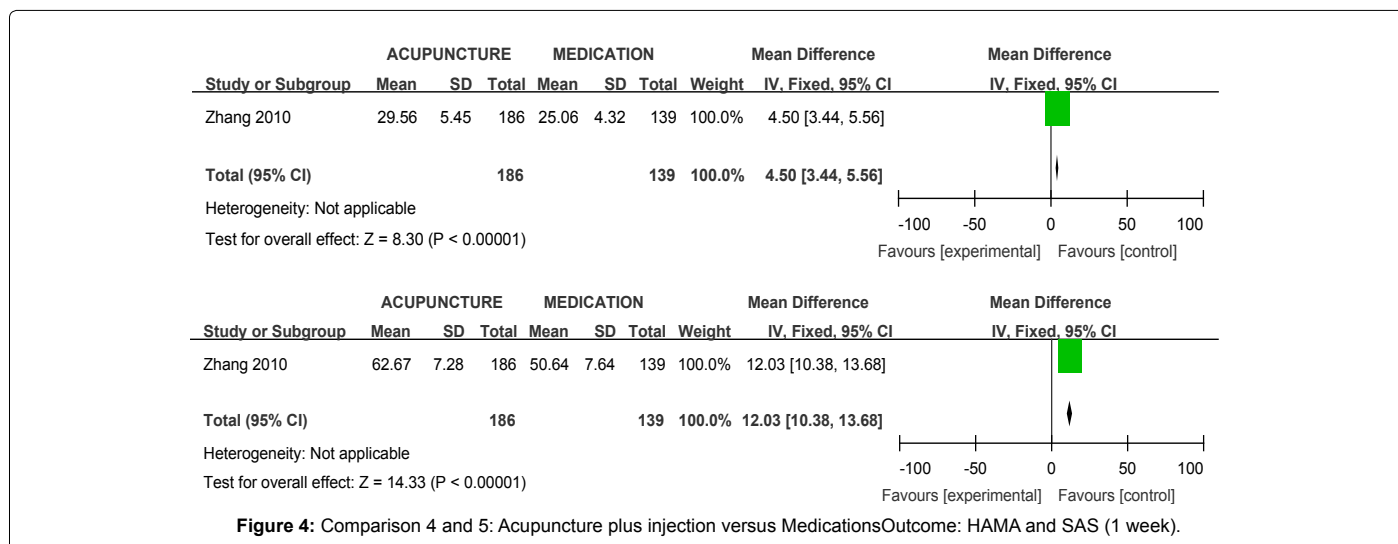


Figure 4: Comparison 4 and 5: Acupuncture plus injection versus Medications Outcome: HAMA and SAS (1 week).

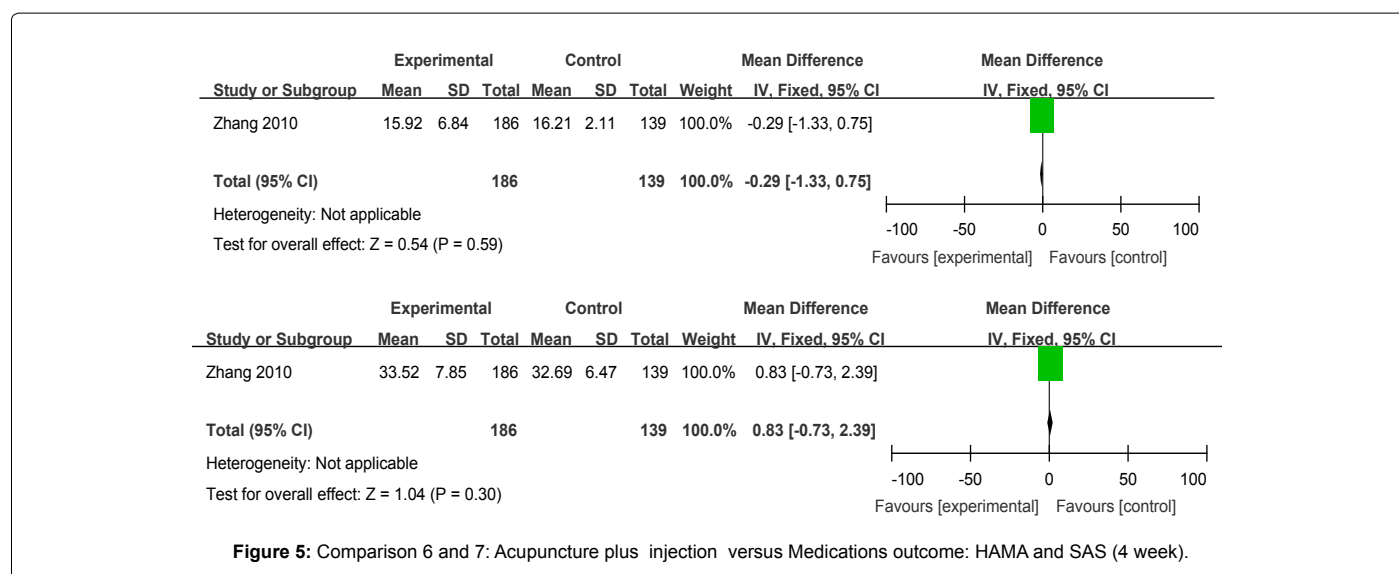


Figure 5: Comparison 6 and 7: Acupuncture plus injection versus Medications outcome: HAMA and SAS (4 week).

## Discussion

The results could not be combined because of the heterogeneity, such as the diversity of the needling technique, combination with other therapies, duration of treatment, assessment tools. 3 RCTs suggested that no differences were found in short-term efficacy of acupuncture compared with drug therapy. And 2 RCTs showed that adverse events were rare with acupuncture therapy than that of medication. But follow-up and long-term efficacy of acupuncture is unknown in all 3 RCTs.

ALL 3 trials used correct randomization sequence generation; only one trial reported allocation concealment. No trial blinded the participants or physicians or treatment evaluator. 3 trials had few withdrawals or dropouts. Additionally, no trial strictly followed the standards of reporting guidelines (Standards for Reporting Interventions in Controlled Trials of Acupuncture). There was poor reporting of needling details and practitioner background, which may highly influence the effects of acupuncture. Due to the small number of included trials and these methodology problems, we could not draw a robust conclusion. Two suggestions are recommended for Future Research. Firstly the future researches provide detailed reports based on the Consolidated Standards of Reporting Trials (CONSORT) statement. Secondly follow-up should be taken seriously, intent-to-treat analysis should be conducted to evaluate therapeutic effects.

## Conclusion

Even though some methodological shortcomings influence the quality of the included studies, this review still suggests that acupuncture was an effective alternative therapy for generalized anxiety is safe.

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