



Efficacy of Complementary and Alternative Medicine Therapies for Posttraumatic Stress Disorder

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PREFACE

Health Services Research & Development Service's (HSR&D's) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers, as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout VA.

HSR&D provides funding for four ESP Centers and each Center has an active VA affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence,
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of HSR&D field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at nicole.floyd@va.gov.

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EVIDENCE REPORT

INTRODUCTION

Posttraumatic stress disorder (PTSD) is among the most common Axis I disorders, with an estimated lifetime prevalence in the U.S. of approximately 7 percent.¹ PTSD is often chronic and is associated with significant adverse consequences, including high rates of depression and other psychiatric comorbidities; substance abuse; suicidality; impaired social, occupational, and family functioning; decreased quality of life; and increased rates of medical morbidity, health risk behaviors, and health service use.¹⁻⁹ PTSD is the emotional disorder most frequently associated with combat and other potentially traumatic experiences that may occur during the course of military service (e.g., sexual assault, motor vehicle injury). Over 2.2 million U.S. troops have deployed in Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF).¹⁰ One anticipated consequence of this sustained period of military operations is the increased incidence of PTSD among Veterans. Among OEF/OIF Veterans who received Department of Veterans Affairs (VA) care between 2002 and 2008, 22 percent were diagnosed with PTSD.¹¹ In addition to increased mental health service use among this newest generation of Veterans, the VA has witnessed the sharpest increase in mental health service use among Vietnam-era Veterans.¹² As the VA strives to anticipate and serve the treatment needs of the Veteran population, including those returning from current Middle East conflicts as well as Veterans of previous service eras, identifying and implementing effective PTSD treatment approaches remains a critical priority.

Complementary and alternative medicine (CAM) interventions are popular among consumers and are widely employed to treat diverse physical and mental health conditions.¹³ The results of a recent national survey show that nearly 38 percent of U.S. adults use CAM approaches to manage a range of physical and emotional health concerns, including pain, anxiety, and depression.^{14,15} Such widely used practices deserve careful evaluation and may hold promise as either adjunctive or primary PTSD therapies. Thus, this evidence synthesis was requested by VA Research and Development to inform decisions on the need for research in this area. This report reviews the evidence for common CAM approaches for PTSD—excluding natural products such as nutritional supplements—and examines mind-body therapies, manipulative and body-based practices, and practices that are movement-based or involve energy therapies.

BACKGROUND

The current VA/Department of Defense (DoD) Clinical Practice Guideline for the Management of Posttraumatic Stress (October 2010)¹⁶ recommends the following evidence-based, first-line therapies for PTSD: (1) trauma-focused cognitive behavioral psychotherapies, (2) stress inoculation training (SIT), and (3) pharmacotherapies. These recommendations are largely consistent with previously published practice guidelines and systematic reviews (e.g., Bisson and Andrew,¹⁷ Foa and colleagues,¹⁸ Institute of Medicine¹⁹).

Overview of Current Evidence-based PTSD Therapies

Trauma-focused psychotherapies

The category of trauma-focused psychotherapies incorporates several multicomponent, PTSD-specific interventions that share a theoretical foundation in cognitive behavioral principles. Consistent with a cognitive behavioral framework, the key components of trauma-focused psychotherapies may include *in vivo* and narrative/imaginal exposure as well as cognitive restructuring exercises. These treatments are designed to decrease emotional response through habituation and to modify maladaptive thoughts, behaviors, and emotions associated with PTSD. Most trauma-focused psychotherapy protocols combine administration of these exercises with psychoeducation and training in relaxation and anxiety-management techniques. Of note, several commonly employed relaxation techniques, such as breathing and muscle relaxation, are also consistent with CAM approaches. However, in the case of trauma-focused psychotherapies, these strategies are not hypothesized to be core mechanisms of change. Rather, they are introduced early in treatment to support the patient's later engagement in key trauma-focused elements of treatment (e.g., exposure techniques and cognitive exercises).

The most well established of the trauma-focused psychotherapies are prolonged exposure therapy, cognitive processing therapy, and eye movement desensitization and reprocessing (EMDR). Although the comparative efficacy of these interventions has not yet been established,¹⁷ collectively the category of trauma-focused therapies has a strong empirical base. On average, 56 percent of patients who enter treatment (intent-to-treat) and 67 percent of patients who complete treatment no longer meet criteria for PTSD at posttreatment.²⁰ In clinical trials, trauma-focused therapies show large effects compared to waitlist control (average effect size = 1.11) and moderate effects compared to supportive therapy (average effect size = 0.82).²⁰

Stress inoculation training approaches

SIT protocols for PTSD provide training in anxiety management and coping skills to “inoculate” against heightened stress responses that are presumed central to the maintenance of PTSD. SIT protocols provide a tool kit of cognitive behavioral and mind-body stress management techniques, including progressive muscle relaxation, breathing retraining, positive thinking and self-talk, assertiveness training, and thought stopping.¹⁶ As with trauma-focused psychotherapies, several CAM techniques (e.g., release of muscle tension and breathing techniques to invoke relaxation) are common components of these interventions. However, SIT approaches (like trauma-focused psychotherapies) are theoretically grounded in cognitive behavioral theories of change and impart training in cognitive behavioral stress management techniques. Hence, for this review, and consistent with the theoretical basis of this treatment approach, SIT is considered a cognitive behavioral intervention.

Pharmacotherapies

First-line, evidence-based pharmacotherapies for PTSD include selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs), administered as monotherapies.^{16,18,21} Both SSRIs and SNRIs are presumed to improve psychobiological dysfunction believed to be characteristic of the syndrome of PTSD. Of the SSRIs, the strongest evidence base currently exists for paroxetine and sertraline, for which response rates are near 60 percent.^{21,22}

Among the SNRIs, venlafaxine has the strongest support.¹⁶ For example, one recent randomized controlled trial (RCT) found that 78 percent of patients treated with venlafaxine experienced a positive clinical response (i.e., > 30% decrease in symptom severity) although only 40 percent achieved remission.²³ In contrast to current clinical practice guideline recommendations, it should be noted that the Institute of Medicine's recent review of PTSD therapies (2007)¹⁹ concluded that there is insufficient evidence to support the use of pharmacotherapies for PTSD. In response to this controversial recommendation, one committee member appended¹⁹ an alternative conclusion in support of SSRIs as well as novel antipsychotics. Despite current controversies, pharmacotherapies—particularly SSRIs and SNRIs—are widely accepted as standard first-line treatment.

Limitations of Current Evidence-based PTSD Therapies

Despite mounting empirical support for the treatments summarized above and tremendous efforts within the clinical research community to refine and optimize these approaches, each is associated with limitations and potential barriers to broad dissemination and uptake. Issues of access, patient preference/acceptability, and suitability are the primary limiting factors. For example, trauma-focused psychotherapies may provoke emotional responses, and some patients may have difficulty managing these reactions, or may choose not to engage in therapies that can cause emotional (albeit short-term) discomfort. Thus, the current VA/DoD Clinical Practice Guideline recommends careful screening of patients' suitability for these modalities and recommends against their use with certain patients (e.g., those with current substance abuse, psychosis, or health problems for which intense physiological arousal is contraindicated).¹⁶ Also, all current evidence-based psychotherapies require specialized training and frequent provider contact, which may limit their accessibility. This potential limitation is of particular relevance for patients located in areas in which clinical resources are limited (e.g., rural) and those whose schedules cannot readily accommodate frequent sessions (e.g., because of work constraints or lack of childcare). Finally, psychotherapies are typically delivered in mental health specialty clinics, which may present a barrier for those concerned about perceived stigma associated with receiving care in a mental health setting, or for those who distrust mental health providers.²⁴

In contrast to psychotherapies for PTSD, pharmacotherapies generally require less frequent and shorter contact with a provider and are routinely administered in both mental health and primary care clinics. However, some patients are not amenable to pharmacological interventions,²⁵ and current evidence indicates that nearly 27 percent of patients will prematurely discontinue SSRIs due to treatment failure or adverse side effects, including sexual dysfunction, weight gain, and sleep disturbance.²⁶ Finally, existing studies suggest that medications alone are often not sufficient to relieve symptoms, and there is some evidence that men are less likely than women to benefit from pharmacological PTSD treatments.²⁷ Therefore, current evidence-based treatments for PTSD are not always appropriate, well-tolerated, accessible, adequate, or congruent with patient preferences.

Complementary and Alternative Medicine

CAM is commonly used to describe a wide range of therapies that are not generally considered standard components of modern medicine as practiced by physicians in the U.S. Yet, many CAM treatments, such as acupuncture, are part of traditional medical practices in other parts

of the world. The National Center for Complementary and Alternative Medicine (NCCAM) in the National Institutes of Health (NIH) has proposed a classification system for CAM therapies that includes natural products (e.g., dietary supplements, herbal remedies, probiotics), mind-body medicine (e.g., meditation, yoga, acupuncture), manipulative and body-based practices (e.g., spinal manipulation, massage therapy), whole medical systems (e.g., traditional Chinese medicine, Ayurvedic medicine), and other alternative practices (e.g., light or magnet therapy, movement therapies). Although this definition and classification system is helpful, it is imperfect since some treatments, such as biofeedback, are considered conventional treatment by some experts and CAM treatment by others. For some CAM therapies, such as acupuncture, there is a growing body of scientific literature evaluating efficacy or possible mechanisms of action. However, for many CAM therapies there remains a lack of scientific evidence on efficacy, harms, indications, appropriate dosing, or mechanisms of action.

Rationale for an Evidence-based Synthesis of CAM Therapies for PTSD

CAM interventions are widely requested and used by mental health consumers including Veterans and active duty personnel; mental health–related concerns are among the most common reasons for seeking care from a CAM provider.^{13-15,28,29} If efficacious, these treatments may merit consideration as either first-line or adjunctive PTSD treatments. Most CAM treatments considered in this report are noninvasive or minimally invasive; considered unlikely to result in adverse side effects; and in some cases may be more congruent with individual treatment preferences than currently recommended traditional treatment options. Numerous stakeholders have expressed strong interest in fostering the evidence base for these approaches in PTSD.^{16,30} Consistent with these directives, this evidence synthesis was requested by VA Research and Development to inform decisions on the need for further research in this area. This report thus reviewed the evidence for common CAM approaches for treating PTSD.

METHODS

TOPIC DEVELOPMENT

This review was commissioned by the Department of Veterans Affairs' Evidence-based Synthesis Program. The key questions (KQs) were developed after a topic refinement process that included a preliminary review of published, peer-reviewed literature and consultations with content experts and key stakeholders in the treatment of PTSD. During this topic refinement process, selected CAM therapies were prioritized for the report; natural products (e.g., dietary supplements) were excluded. CAM therapies were classified using categories proposed by the NCCAM, and the KQs reflect this classification.

The final KQs were:

KQ 1. In adults with PTSD, are mind-body complementary and alternative medicine therapies (e.g., acupuncture, yoga, meditation) more efficacious than control for PTSD symptoms and health-related quality of life?

KQ 2. In adults with PTSD, are manipulative and body-based complementary and alternative medicine therapies (e.g., spinal manipulation, massage) more efficacious than control for PTSD symptoms and health-related quality of life?

