VA/DOD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF POSTTRAUMATIC STRESS DISORDER AND ACUTE STRESS DISORDER

Department of Veterans Affairs

Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

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Table of Contents

I. Introduction **5**

II. Background **5**

A. Definition of Traumatic Events 5

B. Acute Stress Reaction and Diagnosis of Acute Stress Disorder 6

C. Diagnosis of Posttraumatic Stress Disorder 8

D. DSM-IV versus DSM-5: Clinical Practice Guideline Implications 11

E. Epidemiology and Impact 13

III. About this Clinical Practice Guideline **16**

A. Methods 16

B. Summary of Patient Focus Group Methods and Findings 20

C. Conflicts of Interest 21

D. Scope of this Clinical Practice Guideline 21

E. Highlighted Features of this Clinical Practice Guideline 22

F. Patient-centered Care 22

G. Shared Decision Making 23

H. Background on Co-occurring Conditions with Posttraumatic Stress Disorder 23

I. Implementation 24

IV. Guideline Work Group **26**

V. Algorithm **27**

Module A: Acute Stress Reaction/Disorder 28

Module B: Assessment and Diagnosis of Posttraumatic Stress Disorder 30

Module C: Management of Posttraumatic Stress Disorder 32

VI. Recommendations **33**

A. General Clinical Management 37

B. Diagnosis and Assessment of Posttraumatic Stress Disorder 39

C. Prevention of Posttraumatic Stress Disorder 41

D. Treatment of Posttraumatic Stress Disorder 44

E. Treatment of Posttraumatic Stress Disorder with Co-occurring Conditions 72

VII. Knowledge Gaps and Recommended Research **76**

A. Shared Decision Making and Collaborative Care 76

B. Treatments for Acute Stress Disorder and Preventing Posttraumatic Stress Disorder 76

C. Treatments for Posttraumatic Stress Disorder 76
D. Non-Pharmacologic Biological Treatments for Posttraumatic Stress Disorder 78
E. Technology-based Treatments for Posttraumatic Stress Disorder 78
F. Treatments for Posttraumatic Stress Disorder with Comorbidities and Co-occurring Conditions. 78

Appendix A: Evidence Review Methodology 79
A. Developing the Scope and Key Questions 79
B. Conducting the Systematic Review 83
C. Convening the Face-to-face Meeting 87
D. Grading Recommendations 88
E. Recommendation Categorization 91
F. Drafting and Submitting the Final Clinical Practice Guideline 93

Appendix B: Patient Focus Group Methods and Findings 95
A. Methods 95
B. Patient Focus Group Findings 95

Appendix C: Pharmacotherapy Dosing Table 97

Appendix D: Evidence Table 98

Appendix E: 2010 Recommendation Categorization Table 104

Appendix F: Participant List 140

Appendix G: Literature Review Search Terms and Strategy 142
A. Topic-specific Search Terms 142
B. Search Strategies 156

Appendix H: Abbreviation List 183

References 186

I. Introduction

The Department of Veterans Affairs (VA) and the Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the "…Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System," by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with posttraumatic stress disorder (PTSD) and acute stress disorder (ASD), thereby leading to improved clinical outcomes.

In 2010, the VA and DoD published a CPG for the Management of Post-Traumatic Stress and Acute Stress Reaction (2010 PTSD CPG), which was based on evidence reviewed through March 2009. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of PTSD and other stress related disorders, such as ASD and other acute reactions to trauma (sometimes referred to as acute stress reactions [ASR]). Improved recognition of the complex nature of ASR, ASD, and PTSD has led to the adoption of new or refined strategies to manage and treat patients with these conditions.

Consequently, a recommendation to update the 2010 PTSD CPG was initiated in 2015. The updated CPG includes objective, evidence-based information on the management of PTSD and related conditions. It is intended to assist healthcare providers in all aspects of patient care, including, but not limited to, diagnosis, treatment, and follow-up. The system-wide goal of developing evidence-based guidelines is to improve the patient's health and well-being by guiding health providers who are taking care of patients with PTSD along the management pathways that are supported by evidence. The expected outcome of successful implementation of this guideline is to:

- Enhance assessment of the patient's condition and determine the best treatment method in collaboration with the patient and, when possible and desired, the patient's family and caregivers
- Optimize the patient's health outcomes and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care

II. Background

A. Definition of Traumatic Events

A traumatic event is defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) as an event (or series of events) in which an individual has been personally or indirectly exposed to actual or threatened death, serious injury, or sexual violence. There is a wide spectrum of psychological responses to traumatic events, ranging from normal, transient, non-debilitating symptoms to a transient ASR to an acute, time-limited and clinically-significant clinical disorder (ASD) to a persistent disorder (PTSD) that may become chronic, if untreated.

The DSM-5 definition of traumatic events is the same for both ASD and PTSD, and one can meet the trauma definition with any one of four criteria (A1-A4) (see Table 1 and Table 2). Criterion A1 is direct exposure to traumatic events such as actual or threatened death, serious injury (e.g., military combat, physical attack, torture, man-made/natural disasters, accidents, incarceration, and exposure to war-zone/urban/domestic violence) or sexual violence or assault. Criterion A2 is witnessing such events and includes people who directly observed such events, but were not harmed themselves. Criterion A3 is indirect exposure such as learning that a loved one was exposed to a traumatic event; if the loved one died during such an event, Criterion A3 would only be met if the death was violent or accidental. Criterion A4 applies to exposure to repeated or extreme details of trauma, such as seeing dead body parts or severely injured people as part of one's professional duties (e.g., medical, law enforcement, mortuary affairs, and journalism personnel).

B. Acute Stress Reaction and Diagnosis of Acute Stress Disorder

ASR is defined as a transient normal reaction to traumatic stress and is not a DSM-5 diagnosis, although symptoms may be temporarily debilitating. Onset of stress-related signs and symptoms may be simultaneous or within minutes of the traumatic event or may follow the trauma after an interval of hours or several days. In most cases, symptoms will resolve rapidly with simple measures, such as reassurance, rest, and ensuring safety.

Combat and operational stress reaction (COSR) is the military analog of ASR and reflects a normal, transient, acute reaction to a high-stress operational or combat-related traumatic event in a military occupational setting. ASR/COSR can present with a broad group of physical, mental, behavioral, and emotional symptoms and signs (e.g., depression, fatigue, anxiety, panic, decreased concentration/memory, hyperarousal, dissociation). Identification of a patient with ASR/COSR symptoms is based on observation of behavior and function as well as clinical assessments since there is insufficient evidence to recommend a specific screening tool. With regard to COSR, a Service Member's role and functional capabilities should also be considered as well as the complexity and importance of his or her job. Symptoms of COSR and ability to function in an operational mission should be documented and collateral information pertaining to stressors or the medical history can be obtained from unit leaders, coworkers, or peers. Individuals who experience ASR or COSR should receive a comprehensive assessment of their symptoms or behavioral signs to include details about the time of onset, frequency, course, severity, level of distress, work performance, functional impairment, and other relevant information. Additionally, the individual should be assessed for medical causes of acute changes in behavior. Military policy indicates that Service Members with COSR who do not respond to initial supportive interventions may warrant referral or evacuation, though the general principle of care is to provide treatment as close to the Service Member's unit/team as possible. If ASR/COSR continues beyond three days with persistent limitations of functioning, it is necessary to monitor Service Members for the possible development of ASD.

ASD, a diagnosis defined by DSM-5 (see Table 1 for full criteria), can also occur after exposure to a traumatic event. Symptoms must last at least three days but less than one month after exposure to the traumatic event for an individual to be eligible for this diagnosis.

Individuals with ASD must have been exposed to a traumatic stressor (Criteria A1-A4). In addition, they must exhibit at least nine out of 14 possible symptoms that are nested within five diagnostic clusters (Table 1). Symptoms need to cause significant distress or functional impairment.

Table 1. DSM-5 Diagnostic Criteria for Acute Stress Disorder*[2]

Diagnostic Criteria for ASD
Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways: 1. Directly experiencing the traumatic event(s) 2. Witnessing, in person, the event(s) as it occurred to others 3. Learning that the event(s) occurred to a close family member or close friend **Note:** In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental. 4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse) **Note:** This does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.
Criterion B. Presence of nine (or more) of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal, beginning or worsening after the traumatic event(s) occurred: **Intrusion Symptoms** 1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s) 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s) 3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring (such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings) 4. Intense or prolonged psychological distress or marked physiological reactions in response to internal or external cues that symbolize or resemble an aspect of the traumatic event(s) **Negative Mood** 5. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, loving feelings) **Dissociative Symptoms** 6. An altered sense of reality of one's surroundings or oneself (e.g., seeing oneself from another's perspective, being in a daze, time slowing) 7. Inability to remember an important aspect of the event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs) **Avoidance Symptoms** 8. Efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s) 9. Efforts to avoid external reminders (e.g., people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s) **Arousal Symptoms** 10. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep) 11. Irritable behavior and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects 12. Hypervigilance 13. Problems with concentration 14. Exaggerated startle response

Diagnostic Criteria for ASD
Criterion C. Duration of the disturbance (symptoms in Criterion B) is three days to one month after trauma exposure. **Note:** Symptoms typically begin immediately after the trauma, but persistence for at least three days and up to a month is needed to meet disorder criteria.
Criterion D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Criterion E. The disturbance is not attributable to the physiological effects of a substance (e.g., medication or alcohol) or another medical condition (e.g., mild traumatic brain injury) and is not better explained by brief psychotic disorder.

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C. Diagnosis of Posttraumatic Stress Disorder

PTSD is a clinically-significant condition with symptoms that have persisted for more than one month after exposure to a traumatic event (Criteria A1-A4) and caused significant distress or impairment in social, occupational, or other important areas of functioning (see Table 2 for full criteria). Criterion A for PTSD is the same as criterion A for ASD; however, ASD can only be within the first month after the traumatic event. After one month, the diagnostic question is whether PTSD is present. Individuals with PTSD must exhibit a specific number of symptoms from each symptom cluster (Criteria B-E). PTSD symptoms must persist for at least one month after the traumatic event (Criterion F) and result in significant distress or functional impairment (Criterion G). PTSD can also have a delayed expression, when full diagnostic criteria are not met until at least six months after exposure to the traumatic event. PTSD can appear alone as the only diagnosis, or more commonly, with another co-occurring DSM-5 disorder, such as a substance use disorder (SUD), mood disorder, or anxiety disorder. PTSD is also strongly associated with functional difficulties, reduced quality of life, and adverse physical health outcomes.

Table 2. DSM-5 Diagnostic Criteria for Posttraumatic Stress Disorder*[2]

DSM-5 Diagnostic Criteria for PTSD
Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways: 1. Directly experiencing the traumatic event(s) 2. Witnessing, in person, the event(s) as it occurred to others 3. Learning that the traumatic event(s) occurred to a close family member or close friend **Note:** In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental. 4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse) **Note:** This does not apply to exposure through electronic media, television, movies or pictures unless this exposure is work-related.

DSM-5 Diagnostic Criteria for PTSD
Criterion B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred. 1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s) 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s) 3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring (such reactions may occur on a continuum with the most extreme expression being a complete loss of awareness of present surroundings) 4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s) 5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s)
Criterion C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following: 1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s) 2. Avoidance or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s)
Criterion D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred as evidenced by two or more of the following: 1. Inability to recall an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs) 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad.", "No one can be trusted.", "The world is completely dangerous.", "My whole nervous system is permanently ruined.") 3. Persistent distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others 4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, shame) 5. Markedly diminished interest or participation in significant activities 6. Feeling of detachment or estrangement from others 7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, loving feelings)
Criterion E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects 2. Reckless or self-destructive behavior 3. Hypervigilance 4. Exaggerated startle response 5. Problems with concentration 6. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep)
Criterion F. Duration of the disturbance (symptoms in Criteria B, C, D, and E) is more than one month.
Criterion G. The disturbance causes clinically significant distress or impairment in social, occupation, or other important areas of functioning.

DSM-5 Diagnostic Criteria for PTSD
Criterion H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition. *Specify* whether: **With dissociative symptoms:** The individuals symptoms must meet the criteria for PTSD and in addition, in response to the stressor, the individual experiences persistent or recurrent symptoms of either of the following: 1. Depersonalization: Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream, feeling a sense of unreality of self or body, time moving slowly) 2. Derealization: Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted) **Note**: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (e.g., blackouts, behavior during alcohol intoxication) or another medical condition (e.g., complex partial seizures). *Specify* if: **With delayed expression:** If the full diagnostic criteria are not met until at least six months after the event (although the onset and expression of some symptoms may be immediate).

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Specific Diagnostic Issues and Questions

- As shown in Table 2, the **Dissociative Subtype of PTSD** is diagnosed when an individual meets all diagnostic criteria for PTSD and also exhibits depersonalization or derealization.
- Also shown in Table 2, **PTSD with delayed expression** is diagnosed if full diagnostic criteria are not met until at least six months after exposure to the traumatic event.
- **Subthreshold PTSD** (also sometimes designated as **partial PTSD** or **subsyndromal PTSD**) is a diagnosis used by clinicians to characterize individuals with clinically significant posttraumatic reactions who fail to meet full PTSD criteria (often for lack of one or two symptoms). The DSM-5 diagnosis for such individuals is **Other Specified Trauma and Stress-Related Disorder (309.89)**. Unfortunately, we currently lack an approved case definition for subthreshold PTSD. Individuals designated as such in one research study may have met different criteria in another study. Furthermore, participants in the clinical trials cited in this CPG were diagnosed with full rather than subthreshold PTSD. As a result, we cannot be certain how well our recommendations for treatment of full PTSD apply to those with subthreshold PTSD. (See the DSM-IV versus DSM-5: Clinical Practice Guideline Implications section below regarding a reasonable clinical approach to individuals with subthreshold PTSD.)
- **"Complex PTSD"** [3] is a term used to characterize traumatized individuals who, in addition to usually meeting full PTSD diagnostic criteria, also exhibit prominent behavioral difficulties (such as impulsivity and self-destructive actions), emotional difficulties (such as affect lability), cognitive difficulties (such as dissociation), interpersonal difficulties, and somatization. The DSM-5 does not recognize complex PTSD as a distinct, valid, and empirically-based diagnosis. Furthermore, the recommendations in this CPG apply to individuals who meet DSM-5 criteria for PTSD whether or not some clinicians might conclude that they also appear to have "complex PTSD."

D. DSM-IV versus DSM-5: Clinical Practice Guideline Implications

The diagnostic criteria for PTSD underwent substantial changes between the DSM-IV (published in 1994) and the DSM-5, which was published in 2013. As with other mental disorders, we lack biological markers for PTSD, making a provider dependent on the self-reported presence or absence of specific symptoms in making the diagnosis. Changes in the criteria for PTSD may carry significant implications for the diagnosis and treatment of the disorder.

Changes to the PTSD diagnostic criteria included modifying the definition of a traumatic event to note that the sudden death of a loved one had to involve traumatic circumstances to qualify as a trauma, and to eliminate the requirement that the traumatic event be accompanied by particular emotional reactions, specifically fear, helplessness, or horror. Changes to the symptom criteria for PTSD included adding three new symptoms to the diagnosis. These symptoms, a persistent and distorted sense of blame for the trauma or its consequence, persistent negative emotions, and reckless or self-destructive behavior, increased the total number of symptoms from 17 to 20. In addition, the descriptions of eight of the original 17 symptoms were revised or rewritten, with changes ranging from minor to substantial. The symptom criteria for PTSD were also rearranged into four symptom clusters instead of the three present in earlier versions of the DSM. Effectively, symptoms in the DSM-IV cluster of "Avoidance and numbing" were divided into an "Avoidance" cluster and a "Negative alterations in cognition and mood" cluster that includes five DSM-IV symptoms and two newly added symptoms. Although the DSM-5 retained the diagnostic requirement that symptoms from all clusters be present, the changes in the number of symptoms, definitions of symptoms, and specific symptoms included in each cluster effectively changed the criteria used to make a diagnosis.

At the time this CPG was prepared, the full consequences of the changes to the diagnostic criteria were not clear. The changes generated considerable controversy and rigorous debate within the clinical and research community. A full exploration of these controversies is beyond the scope of this guideline, but two issues raised are of particular importance in the application of this guideline. First, there are questions about the impact of the diagnostic changes on the actual diagnosis of the disorder, and the potential that the new definition excludes people who would have met the previous diagnosis. Second, there are questions about the appropriate application of treatments developed and tested using DSM-IV criteria to patients diagnosed with the DSM-5 criteria.[4,5]

With regard to the impact of the changes to the DSM on the diagnosis of PTSD, four logical possibilities arise: (1) an individual may meet criteria under **both DSM-IV and DSM-5**; (2) an individual may not meet criteria under either **DSM-IV or DSM-5**; (3) an individual may meet criteria under **DSM-IV but not DSM-5**; or (4) an individual may meet criteria under **DSM-5 but not DSM-IV**. Based on the available literature, some authors have concluded that a significant number of individuals (upwards of 50%) would be diagnosed with PTSD under one set of criteria but not the other (i.e., discordant diagnoses - 3 and 4 above).[4] Other authors examining the same literature have concluded that the two diagnostic rubrics result in much less inconsistency in diagnostic classification (i.e., concordant diagnoses - 1 and 2 above).[5] A full understanding of the impact of the changes to DSM criteria for PTSD awaits further study, but it is likely that the effect of these changes will depend on factors such as the method of assessment, assessment setting, timing of the assessment relative to the trauma, and the nature of the trauma.

For clinicians, the possibility that changes in the DSM criteria for PTSD could alter the diagnostic determination, change a treatment plan, or alter a disability determination raises questions. Indeed, the PTSD CPG Work Group was faced with this challenge as it developed this guideline. In an effort to put forward a useful guideline based on existing research, the Work Group adopted an approach that balanced logic, empirical data, and practicality.

At the time that this guideline was prepared, both the VA and DoD had adopted the DSM-5 criteria, so clinicians are expected to base their diagnosis on these criteria. In contrast, however, all of the clinical trials reviewed in the preparation of this guideline utilized the DSM-IV (or earlier) criteria, raising potential questions as to the applicability of the present guideline. In situations where the diagnostic determination (either presence or absence of PTSD) is consistent under the DSM-IV and DSM-5 criteria, there are no particular conflicts. When PTSD is present, one would apply this guideline and when PTSD is clearly absent, one would not. Questions arise, however, when PTSD would be diagnosed under one set of criteria but not the other, or when significant PTSD symptoms are present but the diagnostic criteria are not met (subthreshold PTSD).

Concerning situations in which diagnoses using the different criteria are discordant or where the DSM-IV-based diagnosis is unknown, the Work Group believes the present guideline reflects the best, empirically-based treatment recommendations. This can be illustrated by examining three clinical scenarios: two involving discordant diagnoses and one involving subthreshold PTSD.

Scenario 1: In the case of a patient who has been diagnosed with PTSD based on DSM-IV criteria, retains symptoms of PTSD, but who does not meet DSM-5 criteria, the present guideline may be used with confidence to make treatment decisions because they were developed based on studies that used the same DSM-IV criteria.

Scenario 2: In the case of a patient who has not been previously diagnosed with PTSD based on DSM-IV criteria (or the DSM-IV diagnosis is unknown) but **does** meet DSM-5 criteria, the clinician must make treatment decisions although empirical outcome data using DSM-5 criteria are lacking. In this case, the present guideline, based on research using DSM-IV criteria, is assumed to provide the best available projection of effective treatments for DSM-5 PTSD.

Scenario 3: A patient who does not meet DSM-5 criteria for PTSD but does have a number of PTSD symptoms accompanied by clinically-significant distress or impairment is often referred to as "subthreshold PTSD," although there is no agreed-upon definition of subthreshold PTSD. As there are no randomized controlled trials (RCTs) examining treatments specifically for subthreshold PTSD, we are unable to make recommendations regarding evidence-based treatments in this situation. Clinicians are encouraged to use their clinical judgment in collaboration with the patient to weigh the potential risks and benefits of using or withholding an evidence-based PTSD treatment for someone with subthreshold PTSD. If additional guidance is needed to make a decision in such cases, clinicians may elect to repeat the diagnostic assessment using the DSM-IV criteria. Though impractical in many situations, the additional data provided by confirming, or not confirming, a PTSD diagnosis using the earlier criteria would help to ensure that these patients benefit from the wealth of treatment evidence derived using the earlier diagnostic criteria.

E. Epidemiology and Impact

Estimates of the prevalence of PTSD depend on both sample characteristics and study methods. Sample characteristics include the population of study (e.g., general population, Veterans, or Service Members; U.S. versus other countries; treatment-seeking versus not treatment-seeking). Study methods include the sampling strategy and the method of PTSD assessment and diagnosis. In addition, various risk and protective factors modify prevalence estimates such as military factors (e.g., service era, branch of service, time since deployment, combat exposure), demographic factors (e.g., age, gender, race/ethnicity), and type and amount of trauma exposure.

a. General Population

The Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study found a lifetime PTSD prevalence of 6.4% overall in a sample of over 34,000 U.S. adults.[6] The sample was surveyed in 2004-2005 as a representative sample that reflected the population based on characteristics including region, age, gender, and race/ethnicity. Lifetime PTSD prevalence was higher in women (8.6%) than men (4.1%). The prevalence of lifetime subthreshold partial PTSD was 6.6%. The estimates in the NESARC sample are quite similar to the estimates reported by Kessler et al. in the National Comorbidity Survey-Replication (NCS-R).[7] Like the NESARC, the NCS-R is based on a nationally -representative sample, although the NCS-R data were collected approximately five years earlier. The overall lifetime prevalence of PTSD in the NCS-R was 6.8%, with women higher than men in lifetime prevalence (9.7% compared to 5.2%) and in current prevalence (3.6% compared to 1.8%). Note that although the prevalence estimates in Wave 2 of NESARC and in the NCS-R are based on DSM-IV criteria for PTSD, more recent estimates from Wave 3 of NESARC based on DSM-5 criteria suggest comparable lifetime (6.1%) and current (4.7%) PTSD prevalence estimates.[8]

b. Active Duty U.S. Service Members

In recent years, a number of reviews have examined PTSD prevalence estimates among U.S. Service Members deployed to Iraq and/or Afghanistan.[9-12] Many of the studies in the reviews, however, are based on data collected relatively early during the wars and may not reflect the dynamic changes in the population, such as the cumulative effects of repeated deployments. Richardson et al. reported estimates for current PTSD in U.S. Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) Veterans ranging from 4% to 17%.[12] Kok et al. reported a weighted post-deployment PTSD prevalence of 13.2% in OEF/OIF infantry units, and 6% in the overall population post-deployment.[10] A study by the RAND Corporation in 2008 reported that 14% of a representative sample of 1,965 OEF/OIF Veterans interviewed by telephone met current criteria for PTSD.[13] A review by Ramchand et al. noted an increased prevalence of PTSD in those serving in the Army and Marine Corps as well as among enlisted personnel relative to officers.[14] Combat exposure, however, is the strongest predictor of mental health problems among those deployed to Iraq and Afghanistan.[14] One study found higher rates of PTSD among National Guard members, [15] though in general, similar prevalences have been found by service, branch, or rank adjusted for combat exposure.[14]

Using a random sample of the OEF/OIF military population, two studies based on the Millennium Cohort longitudinal cohort study found that 7.3% to 8.3% of participants who reported combat exposure met criteria for PTSD.[16,17] The estimates included Veterans who had separated by the time the data were

collected, and therefore are not strictly estimates for active duty personnel. However, the Army Study to Assess Risk and Resilience in Service Members (ARMYSTARRS), showed a prevalence of 8.6%, consistent with the Millennium cohort data.[18]

c. Users of Care in the Department of Defense Healthcare System

DoD estimates of incidence and prevalence are derived from administrative medical data of active duty personnel who receive PTSD-related care within the DoD direct care system. During fiscal year 2015, 2.2% of the active duty population was estimated to meet criteria for PTSD. Estimated prevalence was higher among female Service Members (3.2%) than male Service Members (2.0%) and among those who had deployed (3.6%) as compared to those who had not (0.8%).[19]

d. U.S. Veterans

A precise estimate of the prevalence of PTSD in the current population of U.S. Veterans overall has yet to be established. Among non-treatment-seeking Veteran samples, estimates are only slightly higher than in the general population (6.4% to 6.8%).[6,7] In a recent survey of a nationally representative U.S. Veteran sample, 8% screened positive for lifetime PTSD on the PTSD Checklist (PCL).[20] Current (past year) PTSD prevalence was 5%. Lifetime prevalence was higher among female than male Veterans and among younger Veterans than older Veterans. Veterans of all ages reported exposure to many potentially traumatic events, including combat, and the conditional risk for developing PTSD was high for non-combat-related events such as sexual or physical assault.

For various reasons, including barriers to endorsing mental health issues in the military (e.g., stigma, fear, job loss), prevalence estimates among active duty U.S. Service Members may not be representative of PTSD prevalence estimates among U.S. Veterans.

e. Veteran Service Era

Magruder and Yeager reviewed studies of PTSD prevalence related to deployment status by war era.[21] They reported that prevalence of PTSD among OEF/OIF and Operation New Dawn (OND) deployed populations ranged from 5% to 20% and among non-deployed, 3% to 9%. The estimated prevalence of PTSD among deployed populations to the Gulf War ranged from 2% to 24% and among the non-deployed groups from 0.7% to 6%. Among Vietnam War studies, the estimated prevalence of PTSD among deployed populations ranged from 9% to 19%. Among the non-deployed Vietnam era comparison groups, estimates were 1% to 13%. Despite the heterogeneous results for PTSD prevalence, they noted a 1.5- to 3.5-fold increase in PTSD risk with deployment, regardless of war era. The odds of PTSD for deployed versus non-deployed Veterans were lowest among OEF/OIF/OND and highest for Vietnam Veterans.

