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Needle Acupuncture for Posttraumatic Stress Disorder (PTSD)

A Systematic Review

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Preface

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury is interested in determining the efficacy and comparative effectiveness of integrative medicine approaches for psychological health conditions. This document is a systematic review of needle acupuncture for posttraumatic stress disorder, conducted as part of a two-year project on integrative medicine approaches for psychological health conditions. The review will be of interest to military health policymakers and practitioners, civilian health care providers and policymakers, payers (e.g., health plans, employers), and patients.

The authors do not have any conflicts of interest to declare.

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Abstract

This systematic review synthesized evidence from randomized controlled trials (RCTs) to determine the efficacy of needle acupuncture for posttraumatic stress disorder (PTSD; PROSPERO record CRD42015026766).

Through January 2016, we searched nine databases, as well as trial registries and existing systematic reviews, to identify RCTs evaluating the efficacy and safety of needle acupuncture—used adjunctively or as monotherapy—to treat adults with PTSD. Two independent reviewers screened identified literature using predetermined eligibility criteria, extracted study-level information, and assessed the methodological quality of included studies. Outcomes of interest included PTSD symptoms (primary outcome), health-related quality of life, functional status, anxiety and depression symptoms, sleep quality, and adverse events. Meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models. Quality of the body of evidence was assessed using the GRADE approach.

Seven studies (reported in ten publications) with 709 total participants were included. Studies compared acupuncture with treatment as usual (TAU), sham acupuncture, a passive waitlist control, cognitive behavioral therapy, and paroxetine. We found statistically significant effects in favor of acupuncture (as adjunctive or monotherapy) versus any comparator for PTSD symptoms at postintervention (standardized mean difference [SMD] −0.80; 95% confidence interval [CI] −1.59 to −0.01; 6 RCTs; very low quality of evidence) and at a follow-up between one and six months (SMD −0.46; CI −0.85 to −0.06; 4 RCTs; low quality of evidence). No statistically significant effect was identified for depression symptoms at postintervention (SMD −0.58; CI −1.17 to 0.01; 6 RCTs; very low quality of evidence), but the effect was significant at the one- to six-month follow-up (SMD −0.56; CI −0.88 to −0.23; 4 RCTs; low quality of evidence). No significant effects of acupuncture were identified for anxiety symptoms at postintervention (SMD −0.82; CI −2.16 to 0.53; 4 RCTs; very low quality of evidence) and one- to six-month follow-up (SMD −0.35; CI −1.17 to 0.47; 3 RCTs; very low quality of evidence) or for sleep quality (compared with TAU or sham acupuncture) at postintervention (SMD −0.46; CI −3.95 to 3.03; 2 RCTs; low quality of evidence). All other outcomes were reported only in single studies without replication. Safety data suggest that acupuncture is not associated with any serious adverse events, though some participants reported minor or moderate needle pain, superficial bleeding, and hematoma; however, safety was not systematically collected in most studies. We did not detect systematic differences by type of acupuncture, but there were only a few studies in each category and no head-to-head trials were identified. We did not detect systematic differences in effects comparing adjunctive and monotherapy studies, but the number of RCTs was insufficient for robust analyses. We did not detect systematic differences by comparator, but very few studies reported on the same comparator, hindering analyses.

We identified potential benefits of acupuncture for PTSD and depression symptoms compared with control groups in the months following treatment. However, the number of available studies is small, and the quality of evidence is low to very low. Few minor adverse events and no serious adverse events were reported, but safety assessments were limited. Additional well-designed, rigorous, and large RCTs have the potential to further develop the evidence base to provide more-conclusive evidence.

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Introduction

Many people witness or live through one or more traumas—shocking, frightening, or dangerous events—in their lifetimes (Sledjeski, Speisman, and Dierker, 2008). While most people recover from initial stress reactions to witnessing or experiencing traumatic events, some continue to experience problems; posttraumatic stress disorder (PTSD) is a mental health condition that may develop as a result (American Psychiatric Association, 2013; Breslau, 2009; Kessler et al., 2005). PTSD is associated with several negative consequences, including psychiatric comorbidity, high medical costs, poor work performance, familial discord, crime, and suicide risk (Kessler, 2000; Reynolds et al., 2016; Boscarino, 2006; Taft et al., 2007; Smith, Schnurr, and Rosenheck, 2005). Needle acupuncture is hypothesized to help adults with PTSD by causing neurological responses involving the autonomic nervous system, the prefrontal cortex, and several limbic structures in the brain involved in the pathophysiology of PTSD (Hollifield, 2011). This systematic review synthesized evidence from randomized controlled trials (RCTs) to provide reliable estimates of the effectiveness of needle acupuncture for PTSD (PROSPERO record CRD42015026766).

This review was guided by the following key questions (KQs):

- KQ 1: What are the efficacy and safety of needle acupuncture, as an adjunctive or monotherapy, in addressing PTSD symptoms, health-related quality of life, functional status, depression and anxiety symptoms, sleep quality, and adverse events in adults with PTSD compared with treatment as usual (TAU), active treatments, sham acupuncture, waitlists, or no treatment?
    - KQ 1a: Does the effect of needle acupuncture vary by type of acupuncture (e.g., auricular acupuncture)?
    - KQ 1b: Does the effect of needle acupuncture differ if acupuncture is offered as an adjunctive therapy rather than as a monotherapy?
    - KQ 1c: Does the effect of needle acupuncture depend on the comparator?

Methods

To answer our key questions, we conducted a systematic search of electronic databases—PubMed, PsycINFO, Allied and Complementary Medicine (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effect (DARE), Web of Science, Embase, and Published International Literature on Traumatic Stress (PILOTS)—from inception to January 2016 to identify reports of RCTs testing the efficacy and safety of needle acupuncture—used

adjunctively or as monotherapy—to treat adults with PTSD. We also searched the trial registries Cochrane Central Register of Controlled Trials (CENTRAL), Clinicaltrials.gov, and the International Clinical Trials Registry Platform. In addition, bibliographies of existing systematic reviews and included studies were reference-mined. Participants must have been 18 years or older and diagnosed with PTSD. There were no exclusion criteria regarding comparison intervention, trial setting, or language in which the manuscript was published.

Two independent reviewers screened identified literature using predetermined eligibility criteria, extracted prespecified study-level information and outcome data, and assessed the quality of included studies. Outcomes of interest included PTSD symptoms (primary outcome), health-related quality of life, functional status, anxiety and depression symptoms, sleep quality, and adverse events. When possible, meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models; meta-regressions were also conducted when feasible, though a small number of studies makes the ratio of studies to "study-level covariates" potentially too small for the analysis to be sufficiently powered (Borenstein, 2009). Quality of the body of evidence for each outcome was assessed using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach.

Results

Seven RCTs (reported in ten publications), with 709 total participants and conducted in two countries, met inclusion criteria. Studies took place in various health care settings, including outpatient care, inpatient care, and residential care. Participants' average age ranged from approximately 33 to 65 years, and the proportion of males ranged from 32 to 100 percent.

Key Question 1

We identified seven RCTs providing data on the overall efficacy of acupuncture and seven on the overall safety of acupuncture. Overall, we found evidence in support of acupuncture for PTSD symptoms (postintervention: standardized mean difference [SMD] −0.80; 95% confidence interval [CI] −1.59 to −0.01; I^2 90%; 6 RCTs; one- to six-month follow-up: SMD −0.46; CI −0.85 to −0.06; I^2 30%; 4 RCTs), functional status (based on results from one RCT), and depression symptoms (one- to six-month follow-up: SMD −0.56; CI −0.88 to −0.23; I^2 0%; 4 RCTs). The quality of the body of evidence underpinning effect estimates for PTSD symptoms at postintervention and functional status at both time points is very low due to unclear or inadequate intention-to-treat (ITT) analysis procedures, wide confidence intervals, and either considerable heterogeneity (PTSD symptoms) or inability to judge consistency (functional status). Moreover, treatment effect estimates for PTSD symptoms at postintervention were considerably lower and no longer statistically significant when removing a poor quality study with the outlying positive effect in favor of acupuncture (SMD −0.50; CI −1.01 to 0.01; I^2 64%; 5 RCTs). We rated the quality of the body of evidence for one- to six-month follow-up results on

PTSD and depression symptoms to be low due to wide confidence intervals spanning effect sizes with clinically meaningful differences of benefit, and we rated performance bias to be high due to lack of blinding participants in all trials contributing to the analyses.

From reported safety data, we did not find strong evidence indicating that acupuncture is associated with any serious adverse events. Some participants reported minor or moderate needle pain, minor superficial bleeding, and minor hematoma, whereas refusal to continue acupuncture due to fear of needle pain, refusal to continue due to discomfort, and kidney pain were each reported by one (different) participant. However, RCT reports provided little detail about procedures for collecting safety information, making it unclear whether few reports of adverse events were due to few experiences of adverse events or due to instrumentation for detecting adverse events.

Key Question 1a

Two RCTs provided data evaluating auricular (ear) acupuncture (King et al., 2015; Prisco et al., 2013), while five RCTs provided data evaluating some form of Traditional Chinese Medicine (TCM) acupuncture (Engel et al., 2014; Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)—three of which also involved electroacupuncture (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). We did not identify any direct comparisons of auricular acupuncture versus TCM acupuncture. We did not detect statistically significant differences (in indirect comparisons via meta-regression) in effects by type of acupuncture for PTSD or depression symptoms (PTSD symptoms postintervention: p=0.57; depression symptoms postintervention: p=0.19), though we had a limited number of RCTs available for these analyses. Based on a direct comparison from one RCT (Zhang, Yuan, et al., 2010b), we found no statistically significant difference between electroacupuncture and electroacupuncture plus moxibustion for PTSD symptoms and depression symptoms at postintervention, three-month follow-up, or six-month follow-up. However, we did identify statistically significant, clinically small effects in favor of electroacupuncture plus moxibustion (versus electroacupuncture only) for anxiety symptoms at postintervention (SMD 0.37; CI 0.03 to 0.71), three-month follow-up (SMD 0.44; CI 0.10 to 0.77), and six-month follow-up (SMD 0.42; CI 0.08 to 0.76), based on a very low quality body of evidence due to wide confidence intervals and lack of replication.

Key Question 1b

Three RCTs provided data evaluating acupuncture as an adjunctive therapy (Engel et al., 2014; King et al., 2015; Prisco et al., 2013), and four RCTs provided data evaluating acupuncture as a monotherapy (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). Of the three adjunctive RCTs, all co-interventions involved TAU that also served as a comparator (i.e., the intervention contrast was acupuncture plus TAU versus TAU). TAU involved either psychotherapies and medications following the U.S. Department of

Veterans Affairs and U.S. Department of Defense (VA/DoD) Clinical Practice Guideline for Management of Post-Traumatic Stress (Engel et al., 2014), a ten-week residential PTSD treatment program for combat-related PTSD (King et al., 2015), or cognitive behavioral therapy along with psychopharmacology if indicated (Prisco et al., 2013). We did not detect any direct comparisons of acupuncture as adjunctive therapy versus acupuncture as monotherapy. We did not identify statistically significant differences (in indirect comparisons via meta-regression) in effects by type of co-intervention status for PTSD or depression symptoms (PTSD symptoms postintervention: p=0.85; PTSD symptoms follow-up: p=0.96; depression symptoms postintervention: p=0.50; depression symptoms follow-up: p=0.75), though we had a limited number of RCTs available for these analyses.

Key Question 1c

Three RCTs provided data evaluating acupuncture plus TAU versus TAU alone (Engel et al., 2014; King et al., 2015; Prisco et al., 2013), one RCT provided data evaluating acupuncture versus sham acupuncture (Prisco et al., 2013), one RCT provided data evaluating acupuncture versus a passive waitlist control (Hollifield et al., 2007), and four RCTs provided data evaluating acupuncture versus an active comparator, namely either group cognitive behavioral therapy or paroxetine (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). We did not detect statistically significant differences (in indirect comparisons via meta-regression) in effects by type of comparator for the above outcomes (PTSD symptoms postintervention: p=0.98; PTSD symptoms follow-up, p=0.44; depression symptoms postintervention: p=0.78; depression symptoms follow-up, p=0.61; anxiety symptoms postintervention: p=0.90; anxiety symptoms follow-up, p=0.90), though we had a limited number of RCTs available for these analyses.

Conclusions

We identified potential benefits of acupuncture for PTSD symptoms and functional status (compared with control groups) immediately postintervention, though the quality of the body of evidence underpinning these estimates is very low. We consequently have very little confidence that these estimates represent the true effect of acupuncture on these outcomes. We identified a low quality body of evidence suggesting potential benefits of acupuncture for PTSD and depression symptoms (compared with control groups) in the months following completion of acupuncture treatment; it is possible, however, that further research may change both our confidence in these effect estimates and the estimates themselves. We did not identify any evidence to suggest that acupuncture is associated with serious adverse events, though some participants may experience mild adverse events due to needling procedures, and the generally low reporting about adverse events may be due to differential procedures for collecting (or not collecting) safety information. We also did not identify any evidence to suggest that results differ

by type of acupuncture, co-intervention status, or comparator, though these analyses are limited by the small number of identified RCTs and lack of direct comparisons.

Because the number of available studies is small and the quality of evidence is low to very low, additional well-designed, rigorous, and large RCTs are needed to provide more-conclusive evidence on whether acupuncture is efficacious for treating adults with PTSD. Future RCTs should also be reported in compliance with established best practices for reporting acupuncture trials (MacPherson et al., 2002). Researchers, policymakers, funders, and practitioners may wish to establish future priorities on needle acupuncture for PTSD, considering type of needle acupuncture, choice of comparator, co-intervention status, and target outcomes.

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Abbreviations

AMED	Allied and Complementary Medicine
CAM	Complementary and Alternative Medicine
CAPS	Clinician-Administered PTSD Scale
CDSR	Cochrane Database of Systematic Reviews
CENTRAL	Cochrane Central Register of Controlled Trials
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CBT	cognitive behavioral therapy
CI	confidence interval
CPG	Clinical Practice Guideline
DARE	Database of Abstracts of Reviews of Effect
DoD	U.S. Department of Defense
DSM	*Diagnostic and Statistical Manual of Mental Disorders*
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
ITT	intention to treat
KQ	key question
n.s.	no significant effect
PCL	PTSD Checklist
PILOTS	Published International Literature on Traumatic Stress
PTSD	posttraumatic stress disorder
RCT	randomized controlled trial
SD	standard deviation
SMD	standardized mean difference
TAU	treatment as usual
TCM	Traditional Chinese Medicine
USPSTF	U.S. Preventive Services Task Force
VA	U.S. Department of Veterans Affairs

Chapter One: Introduction

Description of the Condition

In their lifetimes, many people witness or live through one or more traumas—shocking, frightening, or dangerous events, such as a motor vehicle accident, sexual assault, domestic violence, physical assault, natural disaster, and armed conflict (Sledjeski, Speisman, and Dierker, 2008). While most people recover from initial stress reactions to witnessing or experiencing traumatic events, some continue to experience problems. Posttraumatic stress disorder (PTSD) is a mental health condition that can develop after a person witnesses or experiences a traumatic event and continues to experience problems, usually developing within three months of experiencing the trauma (American Psychiatric Association, 2013; Breslau, 2009; Kessler et al., 2005). According to the National Comorbidity Survey, current (12-month) and lifetime prevalence of PTSD among trauma-exposed U.S. adults is 3.6 percent and 6.8 percent, respectively (Kessler et al., 2005). Characteristic symptoms of PTSD include re-experiencing intrusive symptoms, avoiding reminders of the event, having negative thoughts and feelings, and experiencing hyperarousal and reactivity (American Psychiatric Association, 2013). PTSD is associated with several negative consequences, including psychiatric comorbidity, high medical costs, poor work performance, familial discord, crime, and suicide risk (Kessler, 2000; Reynolds et al., 2016; Boscarino, 2006; Taft et al., 2007; Smith, Schnurr, and Rosenheck, 2005).

Mental health professionals use several types of interventions for treating people with PTSD. These include cognitive behavioral therapy (CBT) and its variants (e.g., cognitive processing therapy, prolonged exposure therapy, and stress inoculation therapy), other psychotherapies (e.g., interpersonal, supportive, and psychodynamic psychotherapies), family therapy, group therapy, and pharmacotherapies (e.g., selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors), among others (Gartlehner et al., 2013; Management of Post-Traumatic Stress Working Group, 2010). Cochrane reviews provide evidence specifically in support of trauma-focused CBT, group trauma-focused CBT, eye movement desensitization and reprocessing, and nontrauma-focused CBT (Bisson et al., 2013); selective serotonin reuptake inhibitors (Stein, Ipser, and Seedat, 2006); and hydrocortisone (Amos, Stein, and Ipser, 2014) for PTSD. However, many people with PTSD do not seek treatment or do not receive adequate treatment that is empirically based (Institute of Medicine, 2008). Improving access to, the quality of, and evidence underpinning treatments for PTSD are therefore important health policy priorities, particularly for active-duty military and veteran populations in which the prevalence of PTSD is increasing (Institute of Medicine, 2014).

Description of the Intervention

Complementary and alternative medicine (CAM) approaches are increasingly used to help those with PTSD because such approaches can be delivered outside conventional mental health clinics, require less talking and disclosure than psychotherapy, and may not carry the risks of side effects from pharmaceutical interventions (Strauss et al., 2011). Examples of CAM approaches include meditation, relaxation techniques, and—the focus of this review—acupuncture (Strauss and Lang, 2012). Needle acupuncture involves inserting and manipulating thin solid needles into specific documented acupuncture points on the body in order to create a therapeutic impact, and the procedure is thought to provide a safe, simple, and comparatively inexpensive alternative or supplement to traditional PTSD treatments (Prisco et al., 2013). Needle acupuncture is hypothesized to be effective for PTSD by causing neurological responses involving the autonomic nervous system, the prefrontal cortex, and several limbic structures in the brain that are involved in the pathophysiology of PTSD (Hollifield, 2011).

Why It is Important to Do This Review

The current U.S. Department of Veterans Affairs (VA) and U.S. Department of Defense (DoD) Clinical Practice Guideline (CPG) for Management of Post-Traumatic Stress (Management of Post-Traumatic Stress Working Group, 2010) makes two recommendations regarding use of acupuncture for patients with posttraumatic stress. First, the CPG recommends that "acupuncture may be considered as treatment for patients with PTSD" (p. 175), and "there is some evidence that acupuncture may be helpful with the management of Post-Traumatic Stress Disorder, acute or chronic" (p. 176). This recommendation is based on one "properly-done" randomized controlled trial (RCT) rated as "good" quality of evidence (the highest quality for evidence directly linked to a health outcome). The CPG consequently provided a level "B" strength of recommendation (the second-highest level) for acupuncture, meaning the CPG group recommends that clinicians provide acupuncture to eligible patients because they found "good" evidence of a moderate net benefit (i.e., improvement in health outcomes outweighing harm) of the intervention. Second, the CPG states that CAM approaches "may be considered for adjunctive treatment of hyperarousal symptoms, although there is no evidence that these are more effective than standard stress inoculation techniques" (p. 178). However, compared with the recommendation above, this statement is based on level "I" strength of recommendation (the lowest level), meaning the CPG group concluded that the evidence is "insufficient to recommend for or against routinely providing the intervention. Evidence that the intervention is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined" (p. 202). Whenever acupuncture was mentioned for either recommendation, the CPG noted that research focusing on the efficacy of acupuncture for PTSD was relatively limited at the time (Management of Post-Traumatic Stress Working Group, 2010). This review may be used by committees charged with updating CPG guidelines for treatment of PTSD.

A previous systematic review on acupuncture for PTSD concluded that, while encouraging, the evidence of effectiveness of acupuncture for PTSD was incomplete and required further high-quality RCTs (Kim, Heo, et al., 2013). However, this previous review was conducted prior to several recent RCTs on acupuncture for PTSD, included acupressure interventions in addition to needle acupuncture interventions, and did not examine possible moderators of the intervention. The current review aims to provide updated estimates of the effects of acupuncture on PTSD, with a focus on needle acupuncture interventions specifically and with the inclusion of review questions specifically addressing potential sources of variability (moderators) in intervention effects. Given that some interventions for preventing PTSD have even been shown in previous meta-analyses to lead to increased PTSD symptoms over time (Roberts et al., 2009; Rose et al., 2002), rigorous evaluation of treatments under consideration for PTSD guideline recommendations is critical in order to ensure that symptoms and other important outcomes are not exacerbated as a result of treatment.

Objective

This review aims to synthesize evidence from RCTs in order to provide reliable estimates of the efficacy and safety of needle acupuncture for PTSD. The current review was requested by the U.S. Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, which commissioned the RAND Corporation to develop a series of systematic reviews on CAM interventions for such conditions as substance use, major depressive disorder, and PTSD.

Chapter Two: Methods

Key Questions

We performed a systematic review to identify RCTs testing the efficacy and safety of needle acupuncture for treating individuals with PTSD (PROSPERO record CRD42015026766). The following key questions (KQs) guided this systematic review:

- KQ 1: What are the efficacy and safety of needle acupuncture, as an adjunctive or monotherapy, in addressing PTSD symptoms, health-related quality of life, functional status, depression and anxiety symptoms, sleep quality, and adverse events in adults with PTSD compared with treatment as usual (TAU), active treatments, sham acupuncture, waitlists, or no treatment?
  - KQ 1a: Does the effect of needle acupuncture vary by type of acupuncture (e.g., auricular acupuncture)?
  - KQ 1b: Does the effect of needle acupuncture differ if acupuncture is offered as an adjunctive therapy rather than as a monotherapy?
  - KQ 1c: Does the effect of needle acupuncture depend on the comparator?

Search Strategy

The following databases were searched from inception to January 2016: PubMed, PsycINFO, Allied and Complementary Health Database (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effect (DARE), Web of Science, Embase, and Published International Literature on Traumatic Stress (PILOTS). We also searched the clinical trial registries Cochrane Central Register of Controlled Trials (CENTRAL), Clinicaltrials.gov, and the International Clinical Trials Registry Platform (see Appendix A). The search string for each database was developed by the chief reference librarian for RAND's Knowledge Services and was informed by search results of an environmental scan of the literature (as part of unpublished RAND research by Melony Sorbero, Sean Grant, and Susanne Hempel in October 2014), reviews on acupuncture for substance use (Lua and Talib, 2012; Lin, Chan, and Chen, 2012; Cho and Whang, 2009; Kim, Schiff, et al., 2006; Mills et al., 2005; Liu et al., 2009; Gates, Smith, and Foxcroft, 2006; Jordan, 2006), and a previous review on acupuncture for PTSD conducted before several recent trials on acupuncture for PTSD were published (Kim, Heo, et al., 2013). Search strings included terms related to PTSD (e.g., "PTSD," "post-traumatic stress") and needle acupuncture (e.g., "acupuncture," "acupuncture therapy"). We reference-mined included studies and prior systematic reviews related to this topic identified through the electronic search.