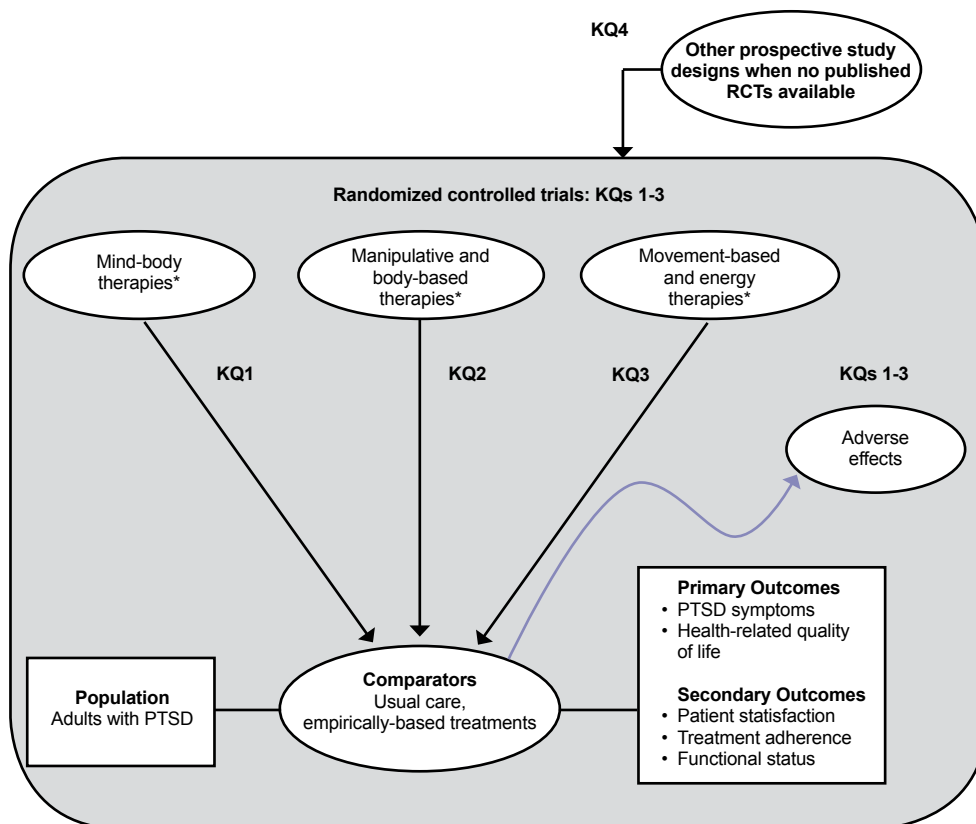
KQ 3. In adults with PTSD, are complementary and alternative medicine therapies that are movement-based or involve energy therapies more efficacious than control for PTSD symptoms and health-related quality of life?

KQ 4. For treatments evaluated in KQs 1–3 that lack randomized controlled trials, is there evidence from other study designs that suggests the potential for treatment efficacy?

ANALYTIC FRAMEWORK

We developed and followed a standard protocol for all steps of this review. Our approach was guided by the analytic framework shown in Figure 1.

Figure 1. Analytic framework for CAM therapies for PTSD



Examples of interventions:

- **Mind-body therapies:** acupuncture, meditation, yoga, deep-breathing exercises, guided imagery, hypnotherapy, progressive relaxation, and tai chi
- **Manipulative and body-based therapies:** spinal manipulation and massage therapy
- **Movement-based therapies:** Feldenkrais method, Alexander technique, Pilates, Rolfing Structural Integration, and Trager Psychophysical Integration
- **Energy therapies:** magnet therapy, light therapy, qi gong, Reiki, and healing touch

SEARCH STRATEGY

We searched English-language publications in MEDLINE® (via PubMed®), Embase®, PsycINFO®, Cumulative Index to Nursing and Allied Health Literature® (CINAHL), and the Cochrane Controlled Trials Registry from database inception through December 22, 2010. Search terms included terms for CAM therapies (acupuncture, mind-body, sensory art, yoga, reflexotherapy, musculoskeletal manipulation), PTSD, and RCTs. We used these limit terms: all adults ≥ 19 years of age, humans, and English. In addition, we searched the Published International Literature on Traumatic Stress (PILOTS) database (April 26, 2011), a specialized PTSD database maintained by the National Center for Posttraumatic Stress Disorder, to identify existing systematic reviews and studies of relaxation treatments.

We supplemented electronic searching by examining the bibliographies of included studies and review articles. When RCTs were not identified, we searched for prospective studies by adapting the sensitive “therapy filter” contained in PubMed clinical queries. To assure completeness, search strategies were developed in consultation with a master librarian. The search terms and MeSH headings for the search strategies appear in Appendix A. In addition to searching the published literature, we searched ClinicalTrials.gov (www.clinicaltrials.gov) (April 7, 2011) to identify studies in progress or completed studies that have not been published in the peer-reviewed literature.

STUDY SELECTION

Using prespecified inclusion/exclusion criteria, two reviewers assessed the list of titles and abstracts. Full-text articles identified by either reviewer as potentially relevant were retrieved for further review. Each article retrieved was reviewed by two reviewers using the eligibility criteria in Appendix B; disagreements were resolved by discussion or by a third reviewer. To be included in the evidence synthesis, a study had to (1) be an RCT, (2) compare an eligible treatment to an empirically-based treatment or to a control condition, and (3) include a sample diagnosed with PTSD. Because relaxation is often used as a placebo control in trials of psychotherapy, we further specified that relaxation interventions must be presented as an active treatment and described in sufficient detail to understand the key components. As noted earlier, studies that included relaxation training introduced within the context of a standard PTSD therapy, such as prolonged exposure or SIT, were conceptualized as non-CAM and thus ineligible for this review. In the absence of any RCT for a given treatment, we examined other prospective study designs. In response to a request from stakeholders, we categorized reasons for exclusion in a subsample of 600 studies excluded during the initial abstract review. Detailed eligibility criteria are described in Table 1.

Table 1. Summary of inclusion and exclusion criteria

Study characteristic	Inclusion criteria	Exclusion criteria
Study design	KQs 1–3: RCTs KQ 4: Other study designs when no RCTs were identified ^a	Non–English language publication Non–peer-reviewed publication
Population	Adults ≥ 19 diagnosed with PTSD using DSM criteria, validated severity measures (e.g., PTSD checklist), or clinical diagnosis Patients in acute-phase treatment (i.e., not selected for treatment-resistant PTSD)	Patients with complicated PTSD or acute suicidality Studies with eligibility criteria requiring a diagnosis of PTSD comorbid with another mental or physical illness (e.g., PTSD and substance abuse)

Study characteristic	Inclusion criteria	Exclusion criteria
Interventions	<p>Any of the following eligible treatments:</p> <ul style="list-style-type: none"> • Mind-body therapies: acupuncture, meditation, yoga, deep-breathing exercises, guided imagery, hypnotherapy, progressive relaxation, and tai chi • Manipulative and body-based therapies: spinal manipulation and massage therapy • Movement-based therapies: Feldenkrais method, Alexander technique, Pilates, Rolfing Structural Integration, and Trager Psychophysical Integration • Energy therapies: magnet therapy, light therapy, qi gong, Reiki, and healing touch 	<p>Interventions used in a continuation or maintenance phase</p> <p>Dietary supplements</p> <p>Standard psychotherapies (e.g., prolonged exposure) and extensions of these therapies (e.g., mindfulness-based cognitive therapy)</p> <p>Relaxation used as a control arm or reported without describing the key components</p> <p>Biofeedback</p>
Comparators	<p>Studies comparing an eligible treatment to a control condition such as usual care (including no treatment), supportive therapy, attention control, sham intervention, or a waitlist</p> <p>Studies comparing an eligible treatment to an empirically based treatment, prolonged exposure, cognitive processing therapy, or antidepressant medication</p>	None
Outcomes	<p>Change in level of PTSD symptoms (i.e., on self-report and/or clinician-administered measures, including remission rates) or change in quality of life (i.e., functional status and health-related quality of life)</p> <p>Social functioning, patient satisfaction with treatment, treatment adherence/retention (e.g., proportion of prescribed sessions that are completed, completion of between-session assignments), and adverse treatment effects</p> <p>Reported at ≥ 6 weeks after treatment initiation</p>	None
Setting	Patients recruited from community or outpatient mental health or general medical settings	Studies conducted outside North America, Western Europe, Australia, or New Zealand. Studies conducted outside of these countries were unlikely to be applicable to VA populations because of important differences in culture and health care systems.

^aThe eligibility criteria for nonrandomized controlled trials matched the criteria for KQs 1–3 except for study design. For each intervention that lacked eligible RCTs, we included prospective studies (nonrandomized controlled trials, controlled before-and-after studies, and prospective cohort studies and case series).

Abbreviations: DSM = Diagnostic and Statistical Manual of Mental Disorders, PTSD = posttraumatic stress disorder, RCT = randomized controlled trial, VA = Veterans Affairs

Studies identified from the ClinicalTrials.gov search were included if they were an RCT of an eligible CAM intervention and evaluated adults with PTSD. In addition, we included completed studies when a MEDLINE search (April 2011) using the name of the principal investigator did not identify a published study reporting clinical outcomes.

DATA ABSTRACTION

A trained researcher abstracted data from published reports into a data abstraction form (Appendix C); a second reviewer overread the abstracted data. We resolved disagreements by consensus among the first and second reviewer or by obtaining a third reviewer's opinion when consensus could not be reached. We abstracted the following data for each included study:

- study design
- setting
- population characteristics
- subject eligibility and exclusion criteria
- number of subjects and providers
- intervention(s)
- comparison(s)
- length of followup
- outcome(s)

For studies identified in ClinicalTrials.gov with no identified peer-reviewed publication of study results, we abstracted a limited set of data: study title, intervention, comparator, funding agency, funding dates, and study status.

QUALITY ASSESSMENT

We assessed the risk of bias pertaining to the key questions using the quality criteria described in the Agency for Healthcare Research and Quality (AHRQ) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* (hereafter referred to as the *Methods Guide*),³¹ adapted for this specific topic. For RCTs, we abstracted data on adequacy of randomization and allocation concealment, comparability of groups at baseline, blinding, completeness of followup and differential loss to followup, whether incomplete data were addressed appropriately, validity of outcome measures and completeness of outcomes reporting, and conflict of interest. Using these data elements, we assigned a summary quality score of Good, Fair, or Poor to individual RCTs. Because non-RCT studies were included for descriptive purposes, we did not assess their quality.

We assessed studies for applicability to U.S. Veterans. In addition to the quality rating for individual studies, we evaluated the overall quality of the evidence for each KQ as proposed by the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group (Appendix D).³²

DATA SYNTHESIS

We critically analyzed studies to compare their characteristics, methods, and findings. We compiled a summary of findings for each KQ or clinical topic and drew conclusions based on a qualitative synthesis of the findings. There were not sufficient studies to perform quantitative meta-analyses. When the evidence was sufficient to estimate an effect, we computed the standardized mean difference (SMD) using Hedges g for continuous outcomes, to facilitate comparisons across studies. The SMD is useful when studies assess the same outcome, but with different measures. In this circumstance, it is necessary to standardize the results for the studies

to a uniform scale to facilitate comparisons and to combine in meta-analysis. We calculated the SMD for each study by subtracting (at posttest) the average score of the control group from the average score of the experimental group and dividing the result by the pooled standard deviations (SDs) of the experimental and control groups. A negative SMD indicates a greater effect in the intervention group. For example, an effect size of -0.5 indicates that the mean decline in PTSD symptom severity for the experimental group is half an SD greater than the mean decline in the control group. SMD is commonly interpreted as small (0.2), moderate (0.5), or large (≥ 0.80).^{33,34}

RATING THE BODY OF EVIDENCE

We assessed the overall body of evidence for outcomes using a method developed by the GRADE Working Group, which classified the grade of evidence across outcomes according to the following criteria:

- High—Further research is very unlikely to change our confidence on the estimate of effect.
- Moderate—Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low—Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Insufficient—Evidence on an outcome is absent or too weak, sparse, or inconsistent to estimate an effect.

PEER REVIEW

A draft version of the report was reviewed by technical experts and clinical leadership, and their comments are provided in Appendix E.

RESULTS

LITERATURE SEARCH

We identified 1776 unique citations from a combined search of MEDLINE® (via PubMed®, n = 353), Embase® (n = 451), CINAHL® (n = 429), PsychINFO® (n = 390), Cochrane Database of Systematic Reviews (n = 32), and the PILOTS database (n = 121). By manual examination of the bibliographies of included studies and review articles, we identified four additional citations. Of these, 1738 were excluded at the title-and-abstract level. Of the 1738 studies excluded at the title-and-abstract level, we reevaluated and categorized the reason for exclusion in a subsample of 600 citations. The most common reasons for exclusion were review article (23%); a drug or a non-CAM intervention (22%); a “standard treatment” (e.g., EMDR or CBT) without a CAM comparator (14%); a sample under 19 years of age (13%); a sample that did not have PTSD (10%); and evaluation of therapies that were neither standard for PTSD nor for CAM (10%).

