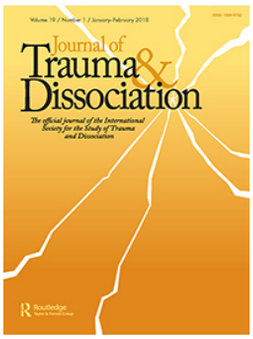

Routledge
Taylor & Francis Group

Journal of Trauma & Dissociation

ISSN: 1529-9732 (Print) 1529-9740 (Online) Journal homepage: https://www.tandfonline.com/loi/wjtd20

Acupuncture for the Treatment of Adults with Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis

Sean Grant, Benjamin Colaiaco, Aneesa Motala, Roberta Shanman, Melony Sorbero & Susanne Hempel

To cite this article: Sean Grant, Benjamin Colaiaco, Aneesa Motala, Roberta Shanman, Melony Sorbero & Susanne Hempel (2018) Acupuncture for the Treatment of Adults with Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis, Journal of Trauma & Dissociation, 19:1, 39-58, DOI: 10.1080/15299732.2017.1289493

To link to this article: https://doi.org/10.1080/15299732.2017.1289493

JOURNAL OF TRAUMA & DISSOCIATION
2018, VOL. 19, NO. 1, 39–58
https://doi.org/10.1080/15299732.2017.1289493

Routledge
Taylor & Francis Group

ARTICLE

OPEN ACCESS Check for updates

Acupuncture for the Treatment of Adults with Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis

Sean Grant, DPhil [a], Benjamin Colaiaco, MA[a], Aneesa Motala, BA[a], Roberta Shanman, MS[a], Melony Sorbero, PhD[b], and Susanne Hempel, PhD[a]

[a]RAND Corporation, Santa Monica, California, USA; [b]RAND Corporation, Pittsburgh, Pennsylvania, USA

ABSTRACT

Acupuncture has been suggested as a treatment for posttraumatic stress disorder (PTSD), yet its clinical effects are unclear. This review aims to estimate effects of acupuncture on PTSD symptoms, depressive symptoms, anxiety symptoms, and sleep quality for adults with PTSD. We searched 10 databases in January 2016 to identify eligible randomized controlled trials (RCTs). We performed random effects meta-analyses and examined quality of the body of evidence (QoE) using the GRADE approach to rate confidence in meta-analytic effect estimates. Seven RCTs with 709 participants met inclusion criteria. We identified very low QoE indicating significant differences favoring acupuncture (versus any comparator) at post-intervention on PTSD symptoms (standardized mean difference [SMD] = −0.80, 95% confidence interval [CI] [−1.59, −0.01], 6 RCTs), and low QoE at longer follow-up on PTSD (SMD = −0.46, 95% CI [−0.85, −0.06], 4 RCTs) and depressive symptoms (SMD = −0.56; 95% CI [−0.88, −0.23], 4 RCTs). No significant differences were observed between acupuncture and comparators at post-intervention for depressive symptoms (SMD = −0.58, 95% CI [−1.18, 0.01], 6 RCTs, very low QoE), anxiety symptoms (SMD = −0.82, 95% CI [−2.16, 0.53], 4 RCTs, very low QoE), and sleep quality (SMD = −0.46, 95% CI [−3.95, 3.03], 2 RCTs, low QoE). Safety data (7 RCTs) suggest little risk of serious adverse events, though some participants experienced minor/moderate pain, superficial bleeding, and hematoma at needle insertion sites. To increase confidence in findings, sufficiently powered replication trials are needed that measure all relevant clinical outcomes and dedicate study resources to minimizing participant attrition.

ARTICLE HISTORY
Received 11 August 2016
Accepted 26 December 2016

KEYWORDS
Alternative medicine; complementary medicine; meta-analysis; posttraumatic stress disorder; systematic review

Posttraumatic stress disorder (PTSD) is a mental health condition that can develop after a person witnesses or experiences a traumatic event (American Psychiatric Association, 2013; Breslau, 2009; Kessler et al., 2005). Characteristic indicators include re-experiencing or intrusive symptoms, avoiding reminders of the event, negative thoughts and feelings, and hyper-

CONTACT Sean Grant sgrant@rand.org RAND Corporation, 1776 Main Street, P.O. Box 2138, Santa Monica, CA 90407-2138, USA.

PROSPERO number for study pre-registration: CRD42015026766

arousal and reactivity (American Psychiatric Association, 2013). Current (12-month) and lifetime prevalence of PTSD among trauma-exposed US adults are 3.6 percent and 6.8 percent, respectively (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 (Boscarino, 2006; Reynolds, Pietrzak, Mackenzie, Chou, & Sareen, 2016; Smith, Schnurr, & Rosenheck, 2005; Taft, Street, Marshall, Dowdall, & Riggs, 2007). However, many people exposed to trauma and who eventually develop PTSD do not seek services or receive adequate empirically based treatment (Institute of Medicine, 2008). Improving access to high-quality treatment is therefore a policy priority.

Complementary and alternative medicine (CAM) approaches are increasingly common for the treatment and management of mental health problems, including PTSD (Strauss, Lang, & Schnurr, 2016). CAM approaches generally refer to techniques that are used in combination with or in lieu of conventional practices from Western medicine (Institute of Medicine, 2005). Examples include meditation, relaxation techniques, and—the focus of this review—acupuncture (Strauss & Lang, 2012). CAM approaches are becoming more widespread because they 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, Coeytaux, McDuffie, Nagi, & Williams Jr., 2011). These advantages may be particularly important given stigma associated with PTSD (Mittal et al., 2013), and the belief held by some patients that talking about their traumatic experiences with a treatment provider would make them feel worse (Ouimette, Brown, & Najavits, 1998). Given the priority of improving access to high-quality treatment for PTSD and the growing adoption of CAM approaches by both practitioners and consumers, clarifying the evidence underpinning particular techniques is imperative to informing policy and guidance about the use of CAM for PTSD.

Acupuncture is a CAM technique that involves inserting and manipulating thin solid needles into specifically chosen points in subcutaneous tissue (or "acupoints") for a given period of time, which, according to Traditional Chinese Medicine (TCM), moves vital energy around the body and thereby restores balance between internal organ systems (Hollifield, 2011). Depending on the targeted diagnosis, procedures vary in dosage (i.e., number, frequency, and duration of sessions), the utilized needling points in subcutaneous tissue, the number of needle insertions per session, depth of needle insertion, type of needle stimulation, needle retention time, needle type, and needling setting (MacPherson et al., 2010). For PTSD, a prominent acupuncture protocol involves twice weekly one-hour sessions for 12 weeks, in which trained acupuncturists insert needles into a primary set of acupoints for all patients as well as flexibly prescribed acupoints tailored to individual

patients' diagnostic patterns (Hollifield, Sinclair-Lian, Warner, & Hammerschlag, 2007). Acupuncture is hypothesized to cause neurological responses involving the autonomic nervous system, the prefrontal cortex, and several limbic structures in the brain that are involved in PTSD pathophysiology (Hollifield, 2011), and it is thought to provide a safe, simple, and comparatively inexpensive alternative or supplement to traditional PTSD treatments (Prisco et al., 2013). However, rigorous research on the clinical effects of acupuncture for PTSD is needed to support its use by healthcare providers and systems.