The most recognized study of Vietnam-era Veterans is the National Vietnam Veterans Readjustment Study (NVVRS) conducted in 1986-1987.[22] Using DSM-III-R PTSD criteria, a lifetime and current prevalence of PTSD estimate of 30.9% and 15.2%, respectively, was reported. Approximately 40 years after the Vietnam War, a follow-up study of the cohort, the National Vietnam Veterans Longitudinal Study (NVVLS), reported a prevalence of current war-zone-related PTSD as 4.5% in men and 6.1% in women based on the Clinician Administered PTSD Scale for DSM-5. Prevalence of lifetime war-zone-related PTSD was 17.0% in men and 15.2% in women.[23] The prevalence of current PTSD from any cause was estimated as 12.2% for male and 8.5% for female theatre Veterans.[23]

The Health of Vietnam-Era Women's Study examined the prevalence of PTSD in Vietnam-era women Veterans.[24] The prevalence of current PTSD according to DSM-5 was 15.9%, 8.1% and 9.1% for the Vietnam, near-Vietnam, and U.S. cohorts who served stateside, respectively. The prevalence of lifetime PTSD was 20.1%, 11.5%, and 14.1%, respectively. It is not clear why the estimates of current and lifetime PTSD are higher in this study than in the NVVLS, but methodologic differences between studies (e.g., use of clinician interview in the NVVLS and lay interview in the all-women's study) may account for the difference. One of the most telling findings was that sexual discrimination or harassment, which is not thought of as war zone exposure, was higher among deployed women and significantly associated with the development of PTSD.

New research conducted by Magruder et al. has examined the long-term trajectories of PTSD in Vietnam-era Veterans and found that while the majority of Veterans remain unaffected by PTSD throughout their lives (79% of those with theater service, 91% with non-theater service), a critical minority (10% of theater Veterans, 4.5% of non-theater Veterans) in 2012 had current PTSD that was either late onset (6.5% theater, 3.3% non-theater) or chronic (4% theater, 1% non-theater).[25] The distribution of longitudinal patterns was significantly different by theater service and confirms that PTSD remains a critical issue for many Vietnam-era Veterans.

The prevalence of PTSD among surviving Veterans of World War II or the Korean Conflict is unknown, but is likely to be lower compared with the prevalence in younger Veterans. The review cited above of prevalence across war eras did not include cohorts prior to the Vietnam War.[21] The nationally representative sample cited above [20] also did not report prevalence by war era, but did report that lifetime and current prevalence were higher in the youngest Veterans (23.4% and 9.1%, respectively, in those age 21-29) compared with the oldest Veterans (age 60+, 3.5% and 2.5%, respectively).[20] Regardless of the specific estimate, these data indicate that some Veterans continue to experience PTSD into old age.

f. Users of Care in the Veterans Health Administration

The VA's Northeast Program Evaluation Center produces an annual data sheet that provides an overview of the PTSD patient population receiving healthcare in the VA. Veterans are defined as meeting a diagnosis of PTSD if they had received at least two visits or one inpatient/residential stay with a diagnosis of PTSD in the prior year. Of the 5,841,668 total Veterans served, 10.6% (N=619,493) who used VA healthcare in fiscal year 2016 were diagnosed with PTSD: 10.2% of men and 15.5% of women.[26] Prevalence data in 2015 was much higher among those Veterans who served in Iraq and/or Afghanistan: 26.7% overall, and 27.3% and 22.5% in men and women, respectively.[27]

g. Impact

PTSD can affect all aspects of a person's functioning and well-being. Pietrzak et al. noted PTSD is associated with nearly all assessed Axis 1 disorders and lifetime suicide attempts, with magnitudes of associations similar to those observed in the NCS-R.[6,7] There are specific increased risks of co-occurring depression and SUD.[20] (See Background on Co-occurring Conditions section.) For example, using DSM-5 criteria in the U.S. Veteran population, Wisco et al. found that 57% of individuals with past-month PTSD met criteria for current major depression, and among those with probable lifetime PTSD, 69% had a lifetime history of alcohol use disorder (AUD). PTSD is also associated with impairments in social and occupational

functioning and overall quality of life.[6,28,29] In addition, PTSD is associated with poorer perceived physical health, increased morbidity, and greater healthcare utilization for physical problems.[30] Findings on mortality are mixed, but generally show that PTSD is associated with increased overall mortality and mortality due to accidental causes.

III. About this Clinical Practice Guideline

This guideline represents an important step toward improving the treatment and management of patients with PTSD in the VA and DoD. As with other CPGs, however, challenges remain, including evidence gaps, the need to develop effective strategies for guideline implementation and to evaluate the effect of guideline adherence on clinical outcomes. This guideline is intended for VA and DoD healthcare practitioners including primary care physicians, nurse practitioners, physician assistants, psychiatrists, psychologists, social workers, nurses, pharmacists, chaplains, addiction counselors, and others involved in the care of Service Members or Veterans with PTSD.

As elaborated in the qualifying statement on page one, this CPG is not intended to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns evolve. This CPG is based on information available by March 2016 and is intended to provide a general guide to best practices. The guideline can assist care providers, but the use of a CPG must always be considered as a recommendation, within the context of a provider's clinical judgment and patient values and preferences, for the care of an individual patient.

A. Methods

The current document is an update to the 2010 PTSD CPG. The methodology used in developing the 2017 CPG follows the *Guideline for Guidelines*,[1] an internal document of the VA and DoD EBPWG. The *Guideline for Guidelines* can be downloaded from http://www.healthquality.va.gov/policy/index.asp. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from within the VA and DoD, known as the Work Group, and ultimately, the development and submission of a new or updated PTSD CPG.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations and writing and publishing a guideline document to be used by providers within the VA/DoD healthcare systems. Specifically, the Champions and Work Group members for this guideline were responsible for identifying the key questions (KQs) of the most clinical relevance, importance, and interest for the management of patients with PTSD. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. The amount of new scientific evidence that had accumulated since the previous version of the CPG was also taken into consideration in the identification of the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group

- Participating throughout the guideline development and review processes

The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified five clinical leaders, Nancy Bernardy, PhD, Matthew Friedman, MD, PhD, and Paula Schnurr, PhD, from the VA as well as Charles Hoge, MD and David Riggs, PhD from the DoD, as Champions for the 2017 PTSD CPG.

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI Institute, and Sigma Health Consulting, LLC, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The first conference call was held in November 2015, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review about the management of PTSD. The group also identified a list of clinical specialties and areas of expertise that are important and relevant to the management of PTSD, from which Work Group members were recruited. The specialties and clinical areas of interest included: ambulatory care, behavioral health, clinical pharmacy, clinical neuropsychology, family medicine, nursing, pharmacology, pharmacy, psychiatry, and psychology.

The guideline development process for the 2017 CPG update consisted of the following steps:

1. Formulating and prioritizing evidence KQs
2. Convening a patient focus group
3. Conducting the systematic review
4. Convening a face-to-face meeting with the CPG Champions and Work Group members
5. Drafting and submitting a final CPG on the management of PTSD to the VA/DoD EBPWG

Appendix A provides a detailed description of each of these tasks.

a. Grading Recommendations

The Champions and Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: [31]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.,:
    - Resource use
    - Equity
    - Acceptability

- Feasibility
- Subgroup considerations

Using this system, the Champions and Work Group determined the relative strength of each recommendation (Strong or Weak). A strong recommendation indicates that the Work Group is highly confident about the balance between desirable and undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they give a weak recommendation.

They also determined the direction of each recommendation (For or Against). A recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option …")

The grade of each recommendation made in the 2017 CPG can be found in the section on Recommendations. Additional information regarding the use of the GRADE system can be found in Appendix A.

b. Reconciling 2010 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence, or as scheduled, subject to time-based expirations.[32] For example, the U.S. Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services.[33] Further, the inclusion criteria for the National Guideline Clearinghouse specify that a guideline must have been developed, reviewed, or revised within the past five years.

The PTSD Guideline Work Group focused largely on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Guideline Work Group considered, with a limited review of the previous supporting evidence, the current applicability of other recommendations that were included in the previous 2010 PTSD CPG, subject to evolving practice in today's environment.

A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE).[34,35] These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories took into account whether or not the evidence that related to a recommendation was systematically reviewed, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current patient care environment and inside the scope of the CPG. Additional information regarding these categories and their definitions can be found in Appendix A. The categories for the recommendations included in the 2017 version of the guideline can be found in the section on Recommendations. The categories for the recommendations from the 2010 PTSD CPG are noted in Appendix E: 2010 Recommendation Categorization Table.

The CPG Work Group recognized the need to accommodate the transition in evidence rating systems from the 2010 PTSD CPG to the current CPG. In order to report the strength of all recommendations using a consistent format (i.e., the GRADE system) the CPG Work Group converted the USPSTF strengths of the recommendation accompanying the carryover recommendations from the 2010 guideline to the GRADE system. As such, the CPG Work Group considered the strength of the evidence cited for each recommendation in the 2010 PTSD CPG as well as harms and benefits, values and preferences, and other implications, where possible. The CPG Work Group referred to the available evidence as summarized in the body of the 2010 PTSD CPG and did not re-assess the evidence systematically. In some instances, peer-reviewed literature published since the 2010 PTSD CPG was considered along with the evidence base used for that CPG.

Where such newer literature was considered when converting the strength of the recommendation from the USPSTF to the GRADE system, it is referenced in the discussion that follows the corresponding recommendation, as well as in Appendix D: Evidence Table.

The CPG Work Group recognizes that, while there are practical reasons for incorporating findings from a previous systematic review, previous recommendations,[36] or recent peer-reviewed publications into an updated CPG, doing so does not involve an original, comprehensive systematic review and, therefore, may introduce bias.

c. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of the CPG. The process for developing the initial draft is described in more detail in Drafting and Submitting the Final Clinical Practice Guideline.

Once a near-final draft of the guideline was agreed upon by the Champions and Work Group members, the draft was sent out for peer review and comment. The draft was posted on a wiki website for a period of 14 business days. The peer reviewers comprised individuals working within the VA and DoD health systems as well as experts from relevant outside organizations designated by the Work Group members. Organizations designated by the Work Group to participate in the peer review and that provided feedback include the following:

- Emory University School of Medicine
- Duke University Medical Center

- New York University Langone Medical Center
- Medical University of South Carolina
- University of Adelaide

The VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their feedback on the CPG. Reviewers were provided a hyperlink to the wiki website where the draft CPG was posted. All reviewer feedback was posted in tabular form on the wiki site, along with the name of the reviewer, for transparency. All feedback from the peer reviewers was discussed and considered by the Work Group. Modifications made throughout the CPG development process were made in accordance with the evidence.

B. Summary of Patient Focus Group Methods and Findings

When forming guideline recommendations, consideration should be given to the values of those most affected by the recommendations: patients. Patients bring perspectives, values, and preferences into their healthcare experience that can vary from those of clinicians. These differences can affect decision making in various situations, and should thus be highlighted and made explicit due to their potential to influence a recommendation's implementation.[37,38] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals with an *a priori set* of assumptions or hypotheses and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership, along with the PTSD CPG Work Group, held a patient focus group prior to finalizing the KQs for the evidence review. The group met on January 25, 2016, at Brooke Army Medical Center, San Antonio Military Medical Center, Fort Sam Houston, Texas. The aim of the focus group and interview was to further the understanding of the perspectives of patients diagnosed with PTSD within the VA and/or DoD healthcare systems. The focus group explored a set of topics related to the management of PTSD, including knowledge of PTSD, treatment options, delivery of care, and the impact and challenges of living with PTSD.

It is important to note the focus group was a convenience sample and the Work Group recognizes the limitations inherent in the small sample size. Less than 10 people were included in the focus group consistent with the requirements of the federal Paperwork Reduction Act, 1980. The Work Group acknowledges that the sample of patients included in this focus group is likely not representative of all VA and DoD patients diagnosed with PTSD. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to PTSD care in the VA and DoD and the patients' broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus group. These limitations, as well as others, were considered during the guideline development as the information collected from the discussion was being used. Recruitment for participation in the focus group was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facility at which the focus group took place.

The following concepts are ideas and suggestions about aspects of care that are important to patients and emerged from the discussion. These concepts were important parts of the participants' care and added to the Work Group's understanding of patient values and perspectives. The Work Group considered the focus group feedback while assessing the strength of each recommendation and continued to consider the

feedback throughout the PTSD CPG development process. Additional details regarding the patient focus group methods and findings can be found in Appendix B: Patient Focus Group Methods and Findings.

PTSD CPG Focus Group Concepts
A. Using shared decision making, consider treatment options and develop a treatment plan based on patient-specific goals, values, and preferences.
B. Educate patients about treatment options, including benefits and risks, side effects, and expectations.
C. Involve family members in accordance with patient preferences and maintain open, trusting, and respectful relationships with patients and their families.
D. Take active steps to improve the perception of and stigma surrounding PTSD.
E. Work with appropriate providers to ensure continuity and accessibility of high-quality care within and between VA and DoD healthcare systems.

C. Conflicts of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in the past 24 months. Verbal affirmations of no COI were used as necessary during meetings throughout the guideline development process. The project team was also subject to random web-based surveillance (e.g., ProPublica).

If a project team member reported a COI (actual or potential), then it was reported to the Office of Evidence Based Practice. It was also discussed with the PTSD CPG Work Group in tandem with their review of the evidence and development of recommendations. The Office of Evidence Based Practice and the PTSD CPG Work Group determined whether or not action, such as restricting participation and/or voting on sections related to the conflict or removal from the Work Group, was necessary. If it was deemed necessary, action to mitigate the COI was taken by the Champions and Office of Evidence Based Practice, based on the level and extent of involvement. No conflicts of interest were identified for the PTSD CPG Work Group members or Champions. Disclosure forms are on file with the Department of Veterans Affairs Evidence Based Practice Program office and available upon request.

D. Scope of this Clinical Practice Guideline

Regardless of setting, any patient in the healthcare system should ideally have access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances.

Guideline recommendations are intended to be patient-centered. Thus, treatment and care should take into account a patient's needs and preferences. Good communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. Use of an empathetic and non-judgmental approach facilitates discussions sensitive to gender, culture, ethnic, and other differences. The information that patients are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. It should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family involvement should be considered, if appropriate.

This CPG is designed to assist providers in managing or co-managing patients with PTSD and related conditions (e.g., ASD). Moreover, the patient population of interest for this CPG is adults who are eligible for care in the VA and DoD healthcare delivery systems. It includes Veterans as well as deployed and non-

deployed active duty Service Members, Guard, and Reserve. This CPG does not provide recommendations for the management of PTSD in children or adolescents.

The literature review encompassed interventional studies (primarily RCTs) published between March 2009 and March 2016, and targeted 12 KQs focusing on the means by which the delivery of healthcare could be optimized for patients with PTSD. The selected KQs were prioritized from many possible KQs. Due to resource constraints, a review of the evidence in all important aspects of care for patients with PTSD was not feasible for the update to this CPG. The methodology used in this systematic evidence review differed from the methodology used in some other published systematic reviews. The methodology for this systematic evidence review relied primarily on existing systematic reviews, supplemented by original articles not represented in those reviews and/or published after the existing review. The process for this guideline produced comprehensive summaries of the conclusions reached by existing systematic reviews or meta-analyses that covered the topics of the KQs. Work Group members pulled the original articles cited within the existing systematic reviews when more information was needed about the results of a particular trial. Work Group members sometimes identified additional relevant articles not identified in the review process or published after March 2016 to supplement the discussion; however, these instances are noted in the text and were not considered when determining the strength and direction of the recommendations. Although the conclusions reached were mostly consistent with the previous guideline, and with other PTSD CPGs, the Work Group acknowledges the limitations of this methodology.

E. Highlighted Features of this Clinical Practice Guideline

The 2017 edition of the VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder (2017 PTSD CPG) is the second update to the original CPG. It provides practice recommendations for the care of populations with PTSD, ASD, and other reactions to trauma (ASR/COSR). A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad spectrum of clinicians engaged in the treatment and management of patients with PTSD and related disorders.

The framework for recommendations in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of treatment, equity of resource availability, and the potential for variation in patient values and preferences. Applicability of the evidence to VA/DoD populations was also taken into consideration. A structured algorithm accompanies the guideline to provide an overview of the recommendations in the context of the flow of patient care and clinician decision making and to assist with training providers. The algorithm may be used to help facilitate translation of guideline recommendations into effective practice.

F. Patient-centered Care

VA/DoD CPGs encourage clinicians to use a patient-centered care approach that is individualized based on patient capabilities, needs, goals, prior treatment experience, and preferences. Whenever possible, all patients in the healthcare system should be offered access to evidence-based interventions appropriate to that patient. When properly executed, patient-centered care may decrease patient anxiety, increase trust in clinicians, [39] and improve treatment adherence.[40] Improved patient-clinician communication through patient-centered care can be used to convey openness to discuss any future concerns.

As part of the patient-centered care approach, clinicians should review the outcomes of previous self-change efforts, past treatment experiences, and outcomes (including reasons for treatment dropout) with the patient. They should explain treatment options to patients including the benefits of accepting a referral to a mental health specialist. The clinician should discuss any concerns the patient has and explore any identified treatment barriers. Lastly, the clinician should involve the patient in prioritizing problems to be addressed and in setting specific goals regardless of the selected setting or level of care.

G. Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage clinicians to focus on shared decision making (SDM). The SDM model was introduced in *Crossing the Quality Chasm,* an Institute of Medicine (now called the National Academy of Medicine) report, in 2001.[41] It is readily apparent that patients with PTSD, together with their clinicians, make decisions regarding which care they choose to engage in. However, patients require sufficient information and time to be able to make informed decisions. Clinicians must be adept at presenting information to their patients regarding individual treatments, expected outcomes, and levels and/or locations of care.

H. Background on Co-occurring Conditions with Posttraumatic Stress Disorder

The vast majority of patients with PTSD will have one or more co-occurring mental health disorders. Comorbid medical and psychiatric conditions are important to recognize because they can modify clinical determinations of prognosis, patient or provider treatment priorities, selection of interventions, and the setting where PTSD care will be provided. Suicidality in particular should be assessed early on and carefully monitored (see Recommendation 4). However, it should be noted that many of the recommended treatments (in particular those in Recommendation 11 and Recommendation 17) in this guideline are effective for patients with considerable complexity and comorbidity.

Because of the many potential etiologies of co-occurring conditions, it is generally best to develop a collaborative care treatment strategy to address these health concerns simultaneously with PTSD symptoms (See Recommendation 2 regarding collaborative care). Some comorbid medical or psychiatric conditions may require early specialist mental health consultation in order to assist in determining treatment priorities. To improve management of PTSD symptoms when they are complicated by the presence of a medical or psychiatric comorbidity, providers may consider the following:

1. Providers should recognize that medical disorders/symptoms, mental health disorders, and psychosocial problems commonly coexist with PTSD and should assess for them during the evaluation and treatment of PTSD.

2. Because of the high prevalence of psychiatric comorbidities in the PTSD population, screening for depression and other psychiatric disorders is warranted (see also the VA/DoD CPGs for the Management of Major Depressive Disorder [MDD][1] and the Management of Bipolar Disorder[2]).
3. Providers should assess and carefully monitor suicide risk (see the VA/DoD CPG for Assessment and Management of Patients at Risk for Suicide[3])
4. Patterns of current and past use of substances by persons with trauma histories or PTSD should be routinely assessed to identify substance misuse or dependency (alcohol, nicotine, prescribed drugs, and illicit drugs) (see also Recommendation 38 on the management of PTSD in the presence of co-occurring SUD and the VA/DoD CPG for SUD[4]).
5. Pain (acute and chronic) and sleep disturbances should be assessed in all patients with PTSD. See Recommendation 39 regarding management of PTSD in the presence of co-occurring sleep disorders.
6. Generalized physical and cognitive health symptoms, also attributed to mild traumatic brain injury (mTBI) and many other causes, should be assessed and managed in patients with PTSD and co-occurring diagnoses (see VA/DoD CPG for the Management of Concussion/mTBI[5] and VA/DoD CPG for the Management of Chronic Multisymptom Illness[6] [CMI]).
7. Associated high-risk behaviors (e.g., smoking, alcohol/drug use, unsafe weapon storage, dangerous driving, unprotected sex, needle sharing, human immunodeficiency virus [HIV], hepatitis risks) should be assessed in patients with PTSD and addressed in the treatment plan.
8. Providers should consider the existence of comorbid conditions when deciding whether to treat patients in the primary care or general mental health setting, or refer them for specialty mental healthcare.
9. Patients with complicated comorbidity may be referred to mental health or PTSD specialty care for evaluation and diagnosis.

I. Implementation

This CPG and algorithm are designed to be adapted by individual healthcare providers with consideration of local needs and resources. The algorithms serve as a tool to prompt providers to consider key decision points in the course of an episode of care.

[1] See the VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/mdd/index.asp

[2] See the VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults. Available at: http://www.healthquality.va.gov/guidelines/mh/bd/index.asp

[3] See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk for Suicide. Available at: http://www.healthquality.va.gov/guidelines/mh/srb/index.asp

[4] See the VA/DoD Clinical Practice Guideline for Management of Substance Use Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/sud/index.asp

[5] See the VA/DoD Clinical Practice Guideline for Management of Concussion/mild Traumatic Brain Injury. Available at: http://www.healthquality.va.gov/guidelines/rehab/mtbi/index.asp

[6] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: https://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

Although this CPG represents the recommended practice on the date of its publication, medical practice is evolving and this evolution requires continuous updating based on published information. New technology and more research will improve patient care in the future. The CPG can assist in identifying priority areas for research and to informing optimal allocation of resources. Future studies examining the results of CPG implementation may lead to the development of new evidence particularly relevant to clinical practice.

IV. Guideline Work Group

Guideline Work Group*	
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V. Algorithm

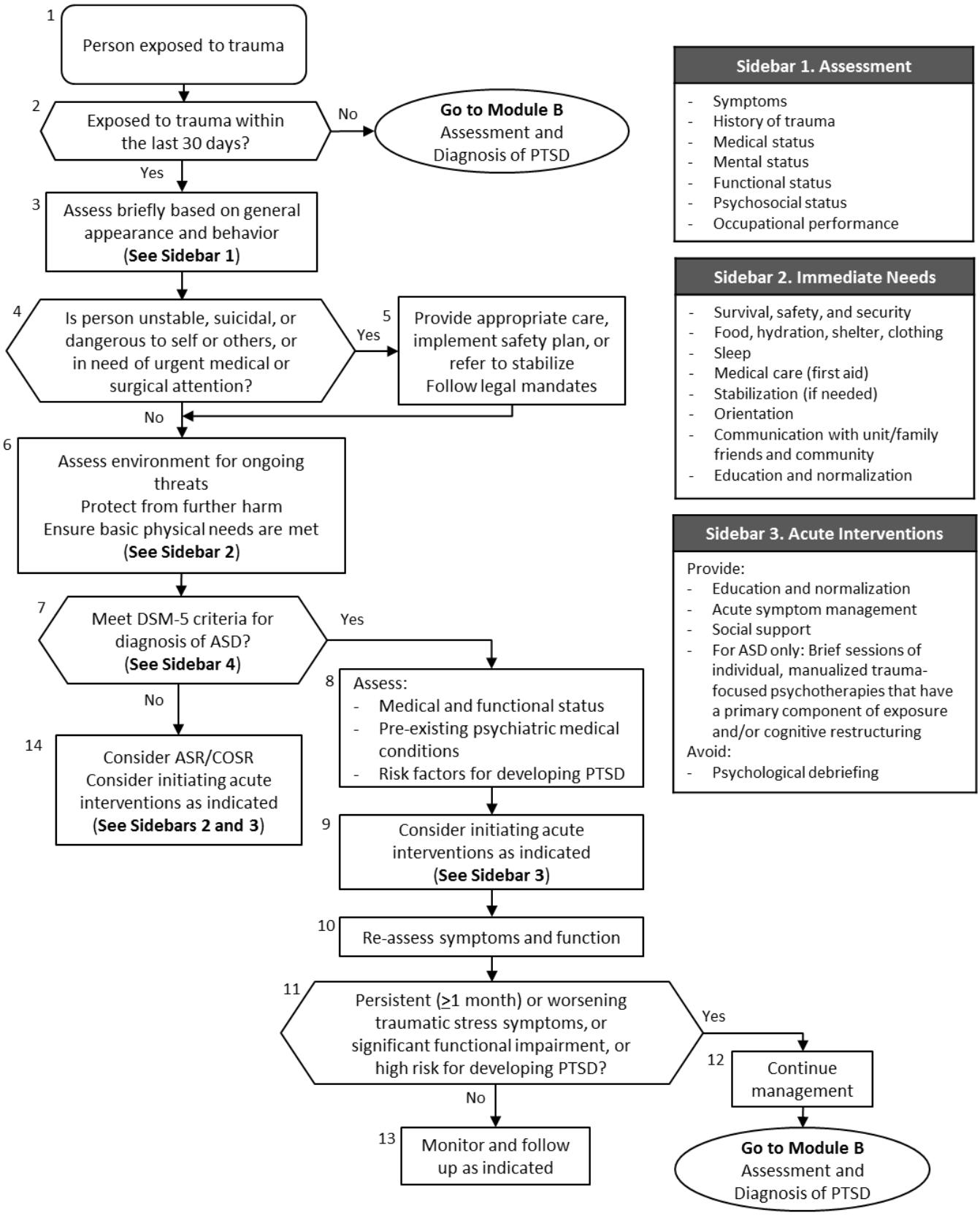
This CPG includes an algorithm that is designed to facilitate understanding of the clinical pathway and decision making process used in management of PTSD. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making and has the potential to change patterns of resource use. Recognizing that some clinical care processes are non-linear, the algorithm format attempts to help the provider to follow a more simplified approach whenever possible in assessing the critical information needed at the major decision points in the clinical process, and includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

A clinical algorithm diagrams a guideline into a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[42]

	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No.
	Rectangles represent an action in the process of care.