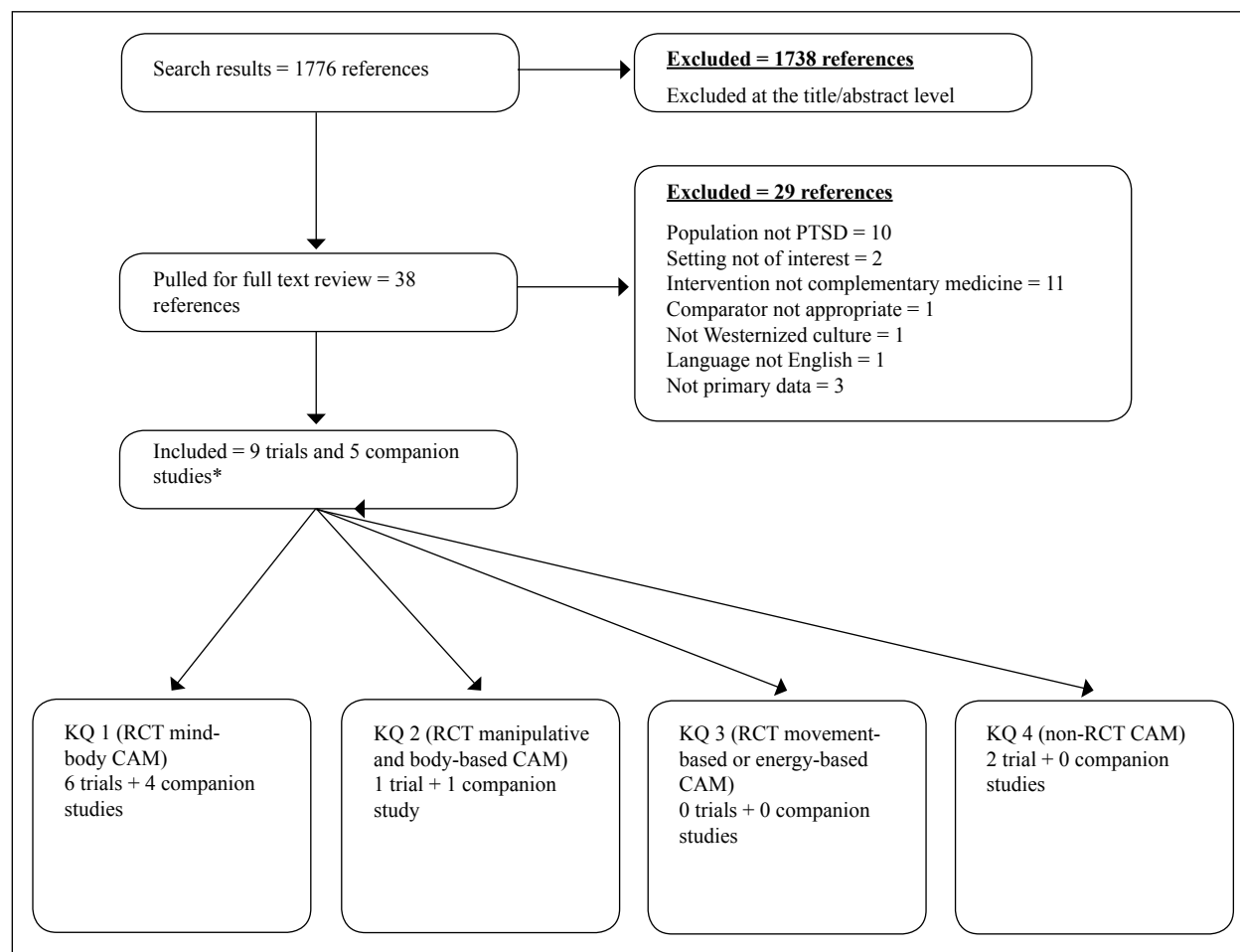
An additional 29 studies were excluded following full-text review. The question of what type of relaxation study was applicable to our report was a complicated one. Our literature search identified six citations that included a relaxation treatment arm but did not meet full eligibility criteria. Of these, one did not evaluate a population with PTSD;³⁵ one was determined not to be CAM because the relaxation was delivered in conjunction with biofeedback;³⁶ two conceptualized the relaxation as a control group rather than an active treatment;^{37,38} and one study with three citations did not describe the key components of the relaxation intervention such that it could not be categorized as CAM or otherwise.³⁹⁻⁴¹

Nine published studies were retained and abstracted for this evidence synthesis, including 7 RCTs (described in 12 articles) and 2 non-RCTs. Five articles contained previously described demographic or descriptive data for the seven RCTs; these studies are referred to as “companion” studies.

Additionally, our search of www.clinicaltrials.gov identified 438 potentially relevant, unpublished trials. Of these, 16 were RCTs of an eligible CAM therapy for PTSD and are described in the applicable KQ sections that follow. There were also three non-RCTs, described in the KQ 4 section.

Figure 2 illustrates each step of our literature search process. Appendix F provides a complete listing of articles excluded at the full-text stage, with reasons for exclusion.

Figure 2. Literature flow diagram



*Reference list includes additional references cited for background and methods plus Web sites relevant to KQs.

Abbreviations: KQ = key question, CAM = complementary and alternative medicine, PTSD = posttraumatic stress disorder, RCT = randomized controlled trial

STUDY CHARACTERISTICS

Basic characteristics of these studies are summarized in Table 2. A total of 7 RCTs (296 subjects) and 2 non-RCTs (41 subjects) met eligibility criteria. Of the RCTs, three evaluated relaxation, two evaluated meditation, and one each evaluated acupuncture and massage interventions. There were no RCTs identified that examined movement-based or energy therapies. To be eligible for participation, all studies required patients to meet DSM criteria for PTSD, and four of the seven RCTs included military Veterans. All studies reported PTSD symptom outcomes, but health-related quality of life (HRQOL), patient satisfaction, social functioning, and adverse effects were reported less frequently. Only one RCT was good quality.

Common study limitations included (1) a lack of power to draw meaningful conclusions, (2) the absence of explanations for missing data and dropouts, and (3) analyses that were performed on completers rather than intent-to-treat samples. In addition, important aspects of the study

design and sample characteristics were frequently unclear in the fair- and poor-quality articles. For example, it was difficult in every case to discern whether the groups being compared were truly comparable at baseline. The nonrandomized studies used prospective cohort and case series designs.

Table 2. Summary of study characteristics

Study	Study design (n)	Quality ^a	Intervention vs. comparator	Outcome measures ^b
<i>RCTs of mind-body interventions: KQ 1</i>				
Bormann et al., 2008 ⁴²	RCT (n = 29)	Fair	Mantram repetition vs. usual care	CAPS, PCL, Q-LES-Q-SF, FACIT-SpEx4, CSQ
Brooks and Scarano, 1985 ⁴³	RCT (n = 25)	Poor	Transcendental meditation vs. psychotherapy	PVSDS, individual items to assess employment status and family problems
Echeburúa et al., 1996 ⁴⁴	RCT (n = 20)	Poor	Progressive muscle relaxation vs. cognitive behavioral therapy	SS-PTSD, SOA
Hollifield et al., 2007 ⁴⁵	RCT (n = 84)	Good	Acupuncture vs. group cognitive behavioral therapy vs. waitlist	PSS-SR, SDI
Vaughan et al., 1994 ⁴⁶	RCT (n = 36)	Fair	Applied muscle relaxation vs. image habituation training vs. EMDR	SI-PTSD, IES
Watson et al., 1997 ⁴⁷	RCT (n = 90)	Poor	Simple relaxation instruction vs. relaxation instruction + deep breathing vs. relaxation instruction + deep breathing and thermal biofeedback	PTSD-I M-PTSD
<i>RCT of manipulative and body-based interventions: KQ 2</i>				
Price, 2006 ^{48,49}	RCT (n = 8)	Poor	Body-oriented therapy (massage) vs. waitlist	CR-PTSD
<i>Non-RCTs of CAM therapies for PTSD: KQ 4</i>				
Abramowitz and Lichtenberg, 2010 ⁵⁰	Prospective cohort (n = 36)	NA	Hypnotherapeutic olfactory conditioning	IES-R
Hossack and Bentall, 1996 ⁵¹	Case series (n = 5); 17 and 29 weeks	NA	Relaxation and visual kinesthetic dissociation	IES

^aStudy quality assessed via key quality criteria described in Agency for Healthcare Research and Quality's (AHRQ's) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.³¹

^bOutcomes limited to those with direct relevance to KQs 1–4 (i.e., PTSD severity/diagnosis, HRQOL).

Abbreviations: CAPS = Clinician-Administered PTSD Scale, CR-PTSD = Crime-Related Post Traumatic Stress Disorder Scale, EMDR = eye movement desensitization and reprocessing, FACIT-SpEx4 = Functional Assessment of Chronic Illness Therapy–Spirituality-Expanded Version 4, IES = Impact of Events Scale, IES-R = Impact of Events Scale–Revised, M-PTSD = Mississippi Scale for Combat-Related PTSD, NA = not applicable, PCL = Posttraumatic Stress Disorder Checklist (-M is military version), PSS-SR = Posttraumatic Symptom Scale–Self Report, PTSD-I = Posttraumatic Stress Disorder Interview, PVSDS = Post-Vietnam Stress Disorder Scale, Q-LES-Q-SF = Quality of Life Enjoyment and Satisfaction Questionnaire–Short Form, RCT = randomized controlled trial, SI-PTSD = PTSD Structured Interview, SOA = Scale of Adaptation, SS-PTSD = Scale of Severity of Posttraumatic Stress Disorder, SDI = Sheehan Disability Inventory

Table 3 summarizes the outcome measures included in this evidence synthesis, listing the abbreviated and full name of each instrument, format, number of items, score range, and interpretation of scoring.

Table 3. Summary of outcome measures

Abbreviation	Name of instrument	Format	# of items	Range	Interpretation
CAPS ^a	Clinician-Administered PTSD Scale	Semistructured interview	17	0–136	Higher score = more severe PTSD symptoms
CR-PTSD ^b	Crime-Related Post Traumatic Stress Disorder Scale	Self-report scale	28	0–112	Higher score = more severe PTSD symptoms
CSQ	Client Satisfaction Questionnaire	Self-report scale	8	8–36	Higher score = more satisfaction with treatment
FACIT-SpEx4	Functional Assessment of Chronic Illness Therapy–Spirituality-Expanded Version 4	Self-report scale	23	0–184	Higher score = better quality of life
IES ^c	Impact of Events Scale	Self-report scale	15	0–75	Higher score = more severe PTSD symptoms
IES-R	Impact of Events Scale–Revised	Self-report scale	22	0–88	Higher score = more severe PTSD symptoms
M-PTSD	Mississippi Scale for Combat-Related PTSD	Self-report scale	35	35–175	Higher score = more severe PTSD symptoms
PCL	PTSD Checklist	Self-report scale	17	17–85	Higher score = more severe PTSD symptoms
PSS-SR	Posttraumatic Symptom Scale–Self-Report	Self-report scale	17	0–51	Higher score = more severe PTSD symptoms
PTSD-I	Posttraumatic Stress Disorder Interview	Structured interview	17	17–119	Higher score = more severe PTSD symptoms
PVSDS	Post-Vietnam Stress Disorder Scale (unpublished)	NR	NR	NR	Higher score = more severe PTSD symptoms
Q-LES-Q-SF	Quality of Life Enjoyment and Satisfaction–Short Form	Self-report scale	14	14–70	Higher score = better quality of life
SDI	Sheehan Disability Inventory	Self-report scale	3	0–30	Higher score = greater functional impairment
SI-PTSD	PTSD Structured Interview	Structured interview	17	0–68	Higher score = more severe PTSD symptoms
SOA	Scale of Adaptation	Self-report scale	6	6–36	Lower score = better adaption to impact of sexual aggression on daily life
SS-PTSDS	Scale of Severity of Posttraumatic Stress Disorder Symptoms	Structured interview	51	0–51	Higher score = more severe PTSD symptoms

^aNumerous scoring strategies exist. The number of items/range of scores presented here refer only to the interview items that assess DSM-IV diagnostic criteria. Additional CAPS items may administered to assess functioning, response validity, and presence of associated symptoms.

^bScore is typically calculated and interpreted as the average item score.

^cThe IES does not assess Cluster D/hyperarousal PTSD symptoms, whereas the IES-R does include items to assess this symptom cluster.

Abbreviations: NR = not reported, PTSD = posttraumatic stress disorder

KEY QUESTION 1: In adults with PTSD, are mind-body complementary and alternative medicine therapies (e.g., acupuncture, yoga, meditation) more efficacious than control for PTSD symptoms and health-related quality of life?

Published literature

We identified six published RCTs that met our criteria for KQ 1. Of these, two examined meditation,^{42,43} one examined acupuncture,⁴⁵ and three examined breathing/relaxation training.^{44,46,47} These studies are summarized in Table 4 and discussed in this section.