Systematic reviews provide the most reliable way to identify benefits and harms associated with treatments (Institute of Medicine, 2011b). Up-to-date systematic reviews that summarize current evidence on treatment effects—and the quality of this evidence—are essential to developing trustworthy practice and policy guidelines (Institute of Medicine, 2011a). Several established psychological and pharmacological approaches for PTSD are supported by evidence from systematic reviews (Amos, Stein, & Ipser, 2014; Bisson, Roberts, Andrew, Cooper, & Lewis, 2013; Stein, Ipser, & Seedat, 2006). The most recent systematic review specifically on acupuncture for PTSD is four years old and was therefore conducted prior to several recent randomized controlled trials (RCTs) on acupuncture for PTSD (Kim et al., 2013). The review authors concluded that the evidence of effectiveness of acupuncture for PTSD is encouraging, yet they included uncontrolled clinical trials that provide less valid estimates of clinical effects, did not consider several important clinical outcomes such as depressive symptoms, quality of life, and sleep quality (Hollifield, 2011), did not analyze outcomes at different time points, and did not involve formal assessments of the quality of the body of evidence to indicate the degree of confidence in the accuracy of estimates of clinical effects. Consequently, updated estimates of the effects of acupuncture on PTSD are needed—particularly by using meta-analytic methods based on a systematic review compliant with standards for ensuring reliable summaries of what the current evidence suggests and the quality of this evidence (Institute of Medicine, 2011b).

Methods

Objective

This systematic review aims to estimate the effects of acupuncture for adults with PTSD. Our primary outcome was PTSD symptoms, and our secondary outcomes were health-related quality of life, functional status, depression and anxiety symptoms, and sleep quality. We registered the review on PROSPERO (CRD42015026766) prior to completing formal screening of search results against eligibility criteria, similar to the rationale for registering

RCTs prior to participant recruitment (Dickersin & Renne, 2003). In addition, we used two methodological guidelines to develop this manuscript: the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009), an evidence- and consensus-based minimum set of items for accurately, comprehensively, and transparently reporting intervention reviews and the Methodological Expectations of Campbell Collaboration Intervention Reviews guidance (Campbell Collaboration, 2014), a set of explicit expectations for reporting systematic reviews on intervention effects.

Search strategy

We searched electronic databases (PubMed, PsycINFO, AMED, CINAHL, Cochrane Database of Systematic Reviews, Other Reviews, CENTRAL, Web of Science, EMBASE, PILOTS) and clinical trial registries (Clinicaltrials.gov, International Clinical Trials Registry Platform) from inception to August 2015, and we conducted an update search in January 2016. Search terms involved variants of "acupuncture" and "posttraumatic stress" (see Online Supplement 1 for the full search strategy). We also reference-mined included studies and relevant systematic reviews identified through our electronic searches.

Eligibility criteria

Inclusion criteria

We included parallel group, individually or cluster-randomized controlled trials with adult participants (male and female) who were 18 years of age or older. Participants must have had a clinical diagnosis of PTSD according to DSM or International Classification of Diseases (ICD) diagnostic criteria, or screen positive for PTSD using a validated measure. We included studies that administered thin or fine solid needles into known acupoints, either as an adjunctive or monotherapy. We included studies involving full-body acupuncture following Traditional Chinese Medicine (TCM), auricular acupuncture, and other specific body sites. Our outcomes of interest for meta-analyses were as follows: PTSD symptoms, health-related quality of life, functional status, depressive and anxiety symptoms, sleep quality, and adverse events.

Exclusion criteria

We excluded studies reported only in conference proceedings or abstracts, though we did not exclude grey literature (e.g., dissertations) or studies by language (we identified eligible studies in Chinese as well as English). We did not exclude studies based on comparator, treatment duration, follow-up period, or setting.

Inclusion screening

Two independent reviewers screened titles and abstracts of retrieved citations using a standardized electronic form. We obtained full texts for citations judged as potentially eligible by one or both reviewers. Two reviewers then screened full texts against the specified eligibility criteria; disagreements were resolved through discussion within the review author team.

Data extraction

The two reviewers independently extracted study-level data on key characteristics of each study's design, sample, setting, interventions, and outcomes using an a priori data collection form in an electronic database (see Online Supplement 2 for a copy of the form). The reviewers used the Cochrane Risk of Bias tool to assess each of the following areas: random sequence generation, allocation concealment, blinding of participants and providers, blinding of outcome assessors, completeness of outcome data, and selective outcome reporting (Higgins et al., 2011). The project lead extracted and analyzed all outcome data, except for a research assistant who extracted data from Chinese language articles (Zhang, Ran et al., 2010a, Zhang, Yuan et al., 2010b). Data from all included studies are documented in a comprehensive evidence table.

Data synthesis

We computed standardized mean difference (SMD) together with the 95% confidence interval (CI) for all studies to facilitate comparison of effects across studies. We conducted random effects meta-analyses using the restricted maximum-likelihood (REML) estimator method for the amount of heterogeneity and the Hartung-Knapp-Sidik-Jonkman adjustment for standard errors (Hartung, 1999; Hartung & Knapp, 2001; Sidik, Jonkman, & Comput Stat Data Anal 2006, 2006) with the "metafor" package (Viechtbauer & Viechtbauer, 2015) in R (version 3.2.3). When multiple measures of the same construct were reported in a study, we chose the measure used most by trials contributing to each meta-analysis in an attempt to reduce statistical heterogeneity, though we also conducted sensitivity analyses to examine whether results differed by measure included in the meta-analysis as applicable. When multiple comparison groups were included in a trial, we included data from one comparison group (in order—sham, TAU, passive, or active) in the meta-analysis, and we conducted sensitivity analyses to examine whether results differed by the comparison group used. For meta-analysis of data with clear outliers, we conducted sensitivity analyses excluding the outliers as appropriate (Greenland & Longnecker, 1992; Hamling, Lee, Weitkunat, & Ambuhl, 2008; Higgins et al., 2011; Orsini, Li, Wolk, Khudyakov, & Spiegelman, 2012). We

investigated publication bias using two different procedures—Begg's rank correlation test for funnel plot asymmetry (Begg & Mazumdar, 1994) and Egger's linear regression test for funnel plot asymmetry (Egger et al., 1997)—given the limited number of expected included studies. We conducted meta-regressions when possible to examine whether there were differences in effect sizes by type of acupuncture, co-intervention, and comparison group.