Eligibility Criteria

Inclusion and exclusion criteria for this review were developed using the framework of participants, interventions, comparators, outcomes, timing, settings, and study design, or PICOTSS:

- *Participants*: Studies were limited to adults, male and female, who were 18 years of age or older. Participants must have had a clinical diagnosis of PTSD according to *Diagnostic and Statistical Manual of Mental Disorders* (DSM) or International Classification of Diseases diagnostic criteria, or screen positive for PTSD using a validated measure with symptoms that are compatible with a PTSD diagnosis (e.g., duration of the disturbance is more than one month).
- *Interventions*: Studies that administered thin or fine solid needles into known acupuncture points, either as an adjunctive or monotherapy, were included. Studies involving full-body acupuncture following Traditional Chinese Medicine (TCM), auricular acupuncture, or other specific body sites, with or without electrostimulation, were included. Studies involving acupuncture via laser, heat, or light were excluded, unless needles were also used. Studies involving dry needling or trigger point and not referring to traditional acupuncture were excluded.
- *Comparators*: Studies that included sham acupuncture (including invasive acupuncture control at nonmeridian points, nonpenetrating acupuncture control, and invasive acupuncture control at nonspecific meridian points), TAU or "standard care," waitlist control, no treatment, or other active treatments were included.
- *Outcomes*: Studies that reported one or more of the following outcomes were included: composite measures of PTSD symptoms or any of the four symptom clusters (intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity), health-related quality of life, functional status (psychological, social, and occupational functioning; reintegration measures), depression and anxiety symptoms, sleep quality, and adverse events.
- *Timing*: Studies could have involved any treatment duration and follow-up period.
- *Setting*: Studies were not limited by setting (e.g., country, physical location of treatment).
- *Study design*: Included studies were limited to parallel group trials or controlled trials that were individually randomized or cluster-randomized. We did not exclude studies by language in which the manuscript was published.

Inclusion Screening

Two independent reviewers (the project lead, who is a doctoral-level, experienced systematic reviewer, and a RAND doctoral student with experience in systematic reviews) screened titles and abstracts of retrieved citations. An initial session piloting the screening form occurred prior to these reviews to ensure similar interpretation of the inclusion and exclusion criteria. Citations judged as potentially eligible by one or both reviewers were obtained as full text. The full-text publications were then screened against the specified inclusion criteria by two independent literature reviewers; any disagreements were resolved through discussion within the review author team.

Data Extraction

The two aforementioned reviewers each independently extracted study-level data in an electronic database. The project lead designed data collection forms with input from the project team. These two reviewers pilot-tested the data collection forms on a few well-reported studies to ensure agreement of interpretation. The project lead extracted all outcome data and performed all analyses.

The following information was extracted from each study:

- *Participants*: gender, age, baseline PTSD scores, comorbid psychological/behavioral health conditions, combat versus noncombat-associated PTSD
- *Interventions*: type of needle acupuncture (TCM, auricular acupuncture, other; specific acupoints), dosage (intensity, frequency, duration), and co-intervention(s)
- *Comparators*: type of comparator
- *Outcomes:* overall PTSD symptoms or any of the four symptom clusters (intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity), health-related quality of life, functional status, depression and anxiety symptoms, sleep quality, and adverse events, for each follow-up point of measurement; for each of these outcomes, we abstracted data on domain, method of measurement, metric of data expression (e.g., means, proportions)
- *Timing*: time-points of outcome assessment
- *Setting*: geographic region, type of health care setting, number of sites
- *Study design*: purpose, recruitment method, inclusion and exclusion criteria, starting and ending sample size, items relevant to risk of bias and quality ratings, and whether a power calculation was reported by study authors.

When several reports for the same study existed, descriptions of participants were compared to ensure that data from the same study populations entered analysis and synthesis only once (i.e., to prevent "double counting" of the same study in an analysis). This situation occurred for two studies (Hollifield et al., 2007; King et al., 2015).

Risk of Bias

The two reviewers assessed the risk of bias of included studies using the Cochrane Risk of Bias tool (Higgins et al., 2011). Specifically, the reviewers assessed risks of bias related to random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and providers (performance bias), blinding of outcome assessors (detection bias), completeness of reporting outcome data (attrition bias), and selective outcome reporting (reporting bias). See Appendix B for an overview of the criteria used to make risk of bias determinations.

Other biases related to the U.S. Preventive Services Task Force (USPSTF)'s criteria for internal validity of included studies were assessed—namely, those related to equal distribution among groups of potential confounders at baseline; cross-overs or contamination between

groups; equal, reliable, and valid outcome measurement; clear definitions of interventions; and intention-to-treat (ITT) analysis (USPSTF, 2008). These criteria were used to rate the quality of evidence of individual included studies using the following guidelines (USPSTF, 2008; Lewin Group and ECRI Institute, 2014):

- *Good*: Comparable groups are initially assembled and maintained throughout the study with at least 80-percent follow-up; reliable, valid measurement is used and applied equally to all groups; interventions are clearly described; all important outcomes are considered; appropriate attention is given to confounders in analysis; ITT analysis is used.
- *Fair*: One or more of the following issues is found in the study: some though not major differences between groups exist at follow-up; measurement instruments are acceptable but not ideal, though are generally applied equally; some but not all important outcomes are considered; some but not all potential confounders are accounted for in analyses. ITT analysis must be done.
- *Poor*: One or more of the following "fatal flaws" is found in the study: initially assembled groups are not comparable or maintained throughout the study; unreliable or invalid measurements are used or applied unequally across groups; key confounders are given little to no attention in analyses; ITT analysis is not used.

Data Synthesis

The primary aim of this systematic review is to identify whether needle acupuncture is effective in improving PTSD symptoms in adults with PTSD. We also aimed to identify whether needle acupuncture is effective in improving health-related quality of life, functional status, depression and anxiety symptoms, and sleep quality, and in reducing adverse events. Therefore, when sufficient data were available, we performed random-effects meta-analyses to pool results across included studies for the outcomes of interest. When multiple measures of the same construct were used (e.g., the PTSD Checklist [PCL] or the Clinician-Administered PTSD Scale [CAPS] for PTSD symptoms), we chose the measure used most by trials contributing to the overall analysis in an attempt to reduce statistical heterogeneity, though we also conducted sensitivity analyses to examine whether results differed by measure. When multiple comparison groups were included in a trial, we chose the data from one comparison group (sham, TAU, passive, and active—in that order), though we also conducted sensitivity analyses to examine whether results differed by the comparison group used. For effect measures, we used the standardized mean difference (SMD), which expresses the size of the intervention effect in a study relative to the variability observed in that study, with 95-percent confidence intervals (CIs) indicating uncertainty in these estimates via the range of values within which one can be reasonably sure that the true effect actually lies. Forest plots for main outcomes were provided for meta-analyses pooling at least three studies. We used the Hartung-Knapp-Sidik-Jonkman method for our random-effects meta-analysis (Hartung, 1999; Hartung and Knapp, 2001; Sidik and Jonkman, 2006). This method may be preferred when the number of studies pooled is small

and when there is evidence of heterogeneity (IntHout, Ioannidis, and Borm, 2014). It has been shown that the error rates are more robust than the previously used DerSimonian and Laird method (Sánchez-Meca and Marín-Martínez, 2008).

Outcomes were grouped by length of follow-up (immediately postintervention and between one and six months). Tests of heterogeneity were performed using the I^2 statistic. Values of the I^2 statistic closer to 100 percent represent higher degrees of heterogeneity, with an I^2 of 30 to 60 percent possibly representing moderate heterogeneity, 50 to 90 percent possibly representing substantial heterogeneity, and 75 to 100 percent possibly representing considerable heterogeneity. Overlapping intervals are recommended as a rough guide for interpreting heterogeneity, rather than as discrete and mutually exclusive thresholds for interpreting I^2 that can be misleading, because the importance of inconsistency depends on several factors in addition to the I^2value (Higgins et al., 2003). Common indices for interpreting the size of clinical effects were used: SMD=0.2 for a small clinical effect, SMD=0.5 for a medium clinical effect, and SMD=0.8 for a large clinical effect (Chen, Cohen, and Chen, 2010). In addition, when sufficient data were available, we conducted subgroup analyses and meta-regressions to address secondary aims of this systematic review. Specifically, we examined whether there were differences in effect sizes between studies conducted in different groups—namely, by type of needle acupunctures (e.g., auricular acupuncture), as a monotherapy versus an adjunctive therapy, and by type of comparison group in the trial. For meta-analyses of data with clear outliers, sensitivity analyses were planned to be conducted *a priori* (excluding the outliers), if appropriate (Greenland and Longnecker, 1992; Orsini et al., 2012; Hamling et al., 2008; Higgins et al., 2011). We also investigated publication bias for all main analyses with sufficient data using Begg's rank correlation test for funnel plot asymmetry (Begg and Mazumdar, 1994) and Egger's test for funnel plot asymmetry (Egger et al., 1997).

Quality of the Body of Evidence

The quality of the body of evidence was assessed for major outcomes using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach (Lewin Group and ECRI Institute, 2014; Balshem et al., 2011), in which the body of evidence is assessed based on the following dimensions: study limitations (low, medium, or high), directness (direct or indirect), consistency (consistent, inconsistent, or unknown), precision (precise or imprecise), and reporting bias (suspected or undetected) (Egger et al., 1997).

The strength of evidence is graded on a four-item scale:

- *High* indicates that the review authors are very confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has few or no deficiencies. As such, the reviewers believe the findings are stable; that is, further research is very unlikely to change confidence in the effect estimate.
- *Moderate* indicates that the review authors are moderately confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has

some deficiencies. As such, the reviewers believe that the findings are likely to be stable, but further research may change confidence in the effect estimate and may even change the estimate.

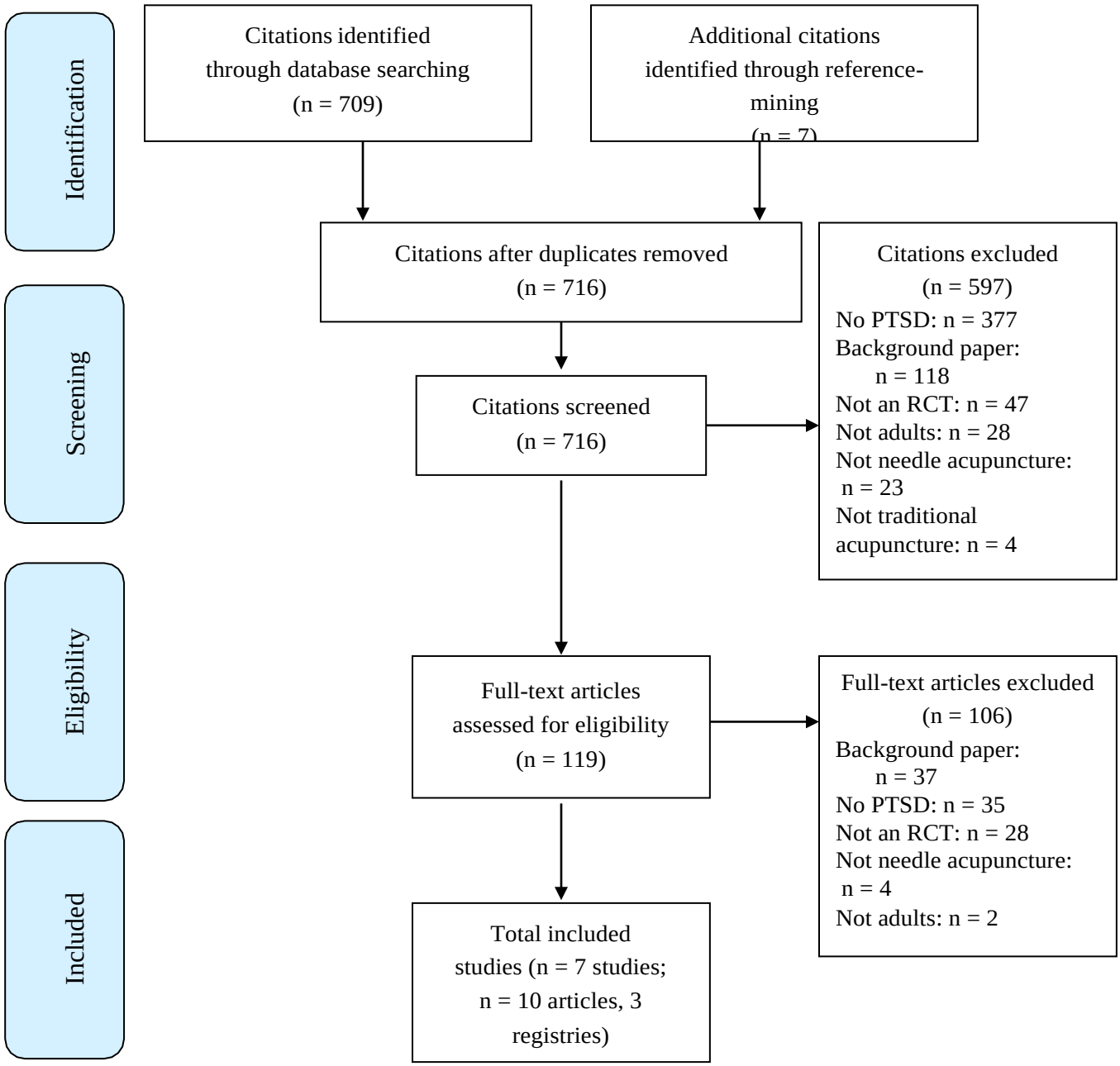
- *Low* indicates that the review authors have limited confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has major or numerous (or both) deficiencies. As such, the reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the effect estimate lies close to the true effect.
- *Very low* indicates that the review authors have very little confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has very major deficiencies. As such, the true effect is likely to be substantially different from the estimated effect; thus, any estimate of effect is very uncertain.

Chapter Three: Results

Results of the Search

We identified 709 citations through our electronic search of databases, as well as seven unique citations through reference-mining of included studies and 28 previous reviews related to needle acupuncture. We therefore examined 716 titles and abstracts (see Figure 3.1).

Figure 3.1. Flow Diagram of Search Results



Full texts were obtained for 119 records identified as potentially eligible by the two reviewers. Of these, 106 articles were excluded at full-text because they were background conceptual or review articles (n=37), did not involve participants with eligible PTSD diagnoses (n=35), did not involve a parallel group RCT (n=28), did not involve needle acupuncture (n=4), or did not involve adult populations (n=2). A list of studies excluded at the full-text review is shown in Appendix C.

Six excluded studies required review team discussion regarding eligibility. Three studies were excluded because the review team ultimately decided that these studies did not require participants to screen positive for or have a diagnosis of PTSD—one involved the use of acupuncture to treat Gulf War Illness (Conboy, St. John, and Schnyer, 2012), the second involved combat stress-induced insomnia, in which one of the five participants was confirmed to not have PTSD (Cronin and Conboy, 2013), and the third involved female child abuse survivors (Dempsey et al., 2014). The fourth study was excluded because acupoint stimulation was used rather than needle acupuncture (Zhang et al., 2011). Two Chinese-language studies were excluded because they did not involve random assignment (Wang and Hu, 2009; Yuan, Liu, and Lai, 2009).

Overall, we identified seven eligible studies, reported across ten articles (see Appendix D). All seven RCTs provided data on the efficacy and safety of needle acupuncture (see Table 3.1).

Table 3.1. Evidence Base for Key Questions

Key Question		Number of RCTs
KQ 1	What are the efficacy and safety of needle acupuncture, as an adjunctive or monotherapy, in addressing PTSD symptoms, health-related quality of life, functional status, depression and anxiety symptoms, sleep quality, and adverse events in adults with PTSD compared with TAU, active treatments, sham acupuncture, waitlists, or no treatment?	7 RCTs with efficacy data 7 RCTs with safety data
KQ 1a	Does the effect of needle acupuncture vary by type of acupuncture (e.g., auricular acupuncture)?	2 auricular acupuncture RCTs 5 TCM acupuncture RCTs 3 RCTs with electroacupuncture
KQ 1b	Does the effect of needle acupuncture differ if acupuncture is offered as an adjunctive therapy rather than as a monotherapy?	3 adjunctive therapy RCTs 4 monotherapy RCTs
KQ 1c	Does the effect of needle acupuncture depend on the comparator?	3 acupuncture + TAU versus TAU RCTs 1 sham acupuncture RCT 1 passive comparator RCT 4 active comparator RCTs

For KQ 1a on the effect of needle acupuncture by type of acupuncture, we identified

- two RCTs evaluating auricular acupuncture (King et al., 2015; Prisco et al., 2013); note that Zhang, Yuan, et al. (2010b) had one trial arm stimulating auricular acupoints, yet it did so using auricular seed-pressing therapy, and therefore is not included as needle auricular acupuncture

- five RCTs evaluating TCM acupuncture (Engel et al., 2014; Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)
- three RCTs that also involved electroacupuncture (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

For KQ 1b on the effect of needle acupuncture as an adjunctive versus a monotherapy, we identified

- three RCTs evaluating acupuncture as an adjunctive therapy (Engel et al., 2014; King et al., 2015; Prisco et al., 2013)
- four RCTs evaluating acupuncture as a monotherapy (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

For KQ 1c on the effect of needle acupuncture being dependent on type of comparator, we identified

- three RCTs evaluating acupuncture plus TAU versus TAU alone (Engel et al., 2014; King et al., 2015; Prisco et al., 2013)
- one RCT evaluating acupuncture versus sham acupuncture (Prisco et al., 2013)
- one RCT evaluating acupuncture versus a passive control (Hollifield et al., 2007)
- four RCTs evaluating acupuncture versus an active comparator (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

Description of Included Studies

Design. All RCTs randomized individual participants, rather than clusters of participants (see Appendix E). Overall, studies assigned 709 participants, ranging in size from 29 (King et al., 2015) to 276 participants (Zhang, Yuan, et al., 2010b), with 84 participants in the study with the median sample size (Hollifield et al., 2007). One study reported that its intended sample size was reached (Zhang, Yuan, et al., 2010b), three studies reported that their intended sample sizes (based on a power calculation) were not reached (Engel et al., 2014; Hollifield et al., 2007; Prisco et al., 2013), and the other three studies did not report any information about a power calculation (King et al., 2015; Wang et al., 2012; Zhang, Ran, et al., 2010a). Four studies were two-arm trials (Engel et al., 2014; King et al., 2015; Wang et al., 2012; Zhang, Ran, et al., 2010a), two studies were three-arm trials (Hollifield et al., 2007; Prisco et al., 2013), and the final study was a four-arm trial (Zhang, Yuan, et al., 2010b).

Setting. Four studies took place in the United States (Engel et al., 2014; Hollifield et al., 2007; King et al., 2015; Prisco et al., 2013), and three studies took place in China (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). Studies took place in various health care settings, such as private offices at a social work clinic (Engel et al., 2014), a residential PTSD treatment facility (King et al., 2015), a VA Medical Center (Prisco et al., 2013), and TCM and psychiatric hospitals (Wang et al., 2012). Three studies involved outpatient care (Engel et al., 2014; Hollifield et al., 2007; Prisco et al., 2013), one involved inpatient care (Wang et al., 2012), one involved residential care (King et al., 2015), and two did not report the care setting

(Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). Most studies took place at one site (Engel et al., 2014; Hollifield et al., 2007; King et al., 2015; Prisco et al., 2013), though one study took place at three sites (Wang et al., 2012), and two studies did not report the number of trial sites (Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

Participants. Average age ranged from 33 to 65 years. One RCT included only males (King et al., 2015), while the reported proportion of males ranged from 32 to 71 percent in other studies. All participants in one study were active-duty military (Engel et al., 2014), all participants were veterans of Operation Enduring Freedom or Operation Iraqi Freedom in two studies (King et al., 2015; Prisco et al., 2013), and the four remaining studies involved civilian samples (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

Interventions. Acupuncture sessions ranged from 30 to 60 minutes per session, from two to four sessions per week, and for three to 12 weeks total in duration. Two studies provided data on auricular acupuncture (King et al., 2015; Prisco et al., 2013), and five studies provided data on TCM acupuncture, including four on TCM acupuncture without electrostimulation (Engel et al., 2014; Hollifield et al., 2007; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b) and three on TCM with electroacupuncture (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

Comparators. Three RCTs provided data on acupuncture plus TAU versus TAU alone (Engel et al., 2014; King et al., 2015; Prisco et al., 2013); TAU involved psychotherapies and medications following the VA/DoD CPG for Management of Post-Traumatic Stress (Engel et al., 2014), a ten-week residential PTSD treatment program for combat-related PTSD (King et al., 2015), or CBT along with psychopharmacology if indicated (Prisco et al., 2013). Only one study reported use of a sham acupuncture comparator, which was structured identically as the true auricular acupuncture in that trial except that nonacupuncture points located on the helix of the ear were used (Prisco et al., 2013). Only one study reported use of a passive comparator, which involved waitlist control participants contacted by the study team only at assessment periods, unless an acute symptom required evaluation (Hollifield et al., 2007). Four RCTs reported use of active comparators; one involved group CBT that met once a week for two hours over 12 weeks (Hollifield et al., 2007), and the other three involved simple oral administration of paroxetine (20 mg) every night for 12 weeks (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

Outcomes. Length of follow-up ranged from immediately postintervention to 6-months postintervention. Six RCTs provided data on PTSD symptoms, one RCT on health-related quality of life, one RCT on functional status, five RCTs on depression symptoms, three RCTs on anxiety symptoms, two RCTs on sleep quality, and seven RCTs on adverse events.

Study Quality and Risk of Bias for Individual Included Studies

The risk of bias and study quality for each of the individual included studies can be found in Table 3.2. According to USPSTF criteria, one study received a "good" quality rating, four were judged to be of fair quality, and two further studies were judged to be of poor quality.

Random sequence generation. Five studies had low risk of selection bias from random sequence generation, and two had an unclear risk of bias.

Allocation concealment. Three studies had low risk of selection bias related to allocation concealment, and four had an unclear risk of bias.

Blinding of participants and providers. All studies were de facto rated high risk of performance bias related to blinding of intervention providers, as it is generally impossible for a provider to be blinded from delivery of acupuncture. One study (Prisco et al., 2013) did potentially mitigate this bias by structuring true and sham acupuncture in an identical fashion and using a standardized script for all acupuncture sessions. Seven studies had high risk of performance bias related to blinding of intervention participants, though one of these studies had low risk of bias for one trial arm that received sham acupuncture (Prisco et al., 2013).