In addition to the published literature, our search of ClinicalTrials.gov identified 16 unpublished or ongoing studies relevant to this question (Table 5).

Table 4. Characteristics of mind-body interventions (KQ 1)

Study and quality rating	Population	Design details	Intervention	Comparator	Outcomes^a
Bormann et al., 2008 ⁴² Fair	N = 29 Trauma: combat Mean age (SD): 56 (6.57) Male: 29 (100%) Military Veterans: 29 (100%)	PTSD diagnosis: DSM-IV by CAPS Key exclusions: Psychotic disorder Severe suicidality Inability to participate in a group Recruitment: PTSD orientation groups, fliers, brochures	6 weekly, 90-minute group sessions of mantram repetition + home practice Led by psychiatric nurses	Usual care	Remission: NR Response: ES = between group differences NR HRQOL: ES = between group differences NR AE: NR Followup duration: 6 weeks (end of treatment)
Brooks and Scarano, 1985 ⁴³ Poor	N = 25 Trauma: combat Mean age (SD): 33.3 (NR) Male: 25 (100%) Military Veterans: 25 (100%)	PTSD diagnosis: DSM-III (means of assessment not specified) Key exclusions: Substance abuse Major tranquilizers Psychiatric hospitalization Suicidal or homicidal Currently practicing TM Recruitment: from mental health clinic	4-day workshop on transcendental meditation (TM), then weekly 60-minute sessions for 11 weeks + home practice 20 minutes/day, twice daily) Led by Maharishi-trained leader	Individual psychotherapy	Remission: NR Response: decreased PTSD symptom severity, p < .05; emotional numbness, p < .025 HRQOL: decreased family problems, p < .05 AE: NR Followup duration: 12 weeks (end of treatment)
Echeburúa et al., 1996 ⁴⁴ Poor	N = 20 Trauma: rape/sex assault Mean age (SD): 22 (6.9) Women: 20 (100%) Veterans: none	PTSD diagnosis: DSM-III-R by SS-PTSDS Key exclusions: Other serious mental illness Time since trauma > 3 months Recruitment: Consecutive patients seeking treatment	Progressive muscle relaxation (PMR) Five 1-hour sessions Intervention not well described	Cognitive restructuring, coping skills training, and PMR	Remission: 5 of 10 treatments vs. 8 of 10 control had no symptoms Response: no between group differences HRQOL: NR AE: NR Followup duration: 5 weeks (end of treatment) and 2,4,7, 13 months

Study and quality rating	Population	Design details	Intervention	Comparator	Outcomes ^a
Hollifield et al., 2007 ⁴⁵ Good	N = 84 Trauma: childhood sexual/physical abuse Mean age (SD): 42.2 (NR) Male: 27 (32.14%) Veterans: none	PTSD diagnosis: DSM-IV by SCID Key exclusions: substance abuse, psychosis, current other active treatment for PTSD Recruitment: clinical referral, advertisement, flyers, other media, professional contacts, word of mouth	Acupuncture (traditional Chinese medicine) with 11 to 14 solid needles placed for 25–40 minutes with manipulation + 15 minutes/day of home-based therapy (ear seeds)	Cognitive behavioral therapy or waitlist	Remission: NR Response (PSS-SR < 16): Acupuncture = 15 (63%), maintained at 24 weeks CBT = 9 (36%), increased to 13 (52%) at 24 weeks Waitlist = 4 (17%), NR at 24 weeks HRQOL: acupuncture and CBT groups improved compared to WL control AE: 1 in acupuncture group Followup duration: 12 weeks (end of treatment) and 24 weeks
Vaughan et al., 1994 ⁴⁶ Fair	N = 36 Trauma: childhood abuse, sexual/physical assault, transportation Mean age (SD): 32 (14.7) Male: 13 (36.11%) Veterans: none	PTSD diagnosis: DSM-III-R by SI-PTSD Key exclusions: severe personality disorder, psychosis Recruitment: from mental health clinic	Applied muscle relaxation (early recognition of anxiety, progressive muscle relaxation, passive muscle (“release-only”) relaxation, cue-controlled relaxation	EMDR or exposure therapy	Remission: no between group differences Response: no between group differences HRQOL: NR AE: NR Followup duration: 2 to 3 weeks (end of treatment) and 24 weeks
Watson et al., 1997 ⁴⁷ Poor	N = 90 Trauma: combat Mean age (SD): 45.6 (NR) Male: 90 (100%) Military Veterans: 90 (100%)	PTSD diagnosis: DSM-III-R by PTSD-I Key exclusions: NR Recruitment: NR	10 weekly, 30-minute sessions of relaxation instruction (RI) or RI + deep breathing instruction	10, weekly, 30-minute sessions of RI, deep breathing + thermal biofeedback	Remission: NR Response: NR HRQOL: NR AE: NR Followup duration: NR

^aIf comparator, outcomes given for intervention versus comparator.

Abbreviations: AE = adverse effects, CAPS = Clinician-Administered PTSD Scale, DSM = Diagnostic and Statistical Manual, EMDR = eye movement desensitization and reprocessing, ES = effect size, HRQOL = health-related quality of life, PCL = PTSD Checklist, PSS-SR = Posttraumatic Symptom Scale–Self Report, PTSD-I = Post-traumatic Stress Disorder Interview. Q-LES-Q-SF = Quality of Life Enjoyment and Satisfaction Questionnaire–Short Form, NR = not reported, NS = not significant, RI = relaxation instruction, SCID = Structured Clinical Interview for DSM, SD = standard deviation, SI-PTSD = PTSD Structured Interview

Meditation

Although various typologies of meditation practice exist, meditation may be broadly classified as concentrative or nonconcentrative (e.g., mindfulness meditation), depending on the manner in which mental attention is entrained. Concentrative techniques are those in which the practitioner intensely focuses on a particular object (e.g., a candle flame, the sensation of breathing, a word or sound) and tries to repeatedly bring focus back to the object if attention falters. In contrast, nonconcentrative techniques encourage practitioners to cultivate awareness and acceptance of all mental events. The goal is to observe moment-to-moment shifts in one's internal experiences without controlling or judging their content.

In this evidence synthesis, we identified two studies^{42,43} involving a total of 54 patients that compared concentrative meditation to control (1 study) or to an active comparator (1 study). Both studies enrolled samples of male combat Veterans into group-based interventions and encouraged regular home practice. Sample sizes were relatively modest ($n = 25$ to 29), treatment length was brief (6 to 12 weeks), and outcomes were assessed at posttreatment only. We did not identify any published studies of nonconcentrative meditative techniques for PTSD.

Bormann and colleagues (2008)⁴² conducted a fair-quality RCT of 29 male combat Veterans who met DSM-IV criteria for PTSD. Participants were recruited from a VA medical center via clinical orientation groups or flyers and brochures. Participants randomized to the mantram intervention received six, 90-minute, weekly group sessions co-led by two psychiatric nurses. Session content included the use of mantram repetition (i.e., the spiritual practice of repeating a sacred word or phrase) to manage PTSD symptoms, slow down thinking to decrease reactivity, and foster mindfulness to train attention. Home practice and self-monitoring were encouraged. Participants randomized to this condition were allowed to maintain usual care, including medications. Patients allocated to the control condition received "usual care" that was not described further. Key inclusion criteria were male VA participants diagnosed with combat-related PTSD. Those with current psychosis or severe suicidality or those deemed unable to participate in a group were excluded.

Outcomes were assessed at posttreatment (6 weeks). PTSD severity was assessed with the Clinician-Administered PTSD Scale (CAPS) and PTSD checklist (PCL). HRQOL was assessed with the Functional Assessment of Chronic Illness Therapy–Spirituality-Expanded Version 4 (FACIT-SpEx4) and Quality of Life Enjoyment and Satisfaction Questionnaire–Short Form (Q-LES-Q-SF). Satisfaction with the mantram intervention was assessed with the Client Satisfaction Questionnaire (CSQ). Adverse effects and treatment adherence (i.e., group session adherence, home practice) were not reported. Steps to ensure treatment fidelity included the use of a treatment manual and expert review of randomly selected session recordings. This trial was conceptualized as a feasibility study, and some of its limitations were consistent with a preliminary effort, including nonblinding of group assignment, failure to report or address missing data, and a lack of followup assessments. In addition, the authors did not report or account for potential baseline between-group differences (e.g., PTSD severity) that may have influenced the findings.

Participants were randomized to the mantram intervention ($n = 14$) or control ($n = 15$). Change scores and effect sizes were provided for all outcome measures. However, because no inferential analyses were conducted, the statistical significance of reported differences was unclear. Posttreatment decreases in the severity of PTSD symptoms were larger in the intervention group

compared to control. For the CAPS, mean change was -4.79 (SD = 7.45) versus -2.64 (SD = 5.44); effect size: -0.33. For the PCL, mean change was -8.79 (SD = 12.64) versus -1.20 (SD = 7.95); effect size: -0.72. A similar pattern of improvement was observed on both measures of HRQOL. For the Q-LES-Q-SF, mean change was 0.64 (SD = 0.93) versus 0.07 (SD = 0.70); effect size: 0.70. For the FACIT-SpEx4, mean change was 10.14 (SD = 9.49) versus 2.64 (SD = 12.62); effect size: 0.67. Eighty-six percent of participants who completed the mantram intervention, including those initially randomized to the waitlist control, rated their treatment satisfaction as “moderate to high” on the CSQ (mean scores not provided).

Brooks and Scarano (1985)⁴³ conducted a poor-quality RCT that allocated 25 patients to either a 12-week transcendental meditation (TM) group (n = 13) or individual psychotherapy (n = 12). TM is a spiritually-based form of mantram. All potential participants were seeking treatment for combat-related trauma symptoms at the Denver Vet Center. No specific inclusion criteria were listed, and it was not clear if all participants met full diagnostic criteria for PTSD. Exclusion criteria included history of psychiatric hospitalization, current suicidal or homicidal ideation, or currently practicing TM. With the exception of the study treatments, the authors did not specify whether participants were able to begin or continue other behavioral or pharmacological therapies during the study period.

TM was taught in a 4-day workshop that included daily 90-minute sessions led by an individual who was trained by Maharishi Mahesh Yogi (TM developer), followed by 11, 1-hour, weekly followup meetings. Home practice for 20 minutes twice daily was recommended. No additional information about the TM trainer was provided. Therapists providing psychotherapy to participants randomized to the comparison condition held a minimum of a master’s degree in social work or psychology. The primary study outcomes, measured at baseline and posttreatment (12 weeks), were the “degree” of PTSD and emotional numbness assessed with the Post-Vietnam Stress Disorder Scale (PVSDS), an unpublished measure. Additional items assessed aspects of HRQOL, including employment status and family problems. Adverse effects (except for discontinuation) were not reported.

Several significant design flaws limited interpretability of study findings, including the use of unpublished and unvalidated measures; failure to describe subject characteristics (although the authors indicated that there were no between-group differences at baseline); no measure of adherence (group attendance, home practice) or treatment fidelity; and failure to measure or report other treatments received during the study period. Because a single interventionist delivered the TM intervention, treatment and therapist effects were confounded. Finally, although not specifically addressed by the authors, this preliminary study enrolled a relatively modest sample size and certainly was not adequately powered for equivalence hypothesis testing (nor was it intended to be).

Comparable proportions of participants in each study arm completed 12 weeks of treatment: 10 (77%) completed TM and 8 (67%) completed individual therapy. Reasons for discontinuation were not reported. Mean pretreatment and posttreatment scores were provided for the PVSDS. However, no information was provided about possible range and interpretation of scores, which largely limited their interpretability. Controlling for pretreatment values, greater reduction in PTSD severity was observed for the TM group (9.70 ± 2.98 to 5.80 ± 4.26) versus psychotherapy group (11.71 ± 2.63 to 10.86 ± 2.85 , $p < .05$). This was also true for the Emotional Numbness Scale for

TM versus psychotherapy (3.70 ± 1.64 to 1.70 ± 1.95 versus 3.75 ± 1.03 to 3.50 ± 1.41 , $p < 0.05$, respectively). At posttreatment, those in the TM group were also more likely to report fewer family problems ($p < 0.05$), whereas no between-group difference in employment status was observed. Within-group, paired t -tests showed significant improvement on all self-reported measures for the TM group and no significant changes at posttreatment for the psychotherapy group.