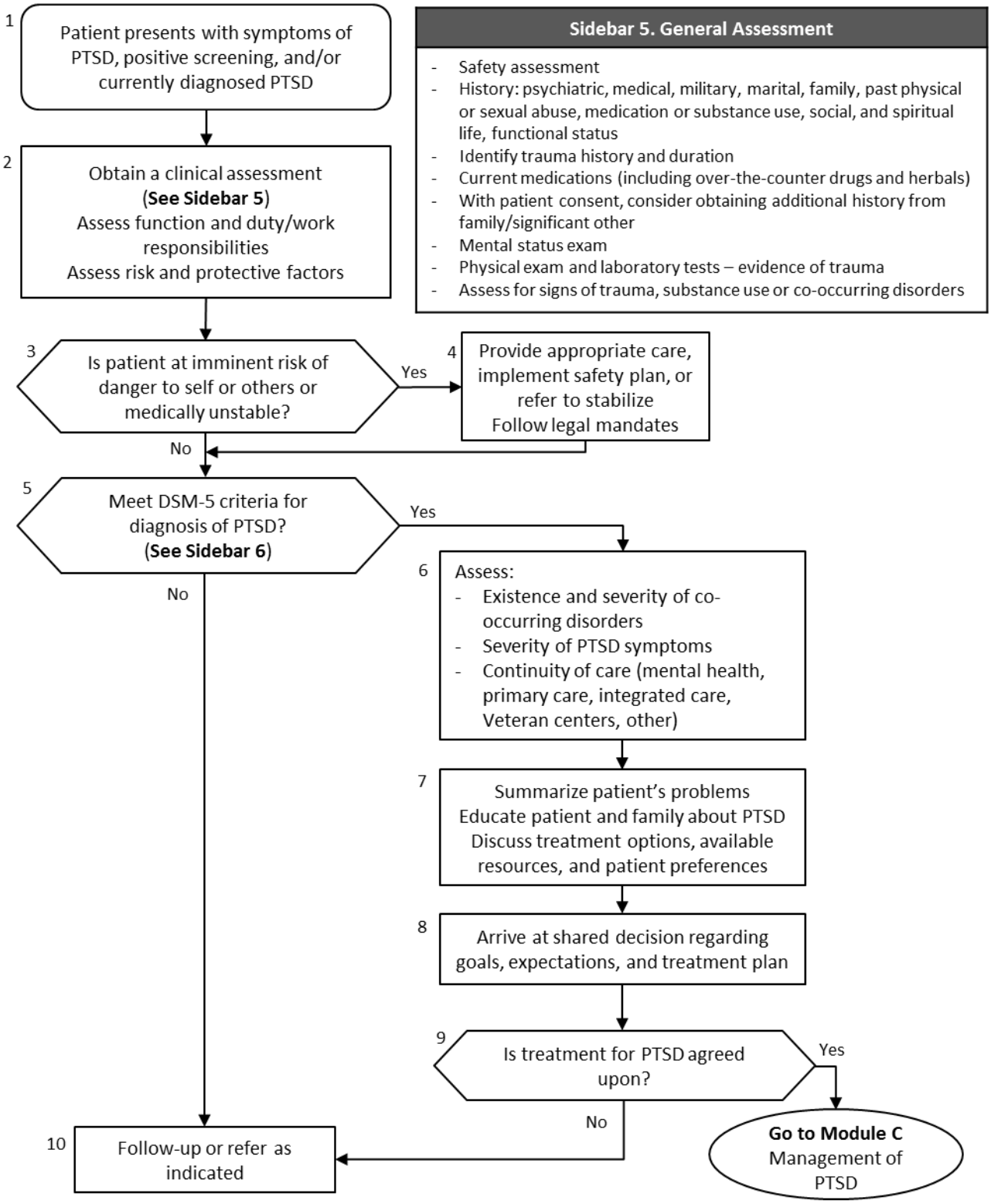
Module A: Acute Stress Reaction/Disorder



Abbreviations: ASD: acute stress disorder; ASR: acute stress reaction; COSR: combat and operational stress reaction; DSM: Diagnostic and Statistical Manual of Mental Disorders; PTSD: posttraumatic stress disorder

Sidebar 4. Diagnostic Criteria for Acute Stress Disorder based on DSM-5	
Criterion A required	Exposure to actual or threatened death, serious injury or sexual violation in one (or more) of the following way(s): 1. Direct exposure 2. Witnessing the event 3. Learning that a close family member or close friend was exposed to a trauma 4. Indirect exposure to aversive details of the trauma, usually in the course of professional duties (e.g., first responders, medics)
Criterion B 9 required	Presence of nine (or more) of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal, beginning or worsening after the traumatic event(s) occurred: The traumatic event is persistently re-experienced, in the following way(s): 1. Intrusive thoughts 2. Nightmares 3. Flashbacks 4. Emotional distress or physical reactivity after exposure to traumatic reminders Negative mood 5. Difficulty experiencing positive affect Dissociative symptoms 6. Altered sense of reality 7. Inability to recall key aspects of the trauma Avoidance of trauma-related stimuli after the trauma, in the following way(s): 8. Trauma-related thoughts or feelings 9. Trauma-related reminders Arousal symptoms 10. Difficulty sleeping 11. Irritability or aggression 12. Hypervigilance 13. Difficulty concentrating 14. Heightened startle reaction
Criterion C	Symptoms last three days to one month after trauma exposure
Criterion D	Symptoms cause significant distress or functional impairment
Criterion E	Symptoms are not due to medication, substance use, or other illness

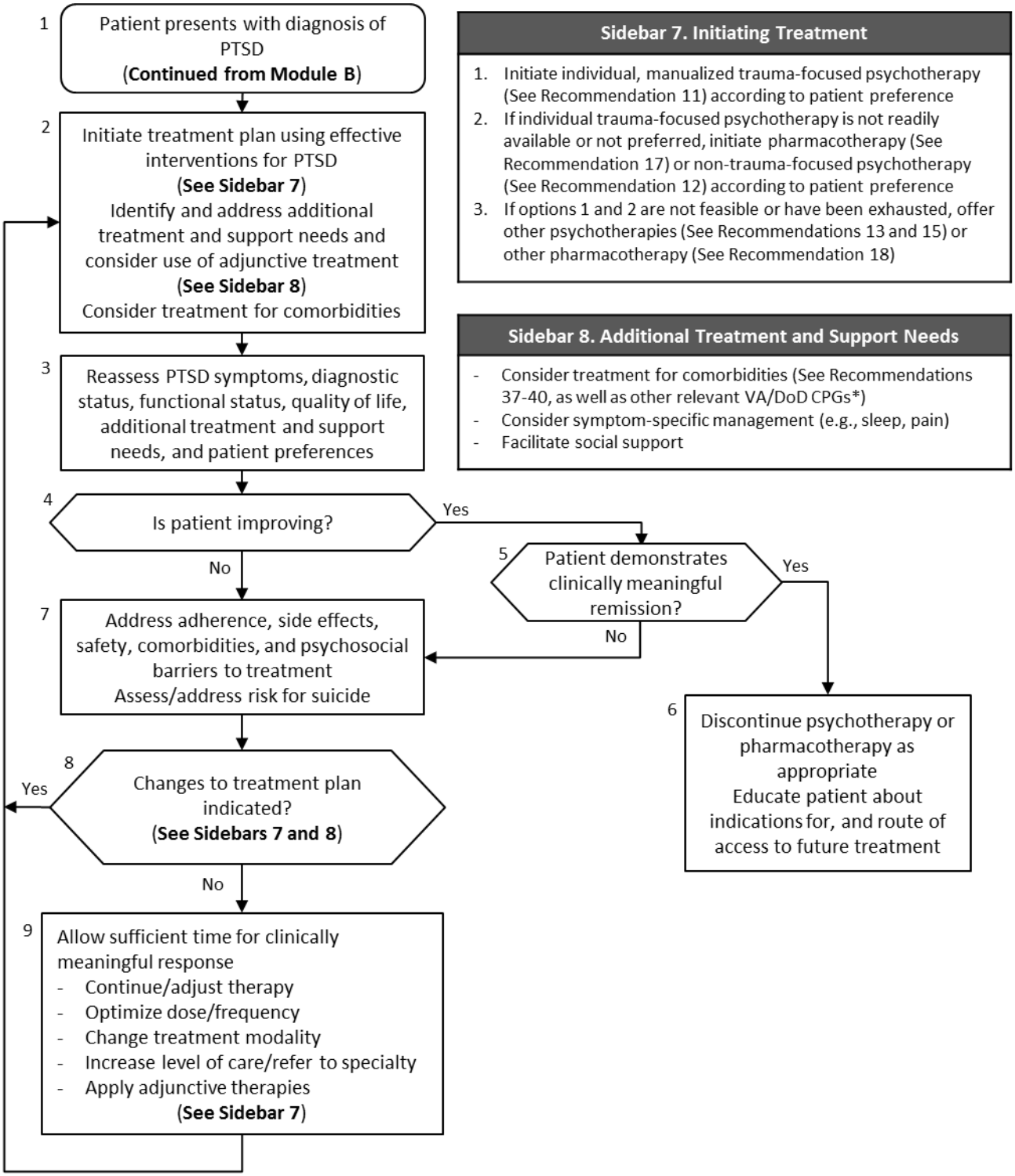
Module B: Assessment and Diagnosis of Posttraumatic Stress Disorder



Abbreviations: DSM: Diagnostic and Statistical Manual of Mental Disorders; PTSD: posttraumatic stress disorder

Sidebar 6. Diagnostic Criteria for Posttraumatic Stress Disorder based on DSM-5	
Criterion A required	The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, in the following way(s): 1. Direct exposure 2. Witnessing the trauma 3. Learning that a relative or close friend was exposed to a trauma 4. Indirect exposure to aversive details of the trauma, usually in the course of professional duties (e.g., first responders, medics)
Criterion B 1 required	The traumatic event is persistently re-experienced, in the following way(s): 1. Intrusive thoughts 2. Nightmares 3. Flashbacks 4. Emotional distress after exposure to traumatic reminders 5. Physical reactivity after exposure to traumatic reminders
Criterion C 1 required	Avoidance of trauma-related stimuli after the trauma, in the following way(s): 1. Trauma-related thoughts or feelings 2. Trauma-related reminders
Criterion D 2 required	Negative thoughts or feelings that began or worsened after the trauma, in the following way(s): 1. Inability to recall key features of the trauma 2. Overly negative thoughts and assumptions about oneself or the world 3. Exaggerated blame of self or others for causing the trauma 4. Negative affect 5. Decreased interest in activities 6. Feeling isolated 7. Difficulty experiencing positive affect
Criterion E 2 required	Trauma-related arousal and reactivity that began or worsened after the trauma, in the following way(s): 1. Irritability or aggression 2. Risky or destructive behavior 3. Hypervigilance 4. Heightened startle reaction 5. Difficulty concentrating 6. Difficulty sleeping
Criterion F required	Symptoms last for more than one month
Criterion G required	Symptoms cause significant distress or functional impairment
Criterion H required	Symptoms are not due to medication, substance use, or other illness

Module C: Management of Posttraumatic Stress Disorder



*VA/DoD CPGs can be found at the following link: https://www.healthquality.va.gov/index.asp. Relevant VA/DoD CPGs to consult may include CPGs for the Management of Major Depressive Disorder, Substance Use Disorder, Bipolar Disorder, Suicide, Chronic Multisymptom Illness, Concussion-mild Traumatic Brain Injury, and others.

Abbreviations: CPG: clinical practice guideline; DoD: Department of Defense; PTSD: posttraumatic stress disorder; VA: Department of Veterans Affairs

VI. Recommendations

#	Recommendation	Strength*	Category†
A. General Clinical Management			
1	We recommend engaging patients in shared decision making (SDM), which includes educating patients about effective treatment options.	Strong For	Not Reviewed, Amended
2	For patients with posttraumatic stress disorder (PTSD) who are treated in primary care, we suggest collaborative care interventions that facilitate active engagement in evidence-based treatments.	Weak For	Reviewed, New-replaced
B. Diagnosis and Assessment of PTSD			
3	We suggest periodic screening for PTSD using validated measures such as the Primary Care PTSD Screen (PC-PTSD) or the PTSD Checklist (PCL).	Weak For	Not Reviewed, Amended
4	For patients with suspected PTSD, we recommend an appropriate diagnostic evaluation that includes determination of DSM criteria, acute risk of harm to self or others, functional status, medical history, past treatment history, and relevant family history. A structured diagnostic interview may be considered.	Strong For	Not Reviewed, Amended
5	For patients with a diagnosis of PTSD, we suggest using a quantitative self-report measure of PTSD severity, such as the PTSD Checklist for DSM-5 (PCL-5), in the initial treatment planning and to monitor treatment progress.	Weak For	Not Reviewed, Amended
C. Prevention of PTSD			
a. Selective Prevention of PTSD			
6	For the selective prevention of PTSD, there is insufficient evidence to recommend the use of trauma-focused psychotherapy or pharmacotherapy in the immediate post-trauma period.	N/A	Reviewed, New-replaced
b. Indicated Prevention of PTSD and Treatment of ASD			
7	For the indicated prevention of PTSD in patients with acute stress disorder (ASD), we recommend an individual trauma-focused psychotherapy that includes a primary component of exposure and/or cognitive restructuring.	Strong For	Reviewed, New-replaced
8	For the indicated prevention of PTSD in patients with ASD, there is insufficient evidence to recommend the use of pharmacotherapy.	N/A	Reviewed, New-replaced
D. Treatment of PTSD			
a. Treatment Selection			
9	We recommend individual, manualized trauma-focused psychotherapy (see Recommendation 11) over other pharmacologic and non-pharmacologic interventions for the primary treatment of PTSD.	Strong For	Reviewed, New-added
10	When individual trauma-focused psychotherapy is not readily available or not preferred, we recommend pharmacotherapy (see Recommendation 17) or individual non-trauma-focused psychotherapy (see Recommendation 12). With respect to pharmacotherapy and non-trauma-focused psychotherapy, there is insufficient evidence to recommend one over the other.	Strong For	Reviewed, New-added

#	Recommendation	Strength*	Category†
b. Psychotherapy			
11	For patients with PTSD, we recommend individual, manualized trauma-focused psychotherapies that have a primary component of exposure and/or cognitive restructuring to include Prolonged Exposure (PE), Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing (EMDR), specific cognitive behavioral therapies for PTSD, Brief Eclectic Psychotherapy (BEP), Narrative Exposure Therapy (NET), and written narrative exposure.	Strong For	Reviewed, New-replaced
12	We suggest the following individual, manualized non-trauma-focused therapies for patients diagnosed with PTSD: Stress Inoculation Training (SIT), Present-Centered Therapy (PCT), and Interpersonal Psychotherapy (IPT).	Weak For	Reviewed, New-replaced
13	There is insufficient evidence to recommend for or against psychotherapies that are not specified in other recommendations, such as Dialectical Behavior Therapy (DBT), Skills Training in Affect and Interpersonal Regulation (STAIR), Acceptance and Commitment Therapy (ACT), Seeking Safety, and supportive counseling.	N/A	Reviewed, New-replaced
14	There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over or in addition to the full therapy protocol.	N/A	Reviewed, New-added
15	We suggest manualized group therapy over no treatment. There is insufficient evidence to recommend using one type of group therapy over any other.	Weak For	Reviewed, New-replaced
16	There is insufficient evidence to recommend for or against trauma-focused or non-trauma-focused couples therapy for the primary treatment of PTSD.	N/A	Reviewed, Amended
c. Pharmacotherapy			
17	We recommend sertraline, paroxetine, fluoxetine, or venlafaxine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy.	Strong For	Reviewed, New-replaced
18	We suggest nefazodone, imipramine, or phenelzine as monotherapy for the treatment of PTSD if recommended pharmacotherapy (see Recommendation 17), trauma-focused psychotherapy (see Recommendation 11), or non-trauma-focused psychotherapy (see Recommendation 12) are ineffective, unavailable, or not in accordance with patient preference and tolerance. (NOTE: Nefazodone and phenelzine have potentially serious toxicities and should be managed carefully.)	Weak For	Reviewed, New-replaced
19	We suggest against treatment of PTSD with quetiapine, olanzapine, and other atypical antipsychotics (except for risperidone, which is a Strong Against, see Recommendation 20), citalopram, amitriptyline, lamotrigine, or topiramate as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks.	Weak Against	Reviewed, New-replaced
20	We recommend against treating PTSD with divalproex, tiagabine, guanfacine, risperidone, benzodiazepines, ketamine, hydrocortisone, or D-cycloserine, as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks.	Strong Against	Reviewed, New-replaced
21	We recommend against treating PTSD with cannabis or cannabis derivatives due to the lack of evidence for their efficacy, known adverse effects, and associated risks.	Strong Against	Reviewed, New-added

#	Recommendation	Strength*	Category†
22	There is insufficient evidence to recommend for or against monotherapy or augmentation therapy for the treatment of PTSD with eszopiclone, escitalopram, bupropion, desipramine, doxepin, D-serine, duloxetine, desvenlafaxine, fluvoxamine, levomilnacipran, mirtazapine, nortriptyline, trazodone, vilazodone, vortioxetine, buspirone, hydroxyzine, cyproheptadine, zaleplon, and zolpidem.	N/A	Reviewed, New-replaced
d. Augmentation Therapy			
23	We suggest against the use of topiramate, baclofen, or pregabalin as augmentation treatment of PTSD due to insufficient data and/or known adverse effect profiles and associated risks.	Weak Against	Reviewed, New-replaced
24	We suggest against combining exposure therapy with D-cycloserine in the treatment of PTSD outside of the research setting.	Weak Against	Reviewed, New-added
25	We recommend against using atypical antipsychotics, benzodiazepines, and divalproex as augmentation therapy for the treatment of PTSD due to low quality evidence or the absence of studies and their association with known adverse effects.	Strong Against	Reviewed, New-replaced
26	There is insufficient evidence to recommend the combination of exposure therapy with hydrocortisone outside of the research setting.	N/A	Reviewed, New-added
27	There is insufficient evidence to recommend for or against the use of mirtazapine in combination with sertraline for the treatment of PTSD.	N/A	Reviewed, New-replaced
e. Prazosin			
28a	For global symptoms of PTSD, we suggest against the use of prazosin as mono- or augmentation therapy.	Weak Against	Reviewed, New-replaced
28b	For nightmares associated with PTSD, there is insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy.	N/A	Reviewed, New-replaced
f. Combination Therapy			
29	In partial- or non-responders to psychotherapy, there is insufficient evidence to recommend for or against augmentation with pharmacotherapy.	N/A	Reviewed, New-replaced
30	In partial- or non-responders to pharmacotherapy, there is insufficient evidence to recommend for or against augmentation with psychotherapy.	N/A	Reviewed, New-replaced
31	There is insufficient evidence to recommend for or against starting patients with PTSD on combination pharmacotherapy and psychotherapy.	N/A	Reviewed, New-added
g. Non-pharmacologic Biological Treatments			
32	There is insufficient evidence to recommend for or against the following somatic therapies: repetitive transcranial magnetic stimulation (rTMS), electroconvulsive therapy (ECT), hyperbaric oxygen therapy (HBOT), stellate ganglion block (SGB), or vagal nerve stimulation (VNS).	N/A	Reviewed, New-replaced
h. Complementary and Integrative Treatments			
33	There is insufficient evidence to recommend acupuncture as a primary treatment for PTSD.	N/A	Reviewed, New-replaced
34	There is insufficient evidence to recommend any complementary and integrative health (CIH) practice, such as meditation (including mindfulness), yoga, and mantram meditation, as a primary treatment for PTSD.	N/A	Reviewed, New-replaced

#	Recommendation	Strength*	Category†
i. Technology-based Treatment Modalities			
35	We suggest internet-based cognitive behavioral therapy (iCBT) with feedback provided by a qualified facilitator as an alternative to no treatment.	Weak For	Reviewed, New-replaced
36	We recommend using trauma-focused psychotherapies that have demonstrated efficacy using secure video teleconferencing (VTC) modality when PTSD treatment is delivered via VTC.	Strong For	Reviewed, Amended
E. Treatment of PTSD with Co-occurring Conditions			
37	We recommend that the presence of co-occurring disorder(s) not prevent patients from receiving other VA/DoD guideline-recommended treatments for PTSD.	Strong For	Reviewed, New-added
38	We recommend VA/DoD guideline-recommended treatments for PTSD in the presence of co-occurring substance use disorder (SUD).	Strong For	Reviewed, New-replaced
39	We recommend an independent assessment of co-occurring sleep disturbances in patients with PTSD, particularly when sleep problems pre-date PTSD onset or remain following successful completion of a course of treatment.	Strong For	Reviewed, New-replaced
40	We recommend Cognitive Behavioral Therapy for Insomnia (CBT-I) for insomnia in patients with PTSD unless an underlying medical or environmental etiology is identified or severe sleep deprivation warrants the immediate use of medication to prevent harm.	Strong For	Reviewed, Amended

*For additional information, please refer to Grading Recommendations.

†For additional information, please refer to Recommendation Categorization and Appendix E: 2010 Recommendation Categorization Table.

A. General Clinical Management

Recommendation

1. We recommend engaging patients in shared decision making (SDM), which includes educating patients about effective treatment options.
   (Strong For | Not Reviewed, Amended)

Discussion

This 2010 PTSD CPG recommendation was not formally addressed in the systematic evidence review for this CPG update. This recommendation has been amended and combines related recommendations from the 2010 guideline. SDM has the goal of considering patient preference in treatment decisions to improve patient-centered care, decision quality, and treatment outcomes. It often involves educating the patient (and family members, as appropriate) on trauma, PTSD and its consequences, and treatment. In SDM, the patient and provider together review treatment options and compare the benefits, harms, and risks of each with the goal of selecting the option that best meets the patient's needs.

A systematic review found that the use of SDM with medical patients was associated with improved communication, decision satisfaction, and recognition and management of the patient's problem.[43] However, the research on SDM for PTSD is minimal. There is one small pilot study that randomized 27 Veterans with PTSD to a SDM intervention or usual care.[44] Those who participated in the SDM intervention were more likely to prefer an evidence-based treatment and more likely to receive an adequate dose of treatment.

Much of the SDM research has focused on evaluating decision aids. Decision aids are tools that educate patients about treatment options as a way to facilitate SDM for health decisions. A systematic review of 115 RCTs that compared decision aids to usual care found that participants who received decision aids were more likely to select a treatment consistent with their values and were less worried about whether they had made the correct decision.[45] There is only one RCT examining a decision aid for PTSD treatment.[46] Consistent with the larger literature about decision aids, the 132 Veterans who received the decision aid (versus usual care) had higher PTSD knowledge and lower conflict about their treatment decision. They were also more likely to select an evidence-based treatment and had better clinical outcomes.

The Work Group based its strong recommendation on the substantial literature supporting SDM in other conditions. The process of SDM maximizes the likelihood that patient preference is taken into account and the benefits outweigh any potential harms. Research should focus on learning more about SDM in the context of making PTSD treatment decisions.

Recommendation

2. For patients with posttraumatic stress disorder (PTSD) who are treated in primary care, we suggest collaborative care interventions that facilitate active engagement in evidence-based treatments.
   (Weak For | Reviewed, New-replaced)

Discussion

The collaborative care model is an evidence-based approach to integrating physical and behavioral health services that is most usually provided within the primary care setting.[47] Collaborative care typically includes: (1) care coordination and care management, (2) regular/proactive monitoring and treatment to achieve outcomes measured using validated clinical rating scales, and (3) regular consultation or referral to appropriate specialists for patients who do not show clinical improvement. Many collaborative care models generally involve a stepped-care approach to symptom management, using a predetermined treatment sequence that starts with simple, low-intensity interventions first. Subsequent treatment steps involving increased complexity and intensity are attempted only after initial treatment is unsuccessful. Care coordination is an integral component of most collaborative care models. Some models also offer telehealth or additional care delivery modalities. Studies of collaborative care reviewed by the Work Group showed variations related to how interventions were delivered, how components of care were structured, and which components of care were delivered. The use of collaborative care interventions that employ or facilitate active engagement in evidence-based PTSD treatments in the primary care setting appears to increase patient follow-through with treatment, improve patient satisfaction, and potentially reduce premature termination from treatment when delivered in the primary care setting.[48-54] Due to study design differences related to the types of collaborative care programs examined, it is difficult to conduct meaningful comparisons across studies; thus, there is a limited body of evidence regarding the effectiveness of specific types of collaborative care interventions for PTSD.[48-53]

The six RCTs reviewed included several types of collaborative care interventions conducted in differing settings (PTSD care management, coordinated anxiety learning and management, technology-enhanced stepped collaborative care, stepped collaborative care, and telemedicine outreach for PTSD). No single consistent protocol was used across the six studies. Half of the studies were conducted among military personnel or Veterans; the rest were conducted with non-military or non-Veteran populations. One recently completed study not included in the systematic evidence review for this CPG (due to the search date cutoff) is the first published RCT with a military population in a military treatment setting that compared this collaborative care model with the usual collaborative care model.[55] The study found that a centrally-assisted collaborative telecare with stepped psychosocial management model appeared to modestly improve outcomes of PTSD and depression treatment among military personnel attending primary care.[55]

Confidence in the quality of evidence for this recommendation was very low to moderate. Among the RCTs reviewed, statistically significant findings included increased patient satisfaction using technology-enhanced stepped collaborative care compared to usual care,[49,50] reduction in PTSD symptoms and PTSD remission across all models of collaborative care studied,[48] and improvements in PTSD and depression when telehealth was used to deliver Cognitive Processing Therapy (CPT) in collaborative care.[50] Care management alone did not appear to be effective for PTSD, whereas the stepped care aspects of the models evaluated did appear to improve outcomes.[48,49,55]

There were no adverse events reported related to this model of care delivery. Given the apparent increased patient follow-through with PTSD treatment and improvement in patient satisfaction correlated with the use of the collaborative care model studies reviewed, the potential benefits outweigh risk of harm. We also considered the potential increased demands on resources required to deliver collaborative

care for PTSD treatment in the primary care setting, which included possible increased staffing to support the model, and potential for this model to reduce clinical productivity, if measured by number of provider treatment encounters alone. More research is needed on the effect of collaborative care on long-term utilization of various healthcare services, on the key components of collaborative care that impact PTSD treatment effectiveness, and on the role of technology-assisted interventions in improving the effectiveness of collaborative care interventions to treat PTSD.

