Evidence-based Practice Center Systematic Review Protocol

Project Title: *Pharmacologic and Nonpharmacologic Treatments of Posttraumatic Stress Disorder*

I. Background and Objectives for the Systematic Review

Posttraumatic stress disorder (PTSD) is a prevalent disorder with significant negative impacts on health, quality of life, and healthcare utilization.[1] Lifetime prevalence of PTSD is estimated to be 6.1 percent in American civilians and 6.9 percent in Veterans.[2,3] Since PTSD was first included by the Diagnostic and Statistical Manual of Mental Disorders, third edition (DSM-III) in 1980, there have been over 300 published randomized controlled trials (RCTs) evaluating vast number of treatments and treatment modalities (e.g., psychotherapy, psychopharmacotherapy, complementary approaches, etc.). Given the large and varied body of evidence, even some of the most comprehensive systematic reviews on PTSD have excluded some intervention types (e.g., complementary and integrative approaches) due to the prohibitively large number of studies that would have to be reviewed.[4] Without a comprehensive database containing all published RCTs on PTSD, clinicians and researchers may need to consult multiple reviews in order to synthesize evidence across studies and evaluate the effectiveness and comparative effectiveness of treatments. However, heterogeneity of review methods, scope, and data presentation make it difficult to synthesize across reviews and have led to variation in conclusions.[5,6] Methodological differences, such as data coding approaches and combining treatment categories for analysis, further limit the generalizability of findings.

Systematic reviews typically abstract a small number of data elements pertinent to the scope of the review due to resource constraints. Furthermore, even when abstracted data are made publicly available, they may be presented in a format that does not readily lend itself to re-analyses without reformatting or re-entry. Hence, there is a need for a single source that provides up-to-date, detailed, comprehensive data on existing PTSD trials to better address current clinical, research, and policy stakeholders' needs. This review seeks to build upon the data repository developed in Technical Brief No. 32,[7] the PTSD Trials Standardized Data Repository, or "PTSD-Repository." This review will build on the PTSD-Repository by including additional data elements and expanding inclusion criteria to interventions targeting comorbid PTSD and substance use disorder (SUD). The PTSD-Repository could (1) serve as a data source for future systematic reviews, meta-analyses, or other cross-study comparisons; (2) help identify research gaps to determine future research priorities; (3) encourage researchers to adopt standard data elements in research and reporting; (4) serve as a source for clinicians seeking information on effectiveness of interventions for patients with particular demographics or exposures; (5) provide the public a source to search for evidence on interventions they or their loved ones are considering; (6) provide policymakers with an up-to-date accounting of evidence to respond to inquiries; and (7) augment and inform the use of existing patient education tools such as PTSD mobile applications[8] or the online PTSD Treatment Decision Aid.[9]

II. The Key Questions

Key Question 1. What pharmacologic interventions have been studied for the treatment of PTSD alone or with comorbid SUD?

Key Question 2. What nonpharmacologic interventions have been studied for the treatment of PTSD alone or with comorbid SUD?