Blinding of outcome assessors. Three studies had a low risk of detection bias related to blinding of outcome assessors, and four had an unclear risk of bias.

Outcome data. Three studies were at low risk of attrition biases related to missing data in the RCT, three had a high risk of bias, and one was unclear.

Selective outcome reporting. One study had a low risk of reporting bias related to subjective outcome reporting, five studies had an unclear risk of bias, and one study had a high risk of bias for outcomes not included in this report or secondary measures of outcomes in this report.

Table 3.2. Study Quality/Risk of Bias for Individual Included Studies

Study ID	Random Sequence Generation (selection bias)	Allocation Concealment (selection bias)	Blinding of Participants (performance bias)	Blinding of Outcome Assessors (detection bias)	Completeness of Reporting Outcome Data (attrition bias)	Selective Outcome Reporting (reporting bias)	Other Biases[a]	USPSTF Quality Rating[b]
Engel et al., 2014	Low	Low	High	Low	Low	High[c]	None	Good
Hollifield et al., 2007	Low	Low	High	Low	High	Unclear	Baseline confounding, ITT analysis	Fair
King et al., 2015	Low	Unclear	High	Unclear	High	Low	ITT analysis	Poor
Prisco et al., 2013	Low	Unclear	Low/High[d]	Unclear	High	Unclear	ITT analysis unclear	Fair
Wang et al., 2012	Unclear	Unclear	High	Unclear	Low	Unclear	ITT analysis unclear	Fair
Zhang, Ran, et al., 2010a	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	All unclear	Poor
Zhang, Yuan, et al., 2010b	Low	Low	High	Low	Low	Unclear	ITT analysis unclear	Fair

NOTES: All trials were de facto "high" risk of bias for blinding of providers.

[a] Other biases include balance of confounders, crossovers/contamination, measurement, intervention definition, and ITT analysis.

[b] The USPSTF criteria (USPSTF, 2008) for study quality involves assessment of various factors related to the internal validity of the study. "Good" is the highest ranking, which involves comparable groups with low attrition, with outcomes being reliably and validly measured and analyzed. "Fair" is the next highest rating, and involves studies with one or a few potential concerns (e.g., some though not major differences between groups exist at follow-up), though ITT was performed. "Poor" is the lowest ranking, and involves studies with one or more "fatal flaws" (e.g., no ITT analysis).

[c] Selective outcome reporting high (Trauma History Questionnaire, PTSD Life Chart Method, Alcohol Use Disorder Identification Test, and diagnostic evaluation by blind assessing acupuncturist assessed but not reported).

[d] Trials that had more than one comparison condition and at least one comparison condition could be considered low risk for participant blinding due to sham acupuncture.

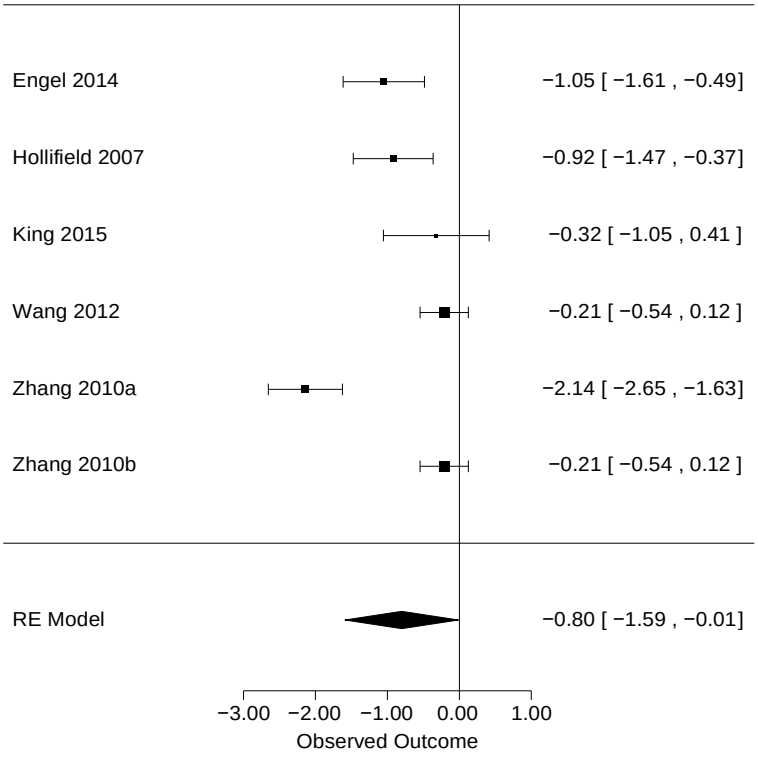
KQ 1: What Are the Efficacy and Safety of Needle Acupuncture, as an Adjunctive or Monotherapy, in Addressing PTSD Symptoms, Health-Related Quality of Life, Functional Status, Depression and Anxiety Symptoms, Sleep Quality, and Adverse Events in Adults with PTSD Compared with TAU, Active Treatments, Sham Acupuncture, Waitlists, or No Treatment?

We identified seven RCTs providing data on the overall efficacy of acupuncture and seven on the overall safety of acupuncture. (A summary of findings and the quality of the body of evidence for each outcome can be found in Table 4.1.)

PTSD Symptoms

Postintervention. Six RCTs (86 percent of RCTs) with 508 total participants (72 percent of randomized participants) reported PTSD symptom data, measured using the PCL, the CAPS, or the Posttraumatic Symptom Scale–Self Report. When data were pooled across these six trials, a large clinical effect in favor of acupuncture (as adjunctive or monotherapy) versus any comparator was observed at postintervention (SMD −0.80; CI −1.59 to −0.01; I^2 90%; 6 RCTs). However, this finding is based on a very low quality body of evidence due to unclear or inadequate ITT analysis procedures, wide confidence intervals, and considerable heterogeneity (see Figure 3.2).

Figure 3.2. Any Acupuncture Versus Any Comparator (PTSD Symptoms, Postintervention SMD)



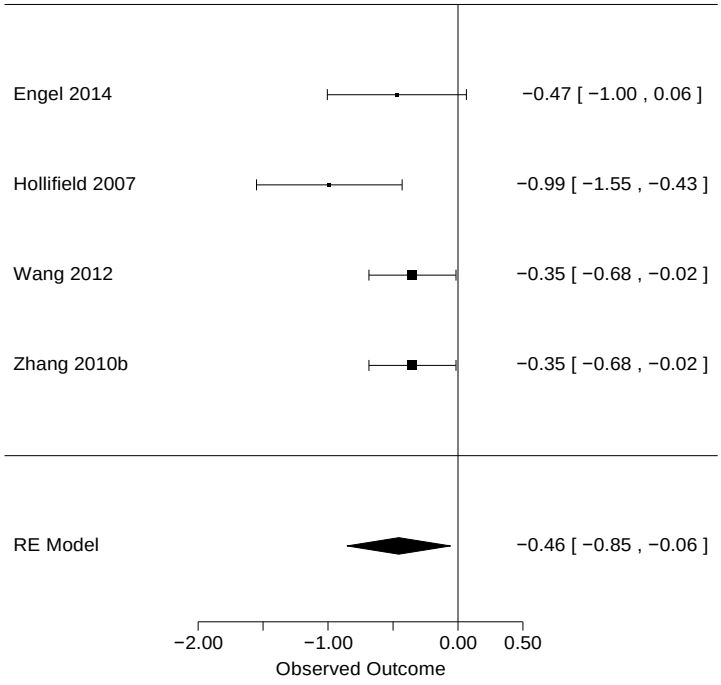
Moreover, all sensitivity analyses for any acupuncture versus any comparator at postintervention were not statistically significant, including the removal of the poor quality study (Zhang, Ran, et al., 2010a), with the outlying positive effect in favor acupuncture (SMD −0.50; CI −1.01 to 0.01; I^2 64%; 5 RCTs), and excluding the three studies related to the Wenchuan County, Sichuan, China, earthquake on May 12, 2008 (SMD −0.83; CI −1.70 to 0.04; I^2 7%; 3 RCTs; see Appendix F, Table 1). However, we found no evidence of publication bias (Egger's test, p=0.77; Begg's test, p=0.44), though we had a limited number of RCTs for these analyses.

In disaggregating the overall analysis by combinations of acupuncture and comparator type, we identified statistically significant, large clinical effects in favor of TCM acupuncture (as monotherapy) versus a passive waitlist control and TCM acupuncture (as adjunctive therapy) plus TAU versus TAU alone. However, results were not statistically significant for TCM acupuncture (as monotherapy) versus active (group CBT or paroxetine) comparators or for auricular acupuncture (as adjunctive therapy) plus TAU versus TAU alone.

Follow-up. Four RCTs (57 percent of RCTs) with 387 total participants (55 percent of randomized participants) provided PTSD symptom data at a follow-up between one and six months. When data were pooled across these four trials, a medium clinical effect in favor of TCM acupuncture (as adjunctive or monotherapy) versus any comparator was observed (SMD −0.46; CI −0.85 to −0.06; I^2 30%). This finding is based on a low quality body of evidence due

to wide confidence intervals and a high risk of performance bias (lack of blinding participants via sham acupuncture comparisons) in all trials contributing to this analysis (see Figure 3.3).

Figure 3.3. Any Acupuncture Versus Any Comparator (PTSD Symptoms, One- to Six-Month Follow-Up SMD)



Almost all sensitivity analyses for any acupuncture versus any comparator at follow-up yielded statistically significant, small to medium effects in favor of acupuncture; however, effects were medium but no longer statistically significant when excluding the studies related to the Wenchuan earthquake (SMD −0.72; CI −4.02 to 2.58; I^2 43%; 2 RCTs; see Appendix F, Table 2). We found no evidence of publication bias (Egger's test, p=0.18; Begg's test, p=0.06), though we had a limited number of RCTs for these analyses. In disaggregating the overall analysis by combinations of acupuncture and comparator type, we identified statistically significant effects in favor of TCM acupuncture (as monotherapy) versus a passive waitlist control and a small clinical effect in favor of TCM acupuncture (as monotherapy) versus active (group CBT and paroxetine) comparators. However, results were not statistically significant for TCM acupuncture (as adjunctive therapy to TAU) versus TAU alone, nor for TCM acupuncture (as monotherapy) versus either a single type (group CBT or paroxetine) of active comparator.

Health-Related Quality of Life

One RCT (20 percent of RCTs) with 55 participants (16 percent of randomized participants) reported health-related quality of life data, measured using the Short Form (SF)-36 Physical Health Component Summary and Mental Health Component Summary scores (Engel et al., 2014). No statistically significant difference between TCM acupuncture (as adjunctive therapy to TAU) versus TAU alone (guideline-concordant PTSD care at a medical center) was observed for physical health-related quality of life using the Physical Health Component Summary (SMD −0.47; CI −1.00 to 0.07; 1 RCT) or for mental health-related quality of life using the Mental Health Component Summary (SMD −0.33; CI −0.86 to 0.21; 1 RCT). The quality of the body of evidence underpinning these effect estimates is very low due to wide confidence intervals and lack of replication.

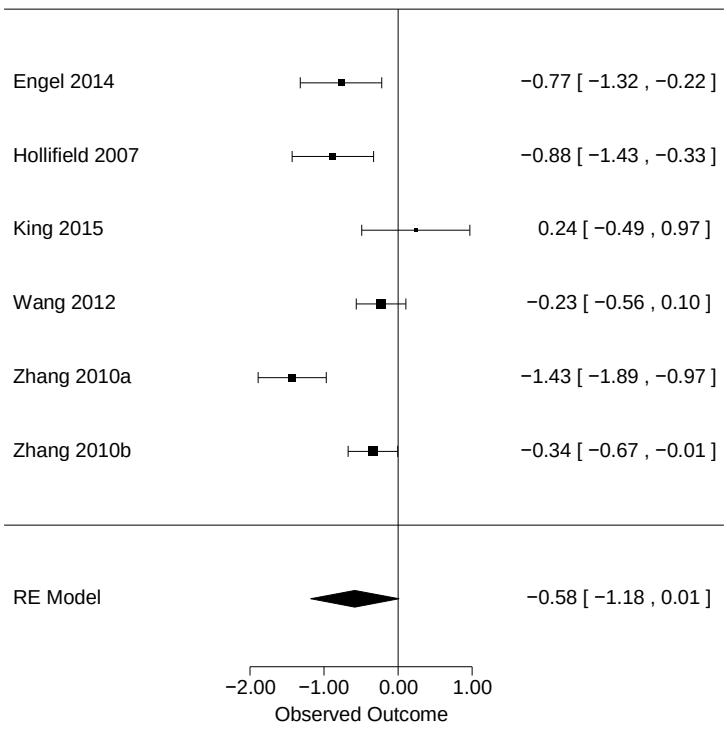
Functional Status

One RCT (20 percent of RCTs) with 56 participants (16 percent of randomized participants) reported functional status data via the Sheehan Disability Inventory (Hollifield et al., 2007). We identified statistically significant, clinically large effects in favor of TCM acupuncture (as monotherapy) versus a passive comparator (waitlist control) at postintervention (SMD −0.83; CI −1.38 to −0.29; 1 RCT) and three-month follow-up (SMD −0.97; CI −1.52 to −0.41; 1 RCT), though these results were based on a very low quality body of evidence and were not significant when comparing acupuncture with an active group CBT comparator (postintervention: SMD −0.25; CI −0.78 to 0.27; 3-month follow-up: SMD −0.16; CI −0.68 to 0.36).

Depression Symptoms

Postintervention. Six RCTs (86 percent of RCTs) with 508 total participants (72 percent of randomized participants) reported depression symptom data, measured using the Beck Depression Inventory II, the Hamilton Depression Scale, the Hopkins Symptom Checklist-25, or the Patient Health Questionnaire. When data were pooled across these six trials, no statistically significant difference between acupuncture (as adjunctive or monotherapy) and any comparator was observed at postintervention (SMD −0.58; CI −1.18 to 0.01; I^2 81%; 6 RCTs). This finding is based on a very low quality body of evidence due to unclear or inadequate ITT analysis procedures, wide confidence intervals, and considerable heterogeneity (see Figure 3.4).

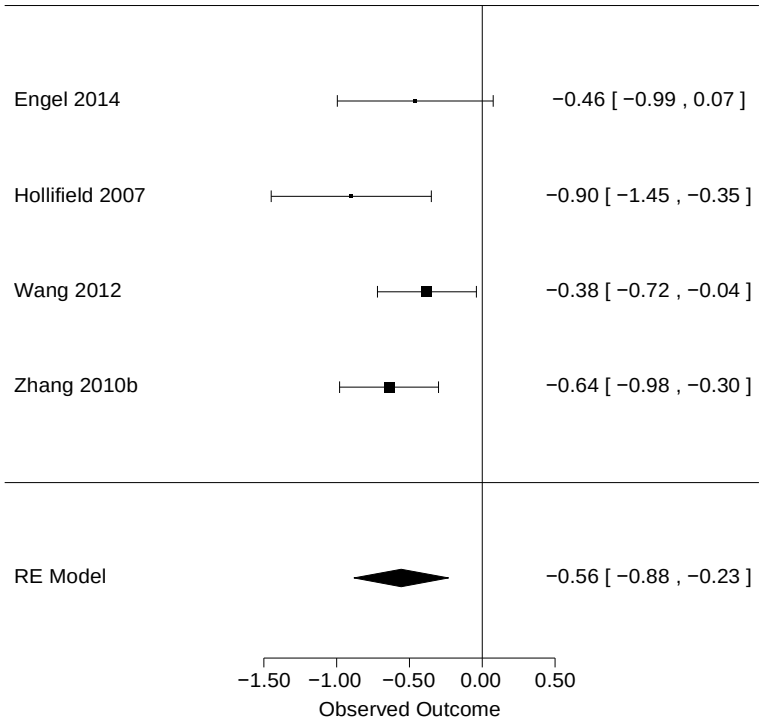
Figure 3.4. Any Acupuncture Versus Any Comparator (Depression Symptoms, Postintervention SMD)



All sensitivity analyses for any acupuncture versus any comparator at postintervention remained not statistically significant, including the sensitivity analysis in which we removed the poor quality study (Zhang, Ran, et al., 2010a), with the outlying positive effect in favor acupuncture (SMD −0.41; CI −0.89 to 0.07; I^2 54%; 5 RCTs), as well as the analysis in which we excluded the three studies related to the Wenchuan earthquake (SMD −0.51; CI −2.00 to 0.98; I^2 72%; 3 RCTs; see Appendix F, Table 3). While we found no evidence of publication bias (Egger's test, p=0.78; Begg's test, p=0.70), we had a limited number of RCTs for these analyses. In disaggregating the overall analysis by combinations of acupuncture and comparator type, we identified statistically significant effects for TCM acupuncture (as monotherapy) versus a passive comparator, and for TCM acupuncture (as an adjunctive therapy to TAU) versus TAU alone; however, results were no longer statistically significant for other disaggregated results.

Follow-up. Four RCTs (57 percent of RCTs) with 387 total participants (55 percent of randomized participants) provided depression symptom data at a follow-up between one and six months. When data were pooled across these four trials, a medium clinical effect in favor of TCM acupuncture (as adjunctive or monotherapy) versus any comparator was observed (SMD −0.56; CI −0.88 to −0.23; I^2 0%). This finding is based on a low quality body of evidence due to wide confidence intervals and a high risk of performance bias (lack of blinding participants via sham acupuncture comparisons) in all trials contributing to this analysis (see Figure 3.5).

Figure 3.5. Any Acupuncture Versus Any Comparator (Depression Symptoms, One- to Six-Month Follow-Up SMD)

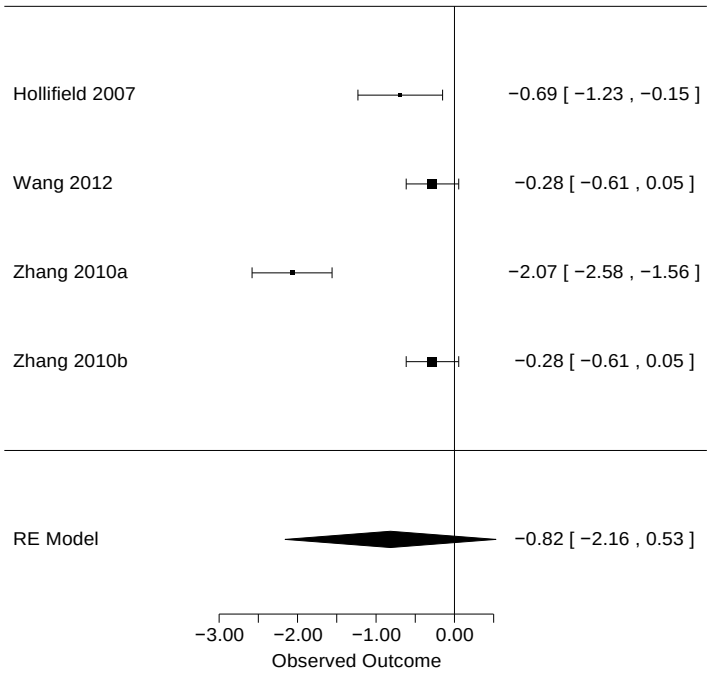


Most but not all sensitivity analyses were statistically significant (see Appendix F, Table 4). While we found no evidence of publication bias (Egger's test, p=0.54; Begg's test, p=0.28), we had a limited number of RCTs for these analyses. In disaggregating the overall analysis by combinations of acupuncture and comparator type, statistically significant results remained only for TCM acupuncture (as monotherapy) versus a passive comparator.

Anxiety Symptoms

Postintervention. Four RCTs (57 percent of RCTs) with 424 total participants (60 percent of randomized participants) reported anxiety symptom data, measured using either the Hamilton Anxiety Scale or the Hopkins Symptom Checklist-25. When data were pooled across the four trials, no statistically significant difference between acupuncture (as monotherapy) and any comparator was observed at postintervention (SMD −0.82; CI −2.16 to 0.53; I^2 92%). This finding is based on a very low quality body of evidence due to unclear or inadequate ITT analysis procedures, wide confidence intervals, and considerable heterogeneity (see Figure 3.6). Findings were not statistically significant for any of our sensitivity analyses, except when excluding the studies related to the Wenchuan earthquake, which leaves only one RCT in the analysis; this RCT reports a clinically medium and statistically significant effect in favor of acupuncture (SMD −0.69; CI −1.23 to −0.15; see Appendix F, Table 5).

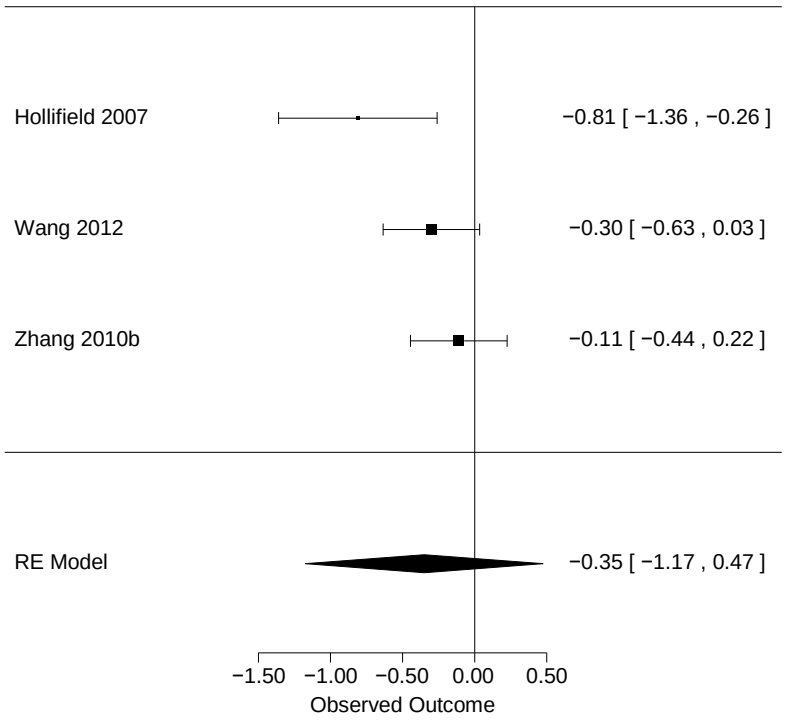
Figure 3.6. Any Acupuncture Versus Any Comparator (Anxiety Symptoms, Postintervention SMD)



In disaggregating the overall analysis by combinations of acupuncture and comparator type, we identified statistically significant results only for TCM acupuncture (as monotherapy) versus a passive comparator.

