

Audience Question

How many are:

Mental health clinicians?

Non-mental health clinicians?

Researchers?

Trainees (graduate students, interns, fellows, etc)?

How many use:

Complementary and alternative Medicine (CAM) therapies in
clinical practice?

CAM therapies personally?

Evidence-based Synthesis Program

Efficacy of Complementary and Alternative Medicine Therapies for Posttraumatic Stress Disorder

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Evidence-based Synthesis Program

Acknowledgements

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- The findings in this document are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs.
- No investigators have any affiliations or financial involvement that conflict with material presented in this report

Evidence-based Synthesis Program (ESP): Program Overview

- Sponsored by VA Office of R&D and HSR&D
- Established to provide timely, accurate reports on healthcare topics identified by VA staff to improve the healthcare of Veterans
- Builds on expertise already in place at the Evidence-based Practice Center (EPC) designated by Agency for Healthcare Research and Quality (AHRQ). Four of these EPCs are also ESP Centers:
 - Durham VA Medical Center
 - VA Greater Los Angeles Health Care System
 - Portland VA Medical Center
 - Minneapolis VA Medical Center

Evidence-based Synthesis Program (ESP): Program Overview

- **Each Center provides ≥ 3 evidence syntheses per year on important clinical practice topics relevant to Veterans in order to:**
 - Develop clinical policies informed by evidence
 - Implement effective services to improve patient outcomes
 - Support VA clinical practice guidelines and performance measures
 - Guide the direction for future research to address gaps in clinical knowledge
- **Topic nomination process facilitated by ESP Coordinating Center (Portland) through online process:**

<http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm>

Evidence-based Synthesis Program (ESP): Program Overview

ESPs work with stakeholders to meet their needs through:

- **Technical Advisory Panel (TAP)**
 - Recruited for each topic to provide content expertise
 - Guides topic development, refines the key questions, and reviews data and draft report
- **External Peer Reviewers & Policy Partners**
 - Review and comment on draft report
 - All reviewer comments are addressed in the final report (often later published in peer-reviewed journal)
- **Final reports posted on VA HSR&D website and disseminated widely through the VA**

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

Efficacy of Complementary and Alternative Medicine Therapies for Posttraumatic Stress Disorder

Published August 2011

Full-length report available on ESP website:
<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

Background: PTSD

Posttraumatic Stress Disorder (PTSD)

- Among most common mental disorders
- Often chronic
- Associated with significant adverse consequences:
 - psychiatric comorbidities (e.g., comorbid depression)
 - substance abuse
 - suicidality
 - impaired functioning
 - decreased quality of life
 - increased rates of medical morbidities, health risk behaviors, and health service use
- Estimated lifetime prevalence in US = 7%

Background: PTSD

PTSD in Veterans

- Increased incidence among Veterans
- PTSD is the mental disorder most commonly associated with combat and other military traumas (sexual assault, MVA, etc.)
- OEF/OIF/OND VA users = 22% diagnosed PTSD (Seal et al., AJPH, 2009)
- Witnessing sharp increase in VA mental health service use by both OEF/OIF/OND and Vietnam-era Veterans
- *As VA strives to anticipate and serve the treatment needs of the growing Veteran population, identifying and implementing effective PTSD treatments remains a critical priority*

Background: Current Treatments

Current First-Line, Evidence-Based Treatments (VA/DoD Clinical Practice Guideline for Management of PTSD, Oct 2010)

- Trauma-focused cognitive behavioral psychotherapies
 - theoretically grounded in CBT
 - multi-component, PTSD specific (+ anxiety mgmt/psychoed)
 - prolonged exposure, cognitive processing therapy, EMDR
 - overlap with CAM (e.g., relaxation strategies prior to exposure)
- Stress inoculation training
 - theoretically grounded in CBT
 - “toolkit” approach of skills to “inoculate” against stress response
 - overlap with CAM (breathing relaxation, muscle relaxation, etc.)
- Pharmacotherapies
 - SSRIs (paroxetine, sertraline) and SNRIs (vanlafaxine)

Background: Current Treatments

Summary

- Mounting empirical support for current EBTs, and strong efforts within clinical research community to refine and optimize these approach
- Yet, each is associated with limitations and potential barrier to broad dissemination and uptake

Primary Limitations of Current Evidence-Based Treatments

- Access
- Specialized provider training/frequent contact
- Suitability
- Side effects (meds)
- Stigma of seeking mental health specialty care

Background: CAM Overview

Complementary and alternative medicine (CAM): includes range of therapies not considered standard to the practice of medicine in US.