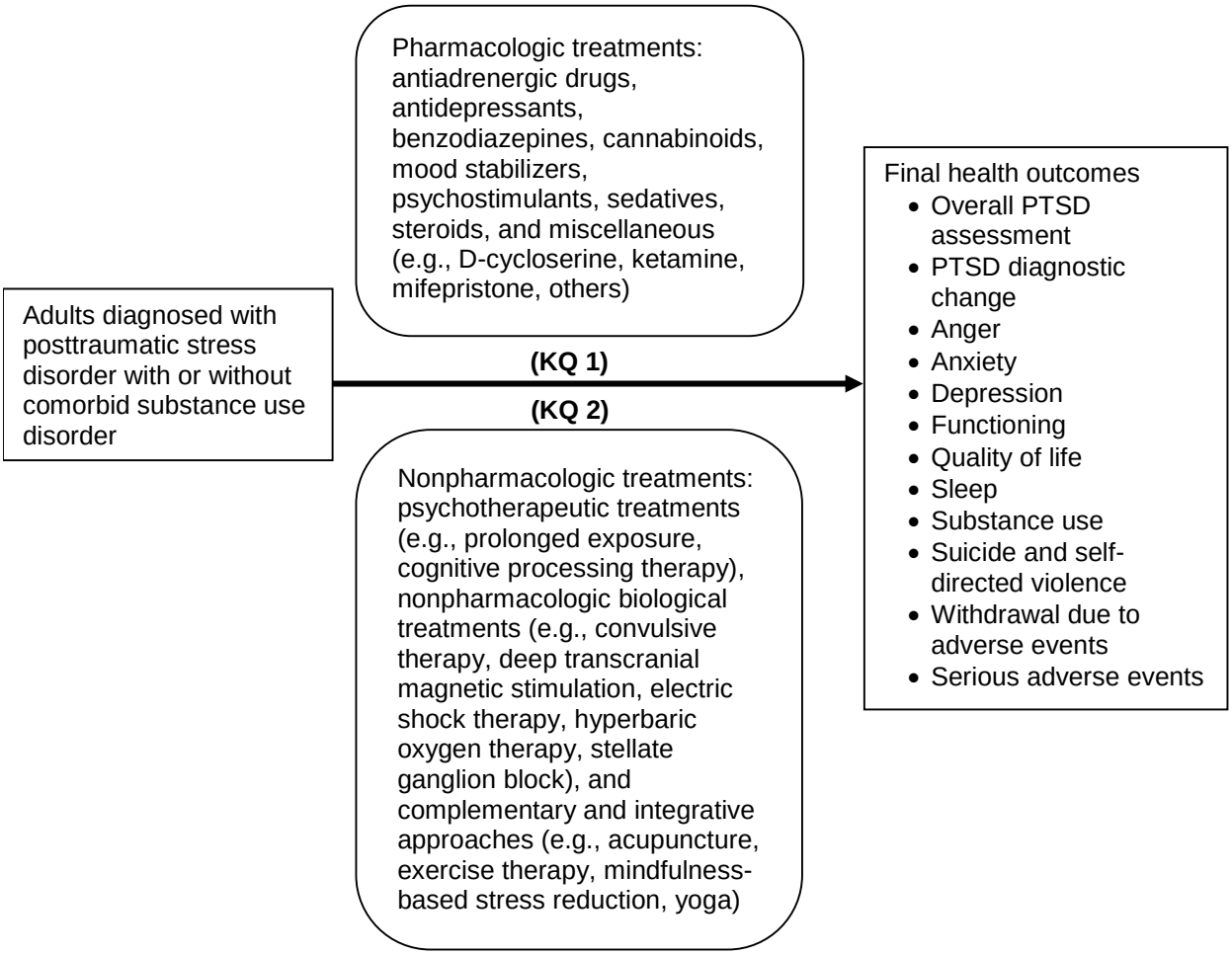
For all Key Questions, the following PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings, Study Design) criteria apply:

- **Population(s):**
  - Adults (≥18 years old) diagnosed with PTSD by a clinician or through patient-reported assessment tool
- **Interventions:**
  - Pharmacologic and nonpharmacologic interventions, including complementary and integrative approaches, for PTSD or comorbid PTSD/SUD
- **Comparators:**
  - Any comparator, including another intervention, waitlist/minimal attention, usual care, or placebo
- **Outcomes:**
  - Overall PTSD outcome, PTSD Diagnostic Change
  - Other outcomes – Anxiety, anger, depression, functioning, quality of life, sleep, substance use, suicide- and self-directed violence, withdrawal due to adverse events, serious adverse events
- **Timing:**
  - No limitation on study duration or length of followup
- **Settings:**
  - No limitation on study setting
- **Study Design:**
  - Randomized controlled trials

III. Analytic Framework

Figure 1 depicts the key questions within the context of the PICOTS inclusion and exclusion criteria presented in Table 1. The figure illustrates how pharmacologic and nonpharmacologic treatments -- which includes psychotherapeutic treatments, nonpharmacologic biological treatments, and complementary and integrative approaches -- may be associated with health and functional outcomes including PTSD symptoms and diagnosis, substance use, anxiety, depression, and quality of life; as well as how these interventions may be associated with harms.

Figure 1. Analytic Framework for Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder



IV. Methods

Criteria for Inclusion/Exclusion of Studies in the Review

Detailed inclusion and exclusion criteria for all KQs are listed in Table 1, and are consistent with the PICOTS above.