B. Diagnosis and Assessment of Posttraumatic Stress Disorder

Recommendation

3. We suggest periodic screening for PTSD using validated measures such as the Primary Care PTSD Screen (PC-PTSD) or the PTSD Checklist (PCL).
   (Weak For | Not Reviewed, Amended)

Discussion

Identification of individuals with PTSD is essential to ensure that they receive appropriate treatment and screening is often considered a key step in the diagnostic process. The Work Group did not review literature on the benefits of screening for PTSD specifically, and in fact, a recent review of screening measures for PTSD that was performed for the VA Evidence-based Synthesis Program noted that no such studies exist.[56] Therefore, this recommendation is based in part on evidence supporting the use of screening for mental health problems, particularly depression in primary care settings. For example, a review of the benefits of depression screening that was conducted by the USPSTF found that screening was associated with improvements of 17% to 87% in response and/or remission.[57]

The recommendation is also based on the availability of psychometrically-sound screening measures as well as consideration of the relative risks and potential benefits of screening.[58,59] In the VA Evidence-based Synthesis Program review of PTSD screening measures, Spoont et al. mention that inaccurately diagnosing PTSD in a patient who does not have PTSD could result in unintended harms to the patient from being labeled with a mental disorder and from side effects of treatment.[56] There are also harms to the healthcare system from the inefficient use of resources. Spoont et al. reported that the positive predictive value—that is, the probability that a person who screens positive has PTSD—was 54% for the PC-PTSD (at the recommended cutpoint of 3) and 58% for the PCL (at the recommended cutpoint of 45).[56] Unfortunately, this means that over 40% of screen positive tests were false positives in the validation studies examined. Additionally, positive predictive value is largely a function of prevalence and is therefore considerably lower in general population and primary care samples compared with samples typically used in validation studies.[60] Spoont et al. also noted that there is potential harm in *not* screening, which could prevent individuals with PTSD from being detected and receiving the care they need.[56] The risks of screening for PTSD can be minimized and potential benefits maximized by using reliable and valid screening measures and by conducting more careful diagnostic evaluation before initiating treatment after a positive screen (see Recommendation 4).

Screening for PTSD can be performed in primary and specialty care settings, and both VA and DoD mandate screening either in context with combat deployments or in primary care settings. Primary care is considered to be an important context for screening because many people with PTSD and other mental

disorders first present in primary care and not in specialty mental healthcare settings.[51] This may be especially true for patients with concerns about stigma.

One-time screening is not recommended because PTSD is a disorder with a fluctuating course for many people. Onset may be delayed, and symptoms may reoccur even after a long period of remission. An individual who is symptom-free at one point may be symptomatic at another. There is no evidence to suggest how frequently screening should occur. VA recommends annual screening for the first five years following separation and then every five years thereafter. DoD recommends routine screening throughout deployment cycles.

A variety of measures are available for PTSD screening.[56] Both VA and DoD have relied most heavily on the PC-PTSD and PCL for various screening purposes. The PC-PTSD, a four-item questionnaire that is generally scored positive if at least three of the four items are endorsed, performs well against both DSM-IV and DSM-5 PTSD diagnoses. The PC-PTSD has been revised to include five items in order to reflect changes to the PTSD diagnostic criteria in DSM-5.[59] Initial validation of the revised scale, the PC-PTSD-5, suggests that a score of three optimizes sensitivity, four optimizes efficiency, and five optimizes specificity. At the time of this guideline, VA and DoD are continuing to use the four-item PC-PTSD, which is reasonable because the PC-PTSD performs well as a screen for PTSD diagnosed according to DSM-5.[59] Research is underway to confirm the optimal cutpoint. The longer 17-item DSM-IV PCL or 20-item DSM-5 PTSD Checklist (PCL-5) also can be used for screening.[58] Data on the DSM-IV version indicated that using different cutpoints optimized screening depending on prevalence, other sample characteristics, and setting.[56,60] Such information is not yet available for the PCL-5, although it is assumed that it will also show comparable variation like the previous screen.[60] For the PCL-5, an overall cutpoint of 33 is recommended for screening in clinical settings based on two studies conducted with Veterans and Service Members whose diagnosis was established by a structured clinical interview.[58] An overall cutpoint of 33 was found to correlate well with DSM-IV and DSM-5 criteria in an epidemiological study of soldiers based on a comparison of PCL and PCL-5 scores, and 38 was determined to be optimally comparable to a higher specificity score of 50 on the original PCL widely used as a cutoff in population prevalence studies.[10,61] No screening measure or cutpoint should be the sole basis for diagnosis (see Recommendation 4).

Recommendation

4. For patients with suspected PTSD, we recommend an appropriate diagnostic evaluation that includes determination of DSM criteria, acute risk of harm to self or others, functional status, medical history, past treatment history, and relevant family history. A structured diagnostic interview may be considered.
   (Strong For | Not Reviewed, Amended)

Discussion

PTSD is associated with a range of comorbid psychological conditions, poorer physical health, increased treatment utilization, impaired functioning, and reduced quality of life.[29,62,63] (See section on Background on Co-occurring Conditions.) Therefore, a comprehensive diagnostic evaluation should include all of these factors. Reardon and colleagues provide an excellent overview of the assessment of PTSD and its comorbidities in adults.[64]

The diagnostic criteria for PTSD are listed in Table 2. Further details are available in the DSM-5 manual [2] and additional guidance about the diagnosis is available in other sources.[65,66]

Diagnosis can be made on the basis of a clinical interview or a structured diagnostic interview such as the Clinician-Administered PTSD Scale (CAPS),[67] Posttraumatic Stress Disorder Symptom Scale Interview for DSM-5 (PSSI-I),[68] or Structured Clinical Interview for DSM-5 (SCID-5).[69] Structured diagnostic interviews can help to enhance the accuracy and completeness of diagnosis. However, the time required for structured interviewing may not be available in primary care and routine specialty mental healthcare settings. If diagnosis is based on clinical interview in any setting, it can be helpful to administer a self-report questionnaire such as the PCL-5 along with other routine self-report screening tools, such as the Patient Health Questionnaire-9 (PHQ-9) and Alcohol Use Disorders Identification Test-Consumption (AUDIT-C).[70-72]

Recommendation

5. For patients with a diagnosis of PTSD, we suggest using a quantitative self-report measure of PTSD severity, such as the PTSD Checklist for DSM-5 (PCL-5), in the initial treatment planning and to monitor treatment progress.
   (Weak For | Not Reviewed, Amended)

Discussion

In addition to their utility in screening and diagnosis, brief questionnaires such as the PCL-5 can be used to assess symptom severity. The PCL-5 consists of 20 items that reflect the symptoms of the PTSD diagnostic criteria. Symptoms are rated on a 5-point scale, ranging from 0=*not at all* to 4=*extremely.* The scale takes 5-10 minutes to complete. The PCL-5 is part of a core set of measures recommended by the Interagency Task Force Work Group on Common Mental Health Measures across VA and DoD.[73] The PCL-5 is also the measure used for PTSD assessment in VA's Measurement Based Care Initiative, which is promoting the use of measurement-based care in mental health.

There are other well-validated measures that can be used to assess severity of PTSD symptoms. The Posttraumatic Diagnostic Scale (PDS) assesses the same DSM-5 criteria and function. For those patients who have previously been assessed using the PCL for DSM-IV, continued use of that measure may be warranted.

A recent systematic review of RCTs of measurement-based care in mental health found that giving providers frequent and timely information about patients' symptom severity during medication and psychotherapy treatment was associated with better patient outcomes.[74] Information about symptom severity was not associated with better outcomes if the information was provided in screening only or infrequently. Because the time frame captured by these scales is within the past month, providers may consider monthly administration as a sufficiently frequent timeframe during an episode of care. However, for some treatments (e.g., Prolonged Exposure [PE], CPT), the time frame has been modified to weekly to allow for more frequent administrations.

C. Prevention of Posttraumatic Stress Disorder

The Work Group approached prevention of PTSD from the perspective of the Institute of Medicine's (now the National Academy of Medicine) definition of prevention which represents an evolution in thinking

beyond primary, secondary, and tertiary prevention.[75] *Universal prevention* strategies target the general population and are not directed at a specific at-risk group. There are currently no recommended strategies for universal prevention of PTSD. *Selective prevention* targets individuals who are at higher than average risk for developing PTSD and includes strategies delivered to trauma-exposed individuals who have not yet developed symptoms or meet criteria for ASD or PTSD. *Indicated prevention* includes strategies to prevent PTSD in individuals with symptoms of ASD or meet criteria for ASD. Because no key questions were included regarding universal prevention of PTSD, we address issues related to selective and indicated prevention.

a. Selective Prevention of Posttraumatic Stress Disorder

Recommendation

6. For the selective prevention of PTSD, there is insufficient evidence to recommend the use of trauma-focused psychotherapy or pharmacotherapy in the immediate post-trauma period. **(N/A | Reviewed, New-replaced)**

Discussion

Studies examining use of individual trauma-focused psychotherapy in the immediate post-trauma period for the selective prevention of PTSD are rare. The seminal single-site study by Rothbaum et al. enrolled individuals who presented to an emergency department within 72 hours of a Criterion A trauma and randomized them to three one-hour sessions of a modified PE intervention (imaginal exposure to the trauma, processing the traumatic material, and in vivo and imaginal exposure homework) spaced one week apart or a waitlist group that received assessments, but no treatment.[76] Compared to waitlist controls, brief trauma-focused cognitive behavioral therapy (CBT) significantly reduced the severity of PTSD symptoms as measured by the PTSD Symptom Scale-Interview Version at four and 12 weeks follow-up. However, there were no significant differences between treatment and waitlist group in the likelihood of developing PTSD at four weeks. The Work Group rated its overall confidence in the existing literature on individual trauma-focused psychotherapy in the immediate post-trauma period for prevention of PTSD as low based on one single site study with moderate to high risk of bias due to high dropout (>30%) at week 12 follow-up. While the findings of the Rothbaum et al. study are promising, the Work Group felt there was not sufficient evidence to recommend use of individual trauma-focused psychotherapy in the immediate post-trauma period to prevent PTSD.

A systematic review of individual psychological debriefing studies included two blinded RCTs using the Critical Incident Stress Debriefing (CISD) strategy in civilian trauma samples.[77] CISD administered immediately after trauma exposure did not reduce incidence of PTSD at six-month follow-up compared to groups that received no debriefing. In fact, individuals with CISD administered immediately following trauma exposure had increased incidence and severity of PTSD at 13-month follow-up.[77]

One study included in the systematic review examined the impact of Battlemind debriefing compared to the standard brief on PTSD symptoms in United Kingdom armed forces.[78] Findings from this cluster-randomized trial revealed no significant impact on PTSD symptoms as measured by self-report. This finding was consistent with prior studies of Battlemind debriefing in U.S. soldiers that found no effect on PTSD compared to a Stress Education control condition except in individuals with high combat exposure.[77]

A number of studies have examined pharmacologic interventions for the selective prevention of PTSD.[79] Medication classes that have been evaluated include beta-blockers, benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), antiepileptic drugs, and glucocorticoids.

Three RCTs compared the early administration of propranolol to placebo in individuals with trauma exposure who were treated in an emergency department.[80-82] Findings indicated no difference in the likelihood of developing PTSD between those who received propranolol and controls.[80-83]

A single RCT compared the early administration of temazepam (within three weeks of trauma) [84] and gabapentin [82] (within 48 hours of trauma) to placebo in individuals with trauma exposure and similarly found no benefit from these medications in the prevention of PTSD.

Four RCTs compared hydrocortisone to placebo for the prevention of PTSD in a variety of acute inpatient medical settings such as intensive care unit, cardiac surgery, emergency room, and trauma center. Compared to placebo, hydrocortisone administration during life-threatening medical illnesses was associated with significantly less PTSD and depression symptoms at three months.[85-88] However, it is unclear if these findings can be generalized to non-medical traumatic events. In addition, variable dosing regimens across studies and concerns about the safety of high-dose glucocorticoid administration limit the utility of hydrocortisone in the selective prevention of PTSD.

The Work Group rated its overall confidence in the existing literature on pharmacotherapy treatment for selective prevention of PTSD as low. Fewer than 10 RCTs evaluated five different medication types and there was wide variation in the administration and dosage of medications and type of trauma included. Evidence was insufficient to recommend any pharmacologic intervention in the immediate post-trauma period to prevent the development of chronic PTSD.[77,89]

b. Indicated Prevention of Posttraumatic Stress Disorder and Treatment of Acute Stress Disorder

Recommendation

7. For the indicated prevention of PTSD in patients with acute stress disorder (ASD), we recommend an individual trauma-focused psychotherapy that includes a primary component of exposure and/or cognitive restructuring.
   (Strong For | Reviewed, New-replaced)

8. For the indicated prevention of PTSD in patients with ASD, there is insufficient evidence to recommend the use of pharmacotherapy.
   (N/A | Reviewed, New-replaced)

Discussion

Two systematic reviews confirmed that compared to supportive counseling or waitlist, individuals with ASD who received brief individual trauma-focused psychotherapy had significantly reduced PTSD symptom severity at follow-up (three to six months).[77,89] However, most studies in the two systematic reviews had small sample sizes and methodologic concerns. Three particularly strong studies from an Australian team headed by Bryant directly compared brief five to six weeks of trauma-focused CBT to supportive counseling in a combined total of 105 civilian survivors of mixed trauma with ASD.[77] Participants with trauma from

motor vehicle or industrial accidents and who met criteria for ASD were randomized to brief trauma-focused CBT (including education about trauma reactions, progressive muscle relaxation training, imaginal exposure to traumatic memories, cognitive restructuring of fear-related beliefs, and graded in-vivo exposure to avoided situations) or supportive counseling. Brief trauma-focused CBT significantly reduced clinician-rated PTSD severity post-treatment, and the incidence of PTSD at six months. Meta-analysis of 10 published RCTs of trauma-focused CBT interventions found a moderate effect size (effect size [ES]=0.54) for preventing PTSD diagnosis at three to six months follow-up, small-to-moderate effects with respect to clinician-rated PTSD symptom severity at three to six month follow-up (ES=0.45), and small effects at long-term follow-up (>12 months; ES=0.34).[89] The meta-analysis found that dropout rates were similar in both groups, with about 20% not completing treatment.

The Work Group rated its overall confidence in the existing literature on brief trauma-focused CBT for selective prevention of PTSD as moderate. More than 15 RCTs evaluating a variety of trauma-focused CBT interventions met the threshold for review. Most of these studies were deemed to be of fair to good quality. Considering the existing data, the Work Group determined that the benefits far outweigh potential harms.

Two studies examined the efficacy of escitalopram versus placebo for indicated prevention in PTSD.[90,91] A study by Suliman et al. randomized individuals who met full DSM-IV criteria or intrusion and hyper-arousal criteria for ASD to escitalopram or placebo less than four weeks after the trauma exposure.[91] There was a significant reduction in PTSD symptoms for both escitalopram and placebo groups at 24 week follow-up, with a significantly greater reduction in CAPS score in the placebo group.[91] A five-armed trial by Shalev et al. compared escitalopram to placebo, waitlist, prolonged exposure, and non-trauma-focused CBT in a sample of individuals who experienced a life-threatening trauma from terrorist activity, motor vehicle accidents, or other accidents, and who met criteria for ASD.[90] Individuals who received prolonged exposure and CBT had significantly lower incidence of PTSD at the five-month follow-up compared to individuals who received waitlist, escitalopram, or placebo.

The Work Group rated its overall confidence in the existing literature on pharmacotherapy treatment for indicated prevention of PTSD as low. Two RCTs evaluated escitalopram in patients with ASD, or ASD symptoms with no evidence of efficacy. One of the trials was small,[91] and the other was considered to have low quality due to the fact that participants could decline up to two of the treatments.[90] Thus, evidence was insufficient to recommend any pharmacologic interventions for the indicated prevention of PTSD in patients with ASD.

D. Treatment of Posttraumatic Stress Disorder

a. Treatment Selection

Recommendation

9. We recommend individual, manualized trauma-focused psychotherapy (see Recommendation 11) over other pharmacologic and non-pharmacologic interventions for the primary treatment of PTSD.
   (Strong For | Reviewed, New-added)

Discussion

The Work Group's recommendation to use individual trauma-focused psychotherapy over pharmacotherapy reflects the current state of the research into PTSD treatment. Although there are few data that reflect direct head-to-head comparisons of trauma-focused psychotherapy and a first-line medication for treating PTSD, two recent meta-analyses compared the treatment effects of psychotherapies and pharmacotherapies.[92,93] The results of these meta-analyses strongly indicate that trauma-focused psychotherapies impart greater change with regard to core PTSD symptoms than pharmacotherapies, and that these improvements persist for longer time periods. This appears true even when restricting the meta-analyses to studies that utilized "active" treatments such as Present-Centered Therapy (PCT) (as opposed to waitlist or treatment as usual) as control groups for psychotherapy studies.

In making this recommendation, the Work Group considered several factors in addition to the apparent differences in the magnitude of change associated with the two treatment modalities. First, the risks for negative side effects or negative reactions to the treatment are generally greater with pharmacologic treatments than with psychotherapies. Second, the positive effects of medication treatment diminish over time and are lost when medications are stopped. Third, comments from participants in the focus group and a growing body of literature indicate a patient preference for psychotherapy over pharmacotherapy.[46,94,95]

Recommendation

10. When individual trauma-focused psychotherapy is not readily available or not preferred, we recommend pharmacotherapy (see Recommendation 17) or individual non-trauma-focused psychotherapy (see Recommendation 12). With respect to pharmacotherapy and non-trauma-focused psychotherapy, there is insufficient evidence to recommend one over the other. **(Strong For | Reviewed, New-added)**

Discussion

The Work Group recognizes that individual trauma-focused psychotherapies may not be readily available in all settings and that not all patients elect to engage in such treatment. When this is the case, the Work Group recommends offering treatment using pharmacologic agents or individual, manualized psychotherapy that is not trauma-focused (such as Stress Inoculation Training [SIT], PCT, and Interpersonal Psychotherapy [IPT]) (see Recommendation 12). Notably, at the time the recommendations were developed, there were no well-designed, well-controlled studies available to the Work Group that directly compared the treatment effects of non-trauma-focused psychotherapy and pharmacotherapy. There are no empirical data to clearly differentiate pharmacotherapy and non-trauma-focused psychotherapy in cases where trauma-focused psychotherapy is unavailable or undesired. However, results of recent meta-analyses suggest that pharmacotherapy or individual non-trauma-focused psychotherapy can help reduce PTSD symptoms when used as the primary treatment modality. Therefore, these treatment modalities should be considered when individual trauma-focused psychotherapy is not available or when a patient declines trauma-focused psychotherapy.[92,93]

The reality is that the growing number of trauma-focused and non-trauma-focused psychotherapies, as well as pharmacologic agents to address PTSD, make it practically impossible to directly compare each psychotherapy treatment to each pharmacotherapy treatment. Thus, it is likely that decisions between

treatment options will continue to rely on clinical judgment and patient preferences, as well as systematic reviews of the growing body of well-controlled trials, such as those used in developing the present recommendation. However, direct comparisons between select non-trauma-focused psychotherapies and select pharmacologic treatments are warranted and will likely prove useful in making clinical decisions which should be done in collaboration with the patient.

b. Psychotherapy

Recommendation

11. For patients with PTSD, we recommend individual, manualized trauma-focused psychotherapies that have a primary component of exposure and/or cognitive restructuring to include Prolonged Exposure (PE), Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing (EMDR), specific cognitive behavioral therapies for PTSD, Brief Eclectic Psychotherapy (BEP), Narrative Exposure Therapy (NET), and written narrative exposure. **(Strong For | Reviewed, New-replaced)**

Discussion

For this CPG, trauma-focused psychotherapy is defined as any therapy that uses cognitive, emotional, or behavioral techniques to facilitate processing a traumatic experience and in which the trauma focus is a central component of the therapeutic process.[96] Although a number of theoretical frameworks have been cited in support of these treatments, extinction learning and cognitive-behavioral models provide the strongest empirical foundation. While trauma-focused psychotherapies differ considerably in their approaches and protocols, most often they involve eight to 16 sessions with varying combinations of the following core techniques: exposure to traumatic images or memories through narrative or imaginal exposure, exposure to avoided or triggering cues in vivo or through visualization, and cognitive restructuring techniques focused on enhancing meaning and shifting problematic appraisals stemming from the traumatic experience(s).

The trauma-focused psychotherapies with the strongest evidence from clinical trials are PE,[97] CPT,[98] and EMDR.[99,100] These treatments have been tested in numerous clinical trials, in patients with complex presentations and comorbidities, compared to active control conditions, have long-term follow-up, and have been validated by research teams other than the developers. Other manualized protocols that have sufficient evidence to recommend use are: specific cognitive behavioral therapies for PTSD,[101-109] BEP,[110-112] NET,[113,114] and written narrative exposure.[115,116]

The various psychotherapies differ in the use and delivery of the core trauma-focused techniques. For example, PE emphasizes imaginal exposure through repeatedly recounting the traumatic narrative out loud (often in present tense, eyes closed, reinforced by being asked to listen to an audio recording of the narrative process between treatment sessions). This is combined with in vivo exposure, and emotional processing of the narrative experience. CPT, and other trauma-focused cognitive therapies, emphasize cognitive restructuring through Socratic dialogue to examine problematic beliefs, emotions, and negative appraisals stemming from the event, such as self-blame or mistrust. EMDR incorporates imaginal exposure through narration and visualization to process the worst image, emotion, and negative cognition associated with the traumatic event, along with a more healthy cognitive reappraisal, with bilateral eye movements or other form of bilateral stimulation intended to create a dual awareness environment to

facilitate processing and relaxation. BEP has a strong psychodynamic perspective,[110-112,117] but also incorporates imaginal exposure, written narrative processes, cognitive restructuring through attention to meaning and integration of the experience, relaxation techniques, and a metaphorical ritual closing to leave the traumatic event in the past and foster a sense of control. NET relies on imaginal exposure through a structured oral life-narrative process that helps patients integrate and find meaning in multiple traumatic experiences across their lifespan. Written narrative exposure alone has been shown to be effective as a stand-alone and simple way to deliver exposure therapy.[115,116]

This recommendation is based on several comprehensive systematic reviews, as well as other studies, and there is high confidence in the evidence overall.[92,93,117,118] Across these trauma-focused therapies, benefits clearly outweigh risks in multiple trials. The choice of a specific approach should be based on clinical considerations, clinician expertise in one or more of these treatment methods, and patient preferences.

There are other psychotherapies that meet the definition of trauma-focused treatment for which there is currently insufficient evidence to recommend for or against their use. Future research is needed to explore the efficacy of novel, emerging treatments.

Recommendation

12. We suggest the following individual, manualized non-trauma-focused therapies for patients diagnosed with PTSD: Stress Inoculation Training (SIT), Present-Centered Therapy (PCT), and Interpersonal Psychotherapy (IPT).
    (Weak For | Reviewed, New-replaced)

Discussion

Although evidence supports the use of trauma-focused psychotherapies for the treatment of PTSD, access to these treatments is not uniform across clinics. In addition, not all patients are willing to participate in treatments that may focus on their trauma to any extent. As a result, some practitioners utilize non-trauma-focused therapies. SIT, PCT, and IPT are the non-trauma-focused therapies with the most evidence derived from clinical trials that have involved direct comparisons with first-line trauma-focused therapies. These treatments differ in their focus and techniques, but are similar in that none of them include a direct exposure to, or cognitive focus on, the traumatic event(s). SIT is a form of cognitive restructuring targeting individual thinking patterns that lead to stress responses in everyday life.[119,120] PCT focuses on current problems in a patient's life that are related to PTSD.[119,121] IPT focuses on the impact that trauma has had on an individual's interpersonal relationships.[122,123]

Evidence for the recommendation supporting non-trauma-focused SIT, PCT and IPT is based largely on two comprehensive meta-analyses, as well as other studies.[117,118] Overall, treatment effects for non-trauma-focused therapies are not as large as those seen in trauma-focused therapies, and the limited number of studies leads to low confidence in the evidence and weak support for the recommendation. However, the evidence shows that these treatments are better than receiving no treatment. A potential advantage of non-trauma-focused treatments is that dropout rates are often lower than those of first-line trauma-focused therapies.

Based on CBT's general effectiveness for treating mental health disorders, it may be appropriate to consider non-trauma-focused CBT when other psychotherapies for PTSD are not available or when non-trauma-focused CBT would be appropriate based on the patient and therapist's agreed upon treatment goals. However, the Work Group could not make a recommendation on this modality because the systematic review did not identify any studies of manualized non-trauma-focused CBT for the treatment of PTSD.