Effect estimates are expressed as Hedges' g—a small study bias-adjusted estimate of the standardized mean difference between acupuncture and comparator interventions. We grouped outcomes by length of follow-up (i.e., immediately post-intervention and longer follow-up at one-to-six months post-intervention) and used the I^2 statistic to assess magnitude of heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). We used conventional indices for interpreting the size of point estimates of effects: 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, & Chen, 2010). We assessed the quality of the body of evidence (QoE) for each outcome using the GRADE approach (Balshem et al., 2011), which involves grading QoE on a 4-item scale (very low, low, moderate, and high) based on four domains (risks of bias, directness of the evidence, consistency of the evidence, and precision of effect estimates) in order to reflect our confidence that effect estimates lie close to true effects and are stable.

Results

Study characteristics

We examined 716 titles and abstracts (Figure 1); of 119 potentially eligible full-texts identified, we excluded 106 articles (see Online Supplement 3 for a full list of excluded full-text articles). We identified seven eligible studies that overall randomized 709 participants (Engel et al., 2014; Hollifield et al., 2007; King et al., 2015; Prisco et al., 2013; Wang, Hu, Wang, Pang, & Zhang, 2012; Zhang, Ran et al., 2010a, Zhang, Yuan et al., 2010b).

Table 1 provides a descriptive overview of included studies (see Online Supplement 4 for extracted data from included studies). All RCTs randomized individual participants. Average age ranged from 33 to 65 years. One RCT included only males (King et al., 2015), while the proportion of males ranged from 32 to 71% in other studies. One study involved active duty military, two involved veterans, and four involved civilian samples. Four studies took place in the United States and three in China. Settings included private offices at a social work clinic, a residential PTSD treatment facility, a VA Medical Center, and TCM and psychiatric hospitals. Three studies involved outpatient care, one inpatient care, and one residential care (two did not report the stage in the clinical pathway). Over

half the studies had an unclear risk of bias related to allocation concealment, blinding of outcome assessors, and selective outcome reporting; nearly half had high risk of attrition bias, and all studies had high risk of performance bias (see Online Supplement 5 for justifications of our risk of bias assessments).

Acupuncture sessions ranged from 30 to 60 minutes per session, 2 to 4 sessions per week, and 3 to 12 weeks total in duration. Two studies provided data on auricular acupuncture and five on TCM acupuncture, with at least 30 different acupoints used for needle insertion across all studies. Three RCTs compared needle acupuncture plus TAU to TAU alone, one to sham acupuncture, one to a passive comparator (wait-list

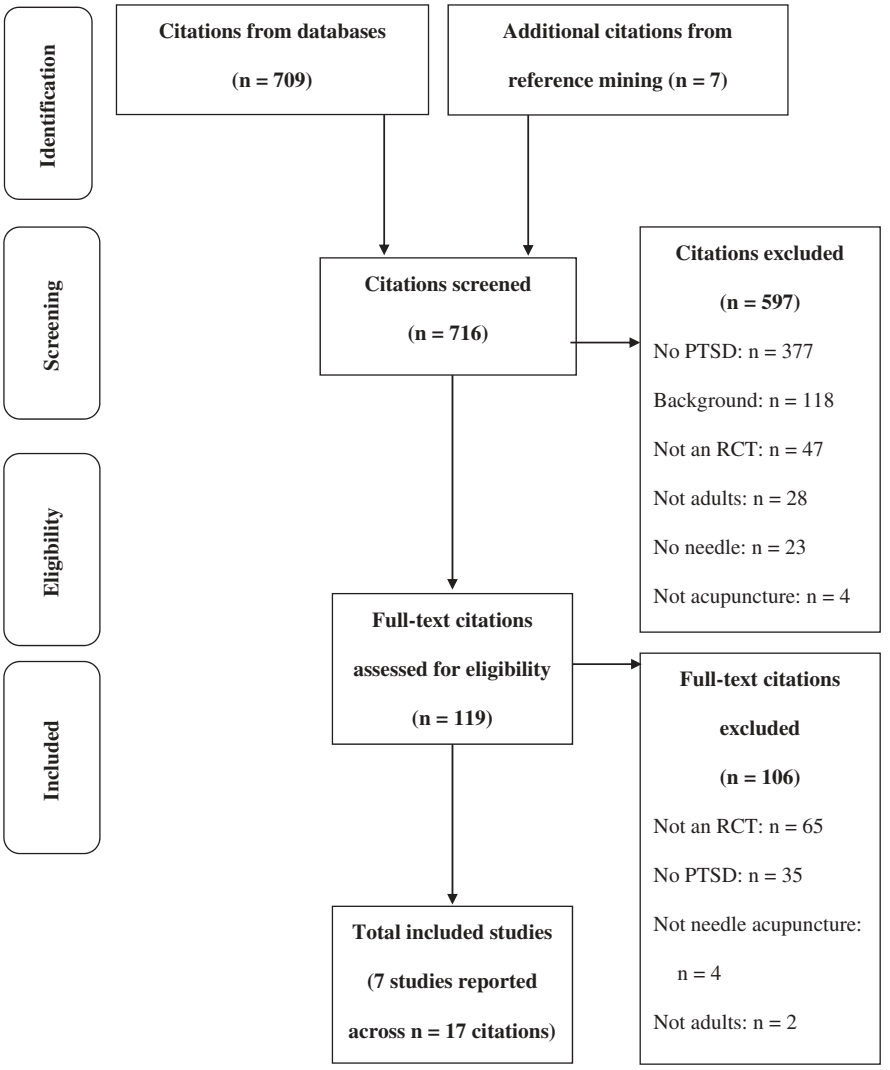

Figure 1. Flow diagram of search results.

Table 1. Evidence table of included studies.

Study	Sample size	Age[a]	Percent male	Country	Baseline PTSD	Acupuncture regimen	Acupoints	Comparator
Engel (2014)	55	Mean: 35 years	69%	US	Mean PCL (SD): 56.1 (11.8) Mean CAPS (SD): 72.9 (16.7)	TCM: 60 minutes, 2x a week/ 4 weeks	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	TAU
Hollifield (2007)	84	Mean: 42 years	32%	US	Mean PSS-SR (SD): Acupuncture: 31.33 (10.10) CBT: 32.52 (6.63) WLC: 30.79 (9.54)	TCM: 60 minutes, 2x a week/ 12 weeks	LR3, PC6, HT7, ST36, SP6, Yintang, GB20, and BL14, 15, 18, 20, 21, 23	CBT, WLC
King (2015)	29	Mean: 33 years	100%	US	Mean duration of PTSD diagnosis (SD): 5.4 (5.1) years	AA: 30 minutes, 3x a week/ 3 weeks	Shen Men, Point Zero, Brain, Thalamus Point, Pineal Gland, Master Cerebral, Insomnia Points 1 and 2, Kidney, Heart, Occiput, and Forehead	TAU
Prisco (2013)	35	Mean: 38 years	71%	US	Mean duration of PTSD symptoms (SD): 5.2 (3.0) years	AA: 45 minutes, 2x a week/ 8 weeks	Shen Men, Kidney (KI, under flap), Sympathetic (under flap), Liver (LR), and Hippocampus	Sham, TAU
Wang (2012)	138	Mean: 48 years	39%	China	Mean CAPS (SD): 65.8 (19.7)	EA: 30 minutes, 3-4x a week/ 12 weeks	Baihui (GV 20), Sishencong (EX-HN 1), Shenting (GV 24), Fengchi (GB 20)	Paroxetine
Zhang (2010a)	92	Range: 18–65 years	35%	China	Minimum duration of PTSD diagnosis of 3 months	EA: 30 minutes, 3x a week/ 12 weeks	Shenyu, Mingmen, Zhishi, Shenting, Shencong points, Baihui, and Fengchi	Paroxetine
Zhang (2010b)	276	Range: 18–65 years	NR	China	Minimum duration of PTSD diagnosis of 3 months	TCM: 30 minutes, 3x a week/ 12 weeks	Shenting, 4 Shencong points, Baihui, and Fengchi	Paroxetine