Table 1. PICOTS: Inclusion and exclusion criteria

PICOTS	Include	Exclude
Populations	• Adults (≥18 years old) with PTSD diagnosed by a clinician or through the administration of a validated clinician-administered or patient-reported assessment tool	• Children (<18 years old) • Diagnosis of acute stress disorder • Studies that do not specify criteria used to diagnose PTSD
Interventions	• Pharmacologic interventions for PTSD or comorbid PTSD/SUD with any pharmacologic component, whether singly, in combination with other treatment categories, or compared with another intervention category • Nonpharmacologic interventions for PTSD or comorbid PTSD/SUD, including complementary and integrative approaches, nonpharmacologic biological treatments, and psychotherapeutic treatments	• Interventions designed to simultaneously target PTSD and comorbid conditions other than SUD if they cannot be standalone PTSD interventions (i.e., interventions targeting PTSD and a comorbidity such as depression are included if the intervention can be a treatment for PTSD alone) • Interventions designed to prevent PTSD
Comparators	• No limitations applied. Direct head-to-head comparison of PTSD interventions were included. • Interventions such as waitlist/minimal attention, usual care, placebo, or other minimally-active treatment (e.g., education or attention control) are categorized as “Controls”	None
Outcomes	• Any overall PTSD outcome	• Studies reporting only individual symptoms or symptom clusters without overall PTSD outcome
Timing	• Any study duration and length of followup	None
Setting	• All study settings	None
Study Design	• RCTs	• Non-RCTs • Selected systematic reviews will be considered as reference check sources of studies to be reviewed for possible inclusion (data will be abstracted from individual studies rather than from systematic reviews) • Partial studies (limited course of treatment), outcome studies (lower dose), experimental treatment manipulations (dismantling)

PTSD = posttraumatic stress disorder; RCTs = randomized controlled trials; SUD = substance use disorder

Literature Search Strategies to Identify Relevant Studies to Answer the Key Questions

Publication Date Range: Electronic databases will be searched for evidence from June 1, 2018, to present, containing three months of overlap with the last database search for Technical Brief No. 32.[7] Additionally, the database from Technical Brief No. 32 will be searched for previously excluded studies related to interventions targeting comorbid PTSD and SUD. An updated literature search will be conducted concurrently with the peer review process and any new literature identified that meets inclusion criteria will be incorporated into the report.

Literature Databases: PTSDpubs (formerly PILOTS), Ovid® MEDLINE®, Cochrane CENTRAL, Embase®, the Cumulative Index to Nursing and Allied Health Literature (CINAHL®), SCOPUS, and PsycINFO®. Search strategies are in Appendix A.

Grey Literature: A gray literature search will not be conducted. Due to the nature of the project, a portal for submission of Supplemental Evidence And Data for Systematic review (SEADS) will not be opened for this project.

Hand Searching: Reference lists of relevant, recent, high-quality systematic reviews or meta-analysis identified in the search will be reviewed to identify RCTs eligible for inclusion.

Process for Selecting Studies: PICOTS described in Section II and criteria in Table 1 will be used to determine eligibility for inclusion and exclusion of abstracts. One investigator will determine eligibility at the title/abstract review stage and a second investigator will review excluded studies. For studies included at the title/abstract review stage, the full-text will be retrieved and reviewed independently for eligibility by two investigators. Any disagreements will be resolved by consensus of the team of investigators.

Data Abstraction and Data Management

After studies are screened and determined to meet inclusion criteria, study design, year, setting, country, sample size, eligibility criteria, source(s) of funding, study characteristics, population characteristics, intervention characteristics, and results will be abstracted using the evidence table developed for Technical Brief No. 32.[7] The evidence table will be in Microsoft® Excel and will include all components in the Statement of Work (see Appendix B for detailed list of data elements). Additional data elements added to this update will be incorporated into the existing evidence table with guidance from the National Center for PTSD (NCPTSD) partner. All study data will be verified for accuracy and completeness by a senior investigator. A record of studies excluded at the full-text level with reasons for exclusion will be maintained.