One limitation of this recommendation is that clinical trials were not specifically designed for individuals who opted out of trauma-focused interventions, the target sub-population for this recommendation. Additionally, these treatments have most often served as an active control condition in clinical trials involving trauma-focused treatments; therefore, it is unknown to what degree they may differentiate from other types of treatment widely used in clinical practice.

Future trials should focus on the effectiveness of these non-trauma-focused treatments with individuals who have refused trauma-focused treatments and on comparing these treatments with less-structured supportive counseling used widely in clinical practice. Such trials will establish the magnitude of non-trauma-focused therapy effect against trauma-focused and other approaches.

Recommendation

13. There is insufficient evidence to recommend for or against psychotherapies that are not specified in other recommendations, such as Dialectical Behavior Therapy (DBT), Skills Training in Affect and Interpersonal Regulation (STAIR), Acceptance and Commitment Therapy (ACT), Seeking Safety, and supportive counseling.
    (N/A | Reviewed, New-replaced)

Discussion

A wide variety of manualized protocols, including DBT,[124] STAIR, [125] ACT,[126] Seeking Safety,[127] hypnosis,[128] brief psychodynamic therapy,[129] and supportive counseling,[104,130,131] have all been used in the treatment of PTSD. However, further research is needed in order to make a recommendation for or against their routine use in patients with PTSD. Some of these treatments have been found to be effective for the treatment of other disorders (e.g., ACT for MDD), but do not have evidence of efficacy in patients with PTSD. A recent randomized trial of OEF/OID Veterans, 80% of whom had a diagnosis of PTSD, that was not included in the systematic evidence review for this guideline, failed to find a difference between ACT and Present-Centered Therapy for PTSD and other outcomes.[132] In addition, a systematic review found that Seeking Safety was not more effective than treatment as usual for reducing PTSD symptoms in patients with PTSD and SUD.[127] STAIR, which was developed to promote the development of skills to enhance participation in trauma-focused treatment among patients with PTSD who had experienced childhood trauma, has not been studied as a stand-alone treatment for PTSD. The Work Group thought it was not possible to make a recommendation for or against supportive counseling. Typically, trauma-focused treatments are superior to supportive counseling in randomized trials.[105,131] Supportive counseling has been shown to be better than waitlist in some trials,[103,104] but the treatment manuals differ so substantially (from relatively inactive [104] to very active [103]) that they do not permit a broad generalization for this approach. The Work Group also thought it was not possible to make recommendations

regarding hypnosis and brief psychodynamic therapy given the limited amount and low quality of evidence for these approaches in PTSD.

It must be acknowledged that this recommendation focusing on time-limited approaches may not adequately address the problems of severe chronicity or inadequate treatment response that can occur in some patients with PTSD, even after successful delivery of one or more courses of trauma-focused psychotherapy or other evidence-based treatments. There is no consensus in the literature on how to optimally approach the care of these patients. Patient preferences and clinical judgment are important in determining the best course of action in such cases.

Recommendation

14. There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over or in addition to the full therapy protocol.
    (N/A | Reviewed, New-added)

Discussion

Relatively few studies have examined whether modifying psychotherapy protocols by adding components of other effective psychotherapies is beneficial, or conversely, whether the components of a multi-component protocol are as effective as the complete protocol. The evidence shows inconsistent results and does not support any strong conclusions. In addition, the Work Group was not aware of studies that were conducted with Veterans or Service Members. There also is insufficient evidence to determine whether the harms and benefits differ for combined or separated treatments relative to the original protocols.

The primary focus of research in this area has been on adding different components to exposure therapy. Several studies have examined the potential benefits of adding cognitive restructuring to exposure, with two studies finding benefit [106,130] and two studies finding no benefit.[97,108] A systematic review of these studies found no added benefit of cognitive restructuring for PTSD symptom severity, loss of PTSD diagnosis, and depression symptoms.[118] An additional study examined the benefits of SIT with the addition of PE relative to SIT alone or PE alone and found all three treatments superior to waitlist and not different from each other.[119]

A dismantling study of CPT, which includes both a written trauma narrative as well as cognitive therapy, examined full CPT versus the separate narrative and cognitive components.[116] The cognitive only group (known as CPT-C) showed faster improvement during treatment on self-rated PTSD outcomes, but the treatments did not differ significantly at post-treatment on clinician-rated PTSD and other outcomes. Based on these findings, the CPT protocol has been modified so that the written narrative is optional, and the standard protocol (now referred to as CPT) includes the cognitive component only.[133] Although there is insufficient evidence to make a general recommendation regarding dismantling psychotherapy protocols, both CPT and CPT-C, as well as written narrative exposure, are included in the evidence recommendation above for trauma-focused psychotherapies.

If modifications to an established protocol (e.g., PE, CPT, EMDR) are clinically necessary, the modifications should be empirically and theoretically guided, and with understanding of the core components of trauma-

focused psychotherapies considered most therapeutically active. Future research using additive and dismantling designs is needed to inform clinical decisions about how to optimize effective treatments.

Recommendation

15. We suggest manualized group therapy over no treatment. There is insufficient evidence to recommend using one type of group therapy over any other.
    (Weak For | Reviewed, New-replaced)

Discussion

The limited data on the efficacy of group therapy for PTSD indicates that it is not as effective as individual therapy. However, some patients with PTSD may prefer manualized group psychotherapy over other treatment formats. Unfortunately, there were few studies published through the time period of our evidence review that informed whether group psychotherapy is as effective as individual psychotherapy. The research has not shown any particular model of manualized trauma-focused or non-trauma-focused group psychotherapy for PTSD to be superior to other active interventions, such as PCT, psychoeducation, or treatment as usual. However, group psychotherapy is better than no treatment in reducing PTSD symptoms.[134]

One study that was published after the search date cutoff, and was therefore not included in the systematic evidence review for this guideline, found that individual CPT was more effective than group CPT for reducing PTSD symptoms, although comparably effective for reducing depression and suicidal ideation.[135] The Work Group considered this study, and it did not change our recommendation. A meta-analysis of 10 studies comparing group psychotherapy to other active interventions found that no single model of group psychotherapy was superior to other group PTSD treatments in reducing PTSD symptoms.[134] A variety of different group therapy modalities were examined across the studies, including trauma-focused CBT, non-trauma-focused CBT, psychoeducation, and PCT. Additionally, a direct head-to-head comparison of group CPT versus group PCT found no significant differences regarding clinician-rated PTSD outcomes.[136] A meta-analysis of six studies [117] plus one additional study [137] compared group psychotherapy for PTSD to waitlist or no treatment. Across studies, group treatment for PTSD was superior to waitlist (i.e., no treatment).

The quality of the evidence is low because of the small number of trials comparing time-limited group psychotherapies to one another and the minimal research comparing group psychotherapy to individual psychotherapy. A trade-off to taking part in group psychotherapy may be that individuals do so at the expense of taking part in individual trauma-focused therapy or other treatments that have greater empirical support. Patient factors that may warrant consideration include a preference for individual trauma-focused psychotherapy, willingness to disclose personal information in group, and potential value of group approaches such as the comradery, milieu, and social support.

Clinical programming that offers group treatment instead of individual treatment may seem like a cost-efficient way to treat more patients more quickly. However, given the absence of evidence that group treatment is as effective as individual trauma-focused psychotherapy, it is not advisable to conclude that group treatment is sufficiently cost-effective. The one study comparing group psychotherapy to individual psychotherapy suggests that group is less effective for treating PTSD.[135] Research is needed to explore the comparative efficacies of different group psychotherapies, including trauma-focused and non-trauma-

focused CBTs. It is important that studies comparing group psychotherapies to individual psychotherapies assess mental health outcomes, dropout rates, and cost-effectiveness.

Recommendation

16. There is insufficient evidence to recommend for or against trauma-focused or non-trauma-focused couples therapy for the primary treatment of PTSD.
    (N/A | Reviewed, Amended)

Discussion

In some cases, Veterans may prefer PTSD treatment that includes attention focused on their intimate relationships. There are no studies that compare individual trauma-focused treatment for PTSD to a couples-based approach. Overall, there is promising but limited evidence in support of trauma-focused couples therapy for PTSD.

Two RCTs found that time-limited trauma-focused couples therapy improved PTSD and relationship satisfaction compared to a waitlist or PTSD education group.[138,139] In one study, couples were randomized to either Cognitive Behavioral Conjoint Therapy (CBCT) or a waitlist.[138] CBCT is a manualized treatment for PTSD that is delivered to couples and focuses on reducing avoidance and challenging core beliefs that are maintaining PTSD and relationship difficulties. The second study randomized Veterans who served in the Iraq or Afghanistan Wars and their partners to either couples therapy or couples-based family education.[139] In this study, couples received Structured Approach Therapy, a manualized treatment that includes education about PTSD and how it affects relationships, emotion activation, and disclosure-based exposures.

Two studies of different treatments, one waitlist and one psychoeducation comparison, suggest trauma-focused couples therapy may reduce PTSD symptoms and improve relationship satisfaction for the identified patient.[138,139] However, there is no evidence that the partner benefits from the PTSD treatment or that a couples approach improves partner-reported relationship satisfaction. Additionally, there are no direct comparisons of individual- versus couples-focused trauma treatment. Given the quality of the empirical findings and that some patients may prefer a couples approach, the Work Group determined that there was insufficient evidence to recommend for or against trauma-focused couples therapy. Research is needed to compare the effectiveness of trauma-focused couples treatment to individual trauma-focused psychotherapy.

c. Pharmacotherapy

Recommendation

17. We recommend sertraline, paroxetine, fluoxetine, or venlafaxine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy.
    (Strong For | Reviewed, New-replaced)

Discussion

Results of three systematic reviews support the use of three SSRIs, sertraline, paroxetine, fluoxetine, and one serotonin norepinephrine reuptake inhibitor (SNRI), venlafaxine, as monotherapy for the treatment of

PTSD.[92,93,140] The most recent meta-analysis included data from over 6,000 participants in 55 studies.[92] Each of these three meta-analyses concluded that sertraline, paroxetine, fluoxetine, and venlafaxine each had stronger evidence to support use in the treatment of PTSD compared to the other SSRIs and SNRIs.

The benefits of these medications outweigh the potential harms. The most frequent adverse effects of SSRIs include sexual dysfunction, increased sweating, gastrointestinal upset, and drowsiness/fatigue. In 2004, the Food and Drug Administration (FDA) issued a box warning stating that, compared to placebo, antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults; however, there does not appear to be an increase in the risk of suicidality in adults beyond age 24 and there may be a reduced risk in adults aged 65 and older. Venlafaxine shares these potential harms and can increase blood pressure at higher dosages. Patients taking SSRIs and SNRIs should have their dose tapered in order to reduce the chances of precipitating a discontinuation reaction, with the exception of fluoxetine (due to its long half-life). Patient preferences and comorbidities should be considered when deciding between these agents. Future research priorities should include further determination of the role and efficacy of antidepressants for the treatment of PTSD.

See Table 3 below and Appendix C: Pharmacotherapy Dosing Table for dosing information.

Table 3. Medication Monotherapy for the Treatment of PTSD by Recommendation and Strength of Evidence

Quality of Evidence*	Recommend For	Suggest For	Suggest Against	Recommend Against	No Recommendation For or Against
Moderate	Sertraline^ Paroxetine^ Fluoxetine Venlafaxine		Prazosin (excluding the treatment of PTSD associated nightmares)		Prazosin for the treatment of PTSD associated nightmares
Low		Nefazodone ±	Quetiapine Olanzapine Citalopram Amitriptyline	Divalproex Tiagabine Guanfacine	Eszopiclone
Very Low		Imipramine Phenelzine±	Lamotrigine Topiramate	Risperidone Benzodiazepines D-cycloserine Hydrocortisone Ketamine	Bupropion Desipramine D-serine Escitalopram Mirtazapine
No Data†					<u>Antidepressants</u> Doxepin Duloxetine‡ Desvenlafaxine Fluvoxamine‡ Levomilnacipran Nortriptyline Trazodone Vilazodone Vortioxetine <u>Anxiolytic/Hypnotics</u> Buspirone‡ Cyproheptadine Hydroxyzine Zaleplon Zolpidem

*The Work Group determined there was no high quality evidence regarding medication monotherapy
^FDA approved for PTSD
±Serious potential toxicity, should be managed carefully
†No data were captured in the evidence review (based on the criteria outlined in Conducting the Systematic Review) and were not considered in development of this table
‡Studies of these drugs did not meet the inclusion criteria for the systematic evidence review due to poor quality

Recommendation

18. We suggest nefazodone, imipramine, or phenelzine as monotherapy for the treatment of PTSD if recommended pharmacotherapy (see Recommendation 17), trauma-focused psychotherapy (see Recommendation 11), or non-trauma-focused psychotherapy (see Recommendation 12) are ineffective, unavailable, or not in accordance with patient preference and tolerance. (NOTE: Nefazodone and phenelzine have potentially serious toxicities and should be managed carefully.) **(Weak For | Reviewed, New-replaced)**

Discussion

Although additional research on nefazodone, imipramine, and phenelzine has been lacking over the past decade, the few previously published placebo-controlled studies demonstrated modest therapeutic effects of these medications for the treatment of PTSD. The confidence in the data yielded from these small studies is low, but the fact remains that nefazodone significantly improved PTSD symptoms in a Veteran population [141] and showed effects equivalent to sertraline in two fair quality trials.[142,143] Recent meta-analyses demonstrate that nefazodone has small-to-medium effect sizes.[92,93] One small controlled study demonstrated measurable therapeutic effects of imipramine and phenelzine in Vietnam combat Veterans.[144]

These medications have fallen out of use by most clinicians due to their unwanted side effect profile, that includes, for example, rare cases of liver toxicity caused by nefazodone, anticholinergic, cardiac, and sedative effects of imipramine, and risk of hypertensive crisis with phenelzine if the patient does not follow a low tyramine diet and avoid contraindicated medications when using monoamine oxidase inhibitors (MAOIs). However, with careful monitoring, these medications can be used safely. Patients may prefer one of these medications due to their sleep-enhancing effects and reduced sexual side effects, but may feel burdened by the need for periodic liver function testing (nefazodone), electrocardiograms (imipramine), or dietary/medication restrictions (phenelzine).

The weak recommendation regarding these medications is due to the limited evidence of their efficacy and known adverse effect profiles. Given the lack of evidence-based alternatives to first-line pharmacotherapy options, and given the promising results in older small single-site trials, more rigorous research on the effectiveness of these three medications, or others in the same classes, is warranted.

Recommendation

19. We suggest against treatment of PTSD with quetiapine, olanzapine, and other atypical antipsychotics (except for risperidone, which is a Strong Against, see Recommendation 20), citalopram, amitriptyline, lamotrigine, or topiramate as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks. **(Weak Against | Reviewed, New-replaced)**

Discussion

We suggest against using quetiapine or olanzapine as monotherapy for the primary treatment of PTSD because of low quality evidence and because the harms outweigh the benefit. A study published outside of our search timeline and apart from the evidence upon which this recommendation is based, assessed the

efficacy of quetiapine as monotherapy for the treatment of PTSD.[145] Despite the moderate effect size demonstrated in the quetiapine RCT, the study had a high risk of bias including a lack of information regarding amount of missing data, analytic method of handling missing data, high attrition, and differential dropout; coupled with quetiapine's known adverse effect profile, these factors necessitated a recommendation suggesting against the use of quetiapine as monotherapy for the treatment of PTSD. (NOTE: The above study was conducted between 2004 and 2008 at two VA medical centers and presented at two national meetings in 2009; it was not published until December 2016 after closure of the evidence review conducted for this CPG. Because of the extensive off-label use of quetiapine to treat PTSD or its symptoms in VA, the Work Group felt an obligation to include the study in the guideline.)

Olanzapine has been evaluated in two small studies with participants who had non-combat-related PTSD; results were mixed.[146,147] In addition, three meta-analyses reached different conclusions on olanzapine's efficacy ranging from a small effect size to no difference from placebo.[92,93,140]

Antipsychotics can produce metabolic adverse effects (harms) that may exacerbate a patient's comorbidities or result in new medical problems. Metabolic effects, including hyperglycemia, new onset diabetes, weight gain and increased lipid concentrations, can occur with all of the atypical antipsychotics. Higher potency second generation antipsychotics (SGAs), also have a higher incidence of producing extrapyramidal effects, including akathisia and pseudo-parkinsonism, as well as hyperprolactinemia, which can result in sexual dysfunction and gynecomastia. All antipsychotics are associated with an increased risk of stroke in elderly patients and death in elderly patients with dementia. These and other adverse effects and drug-drug interactions limit the acceptability of atypical antipsychotics by patients and healthcare providers.

Evidence from a recent meta-analysis concluded that citalopram has insufficient evidence and does not separate from placebo.[92] Additionally, the potential risk of QT-interval prolongation with doses greater than 40 milligrams (mg) per day outweighs the benefits of the medication. One clinical trial of amitriptyline demonstrated a positive effect on depression, but no effect on PTSD symptoms.[148]

A recent systematic review that included a meta-analysis did not find a significant effect size for topiramate or lamotrigine in the treatment of PTSD.[92] (See Recommendation 38 on PTSD and SUD.) In contrast, two previous systematic reviews and meta-analyses concluded that topiramate yielded moderate-to-large effect sizes as monotherapy.[93,149] Two small 12-week placebo-controlled studies were the basis for these meta-analytic findings. In one study, although an improvement in secondary outcomes for PTSD was seen for topiramate over placebo, topiramate monotherapy showed no difference between groups for the primary outcome of total CAPS scores.[150] In a second study, topiramate was not significantly different from placebo, except for the avoidance/numbing symptom cluster in modified intention-to-treat analysis and the CAPS-rated PTSD symptoms for the completer-only analysis.[151] Additionally, rates of remission and change in depression symptoms did not significantly differ between groups. There is only one small study to date that indicates lamotrigine leads to some improvement in avoidance/numbing and re-experiencing symptoms in patients with PTSD.[152] Further study is warranted prior to making recommendations for the use of topiramate or lamotrigine.

Antiepileptic drugs, including topiramate and lamotrigine, have an FDA warning of an increased risk of suicidal thoughts or behaviors. Topiramate is known to cause paresthesias, hyperammonemia, kidney stones, and cognitive side effects, including transient impaired learning and memory. Lamotrigine must be titrated very slowly and carries a risk of serious rash if dose titration recommendations are not followed carefully, especially in combination with valproate.

Recommendation

20. We recommend against treating PTSD with divalproex, tiagabine, guanfacine, risperidone, benzodiazepines, ketamine, hydrocortisone, or D-cycloserine, as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks. **(Strong Against | Reviewed, New-replaced)**

Discussion

Compared to placebo, divalproex monotherapy,[153] and tiagabine monotherapy [154] were not effective in the treatment of PTSD. The divalproex studies were conducted in small samples of Veterans over eight to 12 weeks, which reduced the confidence in results of these studies. A 12-week placebo-controlled tiagabine study included a much larger PTSD sample from the general population and found no difference between groups.[154] A recent meta-analysis also concluded that divalproex and tiagabine were no more effective in treating PTSD than placebo.[92]

Divalproex requires periodic laboratory testing of liver enzymes and platelets and has significant risks of weight gain, hirsutism, polycystic ovarian syndrome, and teratogenicity, which may negatively impact patient acceptability and preferences, especially in women of childbearing potential. Tiagabine is generally well tolerated and is not associated with significant adverse effects. Neither medication has sexual side effects. Antiepileptic drugs, including divalproex and tiagabine, have an FDA box warning for an increased risk of suicidal thoughts or behaviors. We therefore recommend against the use divalproex or tiagabine for the treatment of PTSD due to the lack of efficacy in the context of significant side effects.

Guanfacine was studied in two small trials.[155,156] No effect was seen on measures of PTSD symptom severity for the actively-treated group relative to the placebo group.

We recommend against the use of risperidone as monotherapy for the primary treatment of PTSD due to very low quality of evidence and because the potential harms outweigh the benefits. Only two studies of risperidone as monotherapy have been conducted; both were in women who were either victims of child abuse [157] or sexual assault.[158] Meta-analyses have differed in their effect sizes for risperidone monotherapy compared to placebo, with Watts et al. [93] basing theirs (ES=0.95) on one study [157] and Lee et al.[92] using both studies (ES=-0.48).[157,158]

We recommend against the use of benzodiazepines for the primary treatment of PTSD due to the lack of evidence for effectiveness and because the risks outweigh potential benefits. Historically, benzodiazepines, particularly alprazolam and clonazepam, were frequently used as a primary agent or “as needed” for the treatment of PTSD despite the lack of evidence of efficacy in RCTs. There was no significant difference between alprazolam versus placebo in a small, five-week, randomized controlled study in 10 patients with PTSD.[159] The lack of effect on PTSD symptoms was also seen in an RCT of six patients who received either placebo or clonazepam.[160] Furthermore, alprazolam administration 30

minutes prior to each of five virtual reality exposure sessions reduced the efficacy of exposure therapy and was associated with more severe PTSD symptoms at three-month follow-up.[161] A very low quality systematic review also concluded that benzodiazepines are ineffective for PTSD treatment, are associated with worse overall severity, worse psychotherapy outcomes, aggression, depression, and substance use, and are relatively contraindicated for patients with PTSD.[162]

Because benzodiazepine use is associated with tolerance and dependence, it can be very difficult to discontinue these medications due to significant withdrawal symptoms. Benzodiazepines are also relatively contraindicated in patients with history of traumatic brain injury (TBI), sleep apnea, chronic obstructive pulmonary disorder (COPD), or who have high rates of comorbid alcohol misuse and SUD, particularly Veterans with combat-related PTSD. Furthermore, pre-clinical evidence suggests that benzodiazepines may actually interfere with the extinction of fear conditioning and/or potentiate the acquisition of fear responses and worsen recovery from trauma.[163,164] We, therefore, recommend against the use of benzodiazepines for the primary treatment of PTSD.

Major depression frequently co-occurs with PTSD. Feder et al. evaluated the efficacy of a single intravenous (IV) sub-anesthetic dose of ketamine in patients with PTSD since preliminary evidence suggests that sub-anesthetic doses of IV ketamine has rapid antidepressant effects in treatment-resistant depression. The study compared ketamine versus midazolam in 41 patients with PTSD in a two-week crossover, low quality RCT.[165] Ketamine administration significantly reduced self-rated PTSD symptoms at 24 hours, but not seven days after the infusion. Furthermore, clinician-rated PTSD symptom severity was also not significantly different between subjects given ketamine or midazolam one week after administration. Additionally, there was no significant difference between ketamine and midazolam with respect to the severity of depressive symptoms. Individuals who received ketamine had greater rates of blurred vision, dry mouth, restlessness, nausea and vomiting, headache, and poor coordination compared to midazolam.

In the context of limited information on the efficacy of ketamine in PTSD combined with its significant side effects and potential for abuse, we recommend against the use of ketamine for the primary treatment of PTSD in a clinical setting. Future, well-designed studies could help shed light on the efficacy of ketamine on clinician-rated PTSD and depressive symptoms.

There is no evidence for the efficacy of hydrocortisone in the primary treatment of PTSD. In a randomized, double-blind, placebo-controlled, crossover pilot study evaluating hydrocortisone's effect on automatic memory retrieval in 30 inpatients with PTSD, investigators found no differences between 10 mg and 30 mg hydrocortisone compared to placebo in outcomes for overall PTSD or in intrusions, avoidance, or hyperarousal using the Impact of Event Scale - Revised. Subjects were taking a variety of psychotropic medications including tricyclic antidepressants (TCAs), SNRIs, SSRIs, antipsychotics, and anticonvulsants.[166]

Recommendation

21. We recommend against treating PTSD with cannabis or cannabis derivatives due to the lack of evidence for their efficacy, known adverse effects, and associated risks.
    (Strong Against | Reviewed, New-added)

Discussion

Preliminary evidence that natural and synthetic cannabinoids could improve PTSD symptoms, particularly nightmares, is offset by the significant side effects including tolerance, dependence, withdrawal syndrome, psychosis, cognitive deficits, and respiratory symptoms if smoked. A recent systematic review concluded that the quality of two retrospective and four prospective studies assessing the use of medical marijuana to treat PTSD was very low.[167] The lack of well-designed RCTs evaluating the efficacy of cannabinoids in large samples of patients with PTSD, together with its serious side effects, does not support the use of natural or synthetic cannabinoids as a treatment for PTSD. Additionally, these findings are consistent with the reviews by Steenkamp et al. and Belendiuk et al.,[168,169] as well as the VA Evidence-based Synthesis Program review of cannabinoids for the treatment of PTSD.[170]

Recommendation

22. There is insufficient evidence to recommend for or against monotherapy or augmentation therapy for the treatment of PTSD with eszopiclone, escitalopram, bupropion, desipramine, doxepin, D-serine, duloxetine, desvenlafaxine, fluvoxamine, levomilnacipran, mirtazapine, nortriptyline, trazodone, vilazodone, vortioxetine, buspirone, hydroxyzine, cyproheptadine, zaleplon, and zolpidem.
    (N/A | Reviewed, New-replaced)

Discussion

Medications listed in this recommendation are based on the following criteria: absence of studies, studies reported conflicting results, or studies reporting inconclusive results. As of yet, there are no RCTs that would support the use of any of the above agents as monotherapy. Escitalopram, duloxetine, desvenlafaxine, levomilnacipran, vilazodone, vortioxetine, and fluvoxamine have not been studied sufficiently to warrant a recommendation.

Currently, there is no evidence for the efficacy of bupropion in the treatment of core symptoms of PTSD.[171] However, we recognize that bupropion may be prescribed to manage antidepressant-induced sexual dysfunction, concurrent attention deficit disorder, or smoking cessation in patients with a diagnosis of PTSD.