NIH National Center for Complementary and Alternative Medicine (NCCAM) classification of CAM therapies:

- Mind-body medicine (e.g., meditation, acupuncture, relaxation, yoga)
- Manipulative and body-based practices (e.g., chiropractic, massage)
- Other alternative practices (e.g., energy therapy)
- Natural products (e.g., supplements; not included in current review)
- Whole medical systems (e.g., Aruyvedic; not included in current review)
 - Imperfect classification system (e.g., biofeedback considered conventional and CAM)
 - for many, mechanisms of action poorly understood

Background: Rationale for CAM

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

- Patient preferences: CAM interventions widely used by MH consumers (including Veterans)
- Considered minimally invasive/low anticipated risk of adverse effects
- If efficacious, could increase the breadth of PTSD treatments:
 - first line treatments?
 - adjunctive?
- Numerous stakeholders have expressed strong interest in developing the evidence base for alternative approaches to treatment of PTSD

Background: Rationale for CAM



Methods: Overview

Q: What's so systematic about a systematic evidence review?

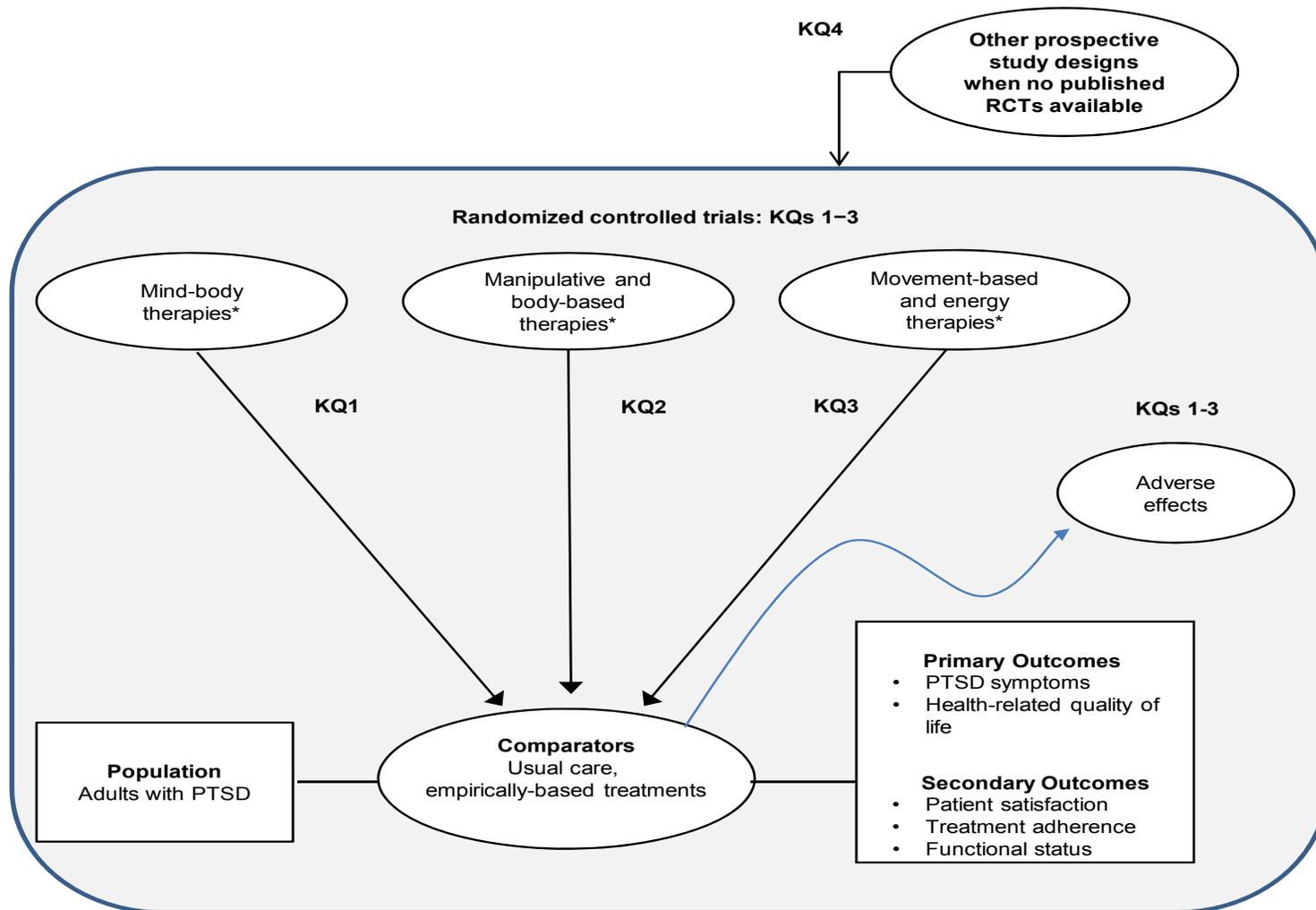
A: Pretty much everything....