Assessment of Methodological Risk of Bias of Individual Studies:

Risk of bias (ROB) assessment will be conducted for RCTs included in Technical Brief No. 32[7] and new RCTs identified from the database search and expanded inclusion criteria. ROB assessment will use the same approach and 12 ROB elements as in Comparative Effectiveness Review (CER) No. 207 Psychological and Pharmacologic Treatments for Adults with Posttraumatic Stress Disorder[4] in accordance with the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Review.*[10] An overall ROB rating (low, medium, high) will be assigned based on satisfaction of each domain (selection, performance, detection, attrition, and reporting bias; see Appendix C for a description of ROB assessment elements). Studies included

in AHRQ CER No. 207 will not be re-evaluated; individual ROB item and overall ratings from the previous CER will be reported in the current report.

With input from the Technical Expert Panel and sponsor (NCPTSD), we will also develop an alternative ROB assessment approach to address limitations in existing ROB approaches. The new ROB approach may include abstracting, describing, or classifying data elements or study characteristics related to risk of bias, but will not include assigning an overall ROB rating to the study in addition to the ROB rating already included as part of the AHRQ methods ROB assessment. The new ROB approach will be piloted in 10 studies included in Technical Brief No. 32,[7] then further refined based on information gleaned from the pilot assessment.

Data Synthesis

For each KQ, data will be abstracted into a detailed evidence table. Characteristics of included studies, such as number of publications by year, study sample size, proportion of studies enrolling community versus military population, and distribution of studies by PTSD assessment method, will be synthesized qualitatively. All studies regardless of overall ROB rating will be incorporated in the qualitative synthesis. Results from studies will not be synthesized quantitatively.

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

Strength of evidence will not be assessed for this review.

Assessing Applicability

Strength of evidence will not be assessed for this review.

V. References

1. Giacco D, Matanov A, Priebe S. Symptoms and subjective quality of life in post-traumatic stress disorder: a longitudinal study. PLoS One. 2013;8(4):e60991. doi: 10.1371/journal.pone.0060991. PMID: 23585868.
2. Kilpatrick DG, Resnick HS, Milanak ME, et al. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. Journal of traumatic stress. 2013 Oct;26(5):537-47. doi: 10.1002/jts.21848. PMID: 24151000.
3. Pietrzak RH, Goldstein RB, Southwick SM, et al. Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Anxiety Disord. 2011 Apr;25(3):456-65. doi: 10.1016/j.janxdis.2010.11.010. PMID: 21168991.
4. Hoffman V, Middleton JC, Feltner C, et al. Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder: A Systematic Review Update. Comparative Effectiveness Review No. 207. (Prepared by the RTI International–University of North Carolina at Chapel Hill Evidence-based Practice Center under Contract No. 290-2015-00011-I for AHRQ and PCORI.) AHRQ Publication No. 18-EHC011-EF. PCORI Publication No. 2018-SR-01. Rockville, MD: Agency for Healthcare Research and Quality; May 2018. doi: 10.23970/AHRQEPCCER207. PMID: 30204376.
5. Cipriani A, Williams T, Nikolakopoulou A, et al. Comparative efficacy and acceptability of pharmacological treatments for post-traumatic stress disorder in adults: a network meta-analysis. Psychol Med. 2018 Sep;48(12):1975-84. doi: 10.1017/s003329171700349x. PMID: 29254516.
6. Stein DJ, Ipser JC, Seedat S. Pharmacotherapy for post traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2006 Jan 25(1):Cd002795. doi: 10.1002/14651858.CD002795.pub2. PMID: 16437445.

7. O'Neil M, McDonagh M, Hsu F, et al. Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: Groundwork for a Publicly Available Repository of Randomized Controlled Trial Data. Technical Brief No. 32. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 19-EHC018-EF. Rockville, MD: Agency for Healthcare Research and Quality; May 2019. doi: 10.23970/AHRQEPCTB32.

8. National Center for PTSD. PTSD Mobile Applications (for Veterans, General Public, Family and Friends). Washington, DC: U.S. Department of Veterans Affairs; 2017. https://www.ptsd.va.gov/public/materials/apps/. Accessed October 24, 2019.

9. National Center for PTSD. PTSD Treatment Decision Aid: The Choice is Yours. U.S. Department of Veterans Affairs. https://www.ptsd.va.gov/apps/decisionaid/. Accessed October 24, 2019.

10. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD:: Agency for Healthcare Research and Quality; 2015. https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview. Accessed October 24, 2019.