Two single-site RCTs with mirtazapine monotherapy versus placebo have been published. Three systematic reviews of these findings have concluded that mirtazapine monotherapy is ineffective and that there was a high risk of bias in both RCTs.[92,93,140] The first study randomized 26 participants to mirtazapine or placebo and found mixed results depending on the outcome measure.[172] Although response rates were significantly greater for mirtazapine (65%) than placebo (22%) and drug performed better than placebo on one secondary PTSD scale; there was no difference found on the primary PTSD outcome. In the second study, 100 participants were openly randomized to mirtazapine or sertraline and both medications were found to be effective in reducing PTSD measures, with no differences between groups.[173] Therefore, in view of mixed results in two methodologically flawed single-site studies, and since the benefits are outweighed by associated risks, there is insufficient evidence to recommend for or against mirtazapine monotherapy for PTSD.

One randomized, double-blind, placebo-controlled crossover study assessed the effects of three weeks of eszopiclone and three weeks of placebo interspersed with one week of washout in 24 patients with PTSD and insomnia who were receiving psychotherapy or antidepressants for more than one month.[174] Eszopiclone significantly improved PTSD symptoms and sleep latency however, the total duration of sleep was not significantly different between patients who were randomized to eszopiclone or placebo.[174] Since the quality of this single study using eszopiclone was low and the reductions in PTSD symptoms were only weakly positive, there is insufficient evidence to recommend for or against the use of eszopiclone for the primary treatment of PTSD.

There is no evidence for the efficacy of D-serine in the primary treatment of PTSD. In a six-week double-blind, placebo-controlled, crossover pilot study of D-serine as monotherapy or add-on to a variety of psychotropic medications (including TCAs, SSRIs, benzodiazepines, and antipsychotics) in 22 outpatients, investigators found a significant reduction in anxiety symptoms and self-reported PTSD scale with D-serine compared to placebo, but only a trend towards improvements in clinician-rated PTSD symptoms using the CAPS.[175]

Given the significant burden of sleep difficulties, relative balance between risks and benefits, and the utility of non-benzodiazepine sedatives/hypnotics in patients with SUD, future studies should evaluate whether primary treatment of insomnia with non-benzodiazepine sedatives/hypnotics can reliably decrease PTSD symptoms. See Recommendation 40 for additional information on insomnia.

d. Augmentation Therapy

Table 4. Medication Augmentation and Combination* Pharmacotherapy for the Treatment of PTSD by Recommendation and Strength of Evidence

Quality of Evidence±	Recommend For	Suggest For	Suggest Against	Recommend Against	No Recommendation For or Against
Moderate			Prazosin (excluding the treatment of PTSD associated nightmares)	Risperidone	Prazosin for the treatment of PTSD associated nightmares
Low			Topiramate	Divalproex Olanzapine	Hydrocortisone
Very Low			Baclofen Pregabalin D-cycloserine†		Mirtazapine and Sertraline^
No data‡				Other atypical antipsychotics	Any drug not listed

*Combination means treatments are started simultaneously; augmentation means one treatment is started after another treatment (all treatments are augmentation unless otherwise noted)
±The Work Group determined there was no high quality evidence regarding medication augmentation and combination therapy
†Outside of a research setting
^Combination treatment
‡No data were captured in the evidence review (based on the criteria outlined in Conducting the Systematic Review) and were not considered in development of this table

Recommendation

23. We suggest against the use of topiramate, baclofen, or pregabalin as augmentation treatment of PTSD due to insufficient data and/or known adverse effect profiles and associated risks.
    (Weak Against | Reviewed, New-replaced)

Discussion

In a study of Veterans with PTSD, topiramate augmentation (of antipsychotics, SSRIs and TCAs, benzodiazepines, and anticonvulsants) did not show a significant difference from placebo in change in PTSD symptoms.[176]

The few published clinical trials with pregabalin and baclofen were small, single-site studies for which the risk of bias was high. Other systematic reviews reached the same conclusion and did not include either baclofen or pregabalin in their final analyses.[92,93,140] In view of inconclusive evidence regarding efficacy and clear evidence regarding adverse effects, we suggest against the use of pregabalin or baclofen augmentation for the treatment of PTSD.

In the only published RCT of baclofen, combat Veterans were randomized to receive medication or placebo as an augmentation agent to citalopram in an eight-week study.[177] Published data only included results for a fraction of those who completed the study. This evidence was considered at very high risk of bias and insufficient to suggest augmentation with baclofen as a treatment for PTSD.

The single published RCT of pregabalin was also an augmentation trial in which 37 soldiers with PTSD, all receiving citalopram or sertraline plus sodium valproate, were randomized to receive either pregabalin or placebo for six weeks.[178] Reduction of scores on the PCL was significantly greater for the pregabalin than for the placebo augmentation group. Although encouraging, this study had substantial methodological and bias concerns, including not reporting the dropout rate, methods of allocation concealment and randomization, and not employing an intention-to-treat analysis, that render these findings insufficient to suggest pregabalin as a treatment augmentation for PTSD.

Recommendation

24. We suggest against combining exposure therapy with D-cycloserine in the treatment of PTSD outside of the research setting.
    (Weak Against | Reviewed, New-added)

Discussion

Combination of exposure therapy with D-cycloserine has not shown consistent benefit for reduction of overall PTSD symptoms based on five studies.[179] While D-cycloserine is inexpensive, the side effect profile is low, and has very good acceptability compared to placebo, one study found lower efficacy of exposure therapy on improving outcomes in combination with D-cycloserine.[179] The lack of overall benefit, low number of randomized trials, and the barriers to implementation suggest that the current state of literature does not support D-cycloserine for combination with exposure therapy. However, some studies have demonstrated that certain subgroups of patients may benefit from D-cycloserine combination.[161] Additional research on the more precise identification of patient subtypes, proper D-cycloserine dose, timing of D-cycloserine administration, and other factors related to D-cycloserine use is warranted. Studies with more precise methodologies are recommended to clarify potential efficacy.

Recommendation

25. We recommend against using atypical antipsychotics, benzodiazepines, and divalproex as augmentation therapy for the treatment of PTSD due to low quality evidence or the absence of studies and their association with known adverse effects.
    (Strong Against | Reviewed, New-replaced)

Discussion

Risperidone and olanzapine are the only atypical antipsychotics to have been studied as augmentation treatment for PTSD. Although researchers found some benefit of SSRI augmentation with olanzapine in 19 Veterans with chronic military-related PTSD compared to placebo, [180] the effect did not achieve statistical significance in a meta-analysis.[92]

Risperidone has been studied in Veterans as an augmentation strategy to antidepressant treatment.[92,93] Two meta-analyses have included studies of risperidone as monotherapy or as treatment augmentation (four trials, N=419).[92,93] The effect sizes were small and any statistically significant improvements were not clinically significant.

VA Cooperative Study #504 [181] randomized 247 Veterans with military-related PTSD deemed resistant to antidepressants to either risperidone augmentation or placebo treatment. After six months, the changes from baseline in CAPS scores were not significant between the two treatment arms. Changes in CAPS subscale scores for re-experiencing and hyperarousal were statistically significant favoring risperidone, but the differences were not considered clinically important. No difference was found in the symptom scales for anxiety, depression, positive or negative symptoms, sleep, or quality of life. The authors concluded that compared to placebo, risperidone did not reduce PTSD symptoms. This is the largest clinical trial of an atypical antipsychotic as a treatment of PTSD to date.

Atypical antipsychotics, other than risperidone and olanzapine, have not been studied as augmentation therapy for PTSD. Since the risks of these medications outweigh the unknown benefits, we recommend against augmentation using atypical antipsychotics.

We recommend against the use of benzodiazepines due to the lack of evidence for effectiveness and because the risks outweigh potential benefits. Historically, benzodiazepines, particularly alprazolam and clonazepam, were frequently used as a primary agent or “as needed” for the treatment of PTSD despite the lack of evidence of efficacy in RCTs. Please see Recommendation 20 for additional information.

Because benzodiazepine use is associated with tolerance and dependence, it can be very difficult to discontinue these medications due to significant withdrawal symptoms. Benzodiazepines are also relatively contraindicated in patients with a history of TBI, sleep apnea, COPD, or who have high rates of comorbid alcohol misuse and SUD, particularly Veterans with combat-related PTSD. Furthermore, pre-clinical evidence suggests that benzodiazepines may actually interfere with the extinction of fear conditioning and/or potentiate the acquisition of fear responses and worsen recovery from trauma.[163,164] We, therefore, recommend against the use of benzodiazepines, even as augmenting agents, in the treatment of PTSD.

A single-site, double-blind study randomized 29 Veterans to divalproex or placebo augmentation of antidepressants (SSRIs, nefazodone, mirtazapine, bupropion, trazodone, and TCAs).[182] No significant differences in mean change in CAPS total or sub-scores were found except for a decrease in avoidance/numbing scores in the placebo arm.

Recommendation

26. There is insufficient evidence to recommend the combination of exposure therapy with hydrocortisone outside of the research setting.
    (N/A | Reviewed, New-added)

Discussion

One small RCT examined whether hydrocortisone enhances the efficacy of exposure therapy in reducing PTSD symptoms.[183] Although this study demonstrated effective combination and noted no side effects of the medication, replication would be necessary to improve confidence in these results. Barriers to implementation include the requirement for a clinician trained in exposure therapy and a prescribing provider to synchronize their efforts. Additional research into identification of certain subtypes of patients, proper hydrocortisone dose, timing of administration, and other factors is warranted. Studies with more precise combination methodologies may demonstrate different results.

Recommendation

27. There is insufficient evidence to recommend for or against the use of mirtazapine in combination with sertraline for the treatment of PTSD.
    (N/A | Reviewed, New-replaced)

Discussion

In the only RCT of combination pharmacotherapy, 36 civilian adults were randomized to sertraline plus mirtazapine (started simultaneously) versus sertraline plus placebo. Treatment groups did not differ in the change in CAPS over 24 weeks.[184] There was a significantly greater reduction of depressive symptoms as well as a greater PTSD remission rate in the combined treatment group (39%) compared to sertraline plus placebo (11%). Based on these methodologically challenged results, we suggest additional research regarding the combination of sertraline with mirtazapine for PTSD treatment be conducted.

e. Prazosin

Recommendation

28a. For global symptoms of PTSD, we suggest against the use of prazosin as mono- or augmentation therapy.
(Weak Against | Reviewed, New-replaced)

28b. For nightmares associated with PTSD, there is insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy.
(N/A | Reviewed, New-replaced)

Discussion

Four small, published trials of variable quality met the threshold for review.[185-188] These trials contained a total of 167 subjects, all of whom were Veterans or active duty Service Members. Most of these trials had promising results, particularly for nightmares. However, in a much larger, well-designed VA Cooperative multi-site trial with 304 subjects, prazosin failed to separate from placebo in the treatment of both global symptoms of PTSD and nightmares.[189] Interestingly, this study had not been published at the time of our review, three years after its completion. Nonetheless, we believed it was important to include in our analysis due to its significance and availability in the public domain (www.clinicaltrials.gov, identifier NCT00532493).

The quality of the four published trials was rated as moderate, based on small-to-medium sample sizes (10-67 subjects per trial), notable design flaws, and the potential for bias. For example, three of the four published trials (along with the VA Cooperative Study) were conducted by the same investigator.[185-187,189] In the fourth published study, only 58% of the subjects met DSM-IV criteria for PTSD.[188] All of these trials also included a mixture of subjects taking prazosin either as monotherapy or to augment existing psychotropic medications, which compromised the Work Group's ability to make separate recommendations for prazosin as mono- and augmentation pharmacotherapy. The quality of the VA Cooperative Study could not be fully rated as it was unpublished. However, the study design was impressive and VA Cooperative Studies are well-known for scientific excellence and methodological rigor.

Several systematic reviews and meta-analyses, none of which reviewed the VA Cooperative Study, have reached differing conclusions regarding the benefit of prazosin for treating PTSD. Lee et al. concluded that prazosin was beneficial at 14-27 weeks as an augmentation medication for the treatment of the global symptoms of PTSD, based on three of the four aforementioned trials.[92] However, Jonas et al. concluded there was insufficient evidence to determine prazosin's efficacy for the global symptoms of PTSD based on two trials.[149] A third, poor quality meta-analysis concluded that prazosin improved sleep quality, nightmares, PTSD symptoms, and global change based on six trials producing medium to large effect sizes.[190]

Global Posttraumatic Stress Disorder Symptoms

We suggest against prazosin as monotherapy or augmentation therapy for global symptoms of PTSD, based on lack of demonstrated efficacy. Two of the three published studies reviewed by the work group, which had 10 and 67 subjects respectively, did find a statistically significant reduction in overall CAPS scores in their prazosin arms compared to controls.[185,187] However, in the third study there was no difference in total CAPS scores.[186] Additionally, in the VA Cooperative Study, which had nearly four times as many subjects, there was no difference in the total CAPS and Clinical Global Impression of Change Scale (CGIC) scores between the prazosin and placebo arms.[189] The VA study demonstrated a placebo effect that appeared larger than that seen in the other trials.

Nightmares and Sleep Quality

Despite the fact that prazosin has been used for managing PTSD-associated nightmares in recent years, we found insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy for nightmares or sleep disturbance associated with PTSD. Specifically, positive results in nearly all

of the smaller studies were contradicted by negative results in the much larger and stronger VA Cooperative Study. In three of the four smaller trials, prazosin significantly decreased recurrent distressing dreams.[185-187] Additionally, in three of the four smaller trials, prazosin significantly improved sleep quality.[186-188] However, in the VA Cooperative Study, there was no difference between prazosin and placebo on recurrent distressing dreams or sleep quality.[189] As mentioned above, the VA study demonstrated a placebo effect that appeared larger than that seen in the other trials.

We recognize that these recommendations constitute a significant reversal of prazosin's role in the current management of PTSD. We are recommending neither for nor against the continuation of prazosin in patients who believe it to be beneficial; the decision to stop or continue prazosin should be individualized and made using SDM. If patients and/or providers decide to discontinue prazosin, we suggest a slow taper of the dose, while monitoring for symptom worsening or reappearance. Prazosin may need to be continued or restarted in some patients.

f. Combination Therapy

Recommendations

29. In partial- or non-responders to psychotherapy, there is insufficient evidence to recommend for or against augmentation with pharmacotherapy.
    (N/A | Reviewed, New-replaced)

30. In partial- or non-responders to pharmacotherapy, there is insufficient evidence to recommend for or against augmentation with psychotherapy.
    (N/A | Reviewed, New-replaced)

31. There is insufficient evidence to recommend for or against starting patients with PTSD on combination pharmacotherapy and psychotherapy.
    (N/A | Reviewed, New-added)

Discussion

Although many patients show clinical improvement in response to recommended evidence-based psychotherapies and/or pharmacotherapies, a sizable proportion of patients are partial- or non-responders. Determining what to do for these patients is a clinically important question, yet the limited evidence available is insufficient to guide clinical decision making. Only a few studies have examined the benefits of administering medication and psychotherapy to either augment a single initial modality following inadequate response, or as a combination at the outset of therapy.

A single study that examined the benefits of sertraline versus placebo for patients following partial response to PE found no added benefit of sertraline augmentation.[191] A study that examined the benefits of PE following eight weeks of treatment with sertraline (versus placebo) found no added benefit of PE augmentation, although post-hoc analysis found that PE (versus continued sertraline monotherapy) improved response among partial responders.[192]

Two studies examined the combination of PE and paroxetine as an initial approach to treatment. In the first, patients who received PE and paroxetine had better outcomes relative to those who received PE and placebo, which suggests that combination treatment is better.[193] In the second, which was based only

on self-reported patient outcomes, patients who received paroxetine and PE did not have better outcomes relative to those who received PE or paroxetine as monotherapy.[194]

None of the studies on augmentation or combination therapy included Veterans or Service Members. Research in these populations is needed to inform clinical decision making. In the absence of evidence to guide decision making, clinicians treating partial- or non-responders should rely on their clinical judgment, use an SDM approach, and take patient preferences into consideration.

g. Non-pharmacologic Biological Treatments

Recommendation

32. There is insufficient evidence to recommend for or against the following somatic therapies: repetitive transcranial magnetic stimulation (rTMS), electroconvulsive therapy (ECT), hyperbaric oxygen therapy (HBOT), stellate ganglion block (SGB), or vagal nerve stimulation (VNS). **(N/A | Reviewed, New-replaced)**

Discussion

Although there is a great deal of interest in rTMS for the treatment of PTSD, data supporting its use is not robust. There are a limited number of trials and a lack of uniformity among studies in terms of location, frequency, and intensity of treatment. A 2014 systematic review identified three RCTs examining the efficacy of rTMS applied to the right dorsolateral prefrontal cortex (DLPFC) for the treatment of PTSD.[195] All three identified RCTs utilized a sham-controlled double-blind design with a clinician-administered outcome metric. Further examination of the individual studies revealed some variability in study design and inconsistency in treatment parameters. For example, Cohen et al. conducted a three-armed study comparing 1 hertz (Hz) or 10 Hz to sham control.[196] The results demonstrated statistically significant improvement for 10 Hz treatment over either sham or 1 Hz. In this trial, low frequency (1 Hz) rTMS failed to separate from sham control. However, the study was limited due to questionable blinding and completers-only data analysis. Watts et al. enrolled 20 subjects randomized into groups for 10 sessions of rTMS targeting the right DLPFC with either 1 Hz treatment or sham control.[197] At two-month follow-up, subjects treated with 1 Hz treatment still had significant improvement over sham control. Boggio et al. also conducted a three-armed study with a total of 30 patients; however patients were randomized to 20 Hz sequences to either right or left DLPFC or sham.[198] Both active controls treatment groups showed statistically significant improvement in clinician-administered scales before and after treatment (but no difference between treatment groups and control), with a larger effect size in the right DLPFC group.[198]

Despite the findings of improvement on clinician-administered scales with rTMS targeting the right DLPFC, there are limitations to the quality of the evidence.[196-198] All three studies used different protocols in terms of frequency of magnetic pulses (20 Hz versus 10 Hz versus 1 Hz). High frequency treatment was effective in both studies where it was included, but in one of the three studies low frequency (1 Hz) rTMS failed to separate from control. As a result, the indicated settings for treatment are unclear. Given the limited number of studies demonstrating efficacy of rTMS for PTSD treatment and the lack of clinical guidance as to location, frequency of dose (Hz), and duration of treatment, we cannot recommend for or against rTMS until additional research has addressed these matters.

There is considerable interest in alternatives to either psychotherapy or pharmacology for the primary treatment of PTSD; however there is currently insufficient evidence to recommend the majority of somatic therapies, including ECT, HBOT, SGB, or VNS. Although there are published case reports supporting the utility of ECT [199] and VNS, [200] there is a lack of published randomized studies.

There is no conclusive evidence that HBOT is effective for treating PTSD. There have been no RCTs or uncontrolled trials specifically focused on patients with PTSD, and there is disagreement about what constitutes an adequate sham treatment. In a DoD study, 72 soldiers with TBI (66% with PTSD) were randomized to standard care (78%), HBOT (54%), or sham HBOT (64%).[201] Baseline scores on the PCL were less severe than in all-PTSD studies, likely because not everyone had PTSD. Scores were still in the severe range. Based on the evidence to date, and the practical and cost concerns, it does not appear that HBOT is a promising treatment for further study.

In addition to small open label trials, SGB has been studied in an open label trial of 166 Service Members followed for up to six months following the procedure.[202] Although the study showed significant reduction in overall PTSD scores, it is limited by its open label design, lack of clinician-administered outcome measures, and completers-only analysis. In a double-blinded RCT using a clinician-administered outcome scale, SGB failed to separate from sham control.[203] Based upon a lack of high quality RCTs supporting the efficacy of ECT, HBOT, SGB, or VNS, the Work Group is unable to recommend the use for the primary treatment of PTSD.

h. Complementary and Integrative Treatments

Recommendation

33. There is insufficient evidence to recommend acupuncture as a primary treatment for PTSD. **(N/A | Reviewed, New-replaced)**

Discussion

The available evidence on acupuncture for the treatment of PTSD is limited. Two low quality RCTs comparing a course of acupuncture to control conditions demonstrated significantly decreased PTSD symptom severity in the acupuncture groups.[204,205] However, neither trial involved a sham control, so a placebo effect cannot be ruled out as an explanation for any positive outcomes. In the first study, Hollifield et al. found that both acupuncture and CBT were effective compared to a waitlist control. Although equivalence or non-inferiority of acupuncture relative to CBT was not tested, the effects appeared similar in both treatments.[204] Engel et al. compared acupuncture in conjunction with usual care to usual care alone and found improvement in PTSD symptoms (based on clinician-rated CAPS scores), depressive symptoms, pain, and overall quality of life in the acupuncture group.[205] No adverse events were reported, although the dropout rate was greater in the acupuncture condition. It should be noted that almost 40% of participants in this study had no medications or counseling, so almost half of the usual care group was effectively a waitlist control group. Finally, a variant of acupuncture called acupoint stimulation, when combined with CBT, was found to be more effective than CBT alone.[206] Since this is a different modality that lacked a sham control condition, the evidence for acupoint stimulation is inconclusive and more research is warranted.

Our overall confidence in the available literature is low. Even though the evidence is trending positively for the use of acupuncture, based on the lack of sham control and other study limitations, the Work Group's assessment was that the current available evidence was still insufficient to recommend acupuncture as a primary treatment modality for PTSD. Safety data suggest that acupuncture is not associated with any serious adverse events, but some participants reported minor/moderate needle pain, superficial bleeding, and hematoma. There is also an insufficient number of staff trained in acupuncture within the VA and DoD healthcare systems to be able to offer it widely. In addition, some patients may not feel comfortable with the procedure, as suggested by the disproportionately high dropout rate in the acupuncture arm of the Engel et al. study.[205] Practitioners should consider factors such as patient preference and treatment availability when determining complementary and integrative health treatment options.

Recommendation

34. There is insufficient evidence to recommend any complementary and integrative health (CIH) practice, such as meditation (including mindfulness), yoga, and mantram meditation, as a primary treatment for PTSD.
    (N/A | Reviewed, New-replaced)

Discussion

The Work Group acknowledges the widespread use of CIH practices as part of the treatment of individuals with PTSD in the DoD and VA healthcare systems. It is important to clarify that we are not recommending against the treatments but rather are saying that, at this time, the research does not support the use of any CIH practice for the primary treatment of PTSD.

Two systematic reviews formed the evidence base to determine which CIH treatments are safe and effective for adults diagnosed with PTSD.[207,208] One systematic review focused on physical activity and exercise,[208] whereas the other summarized the CIH literature more broadly, but included study designs other than RCTs and participants who did not meet the diagnostic threshold for PTSD.[207] Both reviews highlighted the need for improved CIH clinical trial methods, more rigorous reporting, and additional RCTs of CIH interventions. Further research also should focus on analyzing treatment adherence to identify the minimum frequency or duration of practice required for maximum meditation effectiveness.

There were more clinical trials available for meditation than for any other CIH modality. Meditation is a mind-body technique that refers to a broad variety of practices with the general goal of training the mind through regulation of attention and/or emotion to affect functions, symptoms, and state of being. Ten RCTs were reviewed, including five that were specific to mindfulness practices. Grading the body of evidence for meditation overall was complicated by the heterogeneity of the types of meditation that have been assessed. Five RCTs were also specific to mindfulness-based stress reduction (MBSR). MBSR is a manualized protocol that includes didactic training and formal practice in three meditation techniques: body scan, sitting meditation, and mindful yoga. Meditation offered as augmentation to treatment as usual was compared to treatment as usual plus waitlist controls in one of these studies. Studies examining MBSR in group format did not find it to be superior to PCT for clinician-rated CAPS PTSD symptoms [209] or to treatment as usual for self-reported PCL PTSD symptoms.[210] Meditation is promising and may provide a safe, self-administered, and inexpensive intervention for PTSD. Unfortunately, the current research

clearly does not establish its efficacy. Additional high quality trials with adequate power, active control conditions, and longer follow-up periods are needed.

Three studies tested the effects of yoga.[211-213] All included a gentle form of yoga that focused on breathing and meditation and one was trauma-informed yoga. In one study that included patients with subthreshold PTSD, the yoga group participated in twelve 75-minute sessions of Kripalu yoga (weekly for 12 weeks, or twice weekly for six weeks) while controls had weekly group meetings over 12 weeks to complete assessment surveys.[211] The second study evaluated yoga as an augmentation to ongoing supportive psychotherapy.[213] Patients in the yoga group had hour-long weekly trauma-informed yoga sessions for 10 weeks, while controls had 10 weeks of women's health education. Quiones et al. randomized individuals with PTSD to Satyananda yoga versus controls.[212] The yoga group participated in twice weekly sessions of yoga for 16 weeks while controls received usual care. The meta-analysis of these RCTs found that compared to control groups, the yoga interventions reduced PTSD symptoms. No major adverse events were reported in the yoga interventions. However, the Mitchell et al. study was limited by lack of a control treatment and use of self-rated PTSD measures [211] and the Quiones et al. study was limited by a lack of intention-to-treat analysis, use of self-rated PTSD measures, and lack of blinding of outcome assessors.[212] Thus, our overall confidence in the available literature is low.

One systematic review [207] and one RCT [214] compared mantram meditation to waitlist or treatment as usual for PTSD symptoms. The systematic review described a single RCT [215] that randomized 33 patients with PTSD to mantram meditation versus waitlist. Mantram meditation was delivered in 90-minute weekly sessions for six weeks. A second RCT randomized 146 Veterans with military-related PTSD to mantram meditation plus treatment as usual or treatment as usual alone.[214] The mantram intervention consisted of six 90-minute weekly group sessions. This study found that compared to treatment as usual, mantram meditation was associated with reductions in PTSD symptoms as measured by the CAPS, a dropout rate of only 7%, and no reported adverse events. The quality of evidence for the efficacy of mantram was graded as low due to serious limitations and imprecision in effect estimates.