Follow-up. Three RCTs (43 percent of RCTs) with 332 participants (47 percent of randomized participants) provided anxiety symptom data at a follow-up between one and six months. When data were pooled across these three trials, no statistically significant difference was found between acupuncture (as monotherapy) and any comparator (SMD −0.35; CI −1.17 to 0.47; I^2 56%). This finding is based on a very low quality body of evidence due to unclear or inadequate ITT analysis procedures, wide confidence intervals, and substantial heterogeneity (see Figure 3.7). Results were not statistically significant for any sensitivity analysis, except when excluding the studies related to the Wenchuan earthquake, which leaves only one RCT in the analysis; this RCT reports a clinically large and statistically significant effect in favor of acupuncture (SMD −0.81; CI −1.36 to −0.26; see Appendix F, Table 6). In disaggregating the overall analysis by combinations of acupuncture and comparator type, we identified statistically significant results only for TCM acupuncture (as monotherapy) versus a passive comparator.

Figure 3.7. Any Acupuncture Versus Any Comparator (Anxiety Symptoms, One- to Six-Month Follow-Up SMD)



Sleep Quality

Two RCTs (40 percent of RCTs) with 53 total participants (16 percent of randomized participants) reported sleep quality data, measured using either the Insomnia Severity Index (ISI) or the Pittsburgh Sleep Quality Index Global Score. When data were pooled across the two trials, no statistically significant difference between auricular acupuncture (as adjunctive therapy) and any comparator was observed at postintervention (pooled: SMD −0.46; CI −3.95 to 3.03; I^2 0%; King et al., 2015: SMD −0.72; CI −1.47 to 0.04; Prisco et al., 2013: SMD −0.17; CI −0.97 to 0.63). This finding is based on a low quality body of evidence due to high risk of attrition bias and considerably wide confidence intervals. We also did not identify statistically significant results for auricular acupuncture (as adjunctive therapy) plus TAU versus TAU alone (pooled: SMD −0.63; CI −1.89 to 0.63; I^2 0%; low quality of evidence; Prisco et al., 2013: SMD −0.52; CI −1.36 to 0.31) or for auricular acupuncture (as adjunctive therapy) versus sham acupuncture (SMD −0.17; CI −0.97 to 0.63; 1 RCT; very low quality of evidence).

Adverse Events

We identified seven RCTs (100 percent of RCTs) with 709 total participants (100 percent of randomized participants) providing data on the safety of acupuncture. From reported safety data, we did not find strong evidence indicating that acupuncture is associated with any serious adverse events. Only one study explicitly reported that no study-related adverse events were

reported or observed (Engel et al., 2014). Minor to moderate adverse events from acupuncture were reported by a minority of participants in the remaining six studies.

In Hollifield et al. (2007), one participant receiving TCM acupuncture reported kidney pain, which was not reported by any participant in the group CBT and waitlist control comparator groups.

King et al. (2015) reported that one participant in auricular acupuncture dropped out due to uncomfortable feelings while receiving acupuncture. Five other auricular acupuncture participants experienced adverse events during the study period, including one fall, two alcohol-related events, one wrist injury, and one incident of suicidal ideation; four of these adverse events occurred before participants received acupuncture, whereas another (not specified in the report) occurred three days after receipt of acupuncture. The study investigators concluded that none of these adverse events was directly related to the acupuncture intervention.

Prisco et al. (2013) reported that one participant receiving sham acupuncture dropped out because the acupuncture needles were uncomfortable, which was not reported by any participant in the true auricular acupuncture group.

Zhang, Ran, et al. (2010a) monitored adverse events and did not report any, though the authors did not explicitly state that no adverse events were observed.

In Zhang, Yuan, et al. (2010b), some patients (exact number unknown) reported roughness of operational practices, fear of needles, bleeding, hematoma, pain, and fainting; no serious adverse events were reported.

Wang et al (2012) reported the most adverse events of any included study. One participant refused to continue acupuncture for being afraid of pain; in contrast, one participant in the active comparator reported symptoms of giddiness, a second reported symptoms of constipation, and a third reported blurred vision. In the acupuncture group, the following adverse events on behavior, the autonomic nervous system, and the cardiovascular system were experienced during acupuncture (in order of frequency, out of 69 acupuncture participants): minor superficial bleeding (27 participants), minor needle pain (24 participants), minor hematoma (9 participants), and moderate pain (1 participant). Participants in the active comparator (12 weeks of paroxetine) reported numerous adverse events (in order of frequency, out of 69 paroxetine participants): xerophthalmia (36 participants), insomnia (28 participants), appetite loss/anorexia (21 participants), constipation (17 participants), sweat (11 participants), nausea and vomiting (11 participants), headache (11 participants), saliva increase (8 participants), fatigue (7 participants), activity declined (6 participants), diarrhea (6 participants), dizziness (5 participants), excitement or agitation (4 participants), depression (3 participants), blurred vision (3 participants), tachycardia (3 participants), activity increased (2 participants), skin allergy symptom (1 participant), and stuffy nose (1 participant).

KQ 1a: Does the Effect of Needle Acupuncture Vary by Type of Acupuncture?

We aimed to investigate whether any effects of needle acupuncture varied by acupuncture following TCM or acupuncture inserting needles in particular points on the ear (auricular acupuncture). Two RCTs provided data evaluating auricular acupuncture (King et al., 2015; Prisco et al., 2013), while five RCTs provided data evaluating some form of TCM acupuncture (Engel et al., 2014; Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)—three of which also involved electroacupuncture (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). We did not identify any direct head-to-head comparisons of auricular acupuncture versus TCM acupuncture, though one trial provided data on electroacupuncture versus electroacupuncture plus moxibustion.

Auricular

PTSD and depression symptoms. We found no statistically significant difference between auricular acupuncture (as adjunctive therapy) and a TAU comparator (a ten-week, multi-modal residential PTSD treatment program for combat-related PTSD) for PTSD symptoms at postintervention (SMD −0.32; CI −1.05 to 0.42; 1 RCT) and for depression symptoms at postintervention (SMD 0.32; CI −0.49 to 0.97; 1 RCT); these effect estimates are underpinned by a very low quality body of evidence due to high risk of attrition bias, wide confidence intervals, and lack of replication.

Previously reported outcomes. As reported above for KQ 1, we found no statistically significant difference between auricular acupuncture (as adjunctive therapy) and any comparator for sleep quality at postintervention. Regarding adverse events, both King et al. (2015) and Prisco et al. (2013) reported that one participant dropped out due to uncomfortable feelings while receiving acupuncture (true acupuncture in King et al., 2015, and sham acupuncture in Prisco et al., 2013).

TCM Acupuncture

PTSD symptoms. We found no statistically significant difference between TCM acupuncture (as adjunctive or monotherapy) and any comparator for PTSD symptoms at postintervention (SMD −0.89; CI −1.88 to 0.10; I^2 92%; 5 RCTs). This finding is based on a very low quality body of evidence due to unclear or inadequate ITT analysis procedures, wide confidence intervals, and considerable heterogeneity. Results remained not statistically significant for all sensitivity analyses (see Appendix F, Table 7).

Depression symptoms. We identified a statistically significant, medium clinical effect in favor of TCM acupuncture (as adjunctive or monotherapy) versus any comparator for depression symptoms at postintervention (SMD −0.71; CI −1.31 to −0.10; I^2 81%; 5 RCTs). This finding is based on a very low quality body of evidence due to unclear or inadequate ITT analysis

procedures, wide confidence intervals, and considerable heterogeneity. Moreover, results were not statistically significant for half of our sensitivity analyses, including removing the poor quality study (Zhang, Ran, et al., 2010a), with the outlying positive effect in favor of acupuncture (see Appendix F, Table 8).

Previously reported outcomes. As reported above for KQ 1, we identified statistically significant effects for the following outcomes: medium clinical effect in favor of TCM acupuncture (as adjunctive or monotherapy) versus any comparator for PTSD symptoms at a follow-up between one and six months (see Figure 3.3), clinically large effects in favor of TCM acupuncture (as monotherapy) versus a passive comparator (waitlist control) for functional status at postintervention and three-month follow-up, and a medium clinical effect in favor of TCM acupuncture (as adjunctive or monotherapy) versus any comparator for depression symptoms at a follow-up between one and six months (see Figure 3.5). We also identified no statistically significant differences between TCM acupuncture and comparators for the following outcomes: physical and mental health-related quality of life, anxiety symptoms at postintervention (see Figure 3.6), and anxiety symptoms at a follow-up between one and six months (see Figure 3.7). Regarding adverse events, Engel et al. (2014) explicitly reported that no study-related adverse events were reported or observed, whereas Zhang, Ran, et al. (2010a) monitored adverse events and did not report any, though the authors did not explicitly state that no adverse events were observed. Hollifield et al. (2007) and Zhang, Yuan, et al. (2010b) indicated minor adverse events by some patients, and Wang et al (2012) reported numerous minor adverse events. No serious adverse events were reported for any study.

Meta-Regressions

We did not identify statistically significant differences in effects by auricular versus TCM acupuncture for PTSD symptoms postintervention (p=0.57) and depression symptoms postintervention (p=0.19), though we had limited available evidence for these analyses (see Table 3.3).

Table 3.3. Meta-Regression for Effect by Type of Acupuncture

KQ 1a: Does the effect of needle acupuncture vary by type of acupuncture?			
PTSD symptoms (postintervention)	1 auricular, 29 participants 5 TCM, 479 participants	Meta-regression did not suggest a systematic effect (p=0.57)	Very low
Depression symptoms (postintervention)	1 auricular, 29 participants 5 TCM, 479 participants	Meta-regression did not suggest a systematic effect (p=0.19)	Very low

Direct Comparison of Electroacupuncture Versus Electroacupuncture Plus Moxibustion

We found no statistically significant difference between electroacupuncture (with needles) and electroacupuncture (with needles) plus moxibustion for PTSD symptoms at postintervention (SMD −0.13; CI −0.46 to 0.20), three-month follow-up (SMD −0.03; CI −0.36 to 0.31), or six-

month follow-up (SMD −0.01; CI −0.34 to 0.33), as well as for depression symptoms at postintervention (SMD −0.18; CI −0.51 to 0.15), three-month follow-up (SMD −0.26; CI −0.59 to 0.08), or six-month follow-up (SMD −0.33; CI −0.67 to 0.00). We did identify statistically significant, clinically small effects in favor of electroacupuncture plus moxibustion (versus electroacupuncture only) for anxiety symptoms at postintervention (SMD 0.37, 0.03 to 0.71), three-month follow-up (SMD 0.44, 0.10 to 0.77), and six-month follow-up (SMD 0.42, 0.08 to 0.76). However, all of these findings are based on a very low quality body of evidence due to wide confidence intervals and lack of replication.

KQ 1b: Does the Effect of Needle Acupuncture Differ If Acupuncture Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?

Three RCTs provided data evaluating acupuncture as an adjunctive therapy (Engel et al., 2014; King et al., 2015; Prisco et al., 2013), and four RCTs provided data evaluating acupuncture as a monotherapy (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). Of the three adjunctive RCTs, all co-interventions involved TAU that also served as a comparator (i.e., the intervention contrast was acupuncture plus TAU versus TAU alone). TAU involved either psychotherapies and medications following the VA/DoD CPG for Management of Post-Traumatic Stress (Engel et al., 2014), a ten-week residential PTSD treatment program for combat-related PTSD (King et al., 2015), or CBT along with psychopharmacology if indicated (Prisco et al., 2013). We did not identify any direct head-to-head comparisons of acupuncture as adjunctive therapy versus acupuncture as monotherapy.

Adjunctive Therapy

PTSD symptoms. We found no statistically significant effect for acupuncture as adjunctive therapy versus any comparator for PTSD symptoms at postintervention (pooled: SMD −0.72; CI −5.33 to 3.89; I^2 59%; 2 RCTs; Engel et al., 2014: SMD −1.05; CI −1.62 to −0.49; King et al., 2015: SMD −0.32; CI −1.05 to 0.42) based on a very low quality body of evidence due to high risk of attrition bias, wide confidence intervals, and substantial heterogeneity. We also found no statistically significant effect for PTSD symptoms at follow-up (measured using the PCL) (SMD −0.47; CI −1.00 to 0.07; 1 RCT) based on a very low quality body of evidence due to wide confidence intervals and lack of replication. However, results were statistically significant and in favor of acupuncture in sensitivity analyses using one-month rather than two-month PCL data (SMD −1.06; CI −1.63 to −0.49; 1 RCT) and when using two-month CAPS data rather than two-month PCL data (SMD −0.71; CI −1.25 to −0.16; 1 RCT).

Depression symptoms. We found no statistically significant effect for acupuncture as adjunctive therapy versus any comparator for depression symptoms at postintervention (pooled: SMD −0.30; CI −6.71 to 6.11; I^2 79%; 2 RCTs; Engel et al., 2014: SMD −0.77; CI −1.32 to −0.22; King et al., 2015: SMD 0.24; CI −0.49 to 0.97) based on a very low quality body of

evidence due to high risk of attrition bias, wide confidence intervals, and substantial heterogeneity. We also found no statistically significant effect for depression symptoms at follow-up (SMD −0.46; CI −1.00 to 0.07; 1 RCT) based on a very low quality body of evidence due to wide confidence intervals and lack of replication.

Previously reported outcomes. As reported above for KQ 1, we identified statistically significant, clinically large effects in favor of TCM acupuncture (as monotherapy) versus a passive comparator (waitlist control) at postintervention and three-month follow-up (SMD −0.97; CI −1.52 to −0.41; 1 RCT). We also found no statistically significant difference between auricular acupuncture (as adjunctive therapy) and any comparator for sleep quality at postintervention. Regarding adverse events, Engel et al. (2014) explicitly reported that no study-related adverse events were reported or observed, whereas King et al. (2015) and Prisco et al. (2013) indicated minor adverse events by some patients. No serious adverse events were reported for any study.

Monotherapy

PTSD symptoms. We found no statistically significant effect for acupuncture as monotherapy versus any comparator for PTSD symptoms at postintervention (SMD −0.85; CI −2.29 to 0.59; I^2 93%; 4 RCTs). Results did not differ for any sensitivity analyses (see Appendix F, Table 9). We also found no statistically significant effect for acupuncture as monotherapy versus any comparator for PTSD symptoms at a follow-up between one and six months (SMD −0.50; CI −1.32 to 0.32; I^2 53%; 3 RCTs). Results were not statistically significant for all but one sensitivity analysis (see Appendix F, Table 10).

Depression symptoms. We also found no statistically significant effect of acupuncture as monotherapy versus any comparator for depression symptoms at postintervention (SMD −0.70; CI −1.58 to 0.18; I^2 85%; 4 RCTs). Results did not differ for any sensitivity analyses (see Appendix F, Table 11). We also found no statistically significant effect of acupuncture as monotherapy versus any comparator for depression symptoms at a follow-up between one and sixth months (SMD −0.58; CI −1.17 to 0.01; I^2 27%; 3 RCTs). Results did not differ for any sensitivity analyses (see Appendix F, Table 12).

Previously reported outcomes. As reported above for KQ 1, we identified statistically significant, clinically large effects in favor of TCM acupuncture (as monotherapy) versus a passive comparator (waitlist control) for functional status at postintervention and three-month follow-up. We also found no statistically significant differences between acupuncture (as monotherapy) and comparators for anxiety symptoms at postintervention (see Figure 3.6) and at a follow-up between one and sixth months (see Figure 3.7). Regarding adverse events, Zhang, Ran, et al. (2010a) monitored adverse events and did not report any, though the authors did not explicitly state that no adverse events were observed. Hollifield et al. (2007) and Zhang, Yuan, et al. (2010b) indicated minor adverse events by some patients, and Wang et al (2012) reported numerous minor adverse events. No serious adverse events were reported for any study.

Meta-Regressions

We did not identify statistically significant differences in effects by type of co-intervention status for the above outcomes (PTSD symptoms postintervention: p=0.85; PTSD symptoms follow-up: p=0.96; depression symptoms postintervention: p=0.50; depression symptoms follow-up: p=0.75), though we had limited available evidence for these analyses (Table 3.4).

Table 3.4. Meta-Regressions for Effect by Type of Co-Intervention

KQ 1b: Does the effect of needle acupuncture differ if acupuncture is offered as an adjunctive therapy rather than as a monotherapy?			
PTSD symptoms (postintervention)	4 monotherapy, 424 participants 2 adjunctive, 84 participants	Meta-regression did not suggest a systematic effect (p=0.85)	Very low
PTSD symptoms (follow-up)	3 monotherapy, 332 participants 1 adjunctive, 55 participants	Meta-regression did not suggest a systematic effect (p=0.96)	Very low
Depression symptoms (postintervention)	4 monotherapy, 424 participants 2 adjunctive, 84 participants	Meta-regression did not suggest a systematic effect (p=0.50)	Very low
Depression symptoms (follow-up)	3 monotherapy, 332 participants 1 adjunctive, 55 participants	Meta-regression did not suggest a systematic effect (p=0.75)	Very low

KQ 1c: Does the Effect of Needle Acupuncture Depend on the Comparator?

Three RCTs provided data evaluating acupuncture plus TAU versus TAU alone (Engel et al., 2014; King et al., 2015; Prisco et al., 2013), one RCT provided data evaluating acupuncture versus sham acupuncture (Prisco et al., 2013), one RCT provided data evaluating acupuncture versus a passive control (Hollifield et al., 2007), and four RCTs provided data evaluating acupuncture versus an active comparator (Hollifield et al., 2007; Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b).

Sham Acupuncture

Sleep quality. We found no statistically significant difference between TCM acupuncture (as adjunctive therapy) and sham acupuncture for sleep quality at postintervention (SMD −0.17; CI −0.97 to 0.63; 1 RCT) based on a very low quality body of evidence due to high risk of attrition bias, wide confidence intervals, and lack of replication.

Acupuncture Plus TAU Versus TAU Alone

Sleep quality. We found no statistically significant difference between auricular acupuncture (as adjunctive therapy) and TAU for sleep quality at postintervention (pooled: SMD −0.63; CI −1.89 to 0.63; I^2 0%; King et al., 2015: SMD −0.72; CI −1.47 to 0.04; Prisco et al., 2013: SMD −0.52; CI −1.36 to 0.31) based on a low quality body of evidence due to high risk of attrition bias and considerably wide confidence intervals.

Previously reported outcomes. The remainder of results are identical to those presented for acupuncture as adjunctive therapy in KQ 1b—that is, no statistically significant effect for PTSD symptoms at postintervention and at follow-up; no statistically significant effect for depression symptoms at postintervention and at follow-up; and a statistically significant, clinically large effects in favor of acupuncture at postintervention and three-month follow-up based on a very low quality body of evidence.

Passive Comparator

PTSD symptoms. We identified statistically significant, large clinical effects in favor of TCM acupuncture (as monotherapy) versus a waitlist control for PTSD symptoms at postintervention (SMD 0.92; CI −1.47 to −0.36; 1 RCT) and three-month follow-up (SMD −0.99; CI −1.55 to −0.43; 1 RCT). These results are based on a very low quality body of evidence from the same RCT due to high risk of attrition bias, wide confidence intervals, and lack of replication.

Depression symptoms. We identified statistically significant, large clinical effects in favor of TCM acupuncture (as monotherapy) versus a waitlist control for depression symptoms at postintervention (SMD −0.88; CI −1.43 to −0.33; 1 RCT) and three-month follow-up (SMD −0.90; CI −1.45 to −0.35; 1 RCT). These results are based on a very low quality body of evidence from the same RCT due to high risk of attrition bias, wide confidence intervals, and lack of replication.

Anxiety symptoms. We identified a statistically significant, medium clinical effect in favor of TCM acupuncture (as monotherapy) versus a waitlist control for anxiety symptoms at postintervention (SMD −0.69; CI −1.23 to −0.15; 1 RCT). We also identified a statistically significant, large clinical effect in favor of TCM acupuncture (as monotherapy) versus a waitlist control for anxiety symptoms at three-month follow-up (SMD −0.81; CI −1.36 to −0.26). These results are based on a very low quality body of evidence from the same RCT due to high risk of attrition bias, wide confidence intervals, and lack of replication.

Previously reported outcomes. As reported above for KQ 1, we also identified statistically significant, large clinical effects in favor of TCM acupuncture (as monotherapy) versus waitlist control at postintervention and three-month follow-up, though, again, these results were based on a very low quality body of evidence.

Active Comparator

PTSD symptoms. We found no statistically significant difference between TCM acupuncture (as monotherapy) versus an active comparator (group CBT or paroxetine) for PTSD symptoms at postintervention (SMD −0.71; CI −2.20 to 0.78; I^2 93%; 4 RCTs). Results did not differ for all but one sensitivity analysis (see Appendix F, Table 13). However, we found a statistically significant, clinically small effect in favor of TCM acupuncture (as monotherapy) versus an active comparator (group CBT or paroxetine) for PTSD symptoms at a follow-up between one and six months (SMD −0.31; CI −0.59 to −0.02; I^2 0%; 3 RCTs). This finding is based on a low

quality body of evidence due to unclear or inadequate ITT analysis procedures and wide confidence intervals. Results did not substantially differ for all sensitivity analyses (see Appendix F, Table 14).

Functional status. We found no statistically significant difference between TCM acupuncture (as monotherapy) versus group CBT for functional status at postintervention (SMD −0.25; CI −0.78 to 0.27; 1 RCT) and three-month follow-up (SMD −0.16; CI −0.68 to 0.36; 1 RCT). These findings are based on a very low quality body of evidence due to high risk of attrition bias, wide confidence intervals, and lack of replication.

Depression symptoms. We found no statistically significant difference between TCM acupuncture (as monotherapy) versus an active comparator (group CBT or paroxetine) for depression symptoms at postintervention (SMD −0.53; CI −1.47 to 0.41; I^2 86%; 4 RCTs). Results did not differ for all but one sensitivity analysis (see Appendix F, Table 15). We also found no statistically significant difference between TCM acupuncture (as monotherapy) versus an active comparator (group CBT or paroxetine) for depression symptoms at a follow-up between one and six months (SMD −0.40; CI −1.10 to 0.30; I^2 45%; 3 RCTs). Results did not differ for any sensitivity analyses (see Appendix F, Table 16).

Anxiety symptoms. We found no statistically significant difference between TCM acupuncture (as monotherapy) versus an active comparator (group CBT or paroxetine) for anxiety symptoms at postintervention (SMD −0.69; CI −2.13 to 0.75; I^2 93%; 4 RCTs). Results did not differ for all but one sensitivity analysis (see Appendix F, Table 17). We also found no statistically significant difference between TCM acupuncture (as monotherapy) versus an active comparator (group CBT or paroxetine) for anxiety symptoms at a follow-up between one and six months (SMD −0.22; CI −0.49 to 0.05; I^2 0%; 3 RCTs). However, results were inconsistent when utilizing different data from individual trials in the meta-analyses (Appendix F, Table 18).