To summarize, the findings of two short-term RCTs provided limited support for two forms of concentrative meditation for combat-related PTSD. Both studies examined relatively brief group therapy formats in all-male Veteran samples, with demonstrated effects on PTSD severity and HRQOL. However, both were preliminary inquiries, and design limitations compromised interpretability and generalizability of reported findings. Yet, together these studies demonstrate the feasibility of enrolling and retaining male Veterans into meditation group interventions, and both recorded improvement in posttreatment symptoms relative to baseline levels.

Acupuncture

Acupuncture, a branch of traditional Chinese medicine, has been used to treat mental illness in other countries for centuries. It comprises a varied group of procedures that can include needle placement in preselected or individually chosen points; in subcutaneous tissue or muscle; with or without manipulation, electrical stimulation or the use of “ear seeds” in addition to needle placement. However, it is unknown whether acupuncture can be used to treat PTSD successfully.

We identified a single, good-quality RCT by Hollifield and colleagues (2007)⁴⁵ that allocated 84 patients who met DSM-IV criteria for PTSD either to acupuncture ($n = 29$); cognitive behavioral therapy (CBT) sessions ($n = 28$); or a waitlist control ($n = 27$). The intervention period was 12 weeks and comprised 24 acupuncture sessions or weekly group CBT sessions. Participants in the study were recruited by clinician referrals and advertisements in the local media; no VA or DoD settings were included. Key exclusions were comorbid psychotic disorder or substance abuse or current engagement in a PTSD-specific treatment. However, participants could continue stable supportive therapy or prescribed medication for another psychiatric disorder, such as depression.

Biweekly acupuncture treatments were 60 minutes each and included a symptom interview; pulse and tongue evaluation; needle insertion, manipulation, and retention; and Vaccaria seed (or “ear seed”) placement. Participants were instructed to massage the seeds, which were taped to specific points on the ear, for 15 minutes every day between sessions. Treatment was administered by an experienced, licensed acupuncturist trained in traditional Chinese medicine. Weekly, 2-hour group CBT sessions followed a manualized protocol. To equalize amount of attention to the problem the two groups experienced, home practice of CBT methods for 15 minutes/day was also encouraged, but adherence was not measured. The training and experience level of the therapist who led the CBT groups were not specified. Only one interventionist was assigned to each intervention; thus, treatment and therapist effects were confounded.

Assessments were conducted at baseline, 12 weeks (end of treatment), and 6 months (3-month followup). PTSD severity was measured with the Posttraumatic Symptom Scale–Self Report (PSS-SR), and HRQOL was measured with the Sheehan Disability Inventory (SDI). Treatment satisfaction was assessed among those randomized to acupuncture or CBT with a 10-item scale developed by the authors ($\alpha = 0.87$). Neither treatment adherence nor treatment fidelity was reported. Among the 29 participants randomized to acupuncture, 65.5 percent were retained. Five

withdrew before initiation of treatment and thus were not included in the analyzed sample (i.e., no baseline data). An additional five participants withdrew during treatment for the following reasons: incarceration ($n = 1$); conflicting medical treatments ($n = 2$); perceived adverse effects of acupuncture ($n = 1$); and difficulty keeping appointments ($n = 1$). Of the 28 participants randomized to CBT, 75 percent were retained. Three withdrew before treatment, and 4 withdrew during treatment due to difficulty keeping appointments ($n = 2$) and unknown reasons ($n = 2$). Among the 27 participants randomized to waitlist control, 77.8 percent were retained. Three withdrew before treatment, and three withdrew during the study period for unstated reasons. Intent-to-treat analyses included all participants for whom baseline data were available: acupuncture ($n = 24$); CBT ($n = 25$); and waitlist control ($n = 24$). Missing data were estimated using the last-observation-carried-forward method.

Mean PSS-SR scores decreased from baseline to the 12-week assessment in both the acupuncture group (31.3 ± 10.1 to 15.6 ± 13.9) and CBT group (32.5 ± 6.6 to 20.0 ± 10.6 ; $p < .05$) but remained essentially unchanged in the waitlist group (30.8 ± 9.5 to 27.9 ± 12.3). At 6 months, the treatment effects on PTSD symptoms persisted (PSS-SR scores = 15.4, acupuncture; 16.7, CBT; and 27.9, waitlist control). Pairwise contrasts from 0 to 12 weeks were not statistically different between acupuncture and CBT ($p = 0.29$). Pairwise contrasts were statistically significant between both waitlist and acupuncture ($p < 0.01$) and CBT ($p < 0.01$).

Similar findings were observed for all three study arms on the SDI: scores decreased from baseline to the 12-week assessment in both acupuncture (3.8 ± 0.8 to 3.0 ± 1.3) and CBT (4.1 ± 0.8 to 3.3 ± 1.2 ; $p < .05$) but were again essentially unchanged in the waitlist control. SDI scores remained relatively stable across all three groups at 6 months. As with the PSS-SR, pairwise contrasts from baseline to posttreatment for the SDI were not statistically different between acupuncture and CBT ($p = .83$); However, there were statistically significant differences between waitlist and both acupuncture ($p = .01$) and CBT ($p < .01$). Global satisfaction with care was high, and there was no significant difference between groups in both acupuncture and CBT.

In summary, the findings from a single, good-quality RCT suggested that a 12-week course of acupuncture treatments was similar to group CBT (although not powered for equivalence hypothesis testing) and more effective than no acupuncture in reducing PTSD symptoms and improving HRQOL. The clinical improvement associated with acupuncture or CBT persisted for at least 3 months after completion of treatment.

Relaxation

Three studies involving 146 patients^{44,46,47} compared forms of relaxation training to active comparators; one also included a third, attention control arm⁴⁷ Study quality ranged from poor^{44,47} to fair.⁴⁶

The RCT by Echeburúa and colleagues (1996)⁴⁴ randomly assigned 20 women who had experienced sexual aggression in the past 3 months to a CBT-based intervention that included cognitive restructuring plus coping skills training and progressive muscle relaxation (PMR)—or to PMR alone. In this comparative effectiveness design, both interventions consisted of five, 60-minute, weekly sessions administered by a doctoral-level therapist with 5 years' experience conducting CBT for sexual assault-related PTSD. The therapist also was responsible for conducting all study assessments. Participants were recruited from three

psychological counseling centers for women in Spain. All met DSM-III-R criteria for acute PTSD (i.e., symptoms had persisted for > 1 month and < 3 months) per the Scale of Severity of Posttraumatic Stress Disorder Symptoms (SS-PTSDS). Severe psychiatric comorbidity (e.g., schizophrenia, mental deficiency) was the primary exclusion criteria.

The cognitive restructuring plus specific coping skills training intervention included:

- psychoeducation about sexual trauma and PTSD
- introduction of CBT techniques for modifying maladaptive thoughts and feelings related to sexual trauma
- coping skills training including PMR, thought stopping, and distraction
- instructions for self-guided exposure to avoided situations and stimuli

The PMR alone intervention provided psychoeducation and training in progressive muscle relaxation. For both conditions, PMR followed methods proposed by Bernstein and Borkovec.⁵² This study was considered poor quality because of nonblinding of subjects or the assessor/therapist, unclear randomization and allocation concealment, and no intent-to-treat analysis. Power was not calculated a priori and clearly was inadequate for comparative analyses. There was no measure of treatment fidelity, and adherence was unclear. Finally, inclusion of PMR in both intervention arms complicated interpretation of study findings in the absence of a clearer description of how applying this technique may have differed between treatment conditions.

Outcomes were assessed at baseline; posttreatment (5 weeks after baseline); and at approximately 2, 4, 7, and 13 months after baseline (i.e., 1, 3, 6, and 12 months after the end of treatment). It appears that all 20 patients completed treatment and remained in the study through the 13-month assessment. At baseline, mean score on the SS-PTSDS, the primary outcome measure, was 35.5 (SD = 7.96). Within groups, mean scores decreased from baseline to posttreatment, from 36.7 (SD = 8.59) to 12 (SD = 6.94) for the cognitive restructuring plus coping skills group, and from 34.3 (SD = 7.54) to 18.7 (SD = 9.20) for the PMR group. Scores decreased slightly in subsequent assessments in both groups. There were no statistically significant between-group differences. At posttreatment, 8 out of 10 patients (80%) in the cognitive restructuring plus coping skills group and 5 out of 10 (50%) in the PMR group no longer met criteria for PTSD. Additional improvements were observed at the 2-month followup (100% remission in the cognitive restructuring plus coping skills group versus 80% remission in the PMR group), which were retained at the 13-month followup. Results of the Scale of Adaptation (SOA), a measure of functional adaptation to the experience of sexual aggression, reflected significant reductions in both treatment groups, which were retained at the 13-month followup.

In the RCT by Vaughan and colleagues (1994),⁴⁶ applied muscle relaxation (AMR) was compared to eye movement desensitization (EMD) and image habituation training (IHT), a form of exposure therapy. Thirty-six patients with PTSD referred to an outpatient PTSD clinic were randomly assigned to AMR (n = 11), EMD (n = 12), or IHT (n = 13). Participants' trauma histories included violent crime, rape, child abuse, and motor vehicle accident. Schizophrenia and severe personality disorders were exclusions. At baseline, 22 percent reported subclinical levels of Category C (avoidance/numbing) symptoms and thus did not meet full DSM-III-R criteria for PTSD.

Patients were scheduled to attend four sessions over a 2- to 3-week period. The AMR treatment, adapted from Ost (1987),⁵³ taught participants to recognize early signs of anxiety and to apply relaxation techniques to manage and quell anxiety. During the treatment sessions, three increasingly brief, relaxation techniques were sequentially introduced: progressive muscle relaxation, release-only relaxation (i.e., passive muscle relaxation), and cue-controlled relaxation, in which self-instruction to “relax” was paired with the state of relaxation. Participants were expected to practice these techniques between sessions, 40 minutes per day. In the EMD condition (now known as eye movement desensitization and reprocessing [EMDR]), saccadic eye movements (induced by asking the patient to track the therapist’s hand as it moved rapidly across the visual field) were paired with associative elements of the traumatic memory, including imagery, cognition, affect, and physiological sensations. No between-session work was assigned to participants in the EMD group. Patients in the IHT group were required to listen to continuous-loop, audiotaped descriptions of their trauma and to record cognitions and anxiety levels on a homework sheet for 60 minutes per day. The level of education and training of the therapists was not reported, but all were trained in EMD by Francine Shapiro, the originator of the technique. This study was considered fair quality because of ambiguous reporting of methods (including lack of clarity about the adequacy of randomization, nonblinded assessments, inadequate treatment of missing data, lack of intent-to-treat analyses) and inadequate statistical power.

The primary PTSD-related outcome measure was the PTSD Structured Interview (SI-PTSD), assessed by a blinded rater at baseline, posttreatment (2 to 3 weeks), and 3 months. All three treatment groups were associated with significant improvement ($p < 0.001$) in SI-PTSD scores at the posttreatment and 3-month followup. There were no between-group differences in SI-PTSD scores at the baseline, posttreatment, or 3-month assessments. Adverse effects were not reported.

In a 3-arm, 10-week trial, Watson and colleagues (1997)⁴⁷ randomized 90 male Vietnam-era Veterans to 1 of 3 relaxation training conditions: simple relaxation instruction (RI), RI plus deep breathing, or RI plus deep breathing plus thermal biofeedback. All were recruited by a technician at the St. Cloud, Minnesota VA Medical Center; additional details about recruitment procedures were not reported. All met DSM-III-R criteria for PTSD, per the Posttraumatic Stress Disorder Interview (PTSD-I). Additional details about diagnostic procedures or specific inclusion/exclusion procedures were not provided. The technician, who was trained by a doctoral-level psychologist with 7 years’ experience in biofeedback and relaxation therapies, was responsible for recruitment, administration of all study treatments, and all study assessments—and thus was not blinded to treatment group assignment.

All 3 treatment conditions consisted of 10, 30-minute sessions conducted in a quiet, dimly lit laboratory in which participants were seated in a reclining chair and provided 10 minutes to adapt to room temperature before beginning each session. Regardless of treatment group assignment, each participant was attached to a biofeedback apparatus that monitored finger temperature and frontalis muscle tension. Participants randomized to the RI group were instructed to “relax as much as possible” during the sessions. Those in the RI plus deep breathing condition were also given instruction in deep breathing prior to each session and instructed to practice relaxing and deep breathing throughout the 30-minute session. Those in the RI plus deep breathing plus thermal biofeedback condition were additionally told that they would hear a tone, indicating their level of relaxation, and instructed to increase their finger temperature and lower the tone as much as possible by relaxing during the session. Thus, the three treatment arms

could be conceptualized as an attention control (RI), relaxation/CAM intervention (RI + deep breathing), and biofeedback/traditional treatment.