Notes: AA = auricular acupuncture, CAPS = Clinician-administered PTSD Scale, CBT = cognitive behavioral therapy, EA = electro-acupuncture, NR = not reported, PCL = PTSD checklist, PSS-SR = Posttraumatic Symptom Scale-Self Report, PTSD = Posttraumatic Stress Disorder, SD = standard deviation, TAU = treatment as usual, TCM = Traditional Chinese Medicine, US = United States, WLC = wait-list control.

Age of participants is reported either as a mean or a range depending on the information provided in included studies.

control), and four to an active comparator (cognitive behavioral therapy, paroxetine).

Time points for outcomes ranged from immediately post-intervention to short-term (one-to-six months) follow-up. Six of the seven eligible RCTs provided data on PTSD symptoms using the PTSD Checklist (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996), Posttraumatic Symptom Scale-Self Report (Foa, Riggs, Dancu, & Rothbaum, 1993), and Clinician-Administered PTSD Scale (Blake et al., 1995); one study did not include PTSD symptoms as an outcome measure (Prisco et al., 2013). One RCT provided data on health-related quality of life using the 36-Item Short Form Survey, or SF-36 (Ware, Snow, Kosiniski, & Gandek, 1993). One RCT provided data on functional status using the Sheehan Disability Inventory (Sheehan, 1983). Five RCTs provided data on depressive symptoms using the Beck Depression Inventory (Beck, Steer, Ball, & Ranieri, 1996), Hopkins Symptom Checklist (Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974), the Patient Health Questionnaire (Kroenke, Spitzer, & Williams, 2001), and the Hamilton Depression Rating Scale (Hamilton, 1960). Three RCTs provided data on anxiety symptoms using the Hopkins Symptom Checklist (Derogatis et al., 1974) and the Hamilton Anxiety Scale (Maier, Buller, Philipp, & Heuser, 1988). Two RCTs provided data on sleep quality using the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) and Insomnia Severity Index (Bastein, Vallieres, & Morin, 2001).

Effects of acupuncture versus any comparator for adult patients with PTSD

A summary of our findings on acupuncture versus any comparator is located in Table 2. For all analyses below, we found no evidence of publication bias.

PTSD symptoms

We identified a large effect in favor of acupuncture versus any comparator (passive control, TAU, and active intervention) at post-intervention (SMD = −0.80, 95% CI [−1.59, −0.01], I^2 = 90%; $t(5) = -2.61$, $p = 0.05$; see Figure 2) and a medium effect in favor of acupuncture versus any comparator at longer follow-up (SMD = −0.46, 95% CI [−0.85, −0.06], I^2 = 7%; $t(3) = -3.64$, $p = 0.04$; see Figure 3). However, we rated the QoE at post-intervention as "very low" due to high attrition bias in included studies, considerable heterogeneity across studies, a wide confidence interval around the summary point estimate spanning clinically meaningful differences, and sensitivity of results to the inclusion of an outlying poor quality study (see Online Appendix 6 for sensitivity analyses). Additionally, we rated the QoE at follow-up as "low" due to a wide confidence interval around the summary point estimate spanning clinically meaningful differences and high risk of performance bias in included studies. We did not detect statistically

Table 2. Overall effect and subgroup analyses for PTSD symptoms.

Outcome	Studies	SMD (95% CI)	Risk of Bias	Consistency	Directness	Precision	Publication Bias	QoE
PTSD symptoms. (post-intervention)	$k = 6$ $n = 508$	−0.80 (−1.59 to −0.01)	Downgrade 1[a,f]	Downgrade 1[b]	No downgrade	Downgrade 1[d]	$\tau = -0.29$, p = 0.43 t (4) = −0.31, $p = 0.77$	Very low
PTSD symptoms (follow-up)	$k = 4$ $n = 387$	−0.46 (−0.85 to −0.06)	Downgrade 1[g]	No downgrade	No downgrade	Downgrade 1[d]	$\tau = -1.00$, $p = 0.06$ t (2) = −4.17, $p = 0.18$	Low
Physical health-related quality of life (follow-up)	$k = 1$ $n = 55$	−0.47 (−1.01 to 0.07)	No downgrade	Downgrade 2[e]	No downgrade	Downgrade 1[c]	Insufficient evidence to investigate	Very low
Mental health-related quality of life (follow-up)	$k = 1$ $n = 55$	−0.33 (−0.87 to 0.21)	No downgrade	Downgrade 2[e]	No downgrade	Downgrade 1[c]	Insufficient evidence to investigate	Very low
Functional status (post-intervention)	$k = 1$ $n = 56$	−0.83 (−1.38 to −0.29)	Downgrade 1[a]	Downgrade 2[e]	No downgrade	Downgrade 1[d]	Insufficient evidence to investigate	Very low
Functional status (follow-up)	$k = 1$ $n = 56$	−0.97 (−1.53 to −0.42)	Downgrade 1[a]	Downgrade 2[e]	No downgrade	Downgrade 1[d]	Insufficient evidence to investigate	Very low
Depressive symptoms (post-intervention)	$k = 6$ $n = 508$	−0.58 (−1.18 to 0.01)	Downgrade 1[a]	Downgrade 1[b]	No downgrade	Downgrade 1[c]	$\tau = 0.14$, $p = 0.70$ t (4) = 0.29, $p = 0.62$	Very low
Depressive symptoms (follow-up)	$k = 4$ $n = 387$	−0.56 (−0.88 to −0.23)	Downgrade 1[g]	No downgrade	No downgrade	Downgrade 1[d]	$\tau = -0.55$, $p = 0.28$ t (2) = 0.53, $p = 0.54$	Low
Anxiety symptoms (post-intervention)	$k = 4$ $n = 424$	−0.82 (−2.16 to 0.53)	Downgrade 1[a]	Downgrade 1[b]	No downgrade	Downgrade 1[c]	$\tau = -0.60$, $p = 0.25$ t (2) = −1.25, $p = 0.34$	Very low
Anxiety symptoms (follow-up)	$k = 3$ $n = 332$	−0.35 (−1.17 to 0.47)	Downgrade 1[a]	Downgrade 1[b]	No downgrade	Downgrade 1[c]	$\tau = -0.82$, $p = 0.22$ t (1) = −2.52, $p = 0.24$	Very low
Sleep quality (post-intervention)	$k = 2$ $n = 53$	−0.46 (−3.95 to 3.03)	Downgrade 1[a]	No downgrade	No downgrade	Downgrade 1[c]	$\tau = 1.00$, $p = 1.00$	Low

Notes: k = number of randomized controlled trials (RCTs). n = number of participants. SMD < 0 favors needle acupuncture. τ = Kendall's tau for Begg's rank correlation test for funnel plot asymmetry. t = Egger's regression test for funnel plot asymmetry.