Meta-Regressions

We did not identify statistically significant differences in effects by type of comparator for the above outcomes (PTSD symptoms postintervention: p=0.98; PTSD symptoms follow-up: p=0.44; depression symptoms postintervention: p=0.78; depression symptoms follow-up: p=0.61; anxiety symptoms postintervention: p=0.90; anxiety symptoms follow-up: p=0.90), though we had limited available evidence for these analyses (see Table 3.5). Health-related quality of life could not be narratively compared by type of comparator, because it was assessed only in an RCT evaluating acupuncture plus TAU versus TAU alone.

Table 3.5. Meta-Regressions for Effect by Type of Comparator

KQ 1c: Does the effect of needle acupuncture depend on the comparator?			
PTSD symptoms (postintervention)	1 passive, 56 participants 2 TAU, 84 participants 3 active, 368 participants	Meta-regression did not suggest a systematic effect (p=0.98)	Very low
PTSD symptoms (follow-up)	1 passive, 56 participants 1 TAU, 55 participants 2 active, 276 participants	Meta-regression did not suggest a systematic effect (p=0.44)	Very low
Depression symptoms (postintervention)	1 passive, 56 participants 2 TAU, 84 participants 3 active, 368 participants	Meta-regression did not suggest a systematic effect (p=0.78)	Very low
Depression symptoms (follow-up)	1 passive, 56 participants 1 TAU, 55 participants 2 active, 276 participants	Meta-regression did not suggest a systematic effect (p=0.61)	Very low
Anxiety symptoms (postintervention)	1 TAU, 56 participants 3 active, 368 participants	Meta-regression did not suggest a systematic effect (p=0.90)	Very low
Anxiety symptoms (follow-up)	1 TAU, 56 participants 2 active, 276 participants	Meta-regression did not suggest a systematic effect (p=0.90)	Very low

Chapter Four: Discussion

Summary of Findings

Overall, the available evidence in support of acupuncture for PTSD is limited. We identified potential benefits of acupuncture for PTSD symptoms and functional status (compared with control groups) immediately postintervention, though the quality of the body of evidence underpinning these estimates is very low. We consequently have very little confidence that these estimates represent the true effect of acupuncture on these outcomes (i.e., there is uncertainty in the magnitude or stability of these effect estimates). We also identified a low quality body of evidence suggesting potential benefits of acupuncture for PTSD and depression symptoms (compared with control groups) in the months following completion of acupuncture treatment, with results robust to most sensitivity analyses. However, this low quality body of evidence suggests that additional evidence is needed before concluding that effect estimates lie close to the true effect for these outcomes. Therefore, we have limited confidence that these findings are likely to be stable in reflecting the true effect of acupuncture on PTSD and depression symptoms in the months following acupuncture treatment. Further research may still change confidence in these effect estimates and may even change the direction or magnitude of the estimates themselves. Of note, we identified only one RCT that used a sham acupuncture comparator, making it difficult to know whether some results are due to nonspecific or placebo influences. See Table 4.1 for a full summary of findings and quality of the body of evidence for this review.

The available evidence also suggests that acupuncture is not typically associated with serious adverse events, though some participants experienced minor or moderate needle pain, minor superficial bleeding, and minor hematoma, among other reported minor adverse effects. However, the generally low reporting about adverse events may be due to differential procedures for collecting (or not collecting) safety information, making it unclear whether few reports of adverse events were due to few experiences of adverse events or due to the mechanism or instrumentation for detecting adverse events.

We did not identify strong evidence to suggest that results differ by type of acupuncture, co-intervention status, or comparator. Of note, we identified only one RCT that used a sham acupuncture comparator, making it difficult to know whether some results are due to nonspecific effects or placebo influences related to performance bias. Narrative comparisons suggest that results may differ by type of acupuncture and comparator. For example, we found statistically significant results in favor of TCM acupuncture for depression symptoms at postintervention, whereas we did not identify statistically significant effects for auricular acupuncture.

Table 4.1. Summary of Findings and Quality of Evidence

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
KQ 1: Acupuncture versus any comparator							
PTSD symptoms (postintervention)	6 RCTs, 508 participants	SMD −0.80 (CI −1.59 to −0.01), large effect, acupuncture	Downgrade 1[a,f]	Downgrade 1[b]	Direct	Downgrade 1[d]	Very low
PTSD symptoms (follow-up)	4 RCTs, 387 participants	SMD −0.46 (CI −0.85 to −0.06), medium effect, acupuncture	Downgrade 1[m]	No downgrade	Direct	Downgrade 1[d]	Low
Physical health-related quality of life (follow-up)	1 RCT, 55 participants	SMD −0.47 (CI −1.00 to 0.07), n.s.	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Mental health-related quality of life (follow-up)	1 RCT, 55 participants	SMD −0.33 (CI −0.86 to 0.21), n.s.	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Functional status (postintervention)	1 RCT, 56 participants	SMD −0.83 (CI −1.38 to −0.29), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Functional status (follow-up)	1 RCT, 56 participants	SMD −0.97 (CI −1.52 to −0.41), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Depression symptoms (postintervention)	6 RCTs, 508 participants	SMD −0.58 (CI −1.17 to 0.01), n.s.	Downgrade 1[a]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
Depression symptoms (follow-up)	4 RCTs, 387 participants	SMD −0.56 (CI −0.88 to −0.23), medium effect, acupuncture	Downgrade 1[m]	No downgrade	Direct	Downgrade 1[d]	Low
Anxiety symptoms (postintervention)	4 RCTs, 424 participants	SMD −0.82 (CI −2.16 to 0.53), n.s.	Downgrade 1[a]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
Anxiety symptoms (follow-up)	3 RCTs, 332 participants	SMD −0.35 (CI −1.17 to 0.47), n.s.	Downgrade 1[a]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
Sleep quality (postintervention)	2 RCTs, 53 participants	SMD −0.46 (CI −3.95 to 3.03), n.s.	Downgrade 1[a]	No downgrade	Direct	Downgrade 1[c]	Low
Adverse events	7 RCTs, 709 participants	Acupuncture is not associated with any serious adverse events, though some participants reported minor/moderate needle pain, superficial bleeding, and hematoma	Downgrade 2[n]	Downgrade 1[o]	Direct	Downgrade 1[p]	Very low
KQ 1: TCM (monotherapy) versus passive comparator							
PTSD symptoms (postintervention)	1 RCT, 56 participants	SMD −0.92 (CI −1.47 to −0.36), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
PTSD symptoms (follow-up)	1 RCT, 56 participants	SMD −0.99 (CI −1.55 to −0.43), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
Functional status (postintervention)	1 RCT, 56 participants	See KQ 1 (versus any comparator) above	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Functional status (follow-up)	1 RCT, 56 participants	See KQ 1 (versus any comparator) above	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Depression symptoms (postintervention)	1 RCT, 56 participants	SMD −0.88 (CI −1.43 to −0.33), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Depression symptoms (follow-up)	1 RCT, 56 participants	SMD −0.90 (CI −1.45 to −0.35), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Anxiety symptoms (postintervention)	1 RCT, 56 participants	SMD −0.69 (CI −1.23 to −0.15), medium effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Anxiety symptoms (follow-up)	1 RCT, 56 participants	SMD −0.81 (CI −1.36 to −0.26), large effect, acupuncture	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Adverse events	1 RCT, 56 participants	TCM: 1 participant with kidney pain	Downgrade 2[n]	Downgrade 2[e]	Direct	Downgrade 1[p]	Very low
KQ 1: TCM (mono) versus active (CBT + paroxetine)							
PTSD symptoms (postintervention)	4 RCTs, 425 participants	SMD −0.71 (CI −2.20 to 0.78), n.s.	Downgrade 1[a,f]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
PTSD symptoms (follow-up)	3 RCTs, 333 participants	SMD −0.31 (CI −0.59 to −0.02), small effect, acupuncture	Downgrade 1[a]	No Downgrade	Direct	Downgrade 1[d]	Low
Depression symptoms (postintervention)	4 RCTs, 425 participants	SMD −0.53 (CI −1.47 to 0.41), n.s.	Downgrade 1[a,f]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
Depression symptoms (follow-up)	3 RCTs, 333 participants	SMD −0.40 (CI −1.10 to 0.30), n.s.	Downgrade 1[a]	No Downgrade	Direct	Downgrade 1[c]	Low
Anxiety symptoms (postintervention)	4 RCTs, 425 participants	SMD −0.69 (CI −2.13 to 0.75), n.s.	Downgrade 1[a,f]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Anxiety symptoms (follow-up)	3 RCTs, 333 participants	SMD −0.22 (CI −0.49 to 0.05), n.s	Downgrade 1[a]	No Downgrade	Direct	Downgrade 1[c]	Low
Adverse events	4 RCTs, 425 participants	TCM: 1 participant with kidney pain, 1 participant refused to continue due to fear of pain. Unspecified number mentioned fear of needles, bleeding, and pain. Paroxetine: 1 participant constipation, 1 participant blurred vision, 1 participant giddiness. Both: Various other behavior, autonomic nerve, and cardiovascular events.	Downgrade 2[n]	Downgrade 1[o]	Direct	Downgrade 1[p]	Very low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
KQ 1: TCM (mono) versus paroxetine							
PTSD symptoms (postintervention)	3 RCTs, 368 participants	SMD −0.83 (CI −3.58 to 1.92), n.s.	Downgrade 1[l]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
PTSD symptoms (follow-up)	2 RCTs, 276 participants	SMD −0.35 (CI −1.89 to 1.19), n.s.	Downgrade 1[m]	No Downgrade	Direct	Downgrade 1[c]	Low
Depression symptoms (postintervention)	3 RCTs, 368 participants	SMD −0.65 (CI −2.28 to 0.98), n.s.	Downgrade 1[l]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
Depression symptoms (follow-up)	2 RCTs, 276 participants	SMD −0.51 (CI −2.16 to 1.14), n.s.	Downgrade 1[m]	No Downgrade	Direct	Downgrade 1[c]	Low
Anxiety symptoms (postintervention)	3 RCTs, 368 participants	SMD −0.86 (CI −3.40 to 1.68), n.s.	Downgrade 1[l]	Downgrade 1[b]	Direct	Downgrade 1[c]	Very low
Anxiety symptoms (follow-up)	2 RCTs, 276 participants	SMD −0.21 (CI −1.42 to 1.00), n.s.	Downgrade 1[m]	No Downgrade	Direct	Downgrade 1[c]	Low
Adverse events	3 RCTs, 368 participants	TCM: 1 participant refused to continue due to fear of pain. Unspecified number mentioned fear of needles, bleeding, and pain. Paroxetine: 1 participant constipation, 1 participant blurred vision, 1 participant giddiness. Both: Various other behavior, autonomic nerve, and cardiovascular events.	Downgrade 2[n]	Downgrade 1[o]	Direct	Downgrade 1[p]	Very low
KQ 1: TCM (mono) versus CBT							
PTSD symptoms (postintervention)	1 RCT, 57 participants	SMD −0.33 (CI −0.85 to 0.19), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
PTSD symptoms (follow-up)	1 RCT, 57 participants	SMD −0.10 (CI −0.62 to 0.42), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Functional status (postintervention)	1 RCT, 57 participants	SMD −0.25 (CI −0.78 to 0.27), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Functional status (follow-up)	1 RCT, 57 participants	SMD −0.16 (CI −0.68 to 0.36), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Depression symptoms (postintervention)	1 RCT, 57 participants	SMD −0.16 (CI −0.68 to 0.36), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Depression symptoms (follow-up)	1 RCT, 57 participants	SMD −0.04 (CI −0.56 to 0.48), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Anxiety symptoms (postintervention)	1 RCT, 57 participants	SMD −0.17 (CI −0.69 to 0.35), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
Anxiety symptoms (follow-up)	1 RCT, 57 participants	SMD −0.25 (CI −0.77 to 0.27), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Adverse events	1 RCT, 57 participants	TCM: 1 participant with kidney pain	Downgrade 2[n]	Downgrade 1[o]	Direct	Downgrade 1[p]	Very low
KQ 1: TCM (adjunctive) versus TAU							
PTSD symptoms (postintervention)	1 RCT, 55 participants	SMD −1.05 (CI −1.62 to −0.49), large effect, acupuncture	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
PTSD symptoms (follow-up)	1 RCT, 55 participants	SMD −0.47 (CI −1.00 to 0.07), n.s.	Downgrade 1[k]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Physical health-related quality of life (follow-up)	1 RCT, 55 participants	See KQ 1 (versus any comparator) above	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Mental health-related quality of life (follow-up)	1 RCT, 55 participants	See KQ 1 (versus any comparator) above	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Depression symptoms (postintervention)	1 RCT, 55 participants	SMD −0.77 (CI −1.32 to −0.22), medium effect, acupuncture	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[d]	Very low
Depression symptoms (follow-up)	1 RCT, 55 participants	SMD −0.46 (CI −1.00 to 0.07), n.s.	No downgrade	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Adverse events	1 RCT, 55 participants	No study-related adverse events were reported or observed	Downgrade 2[n]	Downgrade 2[e]	Direct	Downgrade 1[p]	Very low
KQ 1: Auricular (adjunctive) versus TAU							
PTSD symptoms (postintervention)	1 RCT, 29 participants	SMD −0.32 (CI −1.05 to 0.42), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Depression symptoms (postintervention)	1 RCT, 29 participants	SMD 0.32 (CI −0.49 to 0.97), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low
Sleep quality (postintervention)	2 RCTs, 53 participants	SMD −0.63 (CI −1.89 to 0.63), n.s.	Downgrade 1[a]	No downgrade	Direct	Downgrade 1[c]	Low
Adverse events	2 RCTs, 53 participants	Auricular: 1 participant dropped out due to uncomfortable feelings while receiving treatment. 1 participant fell, 2 participants had alcohol-related events, 1 participant had a wrist injury, and 1 participant had suicidal ideation before treatment started.	Downgrade 2[n]	Downgrade 1[o]	Direct	Downgrade 1[p]	Very low
KQ 1: Auricular (adjunctive) versus sham acupuncture							
Sleep quality (postintervention)	1 RCT, 24 participants	SMD −0.17 (CI −0.97 to 0.63), n.s.	Downgrade 1[a]	Downgrade 2[e]	Direct	Downgrade 1[c]	Very low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
Adverse events	1 RCT, 24 participants	Sham: 1 participant dropped out because needles were uncomfortable	Downgrade 2[n]	Downgrade 2[e]	Direct	Downgrade 1[p]	Very low
KQ 1a: Does the effect of needle acupuncture vary by type of acupuncture?							
PTSD symptoms (postintervention)	1 auricular, 29 participants; 5 TCM, 479 participants	Meta-regression did not suggest a systematic effect (p=0.57)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
Depression symptoms (post)	1 auricular, 29 participants; 5 TCM, 479 participants	Meta-regression did not suggest a systematic effect (p=0.19)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
KQ 1b: Does the effect of needle acupuncture differ if acupuncture is offered as an adjunctive therapy rather than as a monotherapy?							
PTSD symptoms (postintervention)	4 monotherapy, 24 participants; 2 adjunctive, 84 participants	Meta-regression did not suggest a systematic effect (p=0.85)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
PTSD symptoms (follow-up)	3 monotherapy, 332 participants; 1 adjunctive, 55 participants	Meta-regression did not suggest a systematic effect (p=0.96)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
Depression symptoms (postintervention)	4 monotherapy, 424 participants; 2 adjunctive, 84 participants	Meta-regression did not suggest a systematic effect (p=0.50)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
Depression symptoms (follow-up)	3 monotherapy, 332 participants; 1 adjunctive, 55 participants	Meta-regression did not suggest a systematic effect (p=0.75)	Downgrade 1[g]	No downgrade	Indirect[i]	Downgrade 1[j]	Very low
KQ 1c: Does the effect of needle acupuncture depend on the comparator?							
PTSD symptoms (postintervention)	1 passive, 56 participants; 2 TAU, 84 participants; 3 active, 368 participants	Meta-regression did not suggest a systematic effect (p=0.98)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
PTSD symptoms (follow-up)	1 passive, 56 participants; 1 TAU, 55 participants; 2 active, 276 participants	Meta-regression did not suggest a systematic effect (p=0.44)	Downgrade 1[g]	No downgrade	Indirect[i]	Downgrade 1[j]	Very low
Depression symptoms (postintervention)	1 passive, 56 participants; 2 TAU, 84 participants; 3 active, 368 participants	Meta-regression did not suggest a systematic effect (p=0.78)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
Depression symptoms (follow-up)	1 passive, 56 participants; 1 TAU, 55 participants; 2 active, 276 participants	Meta-regression did not suggest a systematic effect (p=0.61)	Downgrade 1[g]	No downgrade	Indirect[i]	Downgrade 1[j]	Very low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
Anxiety symptoms (postintervention)	1 TAU, 56 participants; 3 active, 368 participants	Meta-regression did not suggest a systematic effect (p=0.90)	Downgrade 1[g]	Downgrade 1[h]	Indirect[i]	Downgrade 1[j]	Very low
Anxiety symptoms (follow-up)	1 TAU, 56 participants; 2 active, 276 participants	Meta-regression did not suggest a systematic effect (p=0.90)	Downgrade 1[g]	No downgrade	Indirect[i]	Downgrade 1[j]	Very low

NOTES: SMD < 0 favors acupuncture. SMD < −0.2 for a small clinical effect, SMD < −0.5 for a medium clinical effect, and SMD < −0.8 for a large clinical effect. Postintervention = immediately following the end of the intervention; follow-up = between one and six months following the end of the intervention. n.s. = no significant effect.

[a] High attrition bias and/or no ITT analysis.
[b] Statistically significant and/or substantial heterogeneity.
[c] Wide confidence interval indicating benefit and harm.
[d] Wide confidence interval spanning effect sizes with clinically meaningful differences.
[e] Cannot judge consistency (only one RCT).
[f] Results changed in statistical significance when removing outlying poor quality study.
[g] Low sample size for meta-regression.
[h] Statistically significant and/or substantial residual heterogeneity.
[i] Based on meta-regression rather than direct comparisons.
[j] Wide confidence intervals for model results (i.e., intercept and factors).
[k] Results statistically significant when using CAPS instead of PCL.
[l] Unclear risks of selection and detection bias.
[m] High risk of performance bias from unblinded participants in all trials underpinning analysis due to lack of sham acupuncture comparators.
[n] Lack of systematic methods to proactively monitor or capture adverse events.
[o] Inconsistent collection and reporting of adverse event data.
[p] Imprecise measurement and/or reporting of adverse events in both trial groups.

In addition, we found no statistically significant differences between acupuncture and either TAU or an active comparator for PTSD symptoms at postintervention or depression symptoms at postintervention and follow-up, yet we did identify statistically significant, clinically large effects in favor of acupuncture versus a passive comparator (waitlist control) for these outcomes. We also found no statistically significant differences between acupuncture and TAU for PTSD symptoms at follow-up, in contrast to statistically significant effects in favor of acupuncture versus a passive comparator (waitlist control) and active comparators (group CBT or paroxetine) for this outcome. Lastly, we found no statistically significant differences between acupuncture and an active comparator for functional status and anxiety symptoms at postintervention and follow-up, yet we did identify statistically significant, clinically medium to large effects in favor of acupuncture versus a passive comparator (waitlist control) for these outcomes. However, we did not detect differences in results by type of acupuncture, co-intervention status, and comparator using meta-regression—though these analyses are limited by the small number of identified RCTs, which makes the ratio of studies to study-level covariates potentially too small for the analysis to be sufficiently powered (Borenstein, 2009).

Significant amounts of statistical heterogeneity for many outcomes indicate that important sources of clinical heterogeneity may be unexplained by some of our analyses and the available data. For instance, acupuncture interventions in our data set and in clinical practice vary by dosage (e.g., number of sessions and weeks), acupoints (e.g., auricular, TCM points), and clinical settings, all of which may provide sources of clinical heterogeneity. Long-term effects of acupuncture are also uncertain, because most outcome data were from postintervention or shortly thereafter, and only two RCTs provided data after three months on a select number of outcomes. Most importantly, having unclear ITT procedures with small trials experiencing some attrition limits confidence in the accuracy and stability of many effect estimates. Of note, though, three RCTs focused solely on active military or veteran populations (Engel et al., 2014; King et al., 2015; Prisco et al., 2013), one of which specifically noted that all patients received care for combat-related PTSD (King et al., 2015).

In addition, three of the seven studies recruited participants who developed PTSD following the same Wenchuan earthquake, which took place in a non-Western culture where acupuncture is a part of traditional medicine (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b). The overall results for PTSD symptoms at postintervention (SMD −0.80; CI −1.59 to −0.01; I^2 90%; 6 RCTs) and at follow-up (SMD −0.46; CI −0.85 to −0.06; I^2 30%; 4 RCTs) were still of the same clinical size yet were no longer statistically significant when removing the earthquake-related studies in sensitivity analyses (postintervention: SMD −0.83; CI −1.70 to 0.04; I^2 7%; 3 RCTs; follow-up: SMD −0.72; CI −4.02 to 2.58; I^2 43%; 2 RCTs). Results for depression symptoms at postintervention (SMD −0.58; CI −1.18 to 0.01; I^2 81%; 6 RCTs) were similar in clinical size and were also not statistically significant when removing the earthquake-related studies in sensitivity analyses (SMD −0.51; CI −2.00 to 0.98; I^2 72%; 3 RCTs); however, results for depression symptoms at follow-up (SMD −0.56; CI −0.88 to −0.23; I^2 0%; 4 RCTs)

were no longer statistically significant when removing the earthquake-related studies (SMD −0.67; CI −3.47 to 2.12; I^2 22%; 2 RCTs). Results for anxiety symptoms at postintervention (SMD −0.82; CI −2.16 to 0.53; I^2 92%; 4 RCTs) and follow-up (SMD −0.35; CI −1.17 to 0.47; I^2 56%; 3 RCTs) were actually statistically significant when removing the earthquake-related studies, though these sensitivity analyses involved only one RCT without replication (postintervention: SMD −0.69; CI −1.23 to −0.15 1 RCT; follow-up: SMD −0.81; CI −1.36 to −0.26, 1 RCT). These sensitivity analyses may be useful for making decisions about U.S. populations, but it is worth noting that these analyses are likely underpowered to detect statistically significant effects compared with the overall analyses, meaning more U.S.-based trials are needed.