1. Topic development
2. Systematic searches of literature
3. Study selection
4. Data abstraction
5. Quality assessment
6. Data synthesis
7. Peer review

Methods: Key Questions

- **Key Question 1:** In adults with PTSD, are mind-body CAM therapies more efficacious than control for PTSD symptoms and health-related quality of life?
- **Key Question 2:** In adults with PTSD, are manipulative and body-based CAM therapies more efficacious than control for PTSD symptoms and health-related quality of life?
- **Key Question 3:** In adults with PTSD, are CAM therapies that are movement-based and energy therapies more efficacious than control for PTSD symptoms and health-related quality of life?
- **Key Question 4:** For treatments evaluated in Key Questions 1-3 that lack randomized controlled trials, is there evidence from other study designs that suggests the potential for treatment efficacy?

Analytic Framework



Methods: Search Strategy

Databases: English-language publications in MEDLINE, Embase, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Controlled Trials Registry, and the Published International Literature on Traumatic Stress (PILOTS) database (targeted search for relaxation studies)

Search terms: Included terms for CAM therapies, PTSD, and randomized controlled trials (RCTs)

Supplemental searches: Bibliographies of individual research and review papers; used the PubMed broad “therapy filter” to identify prospective studies when RCTs were not identified; Clinicaltrials.gov (in progress/completed, unpublished studies)

Methods: Inclusion Criteria

Study design:

- RCTs for KQs 1-3
- Non-RCT, prospective studies when no RCTs identified

Population: Adults \geq 19 yrs w/PTSD by DSM criteria, validated severity measures, or clinical diagnosis; in acute-phase treatment

Interventions: Mind-body, manipulative or body-based, movement-based, or energy therapies

Comparators: Any control condition (including no treatment)

Outcomes: PTSD diagnosis and symptom severity, social functioning, patient satisfaction, quality of life reported \geq 6 weeks post intervention

Setting: Community, outpatient mental health or general medical

Methods: Exclusion Criteria

- Non-English language publication
- Studies not conducted in Westernized countries
- Patient populations with psychosis, acute suicidality, or substance abuse
- Studies that included a CAM therapy in both intervention and control arms
- Interventions commonly considered standard therapy (e.g., biofeedback, or relaxation skills training as part of CBT)
- PTSD as a comorbid rather than primary diagnosis
- Intervention used in a continuation or maintenance phase of treatment
- Relaxation: excluded if control arm and/or description of intervention/CAM components unclear (e.g., “3 relaxation skills taught”)

Methods: Quality Assessment

Assessment of risk of bias: applied quality criteria described in Agency for Healthcare and Research Quality (AHRQ) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*

Data abstraction: for RCTs, data abstracted 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, completeness of outcomes reporting, and conflict of interest

Assigned quality score of Good, Fair, or Poor to individual RCTs

Methods: Data Synthesis

Critically analyzed studies: characteristics, methods, findings

Qualitative synthesis

- Gestalt of findings for each Key Question

Quantitative synthesis

- Could not perform quantitative meta-analyses
- When evidence sufficient, computed Standardized Mean Difference (SMD) using Hedges g
- SMD allows comparisons across studies (different measures, same outcome)