[a] High attrition bias and/or no intention-to-treat analysis. [b] Statistically significant and/or substantial heterogeneity. [c] Wide confidence interval indicating benefit and harm. [d] Wide confidence interval spanning clinically meaningful differences. [e] Cannot judge consistency (only one RCT). [f] Results sensitive to inclusion of poor quality study (see Online Supplement 6). [g] High risk of performance bias from unblinded participants in all trials underpinning analysis due to lack of sham acupuncture comparators.

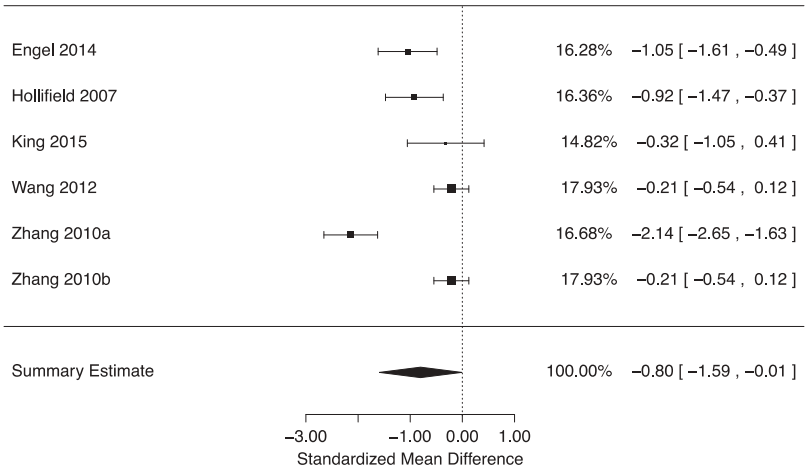

Figure 2. Forest plot for needle acupuncture versus any comparator on PTSD symptoms at post-intervention. Notes: Standardized Mean Difference (SMD) = Hedges' g. SMD < 0 favors needle acupuncture. The reported percentages indicate the weight each study contributes to the meta-analysis. The right hand figures report the SMD [95% Confidence Interval] for each individual study and (at the bottom) the overall estimate from the meta-analysis.

significant differences in effect estimates via meta-regression by type of needle acupuncture (TCM or auricular), (post-intervention: $F[1, 4] = 0.39$, $p = 0.57$), co-intervention status (acupuncture as an adjunctive or as a monotherapy), (post-intervention: $F[1, 4] = 0.04$, $p = 0.85$; follow-up: $F[1, 2] = 0.004$, $p = 0.96$), or comparator (passive control, TAU, or active intervention), (post-intervention: $F[2, 3] = 0.02$, $p = 0.98$; follow-up: $F[2, 1] = 2.13$, $p = 0.44$).

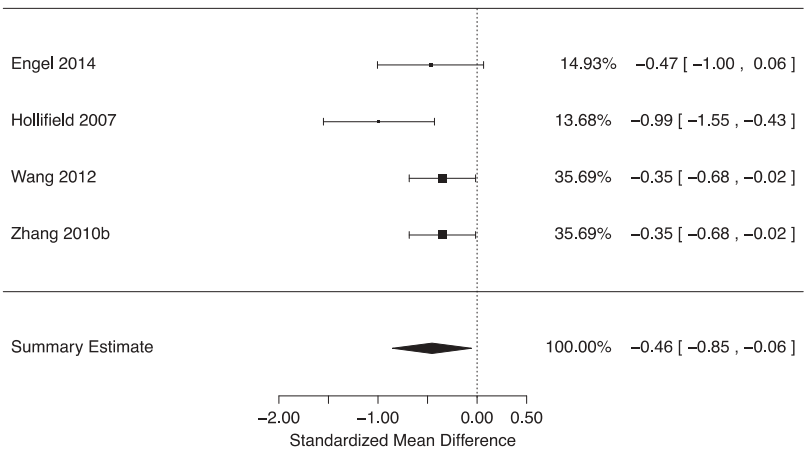

Figure 3. Forest plot for needle acupuncture versus any comparator on PTSD symptoms at one-to-six months follow-up. Notes: Standardized Mean Difference (SMD) = Hedges' g. SMD < 0 favors needle acupuncture. The reported percentages indicate the weight each study contributes to the meta-analysis. The right hand figures report the SMD [95% Confidence Interval] for each individual study and (at the bottom) the overall estimate from the meta-analysis.

Health-Related quality of life

No significant difference was identified between acupuncture and TAU for physical (SMD = −0.47, 95% CI [−1.01, 0.07], $z(0) = -1.72$, $p = 0.09$) and mental health-related quality of life (SMD = −0.33, 95% CI [−0.87, 0.21], $z(0) = -1.21$, $p = 0.23$). We rated the QoE for both outcomes as "very low" due to a wide confidence interval around the summary point estimate spanning clinically meaningful differences and inability to assess consistency in this evidence base due to a lack of replication of results in another RCT. There was insufficient evidence to investigate moderators via meta-regression.

Functional status

We identified a large effect in favor of acupuncture versus wait-list control at post-intervention (SMD = −0.83, 95% CI [−1.38, −0.29], $z(0) = -2.99$, $p = 0.003$) and follow-up (SMD = −0.97, 95% CI [−1.53, −0.42], $z(0) = -3.43$, $p = 0.001$). We rated the QoE for both outcomes as "very low" due to high attrition bias in included studies, a wide confidence interval around the summary point estimate spanning clinically meaningful differences, and lack of replication of results in another RCT. There was insufficient evidence to investigate moderators via meta-regression.

Depressive symptoms

No significant difference was identified between acupuncture and any comparator (passive controls, TAU, and active interventions) at post-intervention (SMD = −0.58, 95% CI [−1.18, 0.01], $I^2 = 82\%$, $t(5) = -2.52$, $p = 0.05$). We rated the QoE at post-intervention as "very low" due to high attrition bias in included studies, considerable heterogeneity across studies, and a wide confidence interval spanning estimates of benefit and harm. We identified a medium effect in favor of acupuncture versus any comparator at longer follow-up (SMD = −0.56, 95% CI [−0.88, −0.23], $I^2 = 0\%$, $t(3) = -5.45$, $p = 0.01$). We rated the QoE at follow-up as "low" due to a wide confidence interval spanning clinically meaningful differences and high risk of performance bias in included studies. We did not detect statistically significant differences in effect estimates via meta-regression by type of needle acupuncture (post-intervention: $F[1, 4] = 2.44$, $p = 0.19$), co-intervention status (post-intervention: $F[1, 4] = 0.56$, $p = 0.50$; follow-up: $F[1, 2] = 0.14$, $p = 0.75$), or comparator (post-intervention: $F[2, 3] = 0.27$, $p = 0.78$; follow-up: $F[2, 1] = 0.84$, $p = 0.61$).