Other Reviews in This Area

The results of this review are comparable to the conclusion of the one previous systematic review on acupuncture for PTSD (Kim, Heo, et al., 2013). As with our review, this previous review concluded that evidence in support of acupuncture for PTSD is encouraging yet not cogent due to the small number of RCTs and participants providing data for meta-analyses. That study also highlighted limitations resulting from the methodological quality of included trials, hindering conclusions that can be drawn from this body of evidence. However, while this previous review included non-randomized evaluations of acupuncture for PTSD, our review focused solely on RCTs and included several additional RCTs published in the interim, providing a different body of evidence underpinning our analyses. Moreover, we conducted a formal assessment of the quality of the body of evidence underpinning outcomes, which allowed us to make more-systematic conclusions about the confidence in the stability and accuracy of our effect estimates in representing true effects of acupuncture on outcomes of interest. While this previous review limited their analyses to PTSD, depression, and anxiety symptoms (as well as adverse events), we investigated additional outcomes of interest reported in RCTs. Furthermore, we investigated results at different time points (i.e., immediately postintervention and at a follow-up between one and six months), allowing us to distinguish effect estimates and our confidence in their representation of true effects at various times postintervention. Lastly, we attempted to investigate moderators (or sources of variability) in potential intervention effects.

Strengths and Limitations

This review has several strengths: an *a priori* research design, duplicate study selection and data extraction of study information, a comprehensive search of electronic databases, inclusion of gray literature (e.g., dissertations or graduate theses), and risk of bias assessments and comprehensive quality of evidence assessments used to formulate review conclusions. However, some limitations are worth noting. First, we focused only on needle acupuncture, whereas related interventions (e.g., acupressure) may yield different effects. Furthermore, we did not contact trial

authors for missing data or to find other potential studies not identified by the search strategy; additional outcome data (if existent), information about potential risks of bias, and other potential studies identified by trial authors have the potential to influence the effect estimates and quality of body of evidence ratings. We also did not search some databases specific to complementary and alternative medicine (e.g., Acubriefs, Acudoc2 RCT) that may yield acupuncture studies not found in major medical databases, such as PubMed (Cogo et al., 2011). In addition, this review was restricted to RCTs. We also did not analyze the potential effect of response expectancies (i.e., participant expectations that acupuncture will have positive effects) due to lack of data on this topic reported in trials, and only one included study used sham acupuncture.

The overall pool of available studies is small, some meta-analyses in this review only pool results from two RCTs, some estimates use data from only one RCT that has not been replicated, and significant heterogeneity also existed for several outcomes. Lastly, the aforementioned attrition biases throughout this evidence also limited confidence in findings.

Implications for Future Research and Practice

The limited available evidence suggests potential benefits of acupuncture for PTSD symptoms and depression symptoms at follow-up points after the acupuncture intervention has been completed. While statistically significant effects were identified for PTSD symptoms and depression symptoms at postintervention, as well as functional status at postintervention and follow-up, the body of evidence for these results was typically of very low quality and not robust to sensitivity analyses (where possible). Because the number of available studies is small, and the quality of evidence is low to very low, additional well-designed, rigorous, and large RCTs are needed to provide more-conclusive evidence about whether acupuncture is efficacious for treating adults with PTSD. Future RCTs should investigate specific PTSD symptom clusters (in addition to overall PTSD symptoms) to clarify whether any of the symptom clusters specifically are sources of any potential patient improvements. Moreover, future trials should include sham comparators to account for possible nonspecific effects; while some contend that it does not serve as a valid "placebo" for acupuncture trials, sham acupuncture is currently the most credible comparator for reducing the risk of performance bias from lack of blinding participants (Tough et al., 2009). Given the potentially chronic nature of PTSD, researchers should also seek to measure outcomes at long-term follow-ups, because only two RCTs provided any outcome data at six months, and no RCTs provided data up to one year postintervention. Future RCTs should also be reported in compliance with the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) recommendations (MacPherson et al., 2002). Researchers, policymakers, funders, and practitioners may wish to establish future priorities on needle acupuncture for PTSD, considering type of needle acupuncture, choice of comparator, co-intervention status, and target outcomes. Committees charged with updating CPGs for treating PTSD may also be interested in using this report as a source of evidence on needle acupuncture.

Appendix A: Search Methodology

PubMed

Time Period Covered:
From Inception to 1/1/2016

Search Strategy:
acupuncture OR "Acupuncture Therapy"[Mesh] OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*) OR auricular acupuncture
AND
"stress disorders, post-traumatic"[MeSH] OR "stress disorders, traumatic, acute"[MeSH] OR "stress disorders" OR "post-traumatic stress" OR "post traumatic stress" OR "posttraumatic stress" OR "trauma" OR "combat trauma" OR "sexual trauma" OR "emotional trauma" OR "traumatic neurosis" OR "acute stress disorder" OR "traumatic stress" OR ("trauma"[tiab] AND "induced"[tiab] AND "spectrum disorder"[tiab]) OR trauma-induced spectrum disorder*[tiab] OR ptsd[tiab]

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PsycINFO

Time Period Covered:
From Inception to 1/1/2016

Search Strategy:
DE "Acupuncture" OR acupuncture OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*) OR auricular acupuncture
AND
DE "Posttraumatic Stress Disorder" OR "stress disorders" OR "post-traumatic stress disorder" OR "posttraumatic stress disorder" OR "post traumatic stress disorder" OR "post-traumatic stress" OR "post traumatic stress" OR "posttraumatic stress" OR "trauma" OR "combat trauma" OR "sexual trauma" OR "emotional trauma" OR "traumatic neurosis" OR "acute stress disorder" OR "traumatic stress" OR ("trauma" AND "induced" AND "spectrum disorder") OR trauma-induced spectrum disorder* OR ptsd
Search modes - Find all search terms

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CINAHL

Time Period Covered:
From Inception to 1/1/2016

Search Strategy:
(MH "Acupuncture+") OR "acupuncture" OR (MH "Acupuncture Points") OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*) OR auricular acupuncture
AND
MH ("Stress Disorders, Post-Traumatic+") OR "stress disorders" OR "post-traumatic stress" OR "post traumatic stress" OR "posttraumatic stress" OR "trauma" OR "combat trauma" OR "sexual trauma" OR "emotional trauma" OR "traumatic neurosis" OR "acute stress disorder" OR "traumatic stress" OR ("trauma" AND "induced" AND "spectrum disorder") OR trauma-induced spectrum disorder* OR ptsd
Search modes - Find all search terms

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Web of Science Indexes **(**SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC)

Time Period Covered:
From Inception to 12/31/2015

Search Strategy:
ts=(acupuncture OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*))
AND
ts=(stress disorders OR post-traumatic stress OR post traumatic stress OR posttraumatic stress OR trauma OR combat trauma OR sexual trauma OR emotional trauma OR traumatic neurosis OR acute stress disorder OR traumatic stress OR (trauma AND induced AND spectrum disorder) OR trauma-induced spectrum disorder* OR ptsd)

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Embase

Time Period Covered:
From Inception to 12/31/2015

Search Strategy:
'acupuncture'/exp OR acupuncture OR 'electro acupuncture' OR (acupoint AND stimulat*) OR (meridian AND needl*) OR 'auricular acupuncture' OR (('chinese medicine'/exp OR 'chinese medicine') AND needl*) OR (auricular AND ('acupuncture'/exp OR acupuncture))

AND
‘stress disorder’:ab,ti OR ‘stress disorders’:ab,ti OR ‘post-traumatic stress disorder’/exp OR ‘post-traumatic stress disorder’ OR ‘posttraumatic stress disorder’/exp OR ‘posttraumatic stress disorder’ OR ‘post traumatic stress disorder’/exp OR ‘post traumatic stress disorder’ OR ‘post-traumatic stress’/exp OR ‘post-traumatic stress’ OR ‘post traumatic stress’/exp OR ‘post traumatic stress’ OR ‘posttraumatic stress’/exp OR ‘posttraumatic stress’ OR trauma:ab,ti OR ‘combat trauma’ OR ‘sexual trauma’ OR ‘emotional trauma’/exp OR ‘emotional trauma’ OR ‘traumatic neurosis’ OR ‘traumatic stress’/exp OR ‘traumatic stress’ OR ‘trauma induced spectrum’ OR ‘acute stress disorder’/exp OR ‘acute stress disorder’ OR ‘trauma-induced spectrum’ OR ‘ptsd’/exp OR ptsd
AND
[humans]/lim
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PILOTS

Time Period Covered:
From Inception to 12/31/2015

Search Strategy:
acupuncture OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR (“chinese medicine” AND needl*)

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Cochrane: CDSR, CENTRAL, and DARE

Time Period Covered:
From inception to 12/31/2015

Search Strategy:
acupuncture or electroacupuncture or electro-acupuncture or (acupoint and stimulat*) or (meridian and needl*) or auricular-acupuncture or (“chinese medicine” and needl*):ti,ab,kw (Word variations have been searched)
AND
“Posttraumatic Stress Disorder” or stress disorders or post-traumatic stress or post traumatic stress or posttraumatic stress or trauma or combat trauma or sexual trauma or emotional trauma or traumatic neurosis or acute stress disorder or traumatic stress or (trauma and induced and spectrum disorder) or trauma-induced spectrum disorder* or ptsd:ti,ab,kw (Word variations have been searched)

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AMED

Time Period Covered:
From Inception to 1/1/2016

Search Strategy:
acupuncture OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*) IN ALL FIELDS PLUS TEXT
AND
stress disorders OR post-traumatic stress OR post traumatic stress OR posttraumatic stress OR trauma OR combat trauma OR sexual trauma OR emotional trauma OR traumatic neurosis OR acute stress disorder OR traumatic stress OR (trauma AND induced AND spectrum disorder) OR "trauma-induced spectrum disorder" OR "trauma-induced spectrum disorders" OR ptsd
IN ALL FIELDS PLUS TEXT

Update:
Time Period Covered:
1/21/2015 to 1/21/2016

Search Strategy:
acupuncture OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*)
IN ALL FIELDS PLUS TEXT
AND
stress disorders OR post-traumatic stress OR post traumatic stress OR posttraumatic stress OR trauma OR combat trauma OR sexual trauma OR emotional trauma OR traumatic neurosis OR acute stress disorder OR traumatic stress OR (trauma AND induced AND spectrum disorder) OR "trauma-induced spectrum disorder" OR "trauma-induced spectrum disorders" OR ptsd
IN ALL FIELDS PLUS TEXT

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Clinicaltrials.gov

Time Period Covered:
From inception to 12/31/2015

Search Strategy:
acupuncture OR electroacupuncture OR electro-acupuncture OR (acupoint AND stimulat*) OR (meridian AND needl*) OR auricular-acupuncture OR ("chinese medicine" AND needl*) OR auricular acupuncture | post-traumatic stress disorder

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International Clinical Trials Registry Platform

Time Period Covered:
From inception to 11/5/2015

Search Strategy:
post-traumatic stress OR posttraumatic stress OR post traumatic stress OR ptsd in the Condition

acupuncture OR electroacupuncture OR electro-acupuncture OR acupoint OR auricular-acupuncture in the Intervention

Appendix B: Cochrane Risk of Bias Criteria

This appendix outlines the criteria used to make risk of bias determinations.

Random sequence generation (selection bias):

- Low risk: The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).
- High risk: The investigators describe a nonrandom component in the sequence generation process. Usually, the description would involve some systematic, nonrandom approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number. Other nonrandom approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgment or some method of nonrandom categorization of participants, for example: allocation by judgment of the clinician; allocation by preference of the participant; allocation based on the results of a laboratory test or a series of tests; allocation by availability of the intervention.
- Unclear risk: Insufficient information about the sequence generation process to permit judgment of low risk or high risk.

Allocation concealment (selection bias):

- Low risk: Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.
- High risk: Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g., a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g., if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.
- Unclear risk: Insufficient information to permit judgment of low risk or high risk. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgment—for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque, and sealed.

Blinding of participants and personnel (performance bias):

- Low risk: Any one of the following: no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- High risk: Any one of the following: no blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
- Unclear risk: Any one of the following: insufficient information to permit judgment of low risk or high risk; the study did not address this outcome.

Blinding of outcome assessment:

- Low risk: Any one of the following: no blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
- High risk: Any one of the following: no blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
- Unclear risk: Any one of the following: insufficient information to permit judgment of low risk or high risk; the study did not address this outcome.

Incomplete outcome data:

- Low risk: Any one of the following: no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.
- High risk: Any one of the following: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; as-treated analysis done with substantial departure of the intervention received from that assigned at randomization; potentially inappropriate application of simple imputation.

- Unclear risk: Any one of the following: insufficient reporting of attrition/exclusions to permit judgment of low risk or high risk (e.g., number randomized not stated, no reasons for missing data provided); the study did not address this outcome.

Selective reporting of outcome data:

- Low risk: Any of the following: the study protocol is available and all of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).
- High risk: Any one of the following: not all of the study's prespecified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g., subscales) that were not prespecified; one or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
- Unclear risk: Insufficient information to permit judgment of low risk or high risk. It is likely that the majority of studies will fall into this category.

Appendix C: Excluded Full-Text Articles

Reason Excluded: Background Paper

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Appendix D: Included Studies

Study	References
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King et al., 2015	King, H. C., D. L. Spence, A. H. Hickey, P. Sargent, R. Elesh, and C. D. Connelly, "Auricular Acupuncture for Sleep Disturbance in Veterans with Post-Traumatic Stress Disorder: A Feasibility Study," *Military Medicine*, Vol. 180, No. 5, 2015, pp. 582–590.
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Appendix E: Evidence Table of Included Studies

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Engel et al., 2014 **References**: Engel et al., 2014 (ClincalTrials.gov: NCT00320138) **Country:** United States **Purpose:** Evaluate a brief course of manual acupuncture for military-related PTSD **Study design:** Individually randomized controlled trial **Recruitment:** Recruited from primary care clinics (68%), self-referrals from advertisements at medical center (19%), referrals from providers/patients (13%) **Quality rating:** Good Valid measurement, >80% follow-up, clear interventions, pre-specified outcomes	**Number of patients:** 55 (28 acupuncture, 27 TAU) **Baseline PTSD:** Mean PCL: 56.1 (standard deviation [SD] 11.8) Mean CAPS: 72.9 (SD 16.7) Used PCL-Civilian version to capture non-combat traumas **Comorbid health conditions:** Mean Beck Depression Inventory: 22.7 (SD 9.9) Mean Numeric Rating Scale: 4.2 (SD 2.4) Mean Physical Health Component Summary: 48.0 (SD 10.9) Mean Mental Health Component Summary: 28.0 (SD 12.4) **Age (Years):** 34.8 (SD 9.7) **Gender:** 38 (69.1%) male **Inclusion criteria:** Active-duty military, aged 18–65, 30+ on PCL, meet criteria for PTSD on CAPS using 1–2 scoring rule **Exclusion criteria:** 1+ PTSD treatment changes in the past 8 weeks, 8+ on Numeric Rating Scale, any acupuncture treatment in past 6 months, pregnant, moderate or severe	**Acupuncture content:** Manualized whole body TCM using hair-thin solid needles (Seirin brand, J type: 0.14, 0.16, and 0.2 mm and L type: 0.2 mm). Manually inserted into muscle/subcutaneous tissue for 15–30 minutes depending on point prescription. Standard sanitation procedures were followed. First 4 sessions were standardized, with each of these used at least once: Urinary bladder 13, 14, 15, 18, 20, 23; Liver 3; Large intestine 4; Heart 5, 7; Pericardium 6; Kidney 3, 9; Ren 4, 15; Du 24; Ear Shenmen; and Yintang. The last 4 sessions allowed individualized treatment based on diagnostic criteria. Participants were randomly assigned to one of three licensed study acupuncturists who practiced regularly and had advanced degrees in TCM. Acupuncturists underwent calibration training prior to the study to ensure treatment fidelity. **Health care setting:** Private offices at social work clinic **Number of sites:** 1 **Level of care:** Outpatient **Dosage:** Two 60-minute sessions per week for four weeks (8 hours total) **Co-interventions:** TAU (see below) **Comparator:** Usual PTSD care at medical center guided by VA/DoD CPG for Management of Post-Traumatic Stress, involving both psychotherapies (e.g., prolonged exposure therapy, nontrauma-focused CBT) and medications (e.g., antidepressants) **Primary endpoint:** PTSD symptoms two months postintervention **Longest follow-up:** Two months postintervention	**PTSD symptoms:** PCL: • Postintervention: SMD −1.05 (CI −1.62 to −0.49), p<0.05 (favors acupuncture) • 1-month follow-up: SMD −1.06 (CI −1.63 to −0.49), p<.05 (favors acupuncture) • 2-month follow-up: SMD −0.47 (CI −1.00 to 0.07), p>0.05 (favors acupuncture) CAPS at 2-month follow-up: SMD −0.71 (CI −1.25 to −0.16), p<0.05 (favors acupuncture) **Health-related quality of life:** SF-36 Mental Health Component Summary score at 2-month follow-up: SMD −0.33 (CI −0.86 to 0.21), p>0.05 (favors acupuncture) SF-36 Physical Health Component Summary score at 2-month follow-up: SMD −0.47 (CI −1.00 to 0.07), p>0.05 (favors acupuncture) **Depression symptoms:** Beck Depression Inventory II: • Postintervention: SMD −0.77 (CI −1.32 to −0.22), p<0.05 (favors acupuncture) • 1-month follow-up: SMD −0.71 (CI −1.26 to −0.17), p<0.05 (favors acupuncture) • 2-month follow-up: SMD −0.46 (CI −1.00 to 0.07), p>0.05 (favors acupuncture)

Study Details	Participants	Intervention/Treatment	Outcomes/Results
reported, ITT analysis used	TBI, psychosis in the past 2 years, serious instability in medical or psychiatric status based on principal investigator or medical monitor judgment, any DSM-IV criterion A traumatic experience in the past 30 days	**Power calculation:** Intended sample size not reached	**Adverse events:** No study-related adverse events were reported or observed

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Hollifield et al., 2007 **References**: Devitt, 2003; Hollifield et al., 2007 (ClinicalTrials.gov: NCT00055354) **Country:** United States **Purpose:** Evaluate the potential efficacy and acceptability of acupuncture for PTSD **Study design:** Individually randomized controlled trial **Recruitment:** Posted flyers (43%), other media (29%), clinics and physicians (14%), professional contacts of the research team (5%), participants' word of mouth (4%), community agencies and therapists (2%), unknown (3%) **Quality rating:** Fair Downgraded from "Good" due to high attrition with questionable ITT analysis (last observation carried forward was used)	**Number of patients:** 84 (29 acupuncture, 28 CBT, 27 waitlist control) **Baseline PTSD:** 62% had traumatic experiences before age 12, 21% between ages 12–17, and 17% after age 18. 38% reported 3+ events. Posttraumatic Symptom Scale–Self Report: • Acupuncture: 31.33 (SD 10.10) • CBT: 32.52 (SD 6.63) • Waitlist control: 30.79 (SD 9.54) **Comorbid health conditions:** Depression (Hopkins Symptom Checklist-25): • Acupuncture: 2.50 (SD 0.70) • CBT 2.63 (SD 0.53) • Waitlist control: 2.61 (SD 0.65) Anxiety (Hopkins Symptom Checklist-25): • Acupuncture: 2.45 (SD 0.57) • CBT 2.40 (SD 0.42) • Waitlist control: 2.26 (SD 0.67) **Age (Years):** Acupuncture: 42.3 (SD 12.1); CBT: 40.9 (SD 13.4); waitlist control: 43.4 (SD 13.5) **Gender:** 27 (32.1%) male **Inclusion criteria:** Posttraumatic Symptom Scale–Self Report score of 16+, DSM-IV PTSD diagnosis, commitment to randomization, no active substance abuse/psychosis, no	**Acupuncture content:** Tailored, whole body, manual TCM using solid needles in subcutaneous tissue or muscle with manipulation. Acupuncturist was a licensed doctor of Oriental Medicine in New Mexico with 4 years postgraduate TCM clinical experience. Participants were evaluated for TCM diagnoses for PTSD to determine flexibly prescribed acupuncture points for each participant; a few standard acupoints were also used. Standard acupuncture point prescription combined front and back treatments to avoid point fatigue (tolerance due to frequent use). Front treatment used 11 needles (bilateral at acupuncture points LR3, PC6, HT7, ST36, SP6, and 1 at Yintang). Back treatment used 14 needles (bilateral at points GB20 and BL14, 15, 18, 20, 21, and 23). There were 15 other points from which up to 3 flexibly prescribed points could be added to the 25 prescribed needles. Different needling techniques for standard points could be used to address participants' specific diagnoses. Viva needles (34 g) were used for most participants and inserted to a depth of 1⁄4 to 1⁄2 in; Seirin (40 g, red) was used for needle-sensitive participants. Needles manipulated at the beginning of treatment and just before needle removal to tonify/reduce points according to diagnosis. Vaccaria seeds ("ear seeds") were also placed at shen men, sympathetic, liver, kidney, and lung points; participants were asked to massage the seeds for 15 minutes per day to help control symptoms. At end of treatment, participants were taught how to place the seeds for symptom management. Lifestyle advice was limited: only in response to direct questions by participants or if a behavior was seriously affecting symptoms related to diagnosis and constitution. **Health care setting:** Did not report **Number of sites:** 1 **Level of care:** Outpatient **Dosage:** Two 60-minute sessions per week for 12 weeks (24 hours). Each session included standard TCM symptom interview (15–20 minutes); pulse and tongue evaluation (2–5	**PTSD symptoms:** Posttraumatic Symptom Scale–Self Report: • Postintervention (versus CBT): SMD −0.33 (CI −0.85 to 0.19), p>0.05 (favors acupuncture) • Postintervention (versus waitlist control): SMD −0.92 (CI −1.47 to −0.36), p<0.05 (favors acupuncture) • 3-month follow-up (versus CBT): SMD −0.10 (CI −0.62 to 0.42), p>0.05 (favors acupuncture) • 3-month follow-up (versus waitlist control): SMD −0.99 (CI −1.55 to −0.43), p<0.05 (favors acupuncture) **Functional status:** Sheehan Disability Inventory: • Postintervention (versus CBT): SMD −0.25 (CI −0.78 to 0.27), p>0.05 (favors acupuncture) • Postintervention (versus waitlist control): SMD −0.83 (CI −1.38 to −0.29), p<0.05 (favors acupuncture) • 3-month follow-up (versus CBT): SMD −0.16 (CI −0.68 to 0.36), p>0.05 (favors acupuncture) • 3-month follow-up (versus waitlist control): SMD −0.97 (CI −1.52 to −0.41), p<0.05 (favors acupuncture) **Depression symptoms:** Depression items on Hopkins Symptom Checklist-25: • Postintervention (versus CBT): SMD −0.16 (CI −0.68 to 0.36), p>0.05 (favors acupuncture) • Postintervention (versus waitlist control): SMD −0.88 (CI −1.43 to −0.33), p<0.05 (favors acupuncture) • 3-month follow-up (versus CBT): SMD −0.04 (CI −0.56 to 0.48), p>0.05 (favors acupuncture)