Methods: “Grading” of Evidence

Rating the Body of Evidence

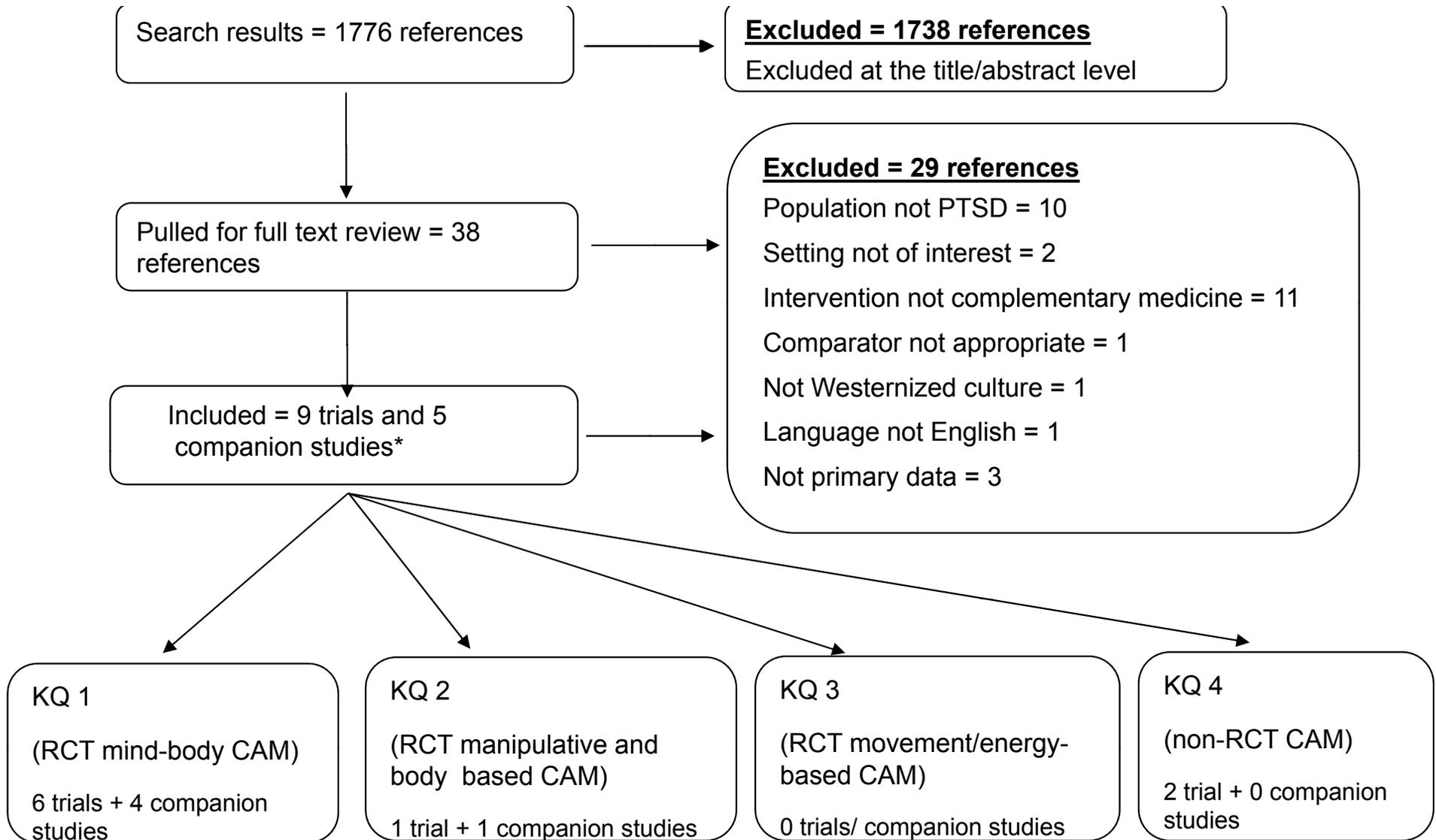
GRADE Working Group criteria for assessing overall body of evidence:

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

Peer Review

- Draft reviewed by technical experts and clinical leadership
- Reviewer comments addressed, incorporated into final report, and listed in Appendix

Literature Flow



Results: ?

Drum roll please.....

Results: Key Question #1

Key Question 1: In adults with PTSD, are mind-body CAM therapies more efficacious than control for PTSD symptoms and health-related quality of life?

- Mind-Body Therapies: acupuncture, meditation, yoga, deep-breathing exercises, guided imagery, hypnotherapy, progressive relaxation, and tai chi
- 6 published RCTs
 - 2 meditation (1 fair, 1 poor)
 - 1 acupuncture (1 good)
 - 3 relaxation (3 poor)
- 16 unpublished /ongoing trials (ClinicalTrials.gov)

Results: Summary of Study Characteristics: KQ#1

Study	Intervention vs. comparator
<i>RCTs of mind-body interventions: KQ 1</i>	
Bormann et al., 2008 (n = 29)	Mantram repetition vs. usual care
Brooks and Scarano, 1985 (n = 25)	Transcendental meditation vs. psychotherapy
Echeburúa et al., 1996 (n = 20)	Progressive muscle relaxation vs. cognitive behavioral therapy
Hollifield et al, 2007 (n = 84)	Acupuncture vs. group cognitive behavioral therapy vs. waitlist
Vaughan et al., 1994 (n = 36)	Applied muscle relaxation vs. image habituation training vs. eye movement desensitization and reprocessing (EMDR)
Watson et al., 1997 (n = 90)	Simple relaxation instruction vs. relaxation instruction + deep breathing vs. relaxation instruction + deep breathing and thermal biofeedback