Anxiety symptoms

No significant difference was identified between TCM acupuncture and any comparator (passive controls and active interventions) at post-intervention (SMD = −0.82, 95% CI [−2.16, 0.53], $I^2 = 94\%$, $t(3) = -1.93$, $p = 0.15$) and follow-up (SMD = − 0.35, 95% CI [−1.17, 0.47], $I^2 = 58\%$, $t(2) = -1.82$,

$p = 0.21$). We rated the QoE at both time points as "very low" due to high attrition bias in included studies, considerable heterogeneity across studies, and a wide confidence interval spanning estimates of benefit and harm. We did not detect statistically significant differences in effect estimates via meta-regression by type of comparator (post-intervention: $F[1,2] = 0.02$, $p = 0.90$; follow-up: $F[1,2] = 0.02$, $p = 0.90$).

Sleep quality

No significant difference was identified between auricular acupuncture and any comparator (TAU and sham acupuncture) at post-intervention (SMD = −0.46, 95% CI [−3.95, 3.03], $I^2 = 0\%$, $t(1) = -1.68$, $p = 0.34$). We rated the QoE as "low" due to high attrition bias in included studies and a wide confidence interval spanning estimates of benefit and harm. There was insufficient evidence to investigate moderators via meta-regression.

Adverse events

All RCTs reported on the safety of acupuncture (Table 3). From reported 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 the few reports of adverse events were due to scarce experiences of or inadequate procedures for detecting adverse events.

Discussion

Summary of findings

Results from meta-analyses of published RCTs indicate positive effects of acupuncture but warrant caution regarding claims that acupuncture is an evidence-based treatment for patients with PTSD based on the best available evidence for key clinical outcomes. We identified potential clinical benefits of acupuncture on PTSD symptoms and functional status immediately post-intervention, as well as PTSD and depressive symptoms in the months following completion of acupuncture treatment. However, based on our QoE assessments, we have limited confidence in the estimates indicating needle acupuncture reduces PTSD and depressive symptoms at follow-up, and we have very limited confidence in the estimates for PTSD symptoms at post-intervention and functional status at both post-intervention and follow-up. Most often, the evidence base underpinning

Table 3. Adverse events in included studies.

Study	Reported adverse events
Engel (2014)	Explicitly reported that no study-related adverse events were reported or observed
Hollifield (2007)	One participant receiving TCM acupuncture reported kidney pain, which was not reported by any participant in the group CBT and wait-list control comparator groups
King (2015)	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 3 days after receipt of acupuncture. The study investigators concluded that none of these adverse events were directly related to the acupuncture intervention
Prisco (2013)	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
Wang (2012)	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 symptom of 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 one case of moderate pain. 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 participants), and stuffy nose (1 participant).
Zhang (2010a)	Monitored adverse events: did not report any but did not explicitly state that no adverse events were observed
Zhang (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

meta-analyses was characterized by small trials that involved significant participant attrition and unclear intention-to-treat analysis procedures, contributing to our limited confidence in effect estimates indicating potential benefits of needle acupuncture for adult patients with PTSD. Consequently, it is very possible that further research could change the direction and magnitude of effect estimates.

We also did not identify systematic effects suggesting that results differ by type of acupuncture, co-intervention status, or comparator, though future trials are needed for better-powered meta-regressions testing these moderators. The available evidence suggests that acupuncture is not typically associated with serious adverse events and that some participants may experience mild adverse events. However, the generally low reporting about adverse events may be due to inadequate or 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 instrumentation for detecting adverse events.

Comparison to other reviews

A previous systematic review on the topic concluded that evidence in support of acupuncture for PTSD is encouraging yet not cogent due to the small number of studies providing data for their meta-analyses and limitations due to the methodological quality of included trials (Kim et al., 2013). The results of this review are compatible with this previous systematic review, though we are less encouraged by the current evidence base. Differences in our conclusions are most likely explained by our inclusion of several additional RCTs published in the interim that led to a larger body of evidence for our analyses, the previous review's inclusion of non-randomized evaluations of acupuncture for PTSD versus our sole focus on RCTs, our investigation of additional outcomes of interest and results at different time-points, and our formal QoE assessments that allowed us to make more systematic conclusions about our confidence in effect estimates.

Limitations and future directions

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 grey literature (e.g., dissertations or graduate theses), and risk of bias assessments and comprehensive QOE assessments used to formulate review conclusions. However, our focus on needle acupuncture provides evidence to this specific CAM technique; other related CAM approaches interventions may yield different effects and be worth future investigation. In addition, we did not contact trial authors for missing data or to identify other potential studies not identified by our search strategy. Significant amounts of statistical heterogeneity for many outcomes also indicated that important sources of clinical heterogeneity remain unexplained. Possible sources of clinical heterogeneity include dosage (e.g., number of sessions and weeks), acupoints (e.g., auricular, TCM points), and clinical settings. We have raw and processed outcome data (see Online Supplement 7), as well as with our accompanying analysis scripts in R (see Online Supplement 8) to facilitate additional analyses by interested investigators.

Future RCTs that are well-designed, rigorous, and sufficiently powered would facilitate an evidence base that can more decisively provide estimates of acupuncture for PTSD. For future researchers interested in further developing this evidence base, we provide several concrete

suggestions based on the current evidence we identified. Firstly, researchers should report RCTs in compliance with reporting standards for acupuncture interventions to facilitate research syntheses (MacPherson et al., 2010). Secondly, given evidence of potential publication bias for withdrawal/craving, researchers should pre-register their trials and report all results regardless of their statistical significance (Dickersin & Renne, 2003). As resources allow, researchers should aim to measure all outcomes targeted by acupuncture when used to treat PTSD; not all RCTs provided data on PTSD symptoms, and the number of RCTs contributing data to health-related quality of life, functional status, and sleep quality was particularly low. Similarly, future RCTs should also measure specific PTSD symptom clusters (in addition to overall PTSD symptoms) to clarify whether there are potential patient improvements in any specific symptom clusters. Moreover, future RCTs should include sham comparators to account for possible non-specific effects. Given the potentially chronic nature of PTSD, researchers should also seek to measure outcomes at longer time points, as only two RCTs provided any outcome data at 6 months, and no RCTs provided data beyond that time point; however, more resources are likely needed to be invested by trial researchers in retaining participants at outcome follow-up time points, given the amount of attrition in the current evidence base. Lastly, future research may wish to explicitly examine and better establish potential neurobiological mechanisms of action of acupuncture prior to further testing in RCTs (Hollifield, 2011).