Study Details	Participants	Intervention/Treatment	Outcomes/Results
	current active treatment specifically for PTSD **Exclusion criteria:** In supportive therapy or taking medication for another psychiatric disorder if the current treatment stable for <3 months or anticipated to change during the study	minutes); needle insertion, manipulation, and retention (25–40 minutes); ear-seed placement (2 minutes). **Co-interventions:** None **Comparator:** Two comparators 1. Group CBT • Once a week for 2 hours over 12 weeks (24 hours). • Used 68-page CBT treatment manual integrating 4 modalities that have direct and theoretical evidence of efficacy. Sessions 1 through 3 use psychoeducation, behavioral activation, and activity planning. Sessions 4 to 10 teach participants classic cognitive restructuring and imagery rehearsal, utilizing material from daily life experiences. Sessions 10 to 12 have participants use classic exposure and desensitization techniques while being encouraged to practice earlier-session skills. • All sessions involve a standard approach of agenda setting, education, review of previous sessions and homework, troubleshooting of therapeutic goals and techniques, new technique training, and establishing commitment to engage in at least 15 minutes per day of homework. 2. Waitlist control • Waitlist participants were in contact with the study team only at the assessment periods unless an acute symptom required evaluation, and they were provided either a study treatment by the investigators or were given referrals for treatment at the end of their participation. **Primary endpoint:** PTSD symptoms at postintervention and 3-month follow-up **Longest follow-up:** 3 months postintervention **Power calculation:** Intended sample size not reached	• 3-month follow-up (versus waitlist control): SMD −0.90 (CI −1.45 to −0.35), p<0.05 (favors acupuncture) **Anxiety symptoms:** Anxiety items on Hopkins Symptom Checklist-25: • Postintervention (versus CBT): SMD −0.17 (CI −0.69 to 0.35), p>0.05 (favors acupuncture) • Postintervention (versus waitlist control): SMD −0.69 (CI −1.23 to −0.15), p<0.05 (favors acupuncture) • 3-month follow-up (versus CBT): SMD −0.25 (CI −0.77 to 0.27), p>0.05 (favors acupuncture) • 3-month follow-up (versus waitlist control): SMD −0.81 (CI −1.36 to −0.26), p<0.05 (favors acupuncture) **Adverse events:** One participant in the acupuncture group reported kidney pain

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: King et al., 2015 **References**: King, 2013; King et al., 2015; King, Moore, and Spence, 2015 **Country:** United States **Purpose:** Examine the feasibility and acceptability of an auricular acupuncture insomnia regimen among Operation Iraqi Freedom and Operation Enduring Freedom veterans with PSTD and sleep disturbance **Study design:** Individually randomized controlled trial **Recruitment:** Convenience sample in a 10-week residential PTSD treatment program for combat-related PTSD **Quality rating:** Poor Significant differential attrition/completion of sleep data; high attrition with no ITT analysis	**Number of patients:** 29 (15 acupuncture, 14 TAU) **Baseline PTSD:** Mean duration of PTSD: 5.4 (SD 5.1) years. Mean duration of PTSD treatment: 2.4 (SD 3.1) years. All in combat-related PTSD treatment. **Comorbid health conditions:** Mean duration of sleep problems: 4.8 (SD 3.5) years **Age (Years):** 33 (SD 7.2) **Gender:** 100% male **Inclusion criteria:** Operation Iraqi Freedom and Operation Enduring Freedom veterans, 18–50 years old, male, DSM-IV PTSD diagnosis, sleep disturbances (one or more of these self-reported symptoms: sleep onset latency >30 minutes, two or more awakenings per night, total sleep time less than 6 hours per night, or the presence of nightmares) **Exclusion criteria:** Significant comorbid conditions, history of moderate or severe traumatic brain injury, known sleep apnea history or other sleep disorder, scoring greater than 3 on the STOP-Bang (snoring, tiredness, observed breathing cessation, pressure related to the presence or treatment of high blood pressure, body mass index, age, neck circumference, and gender) questionnaire, essential tremors	**Acupuncture content:** Standardized auricular acupuncture insomnia acupoints were used: shen men, point zero, brain, thalamus point, pineal gland, master cerebral, insomnia points 1 and 2, kidney, heart, occiput, and forehead. Each acupoint was identified and the ear was cleaned with isopropyl alcohol. A clean insertion technique was used with stainless sterile steel acupuncture needles (0.20 mm diameter, 15 mm in length, D type needles, SEIRIN Corporation, Shizuoka, Japan). Auricular acupuncture treatments were performed on participants in the supine position in a quiet treatment room by the same privileged military acupuncture provider, who had 2 years of clinical experience (more than 500 treatments). **Health care setting:** Residential PTSD Treatment Facility **Number of sites:** 1 **Dosage:** Three 30-minute sessions per week for 3 weeks (4.5 hours) **Level of care:** Residential care **Co-interventions:** TAU (see below) **Comparator:** TAU: a 10-week, multi-modal residential PTSD treatment program for combat-related PTSD that included individual and group cognitive-processing therapy, educational classes, exercise programs, and community involvement. Additionally, all participants resided in berthing with two to four roommates and received 4 hours of psycho-educational sleep didactic in a group setting during the first 3 weeks of PTSD treatment. **Primary endpoint:** Sleep quality at postintervention **Power calculation:** No power calculation reported **Longest follow-up:** Postintervention	**PTSD symptoms:** PCL postintervention: SMD −0.32 (CI −1.05 to 0.42), p>0.05 (favors acupuncture) **Depression symptoms:** Patient Health Questionnaire postintervention: SMD 0.324 (CI −0.49 to 0.97), p>0.05 (favors comparator) **Sleep quality:** Pittsburgh Sleep Quality Index Global Score postintervention SMD −0.72 (CI −1.47 to 0.04), p>0.05 (favors acupuncture) **Adverse events:** One participant dropped out due to uncomfortable feelings while receiving the auricular acupuncture treatment. Five other adverse events occurred: one fall, two alcohol-related events, one wrist injury, and one incident of suicidal ideation. Four of the adverse events occurred in participants who had not yet received the auricular acupuncture treatments. One adverse event occurred in a participant who had received a treatment 3 days before the adverse event. All adverse events were reviewed by a Research Monitor and were deemed unrelated to the treatment. No adverse events directly related to the auricular acupuncture intervention were noted during the study period.

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Prisco et al., 2013 **References**: Prisco et al., 2013 **Country:** United States **Purpose:** Evaluate the feasibility of implementing a group auricular acupuncture intervention as an adjunct treatment for Operation Iraqi Freedom and Operation Enduring Freedom veterans who experience PTSD-related insomnia **Study design:** Individually randomized controlled trial **Recruitment:** Letters, study flyers, and websites were used. Veterans who met initial telephone screening requirements were asked to participate in the full screening process. **Quality rating:** Fair High attrition (30%); ITT analysis used but not described	**Number of patients:** 35 (12 acupuncture, 12 sham, 11 TAU) **Baseline PTSD:** PCL-Military: • Acupuncture: 55.1 (SD 11.4) • Sham: 57.8 (SD 10.3) • TAU: 60.5 (SD 14.4) PTSD symptom duration (years): • Acupuncture: 5.2 (SD 3.0) • Sham: 6.3 (SD 5.4) • TAU: 6.2 (SD 3.2) PTSD-related insomnia duration (years): • Acupuncture: 4.9 (SD 3.0) • Sham: 6.2 (SD 5.6) • TAU: 5.7 (SD 3.4) **Comorbid health conditions:** PTSD-related insomnia duration (years): • Acupuncture 4.9 (SD 3.0) • Sham 6.2 (SD 5.6) • TAU 5.7 (SD 3.4) **Age (Years):** Acupuncture 37.8 (SD 11.4); Sham: 37.9 (SD 10.3); TAU 37.6 (SD 8.0) **Gender:** 25 (71.4%) male **Inclusion criteria:** Combat veterans of the Operation Iraqi Freedom and Operation Enduring Freedom conflicts, diagnosed with PTSD (DSM-IV-TR), had insomnia (as indicated by 8+ on the Insomnia Severity Index), diagnosis of insomnia made after PTSD diagnosis, stable on psychotropic	**Acupuncture content:** Scripted group auricular acupuncture performed in accordance with the established principles and practices of the National Certification Commission for Acupuncture and Oriental Medicine. Using a TCM map as a guide, the true acupuncture intervention used five specific auricular acupuncture points that are thought to help promote sleep: shen men, kidney (KI, under flap), sympathetic (under flap), liver (LR), and hippocampus. The needles were DBC Brand Spring Handle Needles, size 0.16·15 mm. Needle depth depended on the auricle thickness of each participant; needles were inserted until they reached the ear cartilage and to the depth that the needle could stand by itself. No De Qi response was sought during needle insertion, and needles were inserted straight in with no needle manipulation. No guide tubes were used. No additional needling techniques were used after needle insertion. Needles were replaced if they fell out immediately after insertion but were not replaced if they fell out during the remaining treatment time The acupuncturist encouraged all participants at the outset to engage in a state of mindfulness by noting their level of awareness of the surrounding environment and any feelings they might be experiencing; calming background music was played to enhance this milieu. At the end of sessions, participants were encouraged to take a moment to reflect on their acupuncture experiences and recall these experiences when needed. Verbal communication between the participants was kept to a minimum to minimize the potential influence of group dynamics on study outcomes. Performed by a physician with advanced training in auricular acupuncture. A second senior-licensed acupuncturist with more than 20 years of acupuncture experience provided consultative expertise on the development of the protocol and served as the backup acupuncturist. **Health care setting:** VA Medical Center **Number of sites:** 1 **Dosage:** Two 45-minute sessions per week for 8 weeks (12 hours)	**Sleep quality:** Insomnia Severity Index • Postintervention (versus sham): SMD −0.17 (CI −0.97 to 0.63), p>0.05 (favors acupuncture) • Postintervention (versus TAU): SMD −0.52 (CI −1.36 to 0.31), p>0.05 (favors acupuncture) **Adverse events:** One participant in the sham group dropped out because the acupuncture needles were uncomfortable

Study Details	Participants	Intervention/Treatment	Outcomes/Results
	medications for 1 month prior to enrollment in study **Exclusion criteria:** Did not speak English, not competent to sign informed consent, history of moderate or severe TBI, starts use of continuous positive airway pressure or bilevel positive airway pressure during study, severe psychiatric illness (defined as suicidal ideation, homicidal ideation, or psychosis), history of substance dependence (DSM-IV-TR) during the 1 year preceding enrollment in the study, history of illicit substance use for 3 months prior to study enrollment, positive AUDIT-C score (5+) at or during course of study enrollment, received acupuncture during past 3 months, taking Coumadin/heparin/Lovenox, pregnant	**Level of care:** Outpatient **Co-interventions:** Conventional care for PTSD-related insomnia (see TAU below) **Comparator:** Two comparators 1. Sham acupuncture • Structured identically as true auricular acupuncture (except that five nonacupuncture points were used) to control for potential intervention effects • Nonacupuncture points were located on the helix of the ear and selected in consultation with the study acupuncturists and on acupuncture interventions for insomnia 2. TAU • "Conventional care" • Referral to trauma services department • Group and/or individual psychotherapy based on CBT • Evaluation and follow-up by psychiatry if indicated • Psychopharmacology if indicated **Primary endpoint:** Sleep quality (insomnia) **Power calculation:** Intended sample size not reached **Longest follow-up:** Postintervention	

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Wang et al., 2012 **References**: Wang et al., 2012 **Country:** China **Purpose:** To assess the efficacy and safety of electroacupuncture in patients with earthquake-caused PTSD **Study design:** Individually randomized controlled trial **Recruitment:** Initially screened by telephone, with full assessments conducted only for participants who did not report any exclusion criteria during screening **Quality rating:** Fair Downgraded because ITT analysis was not clear, though low attrition (9%)	**Number of patients:** 138 (69 acupuncture, 69 paroxetine) **Baseline PTSD:** CAPS • Acupuncture 65.8 (SD 19.7) • Paroxetine 66.8 (SD 21.3) No combat-related PTSD (all earthquake-caused PTSD) **Comorbid health conditions:** Hamilton Depression Scale: • Acupuncture 13.1 (SD 5.56) • Paroxetine: 12.7 (SD 5.2) Hamilton Anxiety Scale: • Acupuncture 11.6 (SD 5.11) • Paroxetine 11.7 (SD 5.85) **Age (Years):** Acupuncture 48.3 (SD 13.3); Paroxetine 50.3 (SD12.3**)** **Gender:** 54 (39.1%) male **Inclusion criteria:** PTSD diagnosis (DSM-IV-TR), Wenchuan earthquake–caused masses, relief officers and volunteers, ages 18 to 65 years, signed informed consent (participant or immediate family member), have clear consciousness, able to participate in the examination and treatment **Exclusion criteria:** Severe heart, liver, or kidney disorders; have suffered from depression or other mental disorders; “mentally retarded patients”; taking anti-anxiety or	**Acupuncture content:** Electroacupuncture on the scalp: Baihui (GV 20), Sishencong (EX-HN 1), Shenting (GV 24), and Fengchi (GB 20), selected by the introduction of Nomenclature and Location of Acupuncture Points (GB/T12346–006). Sishencong is a group of four points that are located on the vertex of the head, each 1 cun (about the length of the thumb at the knuckle) away from Baihui (GV 20) at four directions (anterior, bilateral, and posterior). Baihui is located on the head, 5 cun directly above the anterior hairline, and 7 cun directly above the posterior hairline. Shenting is located on the head, 0.5 cun directly above the midpoint of the anterior hairline. Fengchi is located in the neck, below the occipital bone, 1 cun above the posterior hairline. Skin at acupoints was routinely disinfected using 75% ethanol. Disposable needles (0.30 × 40 mm, Helio Medical Supplies, Inc., Suzhou, China) were obliquely needled into the point of galea capitis along the scalp up to a 15–30 degree angle. Fengchi was obliquely needled using 1.5-in. stainless steel needles; the direction of the needle tip was microdown on the tip of the nose about 0.5–1.2 in. The direction of the needle tip was forward at Shenting, anterior Shencong, and Baihui. The directions of the needle tip at left-sided, right-sided, and posterior Shencong was toward the Baihui point, and the deeps of needle were about 0.5–1 in. These points were divided into two groups: One group included the points of Shenting, Baihui, left-sided, and right-sided Shencong, and the other group included the points of anterior Shencong, posterior Shencong, left-sided, and right-sided Fengchi. The needles in these two groups were connected with G6805-II electroacupuncture device (Xinsheng Industrial Corporation LTD., Qingdao, China). Prior to the treatment, a 50-hour test was run to assess consistency and calibration of the device in measuring known resistors and capacitors. The needles in the points of shenting, baihui, anterior shencong, and posterior Shencong were connected with positive electrodes, and the needles in the points of left-sided Shencong, right-sided Shencong, left-sided Fengchi, and right-sided Fengchi were connected with negative electrodes, respectively. The two groups were treated with a continuous wave of 100 Hz, and the strength	**PTSD symptoms:** CAPS: • Postintervention: SMD −0.21 (CI −0.55 to 0.12), p>0.05 (favors acupuncture) • 3-month follow-up: SMD −0.33 (CI −0.67 to 0.00), p=.05 (favors acupuncture) • 6-month follow-up: SMD −0.35 (CI −0.69 to −0.02), p<0.05 (favors acupuncture) **Depression symptoms:** Hamilton Depression Scale: • Postintervention: SMD −0.23 (CI −0.56 to 0.11), p>0.05 (favors acupuncture) • 3-month follow-up: SMD −0.35 (CI −0.69 to −0.02), p<0.05 (favors acupuncture) • 6-month follow-up: SMD −0.38 (CI −0.72 to −0.04), p<0.05 (favors acupuncture) **Anxiety symptoms:** Hamilton Anxiety Scale: • Postintervention: SMD −0.28 (CI −0.62 to 0.05), p>0.05 (favors acupuncture) • 3-month follow-up: SMD −0.40 (CI −0.74 to −0.06), p<0.05 (favors acupuncture) • 6-month follow-up: SMD −0.30 (CI −0.64 to 0.03), p>0.05 (favors acupuncture) **Adverse events:** Several reported: • One acupuncture participant refused to continue for being afraid of pain. • One paroxetine participant had symptoms of giddiness. • One paroxetine participant had symptoms of constipation. • One paroxetine participant had symptoms of blurred vision.

Study Details	Participants	Intervention/Treatment	Outcomes/Results
	antidepressant drugs; pregnant or lactating women	of stimulation was tested by the tolerance of patients each time every group. Participants were sitting with backs against the wall and the body fixed. **Health care setting:** TCM and psychiatric hospitals **Number of sites:** 3 **Dosage:** Three or four 30-minute sessions per week for 12 weeks (21 hours) **Level of care:** Inpatient **Co-interventions:** None reported **Comparator:** Active (paroxetine) • simple oral administration of paroxetine (Zhejiang Huahai pharmaceutical Co., LTD, Linhai, Zhejiang, China) • 20 mg every night • six-week treatment cycle, with two consecutive treatments (12 weeks) **Primary endpoint:** PTSD symptoms (follow-up unclear) **Power calculation:** No power calculation reported **Longest follow-up:** 6 months postintervention	• For acupuncture patients with adverse events on behavior, autonomic nerve, cardiovascular system, and so forth, the most frequent side effects reported by the patients were minor needle pain (24 patients, 39.3%), minor superficial bleeding (27 patients, 44.3%), and minor hematoma (9 patients, 14.8%), which were experienced during acupuncture. Only one case of moderate pain (1.64%) was reported in 61 adverse events. • For paroxetine participants with adverse events on behavior, autonomic nerve, cardiovascular system, and so forth, side effects reported were excitement or agitation (4 patients, 2.16%), depression (3 patients, 1.62%), activity increased (2 patients, 1.08%), activity declined (6 patients, 3.24%), insomnia (28 patients, 15.1%), and fatigue (7 patients, 3.78%). • For paroxetine participants with adverse events on autonomic nerve, events mainly included xerophthalmia (36 patients, 3.78%), stuffy nose (1 patients, 0.54%), blurred vision (3 patients, 1.62%), constipation (17 patients, 9.19%), saliva increase (8 patients, 4.32%), sweat (11 patients, 5.95%), nausea and vomiting (11 patients, 5.95%), and diarrhea (6 patients, 3.24%). • For paroxetine participants with adverse events on cardiovascular system, events were mainly dizziness (5 patients, 2.70%), tachycardia (3 patients, 2.62%), and skin allergy symptom (1 patients, 0.54%). • For paroxetine participants with other adverse events, events included appetite loss/anorexia (21 patients, 11.4%) and headache (11 patients, 5.95%).

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Zhang, Ran, et al., 2010a **References**: Zhang, Ran, et al., 2010a **Country:** China **Purpose:** To discuss the therapeutic effects of acupuncture and moxibustion in treating PTSD **Study design:** Individually randomized controlled trial **Recruitment:** Not reported **Quality rating:** Poor All risk of bias items unclear, with no indication of ITT analysis	**Number of patients:** 92 (46 acupuncture, 46 paroxetine) **Baseline PTSD:** PTSD related to the Wenchuan earthquake. Patients had PTSD for a duration of at least 3 months prior to the study. **Comorbid health conditions:** Not reported **Age (Years):** 18–65 **Gender:** 32 (35%) male **Inclusion criteria:** Affected by the Wenchuan earthquake, volunteered to participate in the study, ages 18–65, diagnosed with PTSD using DSM-IV criteria **Exclusion criteria:** Serious heart, liver, kidney diseases; pregnant and breast feeding women; allergic to drugs; suffering from depression or other mental disease	**Acupuncture content:** Electroacupuncture with moxibustion applied to acupoints: Shenyu, Mingmen, Zhishi. Additional acupoints without moxibustion included Shenting, 4 Shencong points, Baihui, and Fengchi. Patients sat on an inclined seat. Their skin was first treated with 75% ethanol for disinfection, and then the needles were introduced to the subgaleal, under an angle of 15–30 degrees. A stainless steel filiform needle of 1.5 cun (about 1.97 in.) was used for the Fengchi acupoint. The needle entered the skin under angle for a depth of 0.5 to 1.2 cun (0.66 to 1.57 in.). The needles were introduced toward the front for the Shenting, front Shencong, and Baihui points. For the left, right, and back Shencong points, the needle was introduced toward the Baihui point for a depth of 0.5 to 1 cun (0.66 to 1.31 in.). Then, needles were connected to the G6805-II electroacupuncture device that uses a continuous wave with frequency of 300–500 Hz per min. The intensity of electrical stimulation was adjusted to the individual tolerance of the patient. The treatment was separated in two groups of acupoints. In the first group, treatment was applied to Shenting, Baihui, and right and left Shencong. In the second group, treatment was applied to the front and back Shencong and left and right Fengchi points. Groups were treated alternately by day. Shengting was connected to the positive electrode, the left Shencong to the negative; Baihui to the positive, right Shencong to the negative; front Shencong to the positive, left Fengchi to the negative; and back Shencong to the positive, right Fengchi to the negative. The electrical stimulation was applied for 30 minutes once a day, 3 times a week every other day, for a continuous trial of 6 weeks, with a total of 18 treatments. **Health care setting:** Not reported **Number of sites:** Not reported **Dosage:** Three 30-minute sessions per week for 12 weeks (18 hours)	**PTSD symptoms:** CAPS severity score at postintervention: SMD −2.14 (CI −2.66 to −1.63), p<0.05 (favors acupuncture) **Depression symptoms:** Hamilton Depression Scale at postintervention: SMD −1.43 (CI −1.89 to −0.97), p<0.05 (favors acupuncture) **Anxiety symptoms:** Hamilton Anxiety Scale at postintervention: SMD −2.07 (CI −2.58 to −1.56), p<0.05 (favors acupuncture) **Adverse events:** Adverse events were monitored and none were reported

Study Details	Participants	Intervention/Treatment	Outcomes/Results
		Level of care: Not reported **Co-interventions:** None reported **Comparator:** Active: paroxetine group (20 mg of paroxetine administered every evening for 12 weeks) **Primary endpoint:** PTSD symptoms at postintervention **Power calculation:** None reported **Longest follow-up:** Postintervention	