VI. Definition of Terms

Not applicable.

VII. Summary of Protocol Amendments

If the EPC needs to amend the protocol, we will give the date of each amendment, describe the change, and provide rationale in this section. Changes will not be incorporated into the protocol.

XIII. Technical Experts

Technical Experts constitute a multi-disciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. The Technical Expert Panel is selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and suggest approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind; neither do they contribute to the writing of the report. They do not review the report, except as given the opportunity to do so through the peer or public review mechanism.

Members of the TEP must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The AHRQ TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

IX. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparing final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The disposition of

comments for systematic reviews and technical briefs will be published 3 months after publication of the evidence report.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers with any financial conflict of interest greater than $5,000 will be disqualified from peer review. Peer reviewers who disclose potential business or professional conflicts of interest can submit comments on draft reports through the public comment mechanism.

X. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Direct financial conflicts of interest that cumulatively total more than $1,000 will usually disqualify EPC core team investigators.

XI. Role of the Funder

This project was funded under Contract No. HHSA 290-2015-00009-I from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The AHRQ Task Order Officer reviewed the EPC response to contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by either the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

APPENDIX A. SEARCH STRATEGIES

Database: Ovid MEDLINE®, Ovid MEDLINE® In-Process & Other Non-Indexed Citations

Pharmacologic interventions

1. stress disorders, post-traumatic/
2. ("posttraumatic stress disorder" or "post traumatic stress disorder" or PTSD).ti,ab.
3. exp Drug Therapy/
4. dt.fs.
5. (medication* or pharmacologic* or pharmaco-therap* or pharmacotherap*).ti,ab.
6. (drug* adj2 (therap* or treatment*)).ti,ab.
7. exp Adrenergic alpha-Antagonists/ or Sympatholytics/ or Doxazosin/ or Prazosin/
8. ("adrenergic alpha antagonist*" or "adrenergic receptor block*" or "alpha adrenergic antagonist*" or "alpha block*" or antiadrenergic* or doxazosin or prazosin or sympatholytic* or terazosin).ti,ab.
9. exp Antipsychotic Agents/
10. ("anti-psychotic*" or antipsychotic* or FGA* or SGA* or aripiprazole or asenapine or brexpiprazole or cariprazine or chlorpromazine or clozapine or fluphenazine or haloperidol or iloperidone or loxapine or lurasidone or olanzapine or paliperidone or perphenazine or pimozide or quetiapine or risperidone or thioridazine or thiothixene or trifluoperazine or ziprasidone).ti,ab.
11. exp Benzodiazepines/
12. (alprazolam or benzodiazepine* or benzodiazepinone* or chlordiazepoxide or clonazepam or clorazepate or diazepam or estazolam or flurazepam or lorazepam or midazolam or oxazepam or quazepam or temazepam or triazolam).ti,ab.
13. exp Monoamine Oxidase Inhibitors/
14. (("monoamine oxidase" adj2 inhibitor*) or MAOI or isocarboxazid or phenelzine or selegiline or tranylcypromine).ti,ab.
15. carbamazepine/ or clonidine/ or lithium/ or pregabalin/ or valproic acid/
16. exp Anticonvulsants/
17. exp Antimanic Agents/
18. exp Cyclohexanecarboxylic Acids/
19. (anticonvuls* or carbamazepine or clonidine or divalproex or gabapentin or lamotrigine or lithium or oxcarbazepine or pregabalin or tiagabine or topiramate or valproate or "valproic acid").ti,ab.
20. exp "hypnotics and sedatives"/ or exp anti-anxiety agents/
21. ("anti anxiety" or antianxiety or buspirone or diphenhydramine or eszopiclone or guanfacine or hydroxizine or hypnotic* or ramelteon or sedative* or suvorexant or tasimelteon or zaleplon or zolpidem or zopiclone).ti,ab.
22. exp Antidepressive Agents/
23. (antidepressant* or "anti-depressant*" or "selective serotonin" or (serotonin adj3 reuptake) or SNRI* or SSRI* or tricyclic or amitriptyline or amoxapine or bupropion or citalopram or clomipramine or desipramine or desvenlafaxine or doxepin or duloxetine or escitalopram or fluoxetine or fluvoxamine or hydroxizine or imipramine or levomilnacipran or maprotiline or milnacipran or mirtazapine or nefazodone or nortriptyline or paroxetine or protriptyline or sertraline or trazadone or trimipramine or venlafaxine or vilazodone or vortioxetine).ti,ab.
24. exp Amphetamines/
25. (amphetamine or armodafanil or atomoxetine or dexmethylphenidate or dextroamphetamine or lisdexamphetamine or MDMA or methamphetamine or methylphenidate or modafanil).ti,ab.