Conclusion

Committees charged with updating practice and policy guidelines for treating PTSD may be interested in using this report as a source of evidence when making recommendations for or against needle acupuncture for this population. Overall, the results of this systematic review warrant caution in promoting acupuncture as an evidence-based treatment for adult patients with PTSD despite identified positive treatment effects. We have limited confidence in estimates indicating that needle acupuncture reduces PTSD and depressive symptoms at follow-up compared to passive controls, TAU, and active interventions, and we have very limited confidence in the estimates for PTSD symptoms at post-intervention and functional status. Moreover, no significant differences were observed between acupuncture and comparators for other outcomes, including no evidence for post-intervention or longer term improves on important psychological outcomes such as anxiety symptoms and sleep quality. Evidence from RCTs does suggest that acupuncture is relatively safe. Larger trials that minimize participant attrition would improve the quality of and confidence in effect estimates.

Acknowledgment

We gratefully acknowledge Patricia Smith and Whitney Dudley for their assistance in article retrieval and formatting aspects of this report. We thank Eugene Han for his help in translating Chinese language articles. We also would like to thank Dr. Paula Schnurr, Dr. Tom Concannon, Dr. Kristie Gore, Dr. Marina Khusid, and Dr. Bradley Belsher for helpful suggestions and content expertise supporting the systematic review this manuscript is based on. The sponsor did not directly participate in the study design, collection, analysis, or interpretation of the data for this manuscript, and they were not involved in the approval of the manuscript for publication or the decision to publish. The authors are solely responsible for the content, and any errors of fact or interpretation are the responsibility of the authors.

Funding

The systematic review was funded through a contract (W91WAW-12-C-0030 14-539) from the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE). The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the views of DCoE or the Department of Defense (DoD).

Disclosure statement

SG's spouse is a salaried employee of Eli Lilly and Company, and owns stock. SG has accompanied his spouse on company-sponsored travel. All other authors declare that they have no conflicts of interest.

ORCID

Sean Grant http://orcid.org/0000-0002-7775-3022

References

American Psychiatric Association. (2013). *The diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Pyschiatric Association.

Amos, T., Stein, D. J., & Ipser, J. C. (2014). Pharmacological interventions for preventing post-traumatic stress disorder (PTSD). *Cochrane Database of Systematic Reviews*, (7), CD006239. doi:10.1002/14651858.CD006239.pub2

Balshem, H., Helfand, M., Schünemann, H. J., Oxman, A. D., Kunz, R., Brozek, J., … Guyatt, G. H. (2011). GRADE guidelines: 3. rating the quality of evidence. *Journal of Clinical Epidemiology*, *64* (4), 401–406. doi:10.1016/j.jclinepi.2010.07.015

Bastein, C. H., Vallieres, A., & Morin, C. M. (2001). Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Medicine*, *2* (4), 297–307. doi:10.1016/S1389-9457(00)00065-4

Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. F. (1996). Comparison of Beck Depression Inventories-IA and-II in psychiatric outpatients. *Journal of Personality Assessment*, *67* (3), 588–597. doi:10.1207/s15327752jpa6703_13

Begg, C. B., & Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics*, *50*, 1088–1101. doi:10.2307/2533446

Bisson, J. I., Roberts, N. P., Andrew, M., Cooper, R., & Lewis, C. (2013). Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane Database of Systematic Reviews*, (12), CD003388. doi:10.1002/14651858.CD003388.pub4

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., & Keane, T. M. (1995). The development of a clinician-administered PTSD scale. *Journal of Traumatic Stress*, *8* (1), 75–90. doi:10.1007/BF02105408

Blanchard, E. B., Jones-Alexander, J., Buckley, T. C., & Forneris, C. A. (1996). Psychometric properties of the PTSD Checklist (PCL). *Behaviour Research and Therapy*, *34* (8), 669–673. doi:10.1016/0005-7967(96)00033-2

Boscarino, J. A. (2006). External-cause mortality after psychologic trauma. *Comprehensive Psychiatry*, *47* (6), 503–514. doi:10.1016/j.comppsych.2006.02.006

Breslau, N. (2009). The epidemiology of trauma, PTSD, and other posttrauma disorders. *Trauma, Violence, and Abuse*, *10* (3), 198–210. doi:10.1177/1524838009334448

Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28* (2), 193–213. doi:10.1016/0165-1781(89)90047-4

Campbell Collaboration. (2014). *Methodological expectations of Campbell collaboration intervention reviews (MEC2IR)*. Oslo, Norway: Author.

Chen, H., Cohen, P., & Chen, S. (2010). How big is a big odds ratio? Interpreting the magnitudes of odds ratios in epidemiological studies. *Communications in Statistics—Simulation and Computation*, *39* (4), 860–864.

Derogatis, L. R., Lipman, R. S., Rickels, K., Uhlenhuth, E. H., & Covi, L. (1974). The Hopkins Symptom Checklist (HSCL): A measure of primary symptom dimensions. In P. Basel (Ed.), *Modern problems in pharmacopsychiatry*. Basel, Switzerland: Karger.

Dickersin, K., & Renne, D. (2003). Registering clinical trials. *Journal of the American Medical Association*, *290* (4), 516–523. doi:10.1001/jama.290.4.516

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *Bmj*, *315* (7109), 629–634.

Engel, C. C., Cordova, E. H., Benedek, D. M., Liu, X., Gore, K. L., Goertz, C., … Ursano, R. J. (2014). Randomized effectiveness trial of a brief course of acupuncture for posttraumatic stress disorder. *Medical Care*, *52* (12 Suppl 5), S57–64. doi:10.1097/mlr.0000000000000237

Foa, E. B., Riggs, D. S., Dancu, C. V., & Rothbaum, B. O. (1993). Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. *Journal of Traumatic Stress*, *6* (4), 459–473. doi:10.1002/jts.2490060405

Greenland, S., & Longnecker, M. P. (1992). Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. *American Journal of Epidemiology*, *135* (11), 1301–1309.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery & Psychiatry*, *23* (1), 56–62. doi:10.1136/jnnp.23.1.56

Hamling, J., Lee, P., Weitkunat, R., & Ambuhl, M. (2008). Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. *Statistics in Medicine*, *27* (7), 954–970. doi:10.1002/sim.3013

Hartung, J. (1999). An alternative method for meta-analysis. *Biometrical Journal*, *41* (8), 901–916. doi:10.17877/DE290R-6916

Hartung, J., & Knapp, G. (2001). A refined method for the meta analysis of controlled clinical trials with binary outcome. *Statistics in Medicine*, *20* (24), 3875–3889. doi:10.1002/sim.1009

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., … Sterne, J. A. (2011). The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *British Medical Journal*, *343*, d5928. doi:10.1136/bmj.d5928

Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *British Medical Journal*, *327*, 557–560. doi:10.1136/bmj.327.7414.557

Hollifield, M. (2011). Acupuncture for posttraumatic stress disorder: Conceptual, clinical, and biological data support further research. *CNS Neuroscience & Therapeutics*, *17* (6), 769–779. doi:10.1111/j.1755-5949.2011.00241.x

Hollifield, M., Sinclair-Lian, N., Warner, T. D., & Hammerschlag, R. (2007). Acupuncture for posttraumatic stress disorder: A randomized controlled pilot trial. *The Journal of Nervous and Mental Disease*, *195* (6), 504–513. doi:10.1097/NMD.0b013e31803044f8

Institute of Medicine. (2005). *Complementary and alternative medicine in the United States*. Washington, DC: National Academies Press.