A number of other CIH modalities were reviewed, including various forms of exercise, natural products such as gingko biloba, and recreational therapies (e.g., sailing), but none were found to have sufficient evidence to support any recommendations regarding their use.[207] Although there is much interest in the area of animal assisted therapy, no studies evaluating the use of interventions with animals, such as equine therapy or canine therapy, met the threshold for inclusion in the review. At this time, there is no evidence to support their use for the primary treatment of PTSD.

Overall, the Work Group recognizes that CIH practices are increasingly offered as part of the treatment of PTSD. These practices hold promise as interventions to improve wellness and promote recovery. Meditation interventions in particular offered as augmentation treatments to treatment as usual—including yoga, MBSR, and mantram repetition—statistically significantly reduced PTSD symptoms compared with all comparators across all sources of trauma. However, at this time there are methodologic concerns that make it difficult to recommend any specific type of meditation. Research is needed to provide more information not only about meditation but other types of CIH as well for the primary and augmentation treatment of PTSD.

i. Technology-based Treatment Modalities

Recommendation

35. We suggest internet-based cognitive behavioral therapy (iCBT) with feedback provided by a qualified facilitator as an alternative to no treatment.
    (Weak For | Reviewed, New-replaced)

Discussion

Several studies have shown beneficial effects of supported iCBT for PTSD symptoms. In each case, support was provided by a qualified facilitator (e.g., care manager, trained peer, therapist) as described in the summary of the studies below.

Three trials utilized therapist support in combination with the internet-based interventions. In a small pilot RCT of 42 individuals, preliminary evidence supported a significant improvement on self-reported PTSD symptoms for therapist-supported iCBT versus waitlist control, although the between-group effect size was small (ES=0.47). Study limitations included a lack of clinician and patient blinding and a small sample size.[216] In a larger study by the same author, 125 individuals were randomized to eight weeks of iCBT with and without exposure components. There was no waitlist comparison or comparison with another treatment. Both groups had significant reductions in clinician-rated PTSD symptoms but there was no between group difference. Study limitations included a lack of assessor blinding and verification of adherence to the treatment protocols, among others.[217] A third study randomized 62 individuals to either iCBT versus delayed treatment group and found significant reductions in clinician-rated PTSD favoring iCBT. The therapist provided guidance and support in the iCBT condition whereas study personnel had weekly contact to answer general questions in the delayed treatment control condition. Study limitations included a lack of screening for comorbidities, the validity of using the CAPS over the phone, and the sample being drawn from the community.[218]

One larger study examined peer support in 303 Veterans that were randomized to either an iCBT intervention or treatment as usual. The iCBT intervention group demonstrated significantly better improvement in self-reported PTSD symptoms. Support for the iCBT was provided by Veteran peers rather than a therapist. Study limitations included an inability to track treatment fidelity, levels of distress (which were measured as mild-to-moderate in degree), and levels of PTSD at the end of the study which potentially could benefit from further treatment.[219]

Some studies have pointed out the particular utility of web-based interventions in certain settings. In a study of 159 patients randomized to either iCBT or to waitlist control, there was significant improvement in the treatment group versus the control group, with effects sustained at three-month follow-up as measured by the PDS.[220]

A small pilot study demonstrated the feasibility of using iCBT in primary care with Veterans.[221] Treatment in primary care may be associated with less stigma than a mental health appointment, making the use of iCBT in primary care an attractive option for those refusing a mental health referral. In a study of 80 Veterans randomized to either iCBT versus optimized usual care in a primary care setting, the iCBT group demonstrated significantly better outcomes on the PTSD Checklist – Civilian Version (PCL-C) than

optimized usual care, which consisted of care management, feedback to the primary care provider, and training on the management of PTSD in primary care settings. A registered nurse provided support to the study participants. Study limitations included a small sample size and the inability to measure treatment adherence.[222]

While there are several limitations to these studies, the Work Group suggests the use of supported iCBT along with the qualifications stated below:

- Clinicians should carefully review the content of any web-based materials to ensure their accuracy and ethical application before recommending their use to patients.
- Web-based approaches may be used when face-to-face interventions are not feasible (e.g., geography limits access to other forms of treatment) or when patients decline more traditional mental health interventions.
- Providers should regularly encourage patients to complete the intervention and endeavor to maintain and strengthen the therapeutic relationship, build patient rapport, stress practice and assignment completion, and ensure adequacy of safety protocols. Availability of telephone contact for initial assessment or other reasons (e.g., emergencies, suicidality/homicidality, or follow-up of specific problems) should be considered.
- Providers using technology-assisted interventions should take steps to ensure that their work complies with the regulations and procedures of the organization in which they are employed, legal standards, and the ethical standards of their professions. Patient confidentiality and safety should be monitored closely.

These interventions may be suggested for patients who refuse other treatment interventions. However, the Work Group's confidence in the quality of evidence for iCBT is low. Moreover, iCBT is not as well supported by the scientific literature as primary treatments for PTSD. The benefits appear to only slightly outweigh the harms. We also recognize that these studies provided oversight to the participants through qualified facilitators familiar with the treatment protocols. There were concerns that unsupervised iCBT or supervision by a peer not adequately trained to deal with a mental health crisis could be a potential harm. Also, there are potential barriers, including knowledge and/or availability of technology, technical support, and cost, which might prevent some individuals from using these approaches.

The Work Group also recognized many potential advantages of iCBT, including increased access to services and reduced stigma in seeking services. These interventions are convenient and can be completed on the patient's own schedule. Participation in supervised iCBT programs could be potentially very helpful to those in remote areas, locations where other services are not readily available, or when irregular hours preclude conventional clinical care. This is a promising area of research and more studies are needed before internet-based interventions can be strongly recommended. Some potential areas of research include human factors in using the technology, monitoring adherence, comparison to in-person PTSD treatments, and studies looking at the types of interventions and their mechanisms of action.

Recommendation

36. We recommend using trauma-focused psychotherapies that have demonstrated efficacy using secure video teleconferencing (VTC) modality when PTSD treatment is delivered via VTC. **(Strong For | Reviewed, Amended)**

Discussion

Sevberal studies have been completed that support the delivery of trauma-focused therapies through VTC, strengthening the support for the use of this modality in the delivery of care.[224-227] Two studies demonstrated the non-inferiority of delivering exposure therapies for Veterans with PTSD through VTC to the home. In a study of 232 Veterans randomized to eight sessions of a combined behavioral activation and therapeutic exposure treatment delivered either in-person or through home-based VTC, both modalities of treatment produced significant improvements in symptoms. The delivery of the intervention through VTC was non-inferior to the in-person delivery of the treatment, meaning that it was shown to be just as good as the standard delivery mechanism.[227] In another study of 52 Veterans receiving eight to 12 sessions of PE either in-person or through home-based VTC, there was a significant reduction in symptoms for both groups, and the outcomes were non-inferior for the VTC group versus the in-person treatment group.[224]

Both individual and group CPT are effective when delivered through VTC. In a study of 126 women with PTSD (including 21 Veterans) receiving individual CPT once to twice weekly for 12 sessions, there was no difference between the in-person delivery of CPT and delivery by VTC, with significant symptom improvements in both groups.[225] An additional study of 125 male Veterans randomized to group CPT-C provided either in-person or through VTC demonstrated significant symptom reduction in both groups, with the treatment outcomes in the VTC group being non-inferior to the in-person treatment group.[226] Another study demonstrated a trend suggesting that delivery of individual CPT to Veterans through VTC was non-inferior to in-person treatment, but the study was underpowered to make any definitive conclusions.[227]

The Work Group has updated and built upon the recommendations from the 2010 PTSD CPG based upon these new studies as described above. Although there are fewer studies examining the delivery of evidence-based treatments through VTC than those delivered in-person, there appears to be similar efficacy for VTC interventions as compared to the in-person delivery of services.

- VTC interventions are encouraged when: in-person interventions are not feasible due to geographic distance between patient and provider or other barriers to patient access (e.g., agoraphobia, physical disability), the patient would benefit from more frequent contact than is feasible with face-to-face sessions, or the patient declines in-person treatment.
- Providers using VTC interventions should endeavor to maintain and strengthen the therapeutic relationship, build patient rapport, stress practice and assignment completion, and ensure adequacy of safety protocols using similar techniques as they do in-person.

- Providers using VTC should take steps to ensure that their work complies with the regulations and procedures of the organization in which they are employed, legal standards, and the ethical standards of their professions. Patient confidentialityand safety should be monitored closely.

The Work Group's confidence in the quality of evidence is moderate. However, there are some concerns associated with treatment delivery through VTC such as technical support, computer literacy, and human factors in using technology. Potential advantages include increased access and decreased stigma. Further research is needed to address these questions.

Although this recommendation is specific to the delivery of trauma-focused therapies tested in VTC settings, the Work Group recognizes that VTC policies across the VA and DoD take a broad interpretation of the literature in making the assumption that any evidence-based outpatient modality being delivered in a face-to-face clinical setting may be considered for VTC delivery. This recommendation should not be interpreted to imply that modalities that have not been specifically tested through VTC are precluded from consideration based upon factors such as research literature outside the scope of this guideline, clinical judgment, SDM, availability of treatment modalities, and others. However, because the recommendations in this guideline are based on empirical evidence, the PTSD Work Group limited the recommendation to those treatments that have demonstrated efficacy.

E. Treatment of Posttraumatic Stress Disorder with Co-occurring Conditions

Recommendation

37. We recommend that the presence of co-occurring disorder(s) not prevent patients from receiving other VA/DoD guideline-recommended treatments for PTSD.
    (Strong For | Reviewed, New-added)

Discussion

Treatment studies of PTSD with various co-occurring disorders have shown that individuals with comorbid conditions can tolerate and benefit from evidence-based individual trauma-focused PTSD treatment, such as PE and CPT. RCTs using various methods rated as fair quality are consistent with these findings. For adults diagnosed with PTSD, treatment safety and effectiveness does not appear to be altered by the presence of comorbidities.

Based on a systematic review of 14 RCTs, the Work Group concluded that the presence of an SUD should not prevent concurrent treatment with evidence-based, trauma-focused therapy for PTSD.[127] A more detailed review of PTSD and co-occurring SUD is provided in Recommendation 38. Similarly, a detailed review of PTSD and co-occurring sleep disturbances is provided in Recommendation 39 and Recommendation 40. RCTs have found good tolerance and efficacy for various trauma-focused PTSD treatments in patients with comorbid psychotic disorders,[228] personality disorders,[122] severe mental illness,[229] dissociation,[230,231] anger,[232] suicidal ideation,[233] and depression.[232] One RCT addressed the issue of the safety of delivering imaginal exposure to patients with PTSD resulting from a cardiovascular event and found no evidence of adverse outcomes from the treatment.[234] The findings from this study suggest that cardiovascular patients should not be prevented from receiving evidence-based PTSD treatments because of safety concerns.

We did not find any studies meeting the threshold for review that examined the common comorbidities of TBI or pain. Well-designed trials looking at the treatment of PTSD and comorbidities, including individuals with multiple co-occurring conditions, are needed. Studies that also examine the patterns and predictors of PTSD and co-occurring condition change are needed to help determine if changes occur concurrently or if changes primarily by PTSD symptoms influence subsequent co-occurring disorder change. However, based on this evidence review, individuals with comorbid disorders should not be excluded from evidence-based treatment for PTSD.

Recommendation

38. We recommend VA/DoD guideline-recommended treatments for PTSD in the presence of co-occurring substance use disorder (SUD).
    (Strong For | Reviewed, New-replaced)

Discussion

Among Veterans with PTSD, rates of problematic drinking range from 12% to 48%.[235] Among Veterans with an SUD, rates of PTSD range from 63% to 76%.[236] Whether or not PTSD and SUDs may be treated concurrently, or if one (typically SUD) must be stabilized prior to treating the other, has historically been a topic of debate among clinicians, primarily due to concerns that individuals with SUDs may not be able to tolerate trauma-focused PTSD treatment.[127] Recent research, however, has shown that patients with PTSD and SUD (including nicotine use disorder) can both tolerate and benefit from concurrent treatment for both conditions, even in the most severe cases.[237]

A 2015 systematic review of 14 controlled trials in individuals with co-occurring PTSD and SUD found that trauma-focused therapies including exposure and cognitive restructuring, when delivered together with SUD interventions, were more likely than SUD treatment alone or treatment as usual to improve PTSD symptoms.[127] Several of these therapies also showed benefit in improving SUD symptoms after five to seven months.[127]

Non-trauma-focused PTSD therapies (e.g., Seeking Safety), when delivered together with an SUD therapy, did not improve PTSD symptoms in individuals with SUDs more than SUD treatment alone or treatment as usual. Evidence of improvement in SUD symptoms is mixed.[127,238,239] Thus, the Work Group does not recommend non-trauma-focused therapies such as Seeking Safety for the treatment of PTSD in the context of co-occurring SUD.

Likewise, medication trials of topiramate (up to 300 mg daily) [240] and prazosin (16 mg daily in divided doses) [241] in patients with comorbid PTSD and AUD failed to demonstrate efficacy in improving the primary symptoms of PTSD, although both medications reduced percent drinking days. In another study, desipramine outperformed paroxetine in reducing drinking days, although both showed some benefit on both drinking and core PTSD symptoms. Interestingly, in the same study, the addition of naltrexone had no effect on outcomes.[242] Combining medication and psychotherapy, however, may be a potentially effective strategy for PTSD and SUD. In one study, adding PE to naltrexone reduced drinking more at six months following treatment completion than naltrexone alone.[237]

The Work Group rated its overall confidence in the literature on treating PTSD and SUDs concurrently as moderate. A number of RCTs evaluating both pharmacotherapy and psychotherapy interventions met the

threshold for review. Most were deemed to be of fair to good quality. In general, the risks of trauma-focused psychotherapies are limited. Patient factors that may warrant consideration include possible denial of their SUD, reluctance to stop using a substance perceived as beneficial for coping with PTSD symptoms, and ambivalence about engaging in treatment for either PTSD or SUDs. Concurrent treatment of PTSD and SUDs also presumes that sufficient resources (e.g., programs, therapists) exist to treat both simultaneously and that providers are skilled in the management of co-occurring disorders. More research is needed to explore the comparative efficacies of different trauma-focused psychotherapies in this population, whether or not different approaches are needed for different substances or patterns of use, and how to improve treatment completion rates.

Recommendation

39. We recommend an independent assessment of co-occurring sleep disturbances in patients with PTSD, particularly when sleep problems pre-date PTSD onset or remain following successful completion of a course of treatment.
    (Strong For | Reviewed, New-replaced)

40. We recommend Cognitive Behavioral Therapy for Insomnia (CBT-I) for insomnia in patients with PTSD unless an underlying medical or environmental etiology is identified or severe sleep deprivation warrants the immediate use of medication to prevent harm.
    (Strong For | Reviewed, Amended)

Discussion

Sleep disturbance is found in 90-100% of Veterans with PTSD.[243,244] Some types of sleep disturbance, such as anxiety about falling asleep due to nightmares, are fairly unique to PTSD. Others, including obstructive sleep apnea, restless leg syndrome, and early morning awakening may occur in patients with PTSD, but are likely to have an alternative etiology and should be considered as co-occurring disorders. Sleep disturbances often do not improve after otherwise effective first-line PTSD treatments.[245,246] It is thus important to examine potential causes of sleep disturbance independently of PTSD, particularly with respect to underlying medical, dietary, and environmental etiologies. A discussion of primary treatments for co-occurring sleep disturbances is beyond the scope of this guideline; interested clinicians may wish to review the CPG on Chronic Insomnia Disorder published by the American College of Physicians in 2016.[247]

Few studies have explicitly evaluated the treatment of sleep disturbance in patients with PTSD. Among 11 studies examined in a 2016 systematic review by Ho et al.,[248] low-to-moderate quality evidence favored the use of CBT-I with and without the addition of Imagery Rehearsal Therapy (IRT) or Exposure, Relaxation, and Rescripting Therapy (ERRT) in patients with PTSD and sleep disturbance. One RCT found that CBT-I improved sleep in Veterans with PTSD; importantly, the gains were still seen at six months post-treatment.[249] CBT-I has also been recommended by the American College of Physicians as the initial treatment for chronic insomnia [247] and web-based CBT-I applications have also shown significant benefit.[250,251] Medication should be considered a second-line intervention at this time following an unsuccessful course of CBT-I treatment, and should include an SDM discussion regarding the harms and benefits of the medication.

Treating nightmares is an integral part of treating sleep disturbance in PTSD. However, the data are somewhat inconclusive regarding the best choice of intervention. Initial studies of IRT in civilian populations were positive,[252,253] but a subsequent, higher-quality trial evaluating the use of IRT in Veterans showed no benefit for nightmare frequency, sleep quality, or PTSD symptoms.[254] Another trial examining the use of IRT administered with CBT-I in Veterans found both objective and subjective improvements in sleep quality, PTSD symptoms, and depression.[255] The study, however, had a waitlist control and lacked a comparison group without the adjunctive IRT, so it is difficult to determine the mechanism of change. Some participants reported difficulty engaging in imagery techniques (a finding noted in several IRT studies), but the protocol overall was acceptable to Veterans and had reasonably high completion rates. Ho et al. assessed the evidence of benefit for ERRT in treating nightmares as being of moderate quality.[248] However, the evidence for ERRT is inconclusive at this time. The two ERRT studies examined by Ho et al. enrolled primarily Caucasian women, had treatment groups numbering fewer than 25 subjects each, did not require a diagnosis of PTSD, and did not include any physiological indices of sleep functioning.[256,257] For information regarding the use of prazosin for nightmares, see section on Prazosin.

The Work Group's overall confidence in the literature on sleep disturbances co-occurring with PTSD is low. However, the risks of treating sleep problems with a discussion of good sleep habits and psychotherapy are very low and patient buy-in is generally quite high due to the potential benefits of sleep on overall health and well-being. At this time, CBT-I continues to offer the strongest evidence and greatest promise. It is a particularly attractive modality because training is widely available in the VA and DoD, it can be delivered in individual or group format, and it requires only a few sessions. Future research should explore the best sequence of treating PTSD and co-occurring sleep disturbance. It should also examine the relative efficacy of effective PTSD treatment versus treatment as usual plus CBT-I in populations with PTSD. Additionally, we need studies evaluating whether or not there is a difference in treating sleep disturbance as an independent condition versus treating it as a component of PTSD. Finally, it may be determined that proactive management of sleep disturbances in Veterans has value in preventing PTSD; more research is needed to explore this possibility.

VII. Knowledge Gaps and Recommended Research

During the development of the 2017 version of the PTSD CPG, the Work Group identified a number of areas for which future research should be conducted. These included, but are not limited to, the following:

A. Shared Decision Making and Collaborative Care

- SDM in the context of making treatment decisions for PTSD
- The effect of collaborative care on long-term utilization of effective PTSD treatment and other healthcare services
- Key components of SDM and collaborative care that impact PTSD treatment effectiveness
- The role of technology-assisted interventions in improving the effectiveness of collaborative care to treat PTSD

B. Treatments for Acute Stress Disorder and Preventing Posttraumatic Stress Disorder

- Studies examining the efficacy and safety of pharmacotherapy and psychotherapy treatments for ASD
- Studies examining the efficacy, safety, and cost effectiveness of pharmacotherapy and psychotherapy treatments to prevent PTSD

C. Treatments for Posttraumatic Stress Disorder

- Issues of access and how to improve access, including accessibility and treatment retention
  - Studies examining how treatment completion rates can be improved
  - Studies to improve treatment motivation and treatment engagement
  - Studies examining the role of treatment choice in retention and the effectiveness of treatment
  - Studies examining models of implementation of effective treatments including costs, value, and feasibility
  - Studies examining novel implementation approaches of effective interventions, such as telehealth, web-based, and primary-care-based models of care
- Comparative efficacy and effectiveness of established treatments
  - Comparative studies of different methods of treatment provisions including couples, family, group, and individually provided interventions
  - Direct comparisons between established treatments, including psychotherapies and pharmacologic treatments
  - Examine treatment approaches for refractory PTSD and sequencing of treatments following partial response

  - Studies including outcomes beyond symptoms such as comorbid conditions, health outcomes, biomarkers, and cost-effectiveness
  - More rigorous research on the effectiveness of pharmacotherapy options
  - Examination of treatment dosing and duration and the impact on outcomes
  - Further investigation of the use of topiramate, prazosin, ketamine and novel therapies in patients with PTSD
- Studies examining treatment effectiveness in different patient populations
  - Studies informing the selection of treatments for specific patient populations, including men and women, various ethnic and racial groups, and various war cohort and trauma exposure groups
  - Examine the influence of service connection, disability, and the process of evaluation on treatment choice, retention, and response in the short and long-term
  - Examination of the effectiveness of practice-based variations/modifications to established psychotherapy protocols to include variations in length, frequency, and number of sessions as well as variations in specific techniques resulting from specific patient population or logistical considerations
- Augmentation of established treatments with other treatment options and/or novel approaches
  - Investigation of factors related to D-cycloserine and hydrocortisone use such as identification of efficacy, patient subtypes, proper dosing, and timing of dose administration
  - Examination of the impact of combining two or more established treatments for PTSD or augmenting an established treatment with a novel treatment
- Clinical trials testing emerging, novel treatments to improve the range of options available to patients
- Research to establish mechanisms of PTSD development and effective treatments to directly inform treatment development and improvement
  - Research examining the use of additive and/or dismantling designs to investigate creating more effective treatments
  - Studies to bring order/parsimony to treatment decision making and development
  - Examination of treatment impact beyond mental health symptoms to larger biological systems
  - Optimize treatment outcomes through mechanism-based treatment modifications
  - Research to better match patients to treatments based on biological or other factors
- Studies examining methods of training and dissemination of effective treatments
  - Best ways to disseminate effective treatments broadly while maintaining fidelity

D. Non-Pharmacologic Biological Treatments for Posttraumatic Stress Disorder

- Studies examining the efficacy of rTMS for PTSD treatment, including studies to identify parameters of effective treatment such as the location and frequency of dose, and duration of treatment
- Studies of acupuncture involving a sham control to examine relationship between placebo effect and improved outcomes
- Adequately powered, actively controlled trials with sufficient follow-up periods for meditation and other types of CIH practices

E. Technology-based Treatments for Posttraumatic Stress Disorder

- Studies examining internet-based interventions including the human factors involved in using the technology, monitoring adherence, comparison to in-person PTSD treatments, and types of interventions offered
- Factors that affect treatment delivery through VTC such as technical support, computer literacy, and human factors in using technology
- Studies examining modified or novel treatment protocols that take advantage of technology-based delivery of care
- Examine potential advantages to technology-based modalities such as increased access and decreased stigma

F. Treatments for Posttraumatic Stress Disorder with Comorbidities and Co-occurring Conditions

- Trials examining the concurrent treatment of PTSD and comorbidities, including individuals with multiple co-occurring conditions
- Studies that examine the patterns and predictors of changes in PTSD symptoms in relation to co-occurring conditions
- Investigation of whether the improvement of PTSD symptoms influences co-occurring conditions and/or if improvements to co-occurring conditions influence PTSD symptoms
- Comparative efficacies of different trauma-focused psychotherapies in populations with co-occurring conditions
- Studies determining the optimal sequence of treating PTSD and co-occurring sleep disturbance, including evaluating whether or not there is a difference in treating sleep disturbance as an independent condition versus treating it as a component of PTSD
- Proactive management of sleep disturbances in Veterans and its role in prevention of PTSD
- Relative efficacy of PTSD treatment versus treatment as usual with CBT-I
- Studies addressing PTSD among older Veterans with dementia and other conditions
- Studies addressing PTSD in the context of advanced illness/end-of-life care

Appendix A: Evidence Review Methodology

A. Developing the Scope and Key Questions

The CPG Champions, along with the Work Group, were tasked with identifying KQs to guide the systematic review of the literature on PTSD. These questions, which were developed in consultation with the Lewin team, addressed clinical topics of the highest priority for the VA and DoD populations. The KQs follow the population, intervention, comparison, outcome, timing and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 provides a brief overview of the PICOTS typology.

Table A-1. PICOTS [258]

P	Patients, Population, or Problem	A description of the patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
I	Intervention or Exposure	Refers to the specific treatments or approaches used with the patient or population. It includes doses, frequency, methods of administering treatments, etc.
C	Comparison	Describes the interventions or care that is being compared with the intervention(s) of interest described above. It includes alternatives such as placebo, drugs, surgery, lifestyle changes, standard of care, etc.
O	Outcome	Describes the specific results of interest. Outcomes can include short, intermediate, and long-term outcomes, or specific results such as quality of life, complications, mortality, morbidity, etc.
(T)	Timing, if applicable	Describes the duration of time that is of interest for the particular patient intervention and outcome, benefit, or harm to occur (or not occur).
(S)	Setting, if applicable	Describes the setting or context of interest. Setting can be a location (such as primary, specialty, or inpatient care).