26. exp Steroids/
27. (DHEA or hydrocortisone or steroid*).ti,ab.
28. exp Cannabinoids/
29. Cannabis/
30. Medical Marijuana/
31. (cannabi* or marijuana or tetrahydrocannabinol or THC).ti,ab.
32. ketamine/
33. ketamine.ti,ab.
34. Propranolol/
35. propranolol.ti,ab.
36. exp Randomized Controlled Trials as Topic/
37. exp Randomized Controlled Trial/
38. double-blind method/ or random allocation/ or single-blind method/
39. Placebos/
40. (random* or control* or trial or sham or placebo* or blind* or dumm* or mask*).ti,ab,kw.
41. (1 or 2) and (or/3-35)
42. 41 and (or/36-40)

Nonpharmacologic interventions
1. stress disorders, post-traumatic/
2. ("posttraumatic stress disorder" or "post traumatic stress disorder" or PTSD).ti,ab.
3. th.fs.
4. exp Psychotherapy/
5. exp Complementary Therapies/
6. exp Convulsive Therapy/
7. Hyperbaric Oxygenation/
8. Transcranial Magnetic Stimulation/
9. exp Rehabilitation/
10. exp Dietary Supplements/
11. exp "Delivery of Health Care, Integrated"/
12. exp Self-Help Groups/
13. exp peer group/
14. exp social support/
15. exp Telemedicine/
16. telephone/ or exp cell phone/
17. (therap* or psychotherap* or counsel* or nonpharma* or non-pharma*).ti,ab.
18. ("alternative medicine" or acupuncture or "animal assist*" or art or "cell phone" or "cognitive behavior*" or CBT or complementary or dance or drama or electroconvulsive or ECT or exercise or "eye movement desensitization and reprocessing" or EMDR or family or "hyperbaric oxygen*" or integrated or meditation or "mind body" or mindfulness or music or "prolonged exposure" or relaxation or "seeking safety" or "self help" or "tai chi" or "tai ji" or "text messag*" or "transcranial magnetic stimulation" or TMS or yoga).ti,ab.
19. exp Randomized Controlled Trials as Topic/
20. exp Randomized Controlled Trial/
21. double-blind method/ or random allocation/ or single-blind method/
22. (random* or control* or trial or sham or blind* or dumm* or mask*).ti,ab,kw.

23. (1 or 2) and (or/3-18)
24. 23 and (or/19-22)

Database: PTSDpubs (formerly PILOTS)
(MAINSUBJECT.EXACT("PTSD") OR MAINSUBJECT.EXACT("PTSD (DSM-III-R)") OR MAINSUBJECT.EXACT("PTSD (DSM-III)") OR MAINSUBJECT.EXACT("PTSD (DSM-IV)") OR MAINSUBJECT.EXACT("PTSD (DSM-5)") OR MAINSUBJECT.EXACT("Complex PTSD") OR MAINSUBJECT.EXACT("PTSD (ICD-11)") OR MAINSUBJECT.EXACT("PTSD (ICD-10)") OR MAINSUBJECT.EXACT("PTSD (ICD-9)") OR (ptsd OR "posttraumatic stress disorder" OR "post-traumatic stress disorder")) AND (MAINSUBJECT.EXACT("Randomized Clinical Trial") OR ti(random* OR control* OR trial))
Additional limits: Scholarly Journals

APPENDIX B. DATA ABSTRACTION ELEMENTS

Data elements added to those abstracted for Technical Brief No. 32[7] are in bold below, and will be abstracted for all studies, including the 318 RCTs included in Technical Brief No. 32.