Institute of Medicine. (2008). *Treatment of posttraumatic stress disorder: An assessment of the evidence*. Washington, DC: National Academies Press.

Institute of Medicine. (2011a). *Clinical practice guidelines we can trust*. Washington, DC: National Academies Press.

Institute of Medicine. (2011b). *Finding what works in health care: Standards for systematic reviews*. Washington, DC: National Academies Press.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry*, *62* (6), 593–602. doi:10.1001/archpsyc.62.7.768

Kim, Y. D., Heo, I., Shin, B. C., Crawford, C., Kang, H. W., & Lim, J. H. (2013). Acupuncture for posttraumatic stress disorder: A systematic review of randomized controlled trials and prospective clinical trials. *Evidence-Based Complementary and Alternative Medicine*, *2013*, 615857. doi:10.1155/2013/615857

King, H. C., Spence, D. L., Hickey, A. H., Sargent, P., Elesh, R., & Connelly, C. D. (2015). Auricular acupuncture for sleep disturbance in veterans with post-traumatic stress disorder: A feasibility study. *Military Medicine*, *180* (5), 582–590. doi:10.7205/MILMED-D-14-00451

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, *16* (9), 606–613. doi:10.1046/j.1525-1497.2001.016009606.x

MacPherson, H., Altman, D. G., Hammerschlag, R., Youping, L., Taixiang, W., White, A., & Moher, D. (2010). Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): Extending the CONSORT statement. *Plos Medicine*, *7* (6), e1000261. doi:10.1371/journal.pmed.1000261

Maier, W., Buller, R., Philipp, M., & Heuser, I. (1988). The hamilton anxiety scale: Reliability, validity and sensitivity to change in anxiety and depressive disorders. *Journal of Affective Disorders*, *14* (1), 61–68. doi:10.1016/0165-0327(88)90072-9

Mittal, D., Drummond, K. L., Blevins, D., Curran, G., Corrigan, P., & Sullivan, G. (2013). Stigma associated with PTSD: Perceptions of treatment seeking combat veterans. *Psychiatric Rehabilitation Journal*, *36* (2), 86–92. doi:10.1037/h0094976

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Journal of Clinical Epidemiology*, *62* (10), 1006–1012. doi:10.1016/j.jclinepi.2009.06.005

Orsini, N., Li, R., Wolk, A., Khudyakov, P., & Spiegelman, D. (2012). Meta-analysis for linear and nonlinear dose-response relations: Examples, an evaluation of approximations, and software. *American Journal of Epidemiology*, *175* (1), 66–73. doi:10.1093/aje/kwr265

Ouimette, P. C., Brown, P. J., & Najavits, L. M. (1998). Course and treatment of patients with both substance use and posttraumatic stress disorders. *Addictive Behaviors*, *23* (6), 785–795. doi:10.1016/S0306-4603(98)00064-1

Prisco, M. K., Jecmen, M. C., Bloeser, K. J., McCarron, K. K., Akhter, J. E., Duncan, A. D., … Reinhard, M. J. (2013). Group auricular acupuncture for PTSD-related insomnia in veterans: A randomized trial. *Medical Acupuncture*, *25* (6), 407–422. doi:10.1089/acu.2013.0989

Reynolds, K., Pietrzak, R. H., Mackenzie, C. S., Chou, K. L., & Sareen, J. (2016). Posttraumatic stress disorder across the adult lifespan: Findings from a nationally representative survey. *American Journal of Geriatric Psychiatry*, *24* (1), 81–93. doi:10.1016/j.jagp.2015.11.001

Sheehan, D. (1983). *The anxiety disease*. New York, NY: Scribner.

Sidik, K., & Jonkman, J. N., & Comput Stat Data Anal 2006. (2006). Robust variance estimation for random effects meta-analysis. *Computational Statistics & Data Analysis*, *50* (12), 3681–3701.

Smith, M. W., Schnurr, P. P., & Rosenheck, R. A. (2005). Employment outcomes and PTSD symptom severity. *Mental Health Services Research*, *7* (2), 89–101. doi:10.1007/s11020-005-3780-2

Stein, D. J., Ipser, J. C., & Seedat, S. (2006). Pharmacotherapy for post traumatic stress disorder (PTSD). *Cochrane Database of Systematic Reviews*, (1), CD002795. doi:10.1002/14651858.CD002795.pub2

Strauss, J. L., Coeytaux, R., McDuffie, J., Nagi, A., & Williams, J. W., Jr. (2011). *Efficacy of complementary and alternative therapies for posttraumatic stress disorder. VA-ESP Project #09-010*. Washington, DC: Department of Veterans Affairs.

Strauss, J. L., & Lang, A. J. (2012). Complementary and alternative treatments for PTSD. *PTSD Research Quarterly*, *23* (2), 1–3.

Strauss, J. L., Lang, A. J., & Schnurr, P. P. (2016). Complementary and Alternative Medicine (CAM) for PTSD. Retrieved 6 August 2016, from http://www.ptsd.va.gov/professional/treatment/overview/complementary_alternative_for_ptsd.asp

Taft, C. T., Street, A. E., Marshall, A. D., Dowdall, D. J., & Riggs, D. S. (2007). Posttraumatic stress disorder, anger, and partner abuse among vietnam combat veterans. *Journal of Family Psychology*, *21* (2), 270–277. doi:10.1037/0893-3200.21.2.270

Viechtbauer, W., & Viechtbauer, M. W. (2015). Package 'metafor'. Retrieved 7 August 2016, from http://cran.r-project.org/web/packages/metafor/metafor.pdf

Wang, Y., Hu, Y. P., Wang, W. C., Pang, R. Z., & Zhang, A. R. (2012). Clinical studies on treatment of earthquake-caused posttraumatic stress disorder using electroacupuncture. *Evidence-Based Complementary and Alternative Medicine*, *2012*, 431279. doi:10.1155/2012/431279

Ware, J., Snow, K. K., Kosiniski, M., & Gandek, B. (1993). *SF-36 health survey: Manual and interpretation guide*. Boston, MA: Quzlity Metric Inc. and The Health Assessment Lab.

Zhang, H., Ran, L., Yuan, X., Wang, K., Hu, Z., & Yang, J. (2010a). Clinical observation on acupuncture and moxibustion in treating post traumatic stress disorder after 5.12 earthquake. *Journal of Chengdu University of TCM*, *33*, 4.

Zhang, H., Yuan, C., Ran, L., Yuan, Q., Yuan, X., Hu, Y., … Yang, J. (2010b). RCT research of different acupuncture therapies in treating posttraumatic stress disorder after Wenchuan "5.12" earthquake. *China Journal of Traditional Chinese Medicine and Pharmacy*, *25*, 105–1510.