Outcomes included PTSD-I total and individual item scores, Mississippi Scale for Combat-Related PTSD (M-PTSD), finger temperature, and frontalis muscle tension. This study was considered poor quality. Key limitations included unclear randomization and allocation concealment; inadequate treatment of incomplete outcome data; nonblinding of subject, provider, and assessor; no intent-to-treat analysis; and no power or sample size calculation/underpowered for comparative analyses. Adverse effects were not reported.

In the completer sample, significant pretreatment versus posttreatment (Week 10) differences were observed for two PTSD symptoms assessed by individual items on the PTSD-I: intrusive memories ($p < .01$) and exaggerated startle response ($p < .05$), as well as M-PTSD total scores ($p < .05$) and middle-finger skin temperature, reported as degrees Fahrenheit ($p < .05$). However, no time-by-treatment group differences were noted. Analysis of outcome data was limited to those who completed at least 9 of the 10 treatment sessions. Those who missed more than one session were replaced by other volunteers; intent-to-treat results were not reported.

To summarize, the findings of three RCTs provided limited support for relaxation interventions for PTSD. However, none of these relatively small studies was adequately powered for comparisons of active treatment groups, and significant design flaws limited interpretability of study findings.

Overall, the findings from six published RCTs that included a mind-body complementary and alternative medicine therapy as an intervention demonstrated the following:

- Meditation techniques were associated with moderate improvements in symptoms and HRQOL compared to usual care only (one fair-quality study) and decreased symptom severity compared to individual psychotherapy (one poor-quality study).
- The clinical effectiveness of a course of acupuncture as a treatment for PTSD was similar to that of group CBT and greater than waitlist control (one good-quality RCT).
- Relaxation training was associated with moderate clinical improvement, but studies were small and favored the active comparator. Because 95 percent confidence intervals were large, an important clinical benefit for active comparators versus relaxation treatment was possible (three poor-quality RCTs).

Unpublished literature

Our search of ClinicalTrials.gov identified 16 RCTs relevant to KQ 1. These studies are summarized in Table 5, organized alphabetically by trial name. We identified eight ongoing trials that are examining the following CAM interventions: acupuncture, emotional freedom techniques, guided imagery/imagery modification, mind-body skills, mindfulness meditation, relaxation, and yoga. In addition, we identified six completed studies for which we could not identify a publication that reported clinical outcomes; they included these interventions: acupuncture, emotional freedom techniques, guided imagery, mindfulness-based stress reduction, and yoga. There was also one trial on yoga with status listed as “unknown.” Of the completed studies, two had funding stop dates of April 2009 or earlier, raising the possibility of publication bias for these interventions. The authors of these two studies were contacted, and for one study (Acupuncture for Posttraumatic Stress Among Military Personnel), a manuscript is in development.

Table 5. Ongoing RCTs of mind-body interventions (KQ 1)

Study title	VA/DoD population?	Intervention	Comparator	Sponsor and clinicaltrials.gov ID	Funding start and stop date	Status
A Controlled Breathing Course for Social & Emotional Health for Vietnam Veterans with Chronic PTSD-RCT ^a	Y	Yoga breathing technique; single group assignment	Not clearly specified	The University of Queensland NCT00256477	Mar 2005–Oct 2005	Completed ^b
Acupuncture for the Treatment of Posttraumatic Stress Among Military Personnel ^a	Y	Acupuncture	Waitlist	Henry M. Jackson Foundation NCT00320138	Mar 2006–Oct 2007	Completed
Effectiveness of Three Different Psychotherapies for Chronic Post-Traumatic Stress Disorder	N	Interpersonal psychotherapy	1. Prolonged exposure 2. Relaxation	NIMH NCT00739765	Apr 2008–Mar 2013	Recruiting
Effect of EFT on Psychological States in a Veterans Population ^a	Y	Emotional Freedom Techniques	Standard care	Soul Medicine Institute NCT0074341	Dec 2008- May 2010	Completed
Efficacy of Yoga for Treatment-Resistant Posttraumatic Stress Disorder	N	Yoga	Women’s health education	Justice Resource Institute NCT00839813	Nov 2008–May 2011	Recruiting
Evaluation of a MCYI as Adjunct of Psychiatric Treatment for Vietnam Veterans With PTSD-RCT ^a	Y	Yoga	Usual care	The University of Queensland NCT00256464	Jun 2007–Jan 2008	Unknown
Evaluation of Telehealth Interventions for Post-Trauma Stress ^a	Y	Mindfulness Telehealth Intervention	Self	Samueli Institute for Information Biology NCT00350584	Feb 2007–Apr 2008	Completed
Examining the Effect of Acupuncture on Sleep Difficulties Related to Post Traumatic Stress Disorder	Y	Acupuncture	1. Sham acupuncture 2. No intervention	Department of Veterans Affairs NCT00868517	Oct 2009–Sep 2011	Recruiting
Guided Imagery for Military Sexual Trauma-Related Posttraumatic Stress Disorder (PTSD) ^a	Y	Guided imagery	Music	Duke University NCT00635635	Oct 2007–Mar 2010	Completed

Study title	VA/DoD population?	Intervention	Comparator	Sponsor and clinicaltrials.gov ID	Funding start and stop date	Status
Mechanistic Pathways of Mindfulness Meditation in Post-Traumatic Stress Disorder	Y	1. Slow breathing 2. Meditation 3. Meditation + slow breathing	Sitting quietly	Oregon Health and Science University NCT00778960	Jan 2009–Sep 2013	Recruiting
Mind-Body Skills Groups for the Treatment of War Zone Stress in Military and Veteran Populations	Y	Mind-body skills	Standard treatment	The Center for Mind-Body Medicine NCT01093053	Sep 2010–Aug 2012	Recruiting
Mindfulness Based Stress Reduction for Posttraumatic Stress Disorder: A Pilot Study ^a	Y	Mindfulness-based stress reduction	Usual care	Seattle Institute for Biomedical and Clinical Research NCT00880152	Sep 2008–Dec 2009	Completed
Neural Correlates of PTSD Prevention With Mindfulness Based Stress Reduction (MBSR) in Iraqi Veterans ^a	Y	Mindfulness-based stress reduction	Supportive therapy	Department of Veterans Affairs NCT01058031	Jan 2007–Nov 2010	Completed
Pilot of Acupuncture to Improve Quality of life in Veterans with Traumatic Brain Injury (TBI) and Post-Traumatic Stress Disorder (PTSD)	Y	Acupuncture	Standard care	Department of Veterans Affairs NCT01060553	Jul 2010–Jun 2011	Recruiting
Psychological Symptom Change in Veterans After Six Sessions of EFT (Emotional Freedom Technique)	Y	Emotional Freedom Technique	Waitlist	Soul Medicine Institute NCT01117545	May 2010–Jun 2013	Recruiting
Study on the Psychotherapeutic Treatment for the Feeling of Being Contaminated After Childhood Sexual Abuse	N	Imagery modification	Waitlist	Goethe University NCT00976859	Sep 2009–Dec 2011	Recruiting

^aNo publication found.

^bAuthor contacted, no results published in peer-reviewed journal as of May 2011.

Abbreviations: NCCAM = National Center for Complementary and Alternative Medicine, NIMH = National Institute of Mental Health, PTSD = posttraumatic stress disorder, RCT = randomized controlled trial

KEY QUESTION 2: In adults with PTSD, are manipulative and body-based complementary and alternative medicine therapies (e.g., spinal manipulation, massage) more efficacious than control for PTSD symptoms and health-related quality of life?

Published literature

We identified one poor-quality RCT by Price (2006)^{48,49} of body-oriented therapy in eight adult female subjects with histories of childhood sexual trauma (Table 6).

Table 6. Characteristics of manipulative and body-based interventions (KQ 2)

Study	Population	Design details	Intervention	Comparator	Outcomes ^a
Price, 2006 ^{48,49}	N = 8 Trauma: rape, childhood physical/sexual abuse Mean age (SD): 38 (NR) Women: 8 (100%) Veterans: none	PTSD diagnosis: Severity of PTSD by PCL Key exclusions: Substance abuse, currently involved in a violent relationship, Not currently in active psychotherapy, Not able to pay 50% of the cost for massage Recruitment: clinical referral	8 weekly 60-minute sessions of body-oriented therapy (massage) + body awareness education and body-mind integration	Waitlist	Remission: Score below clinical cut-off—intervention group, 2 of 4 vs. waitlist group, 1 of 4 Response: symptom improvement, intervention group, p < .01 HRQOL = NR AE = NR Followup duration: 9 weeks (end of treatment)

^aIf comparator, outcomes given for intervention versus comparator.

Abbreviations: AE = adverse effect, NR = not reported, HRQOL = health-related quality of life, PCL = PTSD Checklist

Although formal PTSD diagnosis was not a study inclusion criterion, six of the eight women screened positive for PTSD at study inception, as indicated by baseline administration of the Crime-Related Post Traumatic Stress Disorder Scale (CR-PTSD)—the primary outcome variable. Participants were recruited through clinician referral, free advertisements on women’s groups’ Web sites, and emails to select graduate students; no VA or DoD settings were included. To be included, women had to be in active psychotherapy; be willing to stop any current bodywork one month prior to entering the study; and agree to pay 50 percent of the cost for the study-related bodywork sessions. Exclusion criteria were current substance abuse, involvement in a violent relationship, or psychiatric hospitalization within the last year. There was no requirement to maintain stable dosages of psychotropic medications. Four subjects were randomly allocated to eight, 1-hour sessions of Swedish-type massage, body awareness education, and “body-mind integration” (i.e., exploration of links between internal experiences and physiological sensations). The other four subjects were allocated to a waitlist control. The primary outcome measure, assessed at 9 weeks, was the CR-PTSD.

Pretreatment and posttreatment (Week 9) changes in scores were presented graphically, but axis labels were unclear, which hampered interpretation. Study limitations included incomplete descriptions of study participants, small sample size, and the potential for differing cointerventions across groups. In addition, the principal investigator collected and analyzed all data, and was not blinded to treatment condition. Although not explicitly stated, it appeared that the principal investigator also was the sole interventionist; her level of experience providing bodywork was not stated. This limitation introduces potential bias and confounds treatment and therapist effects. As is common for a small preliminary study, treatment adherence and fidelity were not assessed.

The sample was relatively homogeneous: 89 percent were white; 71 percent reported incomes equal to or greater than \$25,000; and all had at least a bachelor-level education. Sexual orientation was fairly varied—nearly half reported homosexual or bisexual orientations. All subjects had been in psychotherapy at least 1 year (range 1 to 20), and five of eight women were taking psychotropic medications. By Week 9, clinical remission (per recommended screening cutoffs on the CR-PTSD) had occurred in two of four women in the intervention group and one of four women in the waitlist control group. Pretreatment and posttreatment within-group comparisons showed significant improvements for the intervention group but not for the control group on the CR-PTSD; between-group comparisons were not significant.

In summary, the findings from one small, poor-quality RCT in a relatively homogeneous sample provided modest support for the application of body-oriented therapy as an adjunctive treatment for women survivors of childhood sexual assault. We found no RCTs of manipulative or body-based CAM interventions in men, military or Veteran samples, or individuals with PTSD related to more recent traumatic stressors (versus childhood abuse). We were unable to identify published RCTs of other manipulative or body-based CAM interventions, such as chiropractic medicine and naturopathy, or of alternative applications and forms of massage therapy.

Unpublished literature

Our search of ClinicalTrials.gov did not identify any RCTs relevant to KQ 2.

KEY QUESTION 3: In adults with PTSD, are complementary and alternative medicine therapies that are movement-based or involve energy therapies more efficacious than control for PTSD and health-related quality of life?

Our literature search identified no published RCTs of movement-based or energy therapies for PTSD.

Unpublished literature

Our search of ClinicalTrials.gov did not identify any RCTs relevant to KQ 3.

KEY QUESTION 4: For treatments evaluated in KQs 1–3 that lack RCTs, is there evidence from other study designs that suggests the potential for treatment efficacy?