Results: ClinicalTrials.gov

Intervention Type	Completed RCTs (n=7)	Ongoing RCTs (n=8)	Status Unknown (n=1)
Acupuncture	2	2	-
Emotional freedom techniques	1	1	-
Guided imagery	1	1	-
Mind-body skills	-	1	-
Mindfulness-based stress reduction	2	-	-
Mindfulness meditation	-	1	-
Relaxation	-	1	-
Yoga	1	1	1

Results: Key Question #2

Key Question 2: In adults with PTSD, are manipulative and body-based CAM therapies more efficacious than control for PTSD symptoms and health-related quality of life?

- Manipulative and Body-based Therapies: spinal manipulation, massage
- 1 massage (1 poor quality)
- 0 unpublished /ongoing trials (ClinicalTrials.gov)

Results: Key Question #3

- **Key Question 3:** In adults with PTSD, are CAM therapies that are movement-based and energy therapies more efficacious than control for PTSD symptoms and health-related quality of life?
 - Movement-Based Therapies: Feldenkrais method, Alexander technique, Pilates, Rolfing Structural Integration, and Trager Psychophysical Integration
 - Energy Therapies: magnet therapy, light therapy, qi gong, Reiki, healing touch
 - 0 RCTs
 - 0 unpublished /ongoing trials (ClinicalTrials.gov)

Results: Key Question #4

- **Key Question 4:** For treatments evaluated in Key Questions 1-3 that lack randomized controlled trials, is there evidence from other study designs that suggests the potential for treatment efficacy?
 - 2 nonrandomized, prospective studies
 - no quality rating
 - Both multimodal therapies that incorporated CAM techniques (hypnotherapy, guided imagery, relaxation)
 - 2 unpublished /ongoing nonrandomized trials (ClinicalTrials.gov) – both examine yoga interventions

Results: Summary of Study Characteristics: KQ#2&4

<i>RCT of manipulative and body-based interventions: KQ 2</i>	
Price, 2006 (n = 8)	Body-oriented therapy (massage) vs. waitlist
<i>Non-RCT of CAM therapies for PTSD: KQ 4</i>	
Abramowitz and Lichtenberg, 2010 Prospective cohort (n = 36)	Hypnotherapeutic olfactory conditioning
Hossack and Bentall, 1996 Case series (n =5)	Relaxation and visual kinesthetic dissociation

Note: No studies were found that were applicable to KQ#3

Results: ClinicalTrials.gov (No Ongoing Studies)

- Alexander technique
- Craniosacral therapy
- Energy field work
- Feldenkrais
- Magnet therapy
- Pilates
- Reiki
- Tai chi
- Therapeutic touch
- Trager therapy

Summary of Evidence: KQ #1

Mind-Body Therapies

	DOMAINS PERTAINING TO STRENGTH OF EVIDENCE				MAGNITUDE OF EFFECT ^a AND STRENGTH OF EVIDENCE
Number of studies (subjects)	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	N/A	Direct	Imprecise	SMD ^b : <u>-0.32</u> (-1.42 to 0.05) on PCL SDM: <u>-0.70</u> (-1.06 to 0.41) on CAPS
KQ 1: Meditation vs. active treatment					Insufficient SOE
1 (25)	RCT/Poor	N/A	Direct	Imprecise	Not estimated
KQ 1: Acupuncture vs. control					Moderate SOE
1 (84)	RCT/Good	N/A	Direct	Imprecise	SMD: <u>-0.92</u> (-1.51 to -0.32) on PSS-SR
KQ 1: Acupuncture vs. group CBT					Low SOE
1 (84)	RCT/Good	N/A	Direct	Imprecise	SMD: <u>-0.35</u> (-0.91 to 0.22) on PSS-SR