Study Characteristics

a. Author
b. Year of publication
c. Bibliographic citation
d. PubMed ID
e. PTSDpubs (formerly PILOTS) ID number, if available
f. ClinicalTrials.gov identifier
g. Funding source
h. Country/Countries of study sites
i. Site Type (VA/DoD, non-VA/DoD, Mixed, MIL, Non-MIL)
j. Clinical setting
k. Study design
l. Indicate if subscale or symptom cluster data is reported (Y/N)
m. Indicate if subgroup analyses are reported (Y/N)
n. Indicate if psychotherapy providers have graduate degree (Y/N)
o. Indicate if treatment includes group therapy (Y/N)
p. Indicate if allowed PTSD psychotherapy, other psychotherapy, and psychotropic medication co-intervention (Y/N)
q. Diagnostic instrument(s)
r. Operational definition of PTSD (i.e., score or cutoff required for inclusion)
s. Suicide- and self-directed violence-related inclusion/exclusion criteria
t. Psychotic disorder- and symptom-related inclusion/exclusion criteria

Population Characteristics

a. Number of randomized participants
b. Proportion of participants meeting study-defined criteria for PTSD at baseline
c. Mean PTSD severity at baseline
d. Duration of PTSD symptoms
e. % Active duty military
f. % Veteran
g. % Community
h. Mean age
i. % Female
j. Gender and sexual orientation, if reported
k. Race % (by U.S. Census categories)
l. Ethnicity (by U.S. Census categories)
m. % Treatment-naïve
n. % with depression
o. % with substance use disorder
p. % with history of traumatic brain injury
q. Indicate if patients with suicidality were excluded (Y/N)
r. Participants' trauma type(s)
s. Mean number of trauma types and traumatic events experienced per participant

t. % with suicidal ideation/intent/plan/attempt(s) or self-directed violence
u. % with psychotic disorder
v. % with personality disorder
w. % with anxiety disorder
x. % with prior inpatient hospitalization
y. % service connected Veterans

Interventions

a. Intervention classification (pharmacologic, psychotherapy, nonpharmacologic biological, complementary and integrative, mixed, control)
b. Treatment conditions (interventions)
c. Number of participants randomized to each study arm
d. Treatment dose and/or session length
e. Frequency of treatment
f. Duration of treatment
g. Definition of treatment completion and/or adherence
h. Proportion of participants who completed and/or adhered to treatment
i. Mean number of psychotherapy sessions completed or dose of pharmacotherapy
j. Intervention type (PTSD-only, SUD-only, PTSD+SUD, PTSD+other, Control)

Outcomes

a. Primary PTSD outcome measure
b. Method for handling missing data for primary PTSD outcome measure
c. Analysis type of primary PTSD outcome measure (ITT, completer)
d. Statistical analysis method for primary PTSD outcome
e. Assessment time point(s) for primary PTSD outcome
f. Number of participants who completed the primary PTSD outcome assessment
g. Results for primary PTSD outcome (measure score and within-group effect size)
h. Between-group effect size for primary PTSD outcome
i. Proportion of participants who achieved study-defined PTSD diagnostic change
j. Proportion of participants who achieved study-defined clinically meaningful change
k. Results for other PTSD outcome measure(s) for studies that used a clinician-administered measure abstracted as primary PTSD outcome measure
l. Between-group effect sizes for all reported depression outcomes
m. Between-group effect sizes for all reported anxiety outcomes
n. Between-group effect sizes for all reported sleep outcomes
o. Between-group effect sizes for all reported anger outcomes
p. Between-group effect sizes for all reported quality of life outcomes
q. Between-group effect sizes for all reported functioning outcomes
r. Results for all reported substance use outcomes
s. Results for all suicide- or self-directed violence-related outcomes
t. Harms outcomes (withdrawals due to adverse events, serious adverse events)

APPENDIX C. COMPARATIVE EFFECTIVENESS REVIEW No. 207 RISK OF BIAS ASSESSMENT ELEMENTS

a. Was randomization adequate?
b. Was allocation concealment adequate?
c. Were groups similar at baseline?
d. Were outcome assessors masked?
e. Were care providers masked?
f. Were patients masked?
g. Was overall attrition 20% or higher?
h. Was differential attrition 15% or higher?
i. Did the study use intention-to-treat analysis?
j. Did the study use adequate methods for handling missing data?
k. Were outcome measures equal, valid, and reliable?
l. Did study report adequate treatment fidelity (therapist adherence) based on measurement by independent raters?