Published literature

We identified two nonrandomized, prospective studies (Table 7) that assessed clinical outcomes over time among patients with PTSD who received a CAM intervention as defined in the Methods section.

Table 7. Characteristics of nonrandomized CAM treatment studies (KQ 4)

Study	Population	Design details	Intervention	Comparator	Outcomes
Abramowitz and Lichtenberg, 2010 ⁵⁰	Israeli combat Veterans with PTSD by DSM-IV. Mean age: 41.2 (12.2) Women: 0% Veterans: 100%	Prospective cohort (N = 36) Outcomes: 1. Immediately posttreatment (6 weeks) 2. 6 months 3. 1 year	Hypnotherapeutic olfactory conditioning Six 1.5-hour sessions over 6 weeks	NA	Remission: NR Response: IES-R; improvement was significant at the 6-week posttreatment assessment and remained improved at 6 and 12 months
Hossack and Bental, 1996 ⁵¹	Male volunteers who met DSM-III-R criteria for PTSD Mean age: 34.8 (10.26) Women: 0% Veterans: 0%	Multiple baseline design across subjects (N = 5) Outcome: Subjects 1 and 2 received intervention at 3 weeks from baseline; subject 3 received intervention at 6 weeks from baseline; subjects 4 and 5 received intervention at 9 weeks from baseline	4 therapy sessions including Relaxation: Jacobson’s method and guided imagery Two sessions Visual kinesthetic dissociation Two sessions	Baseline	Response: 3 patients reported decrease in intrusive imagery, 1 reported “less clear cut improvement,” and 1 showed “no improvement”

Abbreviations: DSM = Diagnostic and Statistical Manual of Mental Disorders, IES-R = Impact of Events Scale-Revised, NA = not applicable, NR = not reported, PTSD = posttraumatic stress disorder

A prospective cohort study by Abramowitz and Lichtenberg (2010)⁵⁰ involved 36 Israeli veterans with combat-related PTSD and treatment-resistant, olfactory-induced flashbacks. DSM-IV diagnostic criteria were determined by semistructured, clinical interview. Participants underwent a form of brief hypnotherapy that entailed six, 90-minute, weekly hypnotherapeutic olfactory conditioning sessions in addition to standard CBT and stress management strategies (including imaginal exposure to the traumatic event). The core components of the intervention included:

- Session 1: repeated pairing of pleasant memories with a pleasant-smelling essential oil (i.e., classical conditioning)
- Session 2: hypnotic induction, imaginal reexperiencing of functioning well under stress,

paired with hypnotic suggestion that the participant can manage PTSD-related intrusive memories and flashbacks

- Session 3: use of guided imagery, hypnosis, and suggestion around themes of mastery, control, and safety, paired with the pleasant scent identified in the initial session
- Sessions 4 and 5: repeated imaginal exposure to traumatic memories under hypnosis, paired with the pleasant scent
- Session 6: review of treatment gains, new skills, and plans to maintain and use new skills, particularly when triggered by olfactory stimuli

Compared to baseline, the Impact of Events Scale-Revised (IES-R) scores were significantly improved at 6 weeks, 6 months, and 12 months. The investigators also reported significant decreases at 12 months, relative to baseline, in dosage and use of SSRIs, benzodiazepine, and neuroleptic medications.

The multiple baseline case series by Hossack and Bentall (1996)⁵¹ examined a visual-kinesthetic dissociation intervention in five male U.K. residents who reported severe intrusive imagery and met DSM-III-R criteria for PTSD. Study diagnoses were determined by forensic psychiatrists and confirmed by brief clinical interview by the lead author. Participants' trauma histories included surviving an industrial helicopter crash ($n = 1$) and witnessing a crowd surge at a football stadium that resulted in 95 deaths ($n = 4$). In addition to the five participants who completed treatment, a sixth participant enrolled but dropped out during the baseline phase and was not included in study analyses. The Impact of Events Scale (IES), which assesses Cluster B ("reexperiencing") and Cluster C ("avoidance and numbing") symptoms, was the primary measure of PTSD severity. Participants also completed daily diaries of duration, clarity, and related distress. The four-session intervention was administered in two phases:

- Relaxation: In the first two individual sessions, participants were taught to apply progressive muscle relaxation and guided imagery techniques to promote relaxation. Instruction in guided imagery emphasized incorporation of multiple sensory modalities (visual, kinesthetic, auditory, olfactory, and gustatory) in preparation for the next treatment phase.
- Visual-kinesthetic dissociation: In the final two sessions, participants were taught to apply relaxation skills and multisensory imagery techniques to imagine themselves at the cinema and to switch vantage points between being within a film of their trauma (first person), watching the film (second person), and watching themselves watch the film (third person). Using a manualized protocol, participants were then taught to manipulate the color and speed of the film and to run it backward and forward while repeatedly rotating their experience of the image from the first-, second-, and third-person perspectives.

In addition to daily diaries of intrusive events, assessments were conducted at regular intervals across the 17 weeks in which this multiple baseline design study was conducted, as well as 3-month followup (29-week assessment). No descriptive or inferential statistical analyses were conducted. However, visual plots of each participant's symptom change over time were presented and discussed. The authors report "substantial" reductions in IES scores for four of the five participants (although two showed evidence of some posttreatment increase in avoidance).

Daily diary results indicated that four participants reported sizable decreases in the experience of intrusive imagery (maintained at 3-month followup), whereas one experienced a modest increase. The authors noted that daily diary results suggested important (albeit preliminary) differences in how participants responded to the different treatment components: for one participant, relaxation seemed the most potent; for another, visual-kinesthetic dissociation had the greatest impact; and two others seemed to respond to both interventions.

In summary, the two published, nonrandomized studies identified by our systematic search provided little evidence of broad potential efficacy in PTSD for any of the CAM interventions of interest. One study⁵⁰ presented initial pilot findings of a multimodal intervention that included both CAM (hypnotherapy, guided imagery) and imaginal exposure techniques. Although initial findings are promising, the study appears most applicable to the subgroup of combat Veterans who are particularly sensitive to olfactory triggers. Because the study sample was limited to men, it provided no additional information about the potential efficacy of CAM modalities in women. Likewise, a second study in five males provided limited initial information about the feasibility and potential utility of brief CAM intervention that included instruction in relaxation skills and imagery techniques including imaginal exposure.

In addition to these studies, one additional nonrandomized study,⁵⁴ which was published after we conducted our literature search, was identified during the peer review process. In a study by Rosenthal and colleagues (2011), five OEF/OIF Veterans who met DSM-IV diagnostic criteria for combat-related PTSD were instructed in transcendental meditation (TM) by a certified instructor and asked to practice the technique for 20 minutes, twice daily, during the 12-week study period. Clinician support was provided through the study duration via biweekly, face-to-face meetings, as well as telephone, email, and text message contacts. At 8-week followup, patients showed improvements in the clinician-rated PTSD symptom severity (CAPS: *M* change score = 31.4, *p* = 0.02), self-reported PTSD symptom severity (PCL: *M* change score = 24.00, *p* < .02), and self-reported quality of life (Q-LES-Q-SF: *M* change score = -13.00, *p* < 0.01). The results of this small, uncontrolled study provide additional preliminary support for applications of meditation in Veterans with PTSD.⁵⁴

Unpublished literature

Our search of ClinicalTrials.gov identified two non-RCTs relevant to KQ 4. These studies are summarized in Table 8, organized alphabetically by trial name. Both trials examined yoga. One is still recruiting, but the other is completed with a funding stop date of April 2009 or earlier, raising the possibility of publication bias for this intervention.

Table 8. Nonrandomized studies (KQ 4)

Study Title	VA/DOD population?	Intervention	Comparator	Sponsor and clinicaltrials.gov ID	Funding start and stop date	Status
Evaluation of a Yoga Intervention for Post-Traumatic Stress Disorder	Y	Yoga	None	Brigham and Women's Hospital NCT00962403	Aug 2009–Dec 2010	Recruiting
Yoga as a Therapy for Traumatic Experience ^a	Y	Yoga	None	Samueli Institute for Information Biology NCT00269490	Dec 2005–Aug 2007	Completed

^aNo publication found

SUMMARY AND DISCUSSION

This evidence synthesis was requested by VA Research and Development to review and summarize the empirical evidence for applications of common CAM therapies to the treatment of PTSD. Four KQs were identified to examine the efficacy of mind-body therapies (KQ 1), manipulative and body-based therapies (KQ 2), movement-based therapies (KQ 3), and relevant evidence derived from nonrandomized trials of CAM interventions for PTSD (KQ 4).

Our systematic literature search yielded six RCTs relevant to KQ 1, one relevant to KQ 2, and none to KQ 3. For KQ 4, which enabled us to expand our search beyond RCTs to include nonrandomized trials, two additional studies were identified. Most studies reviewed appeared to be preliminary investigations and were underpowered, limited by significant design flaws, and often provided inadequate descriptions of the intervention to permit replication. For each KQ, the evidence reviewed was limited. Indeed, perhaps our most striking finding overall was the relative dearth of available evidence on CAM applications for PTSD, despite clear consumer interest and widespread use of these treatments.

SUMMARY OF EVIDENCE BY KEY QUESTION

For each KQ, we summarize the strength of evidence (SOE) and magnitude of treatment effects in Table 9. Interventions are compared to control or usual care and to active treatments separately. When the strength of evidence was rated insufficient, we did not calculate a treatment effect.

Table 9. Summary of the strength of evidence for KQs 1–3

Number of studies (subjects)	Domains pertaining to strength of evidence				Magnitude of effect ^a and SOE
	Risk of bias: design/quality	Consistency	Directness	Precision	
	Risk of bias: design/quality	Consistency	Directness	Precision	PTSD symptoms: Effect estimate (95% CI)
KQ 1: Meditation vs. usual care					Low SOE
1 (29)	RCT/Fair	Not applicable	Direct	Imprecise	SMD: -0.32 (-1.46 to 0.05), self-report PCL; -0.70 (-1.06 to 0.41), interviewer-based CAPS
KQ 1: Meditation vs. active treatment					Insufficient SOE
1 (25)	RCT/Poor	Not applicable	Direct	Imprecise	Not estimated
KQ 1: Acupuncture vs. control					Moderate SOE
1 (84)	RCT/Good	Not applicable	Direct	Imprecise	SMD: -0.92 (-1.51 to -0.32), self-report PSS-SR
KQ 1: Acupuncture vs. group CBT					Low SOE
1 (84)	RCT/Good	Not applicable	Direct	Imprecise	SMD: -0.35 (-0.91 to 0.22), self-report PSS-SR
KQ 1: Relaxation vs. control					Insufficient SOE
1 (90)	RCT/Poor	Not applicable	Direct	Imprecise	Not estimated

Number of studies (subjects)	Domains pertaining to strength of evidence				Magnitude of effect ^a and SOE
KQ 1: Relaxation vs. other active treatment					Insufficient SOE
2 (56)	RCT/Fair to Poor	Consistent	Direct	Imprecise	Low ^b SMD: 0.41 (-0.42 to 1.24), interviewer based SI-PTSD SMD: 0.79 (-0.13 to 1.71), interviewer based SS-PTSD
KQ 2: Massage vs. control					Insufficient SOE
1 (8)	RCT/Fair	Not applicable	Direct	Imprecise	Not estimated
KQ 3: Movement-based and energy therapies vs. control					Insufficient SOE
None	NA	NA	NA	NA	NA

^aA negative SMD indicates a greater effect for the CAM therapy.

^bSMDs were reported separately for the two studies because a summary estimate was not indicated.

Abbreviations: CI = confidence interval, OR = odds ratio, NA = not applicable, RCT = randomized controlled trial, SMD = standardized mean difference, SOE = strength of evidence

Considered in sum, the highest quality evidence exists for acupuncture. However, strong conclusions cannot reliably be drawn on the basis of a single RCT; replication of findings is required. In addition, the active comparator in this study was group CBT, which is generally considered to be less potent than individual CBT therapies.⁵⁵ The greatest breadth of evidence exists for relaxation interventions—we identified three RCTs that examined forms of breathing and muscle relaxation. In each case, the trials were preliminary and design flaws limited interpretation of study findings, which were positive overall. Further conclusions cannot be made in the absence of well-designed investigations of these modalities.