Study Details	Participants	Intervention/Treatment	Outcomes/Results
Parent study: Zhang, Yuan, et al., 2010b **References**: Zhang, Yuan, et al., 2010b **Country:** China **Purpose:** To study the effectiveness and safety of different acupuncture therapies in treating PTSD after the Wenchuan earthquake **Study design:** Individually randomized controlled trial **Recruitment:** Convenience sample of patients from Jiangyou, Dujiangyan, and Mianyang diagnosed with PTSD from September 2008 to December 2009. **Quality rating:** Fair Downgraded because ITT analysis was unclear, though low risk of attrition bias	**Number of patients:** 276 (69 electroacupuncture, 69 electroacupuncture + moxibustion, 69 electroacupuncture + auricular acupuncture, 69 paroxetine) **Baseline PTSD:** Patients were diagnosed with PTSD using DSM-IV criteria, as a result of Wenchuan earthquake. Patients had PTSD for a duration of at least 3 months prior to the study. **Comorbid health conditions:** Not reported **Age (Years):** 18–65 **Gender:** Not reported **Inclusion criteria:** Affected by the Wenchuan earthquake, volunteered to participate in the study, ages 18–65, diagnosed with PTSD using DSM-IV criteria **Exclusion criteria:** Had an acupuncture treatment within the past 3 months; diagnosed with depression and other mental disease; hereditary mental disease and/or severe heart, liver, or kidney disease; severe physical trauma or mental retardation; currently taking (or took within the past 3 months) psychotropic drugs and/or anxiolytic and antidepressant drugs; pregnant or breast-feeding	**Acupuncture content:** Three acupuncture groups 1. Electroacupuncture. Acupoints used: Shenting, 4 Shencong points, Baihui and Fengchi. Patients sat on a inclined seat. Their skin was first treated with 75% ethanol for disinfection, and the needle was introduced to the subgaleal under an angle of 15–30 degrees. A stainless steel filiform needle of 1.5 cun (about 1.97 in.) was used for the Fengchi acupoint. The needle entered the skin under angle for a depth of 0.5 to 1.2 cun (0.66 to 1.57 in.). The needles were introduced toward the front for the Shenting, front Shencong, and Baihui points. For the left, right, and back Shencong points, the needles were introduced toward the Baihui point for a depth of 0.5 to 1 cun (0.66 to 1.31 in.). Then, needles were connected to the G6805-II electroacupuncture device that used a continuous wave with frequency of 100 Hz. Intensity of electrical stimulation was adjusted to the individual tolerance of the patient. The treatment was separated in two groups of acupoints. In the first group, treatment was applied to Shenting, Baihui, and right and left Shencong. In the second group, treatment was applied to the front and back Shencong and left and right Fengchi points. Groups were treated alternately by day. Shengting was connected to the positive electrode, the left Shencong to the negative; Baihui to the positive, right Shencong to the negative; front Shencong to the positive, left Fengchi to the negative; and back Shencong to the positive, right Fengchi to the negative. The electrical stimulation was applied for 30 minutes once a day, 3 times a week every other day, for a continuous trial of 12 weeks, with a total of 36 treatments. 2. Electroacupuncture + moxibustion. Electroacupuncture was the same as above. Moxibustion was simultaneously applied to acupoints Shenyu, Mingmen, and Zhishi. Patients were lying face down with needles connected to the electrical acupuncture device. In addition, two pieces of moxa of 2 cm each were placed side by side in an moxibustion box. The box was placed horizontally on the lumbar region of the back for about 20 minutes. The treatment was applied 3 times a week, alternating by day, for a continuous period of 12 weeks.	**PTSD symptoms:** CAPS: • Electroacupuncture versus paroxetine postintervention: SMD −0.21 (CI −0.54 to 0.13), p>0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine postintervention: SMD −0.08 (CI −0.41 to 0.25), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine postintervention: SMD −0.10 (CI −0.43 to 0.24), p>0.05 (favors acupuncture) • Electroacupuncture versus paroxetine 3-month follow-up: SMD −0.33 (CI −0.67 to 0.00), p<0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine 3-month follow-up: SMD −0.31 (CI −0.65 to 0.02), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine 3-month follow-up: SMD −0.31 (CI −0.65 to 0.02), p>0.05 (favors acupuncture) • Electroacupuncture versus paroxetine 6-month follow-up: SMD −0.35 (CI −0.69 to −0.02), p<0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine 6-month follow-up: SMD −0.34 (CI −0.68 to −0.01), p<0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine 6-month follow-up: SMD −0.30 (CI −0.64 to 0.03), p>0.05 (favors acupuncture) **Depression symptoms:** Hamilton Depression Scale: • Electroacupuncture versus paroxetine postintervention: SMD −0.34 (CI −0.67 to 0.00, p<0.05 (favors acupuncture)

Study Details	Participants	Intervention/Treatment	Outcomes/Results
		3. Electroacupuncture + auricular acupuncture. Electroacupuncture was the same as above. Simultaneously, treatment was applied to Pizhixia, Shenmen, Jiaogan, Xin, Gan, and Shen acupoints. The patient was sitting on a chair. After the routine disinfection, the auricular acupuncture points were stimulated by using auricular seed pressing therapy for 1–2 minutes. Treatments alternated one ear at a time, with 3 treatments a week for a continuous period of 12 weeks. **Health care setting:** Not reported **Number of sites:** Not reported **Dosage:** Three 30-minute sessions per week for 12 weeks (18 hours) **Level of care:** Not reported **Co-interventions:** None reported **Comparator:** Active: paroxetine group (20 mg paroxetine administered every evening for 12 weeks) **Primary endpoint:** PTSD symptoms at 3 and 6 months postintervention **Power calculation:** Intended sample size was reached **Longest follow-up:** 6 months postintervention	• Electroacupuncture + moxa versus paroxetine postintervention: SMD −0.15 (CI −0.48 to 0.19), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine postintervention: SMD −0.31 (CI −0.65 to 0.03), p>0.05 (favors acupuncture) • Electroacupuncture versus paroxetine 3-month follow-up: SMD −0.44 (CI −0.77 to −0.10), p<0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine 3-month follow-up: SMD −0.11 (CI −0.45 to 0.22), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine 3-month follow-up: SMD −0.29 (CI −0.63 to 0.04), p>0.05 (favors acupuncture) • Electroacupuncture versus paroxetine 6-month follow-up: SMD −0.64 (CI −0.98 to −0.30), p<0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine 6-month follow-up: SMD −0.26 (CI −0.60 to 0.07), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine 6-month follow-up: SMD −0.37 (CI −0.71 to −0.03), p<0.05 (favors acupuncture) **Anxiety symptoms:** Hamilton Anxiety Scale: • Electroacupuncture versus paroxetine postintervention: SMD −0.28 (CI −0.62 to 0.05, p>0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine postintervention: SMD −0.40 (CI −0.74 to −0.06), p<0.05 (favors acupuncture) • Electroacupuncture + auricular versus

Study Details	Participants	Intervention/Treatment	Outcomes/Results
			paroxetine postintervention: SMD −0.30 (CI −0.64 to 0.03), p>0.05 (favors acupuncture) • Electroacupuncture versus paroxetine 3-month follow-up: SMD −0.09 (CI −0.42 to 0.25), p>0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine 3-month follow-up: SMD −0.24 (CI −0.58 to 0.09), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine 3-month follow-up: SMD −0.20 (CI −0.53 to 0.14), p>0.05 (favors acupuncture) • Electroacupuncture versus paroxetine 6-month follow-up: SMD −0.11 (CI −0.45 to 0.22), p>0.05 (favors acupuncture) • Electroacupuncture + moxa versus paroxetine 6-month follow-up: SMD −0.24 (CI −0.58 to 0.09), p>0.05 (favors acupuncture) • Electroacupuncture + auricular versus paroxetine 6-month follow-up: SMD −0.10 (CI −0.44 to 0.23), p>0.05 (favors acupuncture) **Adverse events:** Some patients (number not reported) mentioned roughness of operational practices, fear of needles, bleeding, hematoma, pain, and fainting. No serious adverse events were reported.

Appendix F: Sensitivity Analyses

Table F.1. Sensitivity Analyses: Any Acupuncture Versus Any Comparator (PTSD Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.80; CI −1.59 to −0.01; I^2 90%; 6 RCTs; large clinical effect in favor of acupuncture
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.50; CI −1.01 to 0.01; I^2 64%; 5 RCTs; n.s.
Utilizing group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.70; CI −1.51 to 0.11; I^2 90%; n.s.
Utilizing electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.78; CI −1.59 to 0.03; I^2 91%; n.s.
Utilizing electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.78; CI −1.59 to 0.03; I^2 91%; n.s.
Excluding the three studies on the Wenchuan earthquake (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)	SMD −0.83; CI −1.70 to 0.04; I^2 7%; n.s.

Table F.2. Sensitivity Analyses: Any Acupuncture Versus Any Comparator (PTSD Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.46; CI −0.85 to −0.06; I^2 30%; 4 RCTs; medium clinical effect in favor of acupuncture
3-month follow-up data from Wang et al. (2012) rather than 6-month follow-up data	SMD −0.47; CI −0.90 to −0.04; I^2 32%; medium clinical effect in favor of acupuncture
1-month follow-up data from Engel et al. (2014) rather than 2-month follow-up data	SMD −0.62; CI −1.23 to −0.01; I^2 63%; medium clinical effect in favor of acupuncture
CAPS 2-month follow-up data from Engel et al. (2014) rather than PCL 2-month follow-up data	SMD −0.53; CI −0.99 to −0.07; I^2 40%; medium clinical effect in favor of acupuncture
Group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.33; CI −0.52 to −0.14; I^2 0%; small clinical effect in favor of acupuncture
3-month follow-up data from Zhang, Yuan, et al. (2010b) rather than 6-month follow-up data	SMD −0.47; CI −0.90 to −0.04; I^2 32%; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up SMD −0.47; CI −0.91 to −0.03; I^2 34%; small clinical effect in favor of acupuncture 6-month follow-up SMD −0.47; CI −0.90 to −0.04; I^2 31%; small clinical effect in favor of acupuncture
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up SMD −0.47; CI −0.91 to −0.03; I^2 34%; small clinical effect in favor of acupuncture 6-month follow-up SMD −0.46; CI −0.91 to −0.01; I^2 36%; small clinical effect in favor of acupuncture
Excluding the three studies on the Wenchuan earthquake (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)	SMD −0.72; CI −4.02 to 2.58; I^2 43%; n.s.

Table F.3. Sensitivity Analyses: Any Acupuncture Versus Any Comparator (Depression Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.58; CI −1.18 to 0.01; I^2 81%; 6 RCTs; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.41; CI −0.89 to 0.07; I^2 54%; 5 RCTs; n.s.
Utilizing group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.47; CI −1.06 to 0.12; I^2 80%; n.s.
Utilizing electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.55; CI −1.17 to 0.07; I^2 83%; n.s.
Utilizing electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.58; CI −1.18 to 0.02; I^2 81%; n.s.
Excluding the three studies on the Wenchuan earthquake (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, 2010b)	SMD −0.51; CI −2.00 to 0.98; I^2 72%; n.s.

Table F.4. Sensitivity Analyses: Any Acupuncture Versus Any Comparator (Depression Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.56; CI −0.88 to −0.23; I^2 0%; 4 RCTs; medium clinical effect in favor of acupuncture
3-month follow-up data from Wang et al. (2012) rather than 6-month follow-up data	SMD −0.55; CI −0.90 to −0.20; I^2 0%; medium clinical effect in favor of acupuncture
1-month follow-up data from Engel et al. (2014) rather than 2-month follow-up data	SMD −0.59; CI −0.92 to −0.26; I^2 0%; medium clinical effect in favor of acupuncture
Group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.42; CI −0.79 to −0.05; I^2 18%; small clinical effect in favor of acupuncture
3-month follow-up data from Zhang, Yuan, et al. (2010b) rather than 6-month follow-up data	SMD −0.48; CI −0.79 to −0.17; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b) at 6-month follow-up	SMD −0.43; CI −0.82 to −0.04; I^2 22%; small clinical effect in favor of acupuncture
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.44; CI −0.81 to −0.07; I^2 15%; small clinical effect in favor of acupuncture 6-month follow-up: SMD −0.46; CI −0.79 to −0.13; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b) at 3-month follow-up	SMD −0.41; CI −0.91 to 0.09; I^2= 49%; n.s.
Excluding the three studies on the Wenchuan earthquake (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)	SMD −0.67; CI −3.47 to 2.12; I^2 22%; n.s.

Table F.5. Sensitivity Analyses: Any Acupuncture Versus Any Comparator (Anxiety Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.82; CI −2.16 to 0.53; I^2 92%; 4 RCTs; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.72; CI −2.04 to 0.60; I^2 92%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.69; CI −2.05 to 0.67; I^2 93%; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.26; CI −0.79 to 0.27; I^2 0%; 3 RCTs; n.s.
Group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.69; CI −2.13 to 0.75; I^2 93%; n.s.
Excluding the three studies on the Wenchuan earthquake (Wang et al., 2012; Zhang, Ran, et al., 2010a; Zhang, Yuan, et al., 2010b)	SMD −0.69; CI −1.23 to −0.15; One RCT; medium clinical effect in favor of acupuncture

Table F.6. Sensitivity Analyses: Any Acupuncture Versus Any Comparator (Anxiety Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.35; CI −1.17 to 0.47; I^2 56%; 3 RCTs; n.s.
3-month follow-up data from Wang et al. (2012) rather than 6-month follow-up data	SMD −0.39; CI −1.21 to 0.43; I^2 58%; n.s.
Group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.22; CI −0.49 to 0.05; I^2 0%; n.s.
3-month follow-up data from Zhang, Yuan, et al. (2010b) rather than 6-month follow-up data	SMD −0.34; CI −1.19 to 0.51; I^2 59%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.38; CI −1.05 to 0.29; I^2= 37%; n.s. 6-month follow-up: SMD −0.38; CI −1.05 to 0.29; I^2= 37%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.37; CI −1.09 to 0.35; I^2 44%; n.s. 6-month follow-up: SMD −0.35; CI −1.19 to 0.49; I^2 57%; n.s.
Excluding the three studies on the Wenchuan earthquake (Wang et al., 2012; Zhang, Ran, et al. 2010a; Zhang, Yuan, et al., 2010b)	SMD −0.81; CI −1.36 to −0.26; 1 RCT; large clinical effect in favor of acupuncture

Table F.7. Sensitivity Analyses: TCM Acupuncture Versus Any Comparator (PTSD Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.89; CI −1.88 to 0.10; I^2 92%; 5 RCTs; n.s.
Group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.77; CI −1.80 to 0.26; I^2 92%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.86; CI −1.88 to 0.16; I^2= 92%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.86; CI −1.88 to 0.16; I^2 92%; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.54; CI −1.25 to 0.17; I^2 73%; 4 RCTs; n.s.

Table F.8. Sensitivity Analyses: TCM Acupuncture Versus Any Comparator (Depression Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.71; CI −1.31 to −0.10; I^2 81%; 5 RCTs; medium clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.67; CI −1.33 to −0.01; I^2= 84%; medium clinical effect in favor of acupuncture
Electroacupuncture plus auricular stimulation	SMD −0.70; CI −1.31 to −0.09; I^2 81%; medium clinical effect in favor of acupuncture
Group CBT as the comparator in Hollifield et al. (2007) rather than a waitlist control	SMD −0.57; CI −1.22 to 0.08; I^2 82%; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.48; CI −0.97 to 0.01; I^2 47%; 4 RCTs; n.s.

Table F.9. Sensitivity Analyses: Acupuncture (as Monotherapy) Versus Any Comparator (PTSD Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.85; CI −2.29 to 0.59; I^2 93%; 4 RCTs; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.38; CI −1.31 to 0.55; I^2 62%; 3 RCTs; n.s.
Group CBT as the comparator for Hollifield et al. (2007)	SMD −0.71; CI −2.20 to 0.78; I^2 93%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.82; CI −2.32 to 0.68; I^2 94%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.82; CI −2.31 to 0.67; I^2 94%; n.s.

Table F.10. Sensitivity Analyses: Acupuncture (as Monotherapy) Versus Any Comparator (PTSD Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.50; CI −1.32 to 0.32; I^2 53%; 3 RCTs; n.s.
Group CBT as the comparator for Hollifield et al., 2007	SMD −0.31; CI −0.60 to −0.02; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture data at 3-month follow-up (rather than 6-month follow-up) for Zhang, Yuan, et al. (2010b)	SMD −0.49; CI −1.32 to 0.34; I^2 55%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.49; CI −1.34 to 0.36; I^2 56%; n.s. 6-month follow-up: SMD −0.50; CI −1.33 to 0.33; I^2 54%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.49; CI −1.34 to 0.36; I^2 56%; n.s. 6-month follow-up: SMD −0.48; CI −1.34 to 0.38; I^2 57%; n.s.

Table F.11. Sensitivity Analyses: Acupuncture (as Monotherapy) Versus Any Comparator (Depression Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.70; CI −1.58 to 0.18; I^2 85%; 4 RCTs; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.42; CI −1.19 to 0.35; I^2 50%; 3 RCTs; n.s.
Results did not substantially differ when using group CBT as the comparator for Hollifield et al. (2007)	SMD −0.53; CI −1.47 to 0.41; I^2 86%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.65; CI −1.61 to 0.31; I^2 88%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.69; CI −1.58 to 0.20; I^2 86%; n.s.

Table F.12. Sensitivity Analyses: Acupuncture (as Monotherapy) Versus Any Comparator (Depression Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.58; CI −1.17 to 0.01; I^2 27%; 3 RCTs; n.s.
Group CBT as the comparator for Hollifield et al. (2007)	SMD −0.40; CI −1.10 to 0.30; I^2 45%; n.s.
3-month follow-up (rather than 6-month follow-up) data for Wang et al. (2012)	SMD −0.58; CI −1.22 to 0.06; I^2 36%; n.s.
Electroacupuncture data at 3-month follow-up (rather than 6-month follow-up) for Zhang, Yuan, et al. (2010b)	SMD −0.50; CI −1.09 to 0.09; I^2 24%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.41; CI −1.35 to 0.53; I^2 65%; n.s. 6-month follow-up: SMD −0.45; CI −1.11 to 0.21; I^2 48%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.46; CI −1.18 to 0.26; I^2 43%; n.s. 6-month follow-up: SMD −0.48; CI −1.12 to 0.16; I^2 32%; n.s.

Table F.13. Sensitivity Analyses: Any Acupuncture Versus Active Comparator (PTSD Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.71; CI −2.20 to 0.78; I^2 93%; 4 RCTs; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.23; CI −0.37 to −0.09; I^2 0%; 3 RCTs; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.68; CI −2.21 to 0.85; I^2 94%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.68; CI −2.21 to 0.85; I^2 94%; n.s.

Table F.14. Sensitivity Analyses: Any Acupuncture Versus Active Comparator (PTSD Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.31; CI −0.59 to −0.02; I^2 0%; 3 RCTs; small clinical effect in favor of acupuncture
3-month follow-up (rather than 6-month follow-up) for Wang et al. (2012)	SMD −0.30; CI −0.58 to −0.02; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture data at 3-month follow-up (rather than 6-month follow-up) for Zhang, Yuan, et al. (2010b)	SMD −0.30; CI −0.58 to −0.02; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.29; CI −0.56 to −0.02; I^2 0%; small clinical effect in favor of acupuncture 6-month follow-up: SMD −0.31; CI −0.59 to −0.03; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.29; CI −0.56 to −0.02; I^2 0%; small clinical effect in favor of acupuncture 6-month follow-up: SMD −0.29; CI −0.56 to −0.02; I^2 0%; small clinical effect in favor of acupuncture

Table F.15. Sensitivity Analyses: Any Acupuncture Versus Active Comparator (Depression Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.53; CI −1.47 to 0.41; I^2 86%; 4 RCTs; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.26; CI −0.47 to −0.05; I^2 0%; 3 RCTs; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.48; CI −1.46 to 0.50; I^2 87%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.52; CI −1.46 to 0.42; I^2 86%; n.s.

Table F.16. Sensitivity Analyses: Any Acupuncture Versus Active Comparator (Depression Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.40; CI −1.10 to 0.30; I^2 45%; 3 RCTs; n.s.
3-month follow-up (rather than 6-month follow-up) for Wang et al. (2012)	SMD −0.39; CI −1.09 to 0.31; I^2 47%; n.s.
Electroacupuncture data at 3-month follow-up (rather than 6-month follow-up) for Zhang, Yuan, et al. (2010b)	SMD −0.34; CI −0.77 to 0.09; I^2 0%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.21; CI −0.65 to 0.23; I^2 0%; n.s. 6-month follow-up: SMD −0.27; CI −0.63 to 0.09; I^2 0%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.28; CI −0.64 to 0.07; I^2 0%; n.s. 6-month follow-up: SMD −0.32; CI −0.71 to 0.07; I^2 0%; n.s.

Table F.17. Sensitivity Analyses: Any Acupuncture Versus Active Comparator (Anxiety Symptoms, Postintervention)

Sensitivity Analysis	Result
Reference case	SMD −0.69; CI −2.13 to 0.75; I^2 93%; 4 RCTs; n.s.
Removing the poor quality study (Zhang, Ran, et al., 2010a) with the outlying positive effect in favor of acupuncture	SMD −0.26; CI −0.39 to −0.13; I^2 0%; 3 RCTs; small clinical effect in favor of acupuncture
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.72; CI −2.13 to 0.69; I^2 92%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	SMD −0.69; CI −2.12 to 0.74; I^2 93%; n.s.

Table F.18. Sensitivity Analyses: Any Acupuncture Versus Active Comparator (Anxiety Symptoms, Follow-Up)

Sensitivity Analysis	Result
Reference case	SMD −0.22; CI −0.49 to 0.05; I^2 0%; 3 RCTs; n.s.
3-month follow-up (rather than 6-month follow-up) for Wang et al. (2012)	SMD −0.26; CI −0.66 to 0.14; I^2 0%; n.s.
Electroacupuncture data at 3-month follow-up (rather than 6-month follow-up) for Zhang, Yuan, et al. (2010b)	SMD −0.20; CI −0.50 to 0.10; I^2 0%; n.s.
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b) at 6-month follow-up	SMD −0.21; CI −0.49 to 0.07; I^2 0%; n.s.
Electroacupuncture plus moxibustion (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b)	3-month follow-up: SMD −0.27; CI −0.36 to −0.18; I^2 0%; small clinical effect in favor of acupuncture 6-month follow-up: SMD −0.27; CI −0.36 to −0.18; I^2 0%; small clinical effect in favor of acupuncture
Electroacupuncture plus auricular stimulation (rather than electroacupuncture alone) as the acupuncture intervention in Zhang, Yuan, et al. (2010b) at 3-month follow-up	SMD −0.25; CI −0.39 to −0.11; I^2 0%; small clinical effect in favor of acupuncture

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