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

^bSMD: standardized mean difference; Hedge's g for continuous outcomes

Summary of Evidence: KQ #1

Mind-Body Therapies

	DOMAINS PERTAINING TO STRENGTH OF EVIDENCE				MAGNITUDE OF EFFECT AND STRENGTH OF EVIDENCE
Number of studies (subjects)	Risk of bias: design/quality	Consistency	Directness	Precision	PTSD symptoms: Effect estimate (95% CI)
KQ 1: Relaxation vs. control					Insufficient SOE
1 (90)	RCT/Poor	N/A	Direct	Imprecise	Not estimated
KQ 1: Relaxation vs. other active treatment					Insufficient SOE
2 (56)	RCT/Fair to Poor	Consistent	Direct	Imprecise	SMD : 0.41 (-0.42 to 1.24), SI-PTSD SMD : 0.79 (-0.13 to 1.71), SS PTSD
KQ 2: Massage vs. control					Insufficient SOE
1 (8)	RCT/Fair	N/A	Direct	Imprecise	Not estimated
KQ 3: Movement-based and energy therapies vs. control					Insufficient SOE
None	N/A	N/A	N/A	N/A	N/A

*A negative SMD indicates a greater effect for the CAM therapy

Summary

...and so, in plain English, what does all of that mean, exactly?

Summary: Key Findings

- Highest quality evidence exists for acupuncture
 - acupuncture > wait list control
 - acupuncture \doteq active treatment (group CBT vs individual CBT?)
 - but... strong conclusions cannot be reliably drawn on the basis of a single RCT (further study needed)
- Greatest breadth of evidence exists for relaxation
 - generally associated with moderate improvement
 - but...all 3 studies (breathing, relaxation) are preliminary and have significant design flaws that limit interpretability; preliminary findings favor active comparators (further study needed)

Summary: Key Findings

- Evidence in support of meditation is generally positive
 - meditation > control (usual care)
 - meditation vs. active treatment ?
 - but... based on 2 preliminary studies on concentrative meditation only (further study needed)
- Evidence in support of massage is positive but quite limited
 - 1 RCT with significant design flaws (further study needed)
- Did not identify eligible RCTs of spinal manipulation, movement-based, or energy therapies (KQ 3)
- Overall: studies rarely addressed the issue of adverse effects; retention rates (when reported) similar to current evidence-based approaches

Limitations

- Limited to RCTs in peer-reviewed, English language journals
- No systematic search of the “gray literature”
- Limited to CAM trials conducted in clinical, PTSD samples
- Relaxation therapies: only included those presented as active treatments (versus control) and adequately described (5 otherwise relevant studies excluded, which showed modest effects versus active comparators)
- Did not examine issues of symptom overlap, comorbidity of PTSD and traumatic brain injury, or other unique presentations that may be anticipated among OEF/OIF Veterans
- Did not examine “third-wave psychotherapies” (e.g., mindfulness-based cognitive therapy, acceptance and commitment therapy)
- Scope of search excluded natural products (e.g., nutritional supplements)

Strengths

- Quality over quantity: highly structured, systematic evidence review
- Application of rigorous research methods relatively new to CAM
- Multidisciplinary team included expertise in:
 - research methods
 - internal medicine
 - clinical psychology
 - epidemiology
 - acupuncture research
 - integrative medicine

Conclusions

- Current evidence base is very limited (7 RCTs, 2 prospective trial)
- Overall. published findings are positive
- Research on CAM therapies for PTSD appears to be on the rise, as suggested by the 16 pertinent RCTs we identified in ClinicalTrials.gov
- Glass half empty: limitations of current evidence bases preclude drawing any strong conclusions at this point
- Glass half full: there are numerous, important opportunities for future research in this area!
- Questions remain: efficacy, effectiveness, safety, cost-effectiveness, comparative effectiveness, mechanisms of action, dosing, indications and contraindications, differential responses among subgroups, etc.

Conclusions

- CAM encompasses broad range of treatments, not all of which may hold the same promise for PTSD
- The current absence of a strong signal pointing to any one CAM approach argues for investment in a set of adequately powered trials to evaluate most promising approaches
 - Good-quality early empirical evidence (e.g., acupuncture)
 - Sound theoretical rationale in absence of strong preliminary findings (meditation)
 - And/or promising data gleaned from bench sciences (e.g., compelling animal models)
- For those CAM approaches for which science and theory are less well-developed (e.g., energy therapies), smaller, exploratory pilot studies would be a more prudent next step

Final Thoughts

This is a dynamic and growing field of inquiry.

Results of this review suggest that we can look forward to a more comprehensive evidence base on CAM therapies for PTSD in the near future.

Contact Information

Questions?

**If you have further questions,
feel free to contact:**

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The full, final report and cyberseminar presentation will be available
on the ESP website:

<http://www.hsrdr.research.va.gov/publications/esp/>