The evidence base for meditation therapies is similarly limited by a paucity of well-designed trials, although early evidence is promising. In addition to a lack of scientific rigor and the need to replicate preliminary findings, the current literature is limited to concentrative meditative techniques. No RCTs of other common mind-body interventions, including mindfulness meditation and yoga, were identified in our review of the published, peer-reviewed literature. However, we identified 16 ongoing and/or unpublished studies registered with ClinicalTrials.gov, suggesting that this is a growing area of research. Approximately half of these trials are ongoing, and the majority are recruiting active military and/or Veteran samples. Thus, a significantly larger and broader evidence base may be anticipated within the next several years.

For manipulative and body-based CAM therapies, the evidence base is extremely limited, and for movement-based and energy therapies, we identified no RCTs, published or in progress. Thus, the current and developing evidence bases for these therapies are likely to remain insufficient for clinical or policy recommendations in the near future.

More broadly, the limitations of the current evidence preclude conclusions about specific interventions, populations, formats, settings, appropriate treatment length or “dosing,” or other refinements to the development of these approaches. We found little evidence addressing adverse effects, and retention rates, when reported, were comparable to current evidence-based treatments.

LIMITATIONS

Several limitations of the current review merit mention. First, we limited our literature search to clinical trials published in peer-reviewed, English-language journals. We also searched ClinicalTrials.gov for ongoing and unpublished trials, which served as a proxy “snapshot” of additional evidence that may be anticipated in the near future. However, our search did not extend to the “gray literature,” and thus excluded technical reports, white papers, and other evidence streams and formats that would not have been identified through standard database searches. In addition, we limited our literature search to CAM trials conducted in PTSD samples. Thus, the current review did not consider evidence of CAM applications in other anxiety disorders, major depression, or sleep disorders, for which there is symptom overlap and frequent comorbidity with PTSD. For example, in their review of CAM and self-help treatments for all anxiety disorders (generalized anxiety disorder was most frequently described), Jorm and colleagues⁵⁶ found evidence from at least one well-designed RCT in support of acupuncture, aromatherapy, massage, dance and movement, meditation, relaxation training, and yoga. Other recent evidence reviews and meta-analyses have examined applications of massage in depression;⁵⁷ energy therapies for health and mental health conditions;⁵⁸ mindfulness-based stress reduction for anxiety, depression, pain, and chronic medical conditions;⁵⁹⁻⁶¹ meditation therapy in anxiety disorders;⁶² and vipassana (mindfulness) meditation in a broad range of presentations.⁶³ Evidence of effectiveness in closely related mental illnesses could provide indirect evidence of effectiveness for PTSD.

The current review also did not include applications of CAM treatments in nonclinical populations or noninterventional designs. Because relaxation training has been employed as a placebo control condition in PTSD treatment trials, our inclusion criteria specified that relaxation interventions be presented as active treatment and that the key components be described in sufficient detail. These criteria led to the exclusion of five RCTs of relaxation interventions for PTSD, which otherwise would have met criteria for inclusion in the current review. Of these, two were excluded because relaxation was a control rather than an active comparator,^{37,38} and three were excluded due to lack of detail about the relaxation condition, such that we could not confidently categorize the interventions as CAM.³⁹⁻⁴¹ It merits mention that in these studies, relaxation showed modest effects and performed less favorably than active comparators. Thus, a wider set of inclusion criteria for the current review may have yielded a larger evidence base, and tempered enthusiasm for applications of relaxation-based monotherapies for PTSD. Likewise, we did not examine, or attempt to examine, issues of symptom overlap or comorbidity of PTSD and traumatic brain injury or other unique presentations that may be anticipated among OEF/OIF Veterans. In addition, the scope of our literature search excluded natural products (e.g., nutritional supplements), as was our charge. Finally, our review did not examine third-wave psychotherapies (e.g., mindfulness-based cognitive therapy, dialectical behavior therapy, and acceptance and commitment therapy) and related approaches. Despite some conceptual overlap with CAM and incorporation of CAM techniques such as meditation, these approaches are theoretically grounded in cognitive behavioral theory. They are understood to be extensions of mainstream approaches—and thus are distinct from CAM. Although outside of the scope of the current review, consideration of these strategies may inform broader understanding of the utility of CAM approaches for PTSD. It also merits mention that numerous forms and practices of mindfulness practice exist, such as seated meditation, movement-based practices, and even

the occasional mindful enjoyment of a single raisin. The field may be best served at this stage of treatment development by considering a range of different approaches to cultivating mindfulness skills.

In addition to the above limitations, there are important strengths of our methodological approach as well. First, limiting our review to evidence gleaned from published, peer-reviewed trials allowed us to focus on quality over quantity when examining this relatively undeveloped body of research. Although many CAM approaches have been in practice for thousands of years, the application of rigorous methods to standardize and evaluate the efficacy of these treatments is a relatively new development in the field of interventional PTSD research. In addition, our evidence synthesis was guided by a carefully designed standardized protocol, including a systematic search of research databases and relevant bibliographies, double data abstraction, and use of AHRQ criteria to assess the quality of identified studies. Our multidisciplinary team included expertise in internal medicine, clinical psychology, epidemiology, acupuncture research, and integrative medicine. In sum, this was a highly structured and systematic review of the extant evidence.

RECOMMENDATIONS FOR FUTURE RESEARCH

The limitations of the current evidence preclude our ability to draw strong conclusions to inform clinical practice or public policy regarding optimal use of CAM therapies for PTSD, yet the limitations in the available evidence point to numerous opportunities for future research. Questions remain about the efficacy, effectiveness, safety, cost-effectiveness, comparative effectiveness, mechanisms of actions, dosing, indications and contraindications, and differential response among subgroup populations. There are also unanswered questions about patient and provider preferences and expectations, optimal outcome, adherence and fidelity measures, and resource utilization patterns.

One of the most pertinent questions regarding CAM therapies for PTSD is, What effects might one expect of a given intervention relative to no intervention? This clinically relevant question is best addressed by a randomized clinical trial with a no-treatment (waitlist) comparator. This trial design controls for many threats to internal validity and is particularly appropriate when there are no or few controlled trials. However, study designs that withhold or delay treatment to those with PTSD may not be institutionally feasible or ethically defensible.⁶⁴ In their thoughtful discussion of the methodological challenges inherent in this area of research, Devilly and McFarlane (2009)⁶⁵ question the value and appropriateness of waitlist and placebo-controlled PTSD intervention trials given potential risks (e.g., greater chronicity, comorbidities, suicidality, functional impairments, and financial burden) that may be incurred when available evidence-based treatments are withheld or delayed. As an alternative to the standard RCT design, the authors demonstrate a means of deriving statistical estimates of waitlist control and placebo treatment effect sizes from existing data and applying these estimates to interpret the effects of future treatment innovations. Although this statistical approach has not been used widely, such strategies merit consideration as an alternative to the use of nonactive controls.

Another pertinent question is, To what extent might placebo, or nonspecific effects account for observed clinical outcomes? This question can be hard to answer for CAM therapies, for

which it may be difficult to design a sham procedure that is both truly inert and that appears sufficiently similar to the active intervention to isolate the specific effect of the intervention. The fields of surgical and psychotherapy research have long grappled with similar issues. Strong recommendations and methodological guidelines now exist to guide these efforts.^{66,67} Of the many CAM therapies with potential to serve as a therapeutic option in the treatment of PTSD, acupuncture is arguably the one with the most plausible placebo control. For example, it is possible, in the context of a clinical trial, to administer sham acupuncture such that research subjects are unable to determine with certainty whether they are receiving the true or sham treatment. The current standard in acupuncture research is to compare an active acupuncture intervention to both a sham acupuncture intervention and a no-acupuncture control. This three-arm RCT design makes it possible to simultaneously assess the efficacy or effectiveness and safety of a course of acupuncture while also partially addressing the extent to which nonspecific effects may contribute to observed outcomes.

Although more costly and challenging to conduct, comparative effectiveness designs also may be indicated to give patients and clinicians the most direct evidence about competing treatment options. These trials may be most appropriate and informative after additional preliminary work has fostered a stronger evidence base for CAM treatments of interest. Finally, practical clinical trials, which combine aspects of efficacy and effectiveness designs, merit consideration as a potentially more efficient and actionable alternative to traditional explanatory trials.⁶⁸

Ultimately, the choice of which research strategy to employ should be determined by the key questions and the plausibility and estimates of benefit based on prior research.^{66,69-71} For example, explanatory trials are best suited to address the question, Can this intervention work? and pragmatic trials to address the question, Does this intervention work?⁶⁹ For most CAM treatments, the basic question of “Can it work?” for PTSD has not been answered. Observational studies can provide good evidence about the feasibility of interventions and adverse effects that require large studies or long followup durations to detect. Smeeding and colleagues (2010)⁷² conducted a longitudinal evaluation of the effectiveness of an integrative health clinic and program within the Veterans Affairs Health Care System (VAHCS) for PTSD, chronic pain, stress-related depression, and anxiety. Observational studies of this kind can provide a rich source of information about the feasibility and acceptability of CAM treatments delivered within a VA setting. In addition, high-quality observational studies that show very large treatment effects can provide good evidence of treatment effect. For example, we do not need an RCT to prove the benefits of a good parachute when stepping out of an airplane at altitude. However, our review did not identify observational studies showing very large treatment effects for any of the CAM treatments evaluated. Thus, randomized, placebo (or sham intervention) controlled trials—the gold standard for evaluating intervention effects—will be the most logical design for the majority of studies planned to evaluate CAM interventions. Small exploratory trials would be a logical next step for the CAM interventions that lack any studies of treatment effect.⁶⁷

Whether evaluated in RCTs or observational studies, evaluating CAM therapies is challenging.^{73,74} A complete description of the challenges is beyond the scope of this report, but issues of blinding patients and treating clinicians to the intervention assignment, accounting for the learning curve of procedural-based interventions, identifying the appropriate comparator, procedures to minimize attrition, and monitoring fidelity to the planned intervention are all key

challenges. In addition, research on PTSD has important challenges, including the variety of traumas (e.g., combat, rape), the time since trauma, and the presence of medical or psychiatric comorbidity, all of which may impact treatment response. In addition to these more general challenges, we observed important variability in the completeness and consistency of PTSD outcome reporting. The evidence base for CAM treatments, and PTSD more generally, would be strengthened by a more uniform approach to outcome assessment. For our review, we prioritized PTSD symptom response, HRQOL, and adverse effects as the most important outcomes. Secondary outcomes included patient satisfaction, treatment adherence, and functional status. This prioritization of outcomes should be confirmed with stakeholders and then assessed more consistently across studies. To this end, the PROMIS initiative, an AHRQ-funded effort to develop a common battery of measures for many different conditions, may be a useful resource. Another important limitation of the current evidence base was the descriptions of treatment interventions, which were usually inadequate to permit replication. Glasziou and colleagues⁷⁵ have recently proposed standards for intervention reporting to include sufficient detail to guide replication, including descriptions of the interventionists, the content of the intervention, the treatment setting, how and when the intervention was delivered, and the degree of flexibility permissible. Finally, health services research in the VA could be facilitated by developing procedure codes to capture CAM approaches used in the VA.

CONCLUSIONS

Our systematic review identified seven RCTs and two nonrandomized studies of CAM interventions for PTSD. Our review of relevant studies registered with ClinicalTrials.gov further suggests that this modest empirical foundation is growing. The term CAM encompasses a broad range of treatments—not all of which may hold the same level of promise as applications for PTSD. The current absence of a strong signal pointing to any one CAM approach over others argues for investment in a set of adequately powered trials to evaluate the most promising therapies, rather than a single large trial for any one treatment. Given the current state of evidence, a two-pronged approach may be most appropriate at this stage to move the field forward. That is, a series of adequately powered RCTs may be indicated for select CAM interventions for which there is clear and strong preliminary signal, either based on good-quality, early empirical evidence (e.g., acupuncture), a sound theoretical rationale for efficacy in the absence of strong pilot findings (e.g., meditation), and/or promising data gleaned from the bench sciences (e.g., compelling animal models). For other CAM modalities for which the science and theory are even less well developed, such as energy therapies, more prudence is indicated, suggesting the utility of exploratory pilot studies as the appropriate next step. In addition, the efficiency and ultimate yield of future efforts may be further optimized by consensus agreement about, and concerted efforts to address, limitations identified in the current literature. Broadly, these limitations concern issues of appropriate design, outcome, and replication strategies. There is an opportunity for strategic, well-designed studies to address the substantial gaps in evidence identified in this review.

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