The Champions, Work Group, and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. Table A-2 contains the final set of KQs used to guide the systematic review for this CPG.

a. Population(s)

- ☐ Adults 18 years or older with PTSD or ASD treated in any VA/DoD clinical setting

b. Interventions

- ☐ Key Question 1: Drug classes
  - SSRIs
  - SNRIs
  - TCAs
  - MAOIs
  - Other antidepressants

  - Mood stabilizer/anticonvulsants
  - Antipsychotics
  - Benzodiazepines (anti-anxiety, sedative/hypnotics)
  - Non-benzodiazepine sedative/hypnotics
  - Antianxiety, non-benzodiazepines
  - Peripheral alpha-1 antagonists
  - Other sympatholytics
  - Beta-blockers
  - Psychostimulants
  - Steroids
  - Cannabinoids
  - Other
- Key Question 2: Trauma-focused psychotherapies—therapies that include consciously recalling or activating the traumatic memory either as part (or all) of the presumed therapeutic mechanism or to provide material for other therapeutic techniques (e.g., cognitive restructuring, relaxation, imagery substitution)
  - PE Therapy
  - CPT
  - EMDR
  - Narrative therapy
  - Written exposure therapy
  - Accelerated Resolution Therapy
  - Trauma-focused CBT
  - Cognitive therapy
  - Virtual reality exposure
  - IRT
  - CBCT
  - Mindfulness-based exposure therapy
  - Emotional Freedom Technique/Thought Field Therapy
  - BEP
  - Non-trauma-focused psychotherapies
  - PCT
  - Problem-solving therapy

- SIT
- Mindfulness therapies
- MBSR
- Family therapy
- Behavioral activation
- IPT
- Emotionally Focused Couples Therapy
- ACT
- Relaxation
- Supportive counseling
- Brief psychodynamic therapy
- Neurolinguistic programming (NLP)
- Seeking Safety

☐ Key Question 3: Non-pharmacologic biological treatments

- SGB
- HBOT
- ECT
- TMS

☐ Key Question 4: Complementary and integrative treatments

- Mind-body practices
  - Acupuncture
  - Mindfulness (stand-alone)
  - Meditation
  - Relaxation
  - Mantram
- Natural products
- Animal-assisted therapy
- Creative therapy (e.g., music, art, drama therapy)
- Recreational therapy (e.g., exercise, fishing)
- Progressive muscle relaxation

☐ Key Question 5: See list of interventions for KQ 1 and 2

☐ Key Question 6: See list of interventions for KQ 1 and 2

- ☐ Key Question 7: Group psychotherapy
  - CBT (trauma-focused psychotherapy or non- trauma-focused psychotherapy)
  - Psychodynamic, supportive, or peer group psychotherapy
- ☐ Key Question 8: Collaborative care, integrated care
  - Mental health integration (e.g., primary care mental health integration [PCMHI])
  - Embedded behavioral health
  - Care management models
  - Stepped care
- ☐ Key Question 9: Technology-based modalities
  - Telehealth
  - Virtual reality
  - VTC
  - Telephone based or web-based tools
  - Mobile apps
- Key Question 10: Any intervention in KQ 1–5
- Key Question 11: Any intervention in KQ 1–5 in patients with PTSD with co-morbidity
- ☐ Key Question 12: Peer support

c. Outcomes

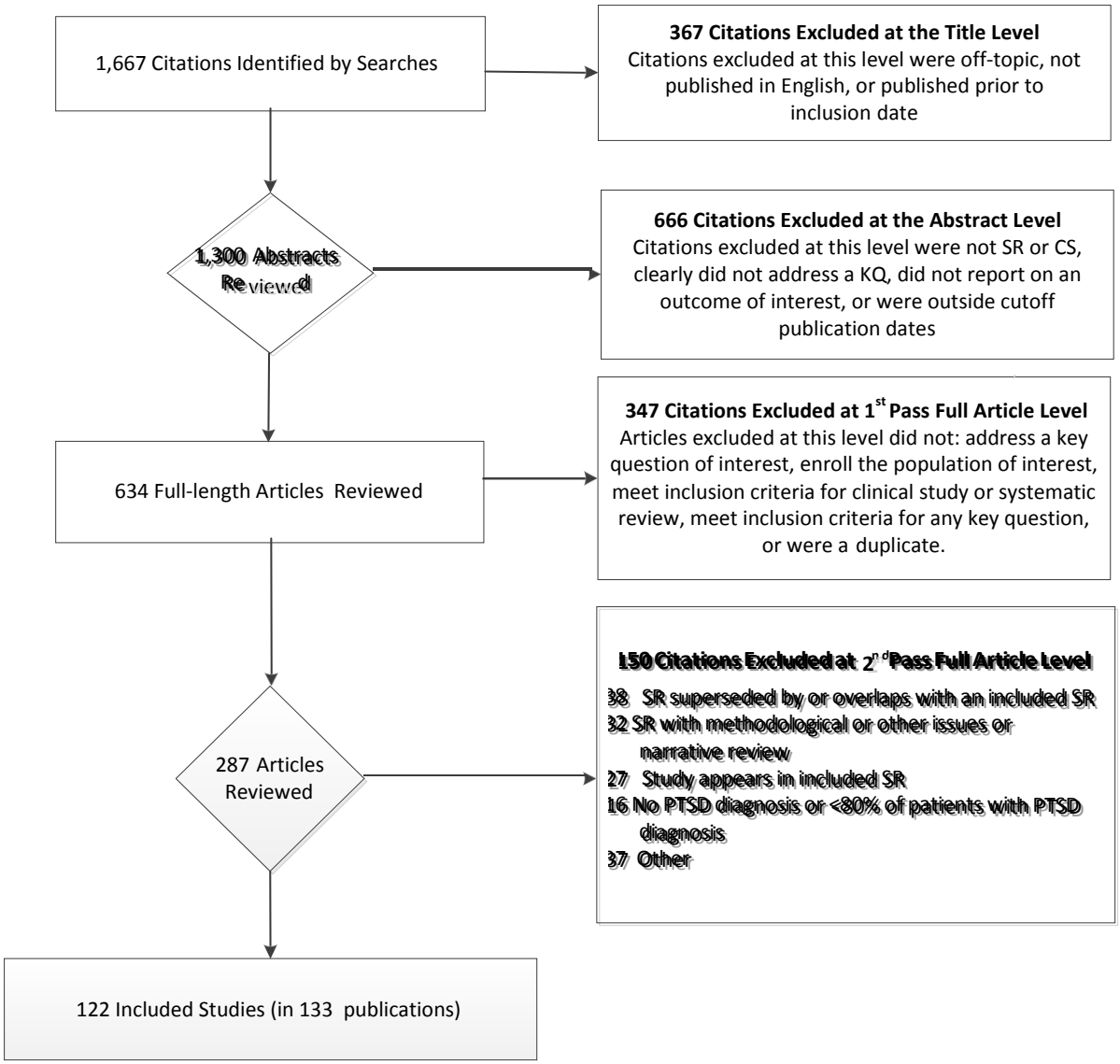
- ☐ Primary outcomes
  - Improvement in global PTSD severity based on CAPS or other validated structured clinical interviews
  - Adverse events
  - Retention/dropout rate
  - Loss of diagnosis/remission
- ☐ Secondary outcomes
  - Self-reported PTSD
  - Specific symptom improvement (e.g., sleep, anger/aggression)
  - Comorbid symptoms (e.g., depression, anxiety, SUD, pain, physical symptoms, sleep, aggression, post-concussive symptoms)
  - Quality of life
  - Functional status
  - Patient satisfaction

B. Conducting the Systematic Review

Extensive literature searches identified 1,667 citations potentially addressing the KQs of interest to this evidence review. Of those, 367 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, or not a full-length article). Overall, 1,300 abstracts were reviewed with 666 of those being excluded for the following reasons: not a systematic review or clinical study, did not address a KQ of interest to this review, did not enroll a population of interest, or published prior to January 2009. A total of 634 full-length articles were reviewed. Of those, 347 were excluded at a first pass review for the following: not addressing a KQ of interest, not enrolling the population of interest, not meeting inclusion criteria for clinical study or systematic review, not meeting inclusion criteria for any KQ, or being a duplicate. A total of 287 full-length articles were thought to address one or more KQs and were further reviewed. Of these, 150 were ultimately excluded. Reasons for their exclusion are presented in Figure A-1 below.

Overall, 122 studies (in 133 publications) addressed one or more of the KQs and were considered as evidence in this review. Table A-2 indicates the number of studies that addressed each of the questions.

Figure A-1. Study Flow Diagram



Abbreviations: CS: comparative study; KQ: key question; PTSD: posttraumatic stress disorder; SR: systematic review

Table A-2. Evidence Base for KQs

Question Number	Question	Number of Studies & Type of Studies
1	For adults diagnosed with PTSD, what is the effectiveness and safety of pharmacotherapy treatments to improve PTSD symptoms? a. Are there specific medications within certain classes (e.g., sertraline within SSRI category) that have evidence of greater efficacy and safety than other medications within the same class?	6 SRs and 7 RCTs
2	For adults diagnosed with PTSD, what is the effectiveness and safety of psychotherapy treatments to improve PTSD symptoms? a. Do any individual non-trauma-focused therapies (e.g., PCT, IPT, SIT) demonstrate equivalent or nearly equivalent efficacy to trauma-focused therapies? b. For the therapies that are effective, is the efficacy of the components of psychotherapies equivalent to the full therapy protocol or components of combined protocols? c. What is the safety and effectiveness of brief interventions to be delivered in primary care or any setting where full interventions are not feasible for improving PTSD symptoms? d. What is the role of peer support in treatment outcomes?	3 SRs (in 4 publications) and 19 RCTs (in 21 publications)
3	For adults diagnosed with PTSD, what is the effectiveness and safety of non-pharmacologic biological treatments, such as stellate ganglion block, hyperbaric oxygen, ECT, or transcranial magnetic stimulation to improve PTSD symptoms?	1 SR and 1 RCT
4	For adults diagnosed with PTSD, are complementary and integrative treatments such as mind-body practices, natural products, animal-assisted therapy, and creative therapy, safe and effective either as primary treatments or adjunctive to standard treatments?	2 SRs and 6 RCTs
5	For adults diagnosed with PTSD, what combined treatment approaches are safe and effective in enhancing treatment response? a. Combination of two or more medication monotherapies b. Augmenting psychotherapy or medication treatment to enhance outcomes c. Combination of psychotherapy with medication	2 SRs and 11 RCTs
6	What is the comparative effectiveness of medication and psychotherapy overall, and within specific classes (e.g., medication versus psychotherapy), for SSRIs versus trauma-focused psychotherapy?	1 SR and 2 RCTs
7	For adults diagnosed with PTSD, what is the effectiveness and safety of CBT (trauma-focused psychotherapy or non-trauma-focused psychotherapy), psychodynamic therapy, supportive psychotherapy, or peer psychotherapy treatments delivered in a group therapy setting? a. What is the effectiveness of group therapy versus individual therapy setting? b. Non-specific group interventions (adjunctively?)	2 SRs and 7 RCTs (in 8 publications)
8	For adults diagnosed with PTSD, what is the effectiveness and safety of collaborative care interventions?	6 RCTs

Question Number	Question	Number of Studies & Type of Studies
9	What is the effectiveness and safety of treatment delivered via technology based modalities? a. What is the comparative effectiveness of treatment delivered by a therapist or licensed health professional via technology based modalities versus in-person? b. What is the comparative effectiveness of treatment delivered via video-teleconferencing based modalities versus telephone based modalities?	19 RCTs
10	What treatments are safe and effective for acute stress disorder or acute stress reaction?	3 SRs (in 4 publications) and 2 RCTs
11	For adults diagnosed with PTSD, is treatment safety and effectiveness altered by presence of comorbidities?	3 SRs, 20 RCTs or secondary analyses of RCTs (in 26 publications) and 2 retrospective cohort studies
12	What is the safety and effectiveness of peer support approaches? a. Stand-alone b. Adjunct therapy	No studies identified
Total Evidence Base		**122 studies (in 133 publications)**

Abbreviations: CBT: cognitive behavioral therapy; ECT: electroconvulsive therapy; IPT: Interpersonal psychotherapy; PCT: present-centered therapy; PTSD: posttraumatic stress disorder; RCT: randomized controlled trial; SIT: Stress Inoculation Training; SSRI: serotonin reuptake inhibitors; SR: systematic review

a. Criteria for Study Inclusion/Exclusion

i. General Criteria

- Clinical studies or systematic reviews published on or after January 1, 2009 to March 2016. If multiple systematic reviews address a KQ, we selected the most recent and/or comprehensive review. Systematic reviews were supplemented with clinical studies published subsequent to the systematic review.
- Studies must be published in English.
- Publication must be a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, and other publications that were not full-length clinical studies were not be accepted as evidence.
- Study must have enrolled at least 20 patients (10 per study group) unless otherwise noted (see Key Question Specific Criteria below)
- Study must have reported on an outcome of interest.
- Study must have enrolled a patient population in which at least 80% of patients were diagnosed with PTSD (or ASD for KQ 10) and were age 18 years or older. If the percentage is less than 80%, then data must have been reported separately for this patient subgroup.

ii. Key Question Specific Criteria

- For KQs 1–10 and 12, acceptable study designs included systematic reviews of RCTs and individual RCTs not evaluated in systematic reviews. If no relevant studies with these designs were found for a given KQ or sub-question, prospective nonrandomized comparative studies were evaluated for inclusion.
- For KQ 11, acceptable study designs included systematic reviews, RCTs, or prospective cohort studies that statistically compared outcomes for patients with PTSD and a co-occurring medical or mental health condition to patients with PTSD and no additional medical or mental health condition. Large retrospective database studies (200 patients minimum) that performed multivariate statistical analyses of the effect of co-occurring conditions on patient outcomes were also acceptable.

b. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in Table A-3, below. Additional information on the search strategies, including topic-specific search terms and search strategies can be found in Appendix G: Literature Review Search Terms and Strategy.

Table A-3. Bibliographic Database Information

Name	Date Limits	Platform/Provider
Bibliographic Databases		
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	2009 to February 2, 2016	Wiley
EMBASE (Excerpta Medica)	2009 to March 3, 2016	Elsevier
Health Technology Assessment Database (HTA)	2009 to February 2, 2016	Wiley
MEDLINE/PreMEDLINE	2009 to March 3, 2016	Elsevier
PILOTS: Published International Literature On Traumatic Stress	2009 to March 9, 2016	ProQuest
PsycINFO	2009 to March 3, 2016	OVIDSP
PubMed (In-process and Publisher records)	2009 to March 3, 2016	NLM
Gray Literature Resources		
The Evidence-based Synthesis Program (ESP) Reports	2009 to March 16, 2016	VA

C. Convening the Face-to-face Meeting

In consultation with the COR, the Champions, and the Work Group, the Lewin Team convened a three and a half day face-to-face meeting of the CPG Champions and Work Group members on August 29-September 1, 2016. These experts were gathered to develop and draft the clinical recommendations for an update to the 2010 PTSD CPG. Lewin presented findings from the evidence review of KQs 1-12 in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review, and asked to categorize and carry forward recommendations from the 2010 PTSD CPG, modifying the recommendations as necessary. The members also developed new clinical practice recommendations not presented in the 2010 PTSD CPG, based on the 2016 evidence review. The subject matter experts were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified GRADE and USPSTF methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

In addition to developing recommendations during the face-to-face meeting, the Work Group members also revised the 2010 PTSD CPG algorithms to reflect the new and amended recommendations. They discussed the available evidence as well as changes in clinical practice since 2010, as necessary, to update the algorithms.

D. Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: [31]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate, e.g.,:
  - Resource use
  - Equity
  - Acceptability
  - Feasibility
  - Subgroup considerations

The following sections further describe each domain.

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid event, resolution of symptoms, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse event, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that the majority of clinicians will offer patients therapeutic or preventive measures as long as the advantages of the intervention exceed the risks and adverse effects. The certainty or uncertainty of the clinician about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?

- Are the desirable effects large relative to undesirable effects?

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease the strength. The evidence review used for the development of recommendations for PTSD, conducted by ECRI, assessed the confidence in the quality of the evidence base and assigned a rate of "High," "Moderate," "Low," or "Very Low."

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

Values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

Other implications consider the practicality of the recommendation, including resources use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost-effectiveness of a therapeutic or preventive measure. For example statin use in the frail elderly and others with multiple co-occurring conditions may not be effective and depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility, and subgroup considerations require similar judgments around the practically of the recommendation.

The framework in Table A-4 was used by the Work Group to guide discussions on each domain.

Table A-4. Evidence to Recommendation Framework

Decision Domain	Judgment
Balance of desirable and undesirable outcomes	
▪ Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa? ▪ Are the desirable anticipated effects large? ▪ Are the undesirable anticipated effects small? ▪ Are the desirable effects large relative to undesirable effects?	Benefits outweigh harms/burden Benefits slightly outweigh harms/burden Benefits and harms/burden are balanced Harms/burden slightly outweigh benefits Harms/burden outweigh benefits
Confidence in the quality of the evidence	
▪ Is there high or moderate quality evidence that answers this question? ▪ What is the overall certainty of this evidence?	High Moderate Low Very low
Values and preferences	
▪ Are you confident about the typical values and preferences and are they similar across the target population? ▪ What are the patient's values and preferences? ▪ Are the assumed or identified relative values similar across the target population?	Similar values Some variation Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	
▪ Are the resources worth the expected net benefit from the recommendation? ▪ What are the costs per resource unit? ▪ Is this intervention generally available? ▪ Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? ▪ Is there lots of variability in resource requirements across settings?	Various considerations

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which combines the four domains.[31] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low.[259] In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or "We recommend offering this option …")
- Weak For (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak Against (or "We suggest not offering this option …")
- Strong Against (or "We recommend against offering this option …")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician or they may be qualified with an explanation about the issues that would lead decisions to vary.

E. Recommendation Categorization

a. Recommendation Categories and Definitions

For use in the 2017 PTSD CPG, a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Clinical Excellence (NICE).[34,35] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2010 PTSD CPG. The categories and definitions can be found in Table A-5.

Table A-5. Recommendation Categories and Definitions

Evidence Reviewed*	Recommendation Category*	Definition*
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

Abbreviation: CPG: clinical practice guideline
*Adapted from the NICE guideline manual (2012) [34] and Garcia et al. (2014) [35]

b. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether or not they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as "New-added," "New-replaced," "Not changed," "Amended," or "Deleted."

"Reviewed, New-added" recommendations were original, new recommendations that were not in the 2010 PTSD CPG. "Reviewed, New-replaced" recommendations were in the previous version of the guideline, but were modified to align with the updated review of the evidence. These recommendations could have also included clinically-significant changes to the previous version. Recommendations categorized as "Reviewed, Not changed" were carried forward from the previous version of the CPG unchanged.

To maintain consistency between 2010 recommendations, which were developed using the USPSTF methodology, and 2017 recommendations, which were developed using the GRADE methodology, it was necessary to modify the 2010 recommendations to include verbiage to signify the strength of the recommendation (e.g., "We recommend," "We suggest"). Because the 2010 recommendations inherently needed to be modified at least slightly to include this language, the "Not changed" category was not used. For recommendations carried forward to the updated CPG with review of the evidence and slightly modified wording, the "Reviewed, Amended" recommendation category was used. This allowed for the wording of the recommendation to reflect GRADE methodology as well as for any other non-substantive (i.e., not clinically meaningful) language changes deemed necessary. The evidence used to support these

recommendations was carried forward from the previous version of the CPG and/or was identified in the evidence review for the update.

Recommendations could have also been designated "Reviewed, Deleted." These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

c. Categorizing Recommendations without an Updated Review of the Evidence

There also were cases in which it was necessary to carry forward recommendations from the previous version of the CPG without a systematic review of the evidence. Due to time and budget constraints, the update of the PTSD CPG could not review all available evidence on management of PTSD, but instead focused its KQs on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated systematic review of the evidence. The support for these recommendations in the updated CPG was thus also carried forward from the previous version of the CPG. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the PTSD CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations which were modified from the 2010 CPG with the updated GRADE language, as explained above.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2017 version of the guideline are noted in the Recommendations. Recommendations 1, 3, 4, and 5 were carried forward from the 2010 PTSD CPG using this method. The categories for the recommendations from the 2010 PTSD CPG are noted in Appendix E: 2010 Recommendation Categorization Table.

F. Drafting and Submitting the Final Clinical Practice Guideline

Following the face-to-face meeting held August 29-September 1, 2016, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2010 PTSD CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2010 PTSD CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki website for a period of 14-20 business days for internal review and comment by the Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in the section titled Peer Review Process. Following the Draft 3 peer review and comment period, a second face-to-face meeting was convened on March 28-29, 2017, to discuss the feedback received and revise the CPG. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the EBPWG for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The Work Group also produced a set of guideline toolkit materials which included a provider summary, pocket cards, and a patient summary. The final 2017 PTSD CPG was submitted to the EBPWG in May 2017.

Appendix B: Patient Focus Group Methods and Findings

A. Methods

As part of the effort to update this CPG, the VA and DoD Leadership held a patient focus group on January 25, 2016, in San Antonio, Texas. The aim of the focus group was to further the understanding of the perspective of patients receiving treatment for PTSD within the VA and/or DoD healthcare systems, as patients are most affected by the recommendations put forth in the CPG. The focus group explored patient perspectives on a set of topics related to the management of PTSD in the VA and DoD healthcare systems, including patients' knowledge of PTSD treatment options, views on the delivery of care, and the impact of PTSD and the challenges it poses.

Participants for the focus group were recruited by VA and DoD Leadership as well as by the PTSD CPG Champions. Patient focus group participants were not designed to be a representative sample of VA and DoD patients who have experienced PTSD. However, recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the guideline development process. Patients were not incentivized for their participation or reimbursed for travel expenses.

The PTSD CPG Champions and Work Group, with support from Lewin, developed a set of questions to help guide the focus group. The focus group facilitator led the discussion using the previously prepared questions as a general guide to elicit the most important information from the patients regarding their experiences and views about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all of the listed questions were addressed. Audio and visual recording equipment was used to record the session. The recording was for internal use only and was distributed to the PTSD Champions and guideline development team. The video was used to document the discussion and synthesize the information.

Ten patients participated in the focus group, however, only nine participants were present at any given time. Seven participants had received care in the DoD healthcare system and three received care in VA facilities. However, at the time of the focus group, the majority of the participants that were receiving care in the DoD healthcare system were either receiving treatment in Warrior Transition Units (WTUs) or were in the process of retiring.

B. Patient Focus Group Findings

a. Using SDM, consider treatment options and develop a treatment plan based on patient-specific goals, values, and preferences

- Use SDM to develop an individualized treatment plan; discuss pros and cons (e.g., benefits, risks, side effects) of each treatment option in conjunction with each patient's goals, priorities, values, and preferences.
- Consider intensive outpatient programs or cognitive behavioral therapy when determining a treatment plan with the patient.
- Discuss pharmacologic options in depth with the patient, including their willingness to take medications and their preferences for adjunctive therapies.

- Consider that patients may prefer group-based outpatient therapies as opposed to individual-based treatment or inpatient treatment.

b. Educate patients about treatment options, including benefits and risks, side effects, and expectations

- Clinicians should be proactive and responsive in providing necessary clinical information in a manner comprehensible to patients and family members; acknowledge that patients will seek and acquire information from other sources (especially the Internet) and encourage patients to proactively seek information from reliable sources.
- When prescribing pharmacologic therapy, provide in-depth and patient-specific education on medication (e.g., side effects, dosing, and safety) during medical visits in conjunction with distributing or otherwise enabling access to educational materials.

c. Involve family members in accordance with patient preferences and maintain open, trusting, and respectful relationships with patients and their families

- Foster family involvement in SDM and patient support in accordance with patient preferences and in a way that is beneficial to the patient.
- Always treat patients and family members with respect.
- Include family members early in treatment discussions, especially regarding what to expect during and after completing treatment.
- Build and maintain trust, respect, and support with the patient and their family.

d. Take active steps to improve the perception of and stigma surrounding PTSD

- Encourage a culture shift surrounding PTSD within the VA and DoD systems; patients often "hide" PTSD while on active duty to comply with "readiness" standards.
- Provide education to patients and have preemptive discussions with Service Members before deployment addressing the prevalence of PTSD and available treatments.
- Consider and offer settings to obtain care that encourage receptiveness to care and respect the privacy of the patient.

e. Work with appropriate providers to ensure continuity and accessibility of high-quality care within and between healthcare systems

- Consult with other providers (e.g., psychiatrists, social workers) and patient advocates as appropriate, especially when patients express the need for more information or other clinical support.
- Provide seamless transitions for pharmacologic treatment, psychotherapy, and other care management within and between VA, DoD, and any other healthcare systems. Patients should not have to encounter abrupt changes in treatment regimens moving from one system to another or have to "start all over" when moving to another system.
- Increase the number of psychiatrists, social workers, and other health providers available to patients with PTSD; inability to locate an available provider may create interruptions in high-quality care.

Appendix C: Pharmacotherapy Dosing Table

Therapeutic Category	Initial Dose	Dose Range	Clinical Considerations: Comorbidities and Safety
Antidepressants ***Monotherapy***			▪ Avoid abrupt discontinuation; withdrawal symptoms with sudden discontinuation of SSRIs and SNRIs, paroxetine and venlafaxine in particular ▪ Paroxetine and sertraline have FDA label indications for treating PTSD ▪ Common adverse effects of the SSRIs and SNRIs include nausea, headache, diarrhea, anxiety, nervousness, sexual dysfunction, agitation, dizziness, hyponatremia or SIADH, and serotonin syndrome ▪ Venlafaxine can elevate blood pressure; caution advised with patients with hypertension
▪ Fluoxetine*	10-20 mg daily	20-80 mg daily	
▪ Paroxetine*	10-20 mg daily	20-50 mg daily	
▪ Sertraline*	25-60 mg daily	50-200 mg daily	
▪ Venlafaxine*	IR: 25 mg 2 or 3 times a day XR: 37.5 mg once daily	75-375 mg in 2-3 divided doses 75-225 mg once daily	
▪ Nefazodone±	25–100 mg 2 times daily	150-600 mg in 2 divided doses	▪ Nefazodone is associated with life-threatening hepatic failure; monitor for signs and symptoms including LFTs; avoid if active liver disease; do not re-challenge ▪ Nefazodone is subject to many drug interactions, particularly those involving CYP3A4 and glycoprotein
▪ Imipramine±	25-75 mg daily	100-300 mg in 1 or 2 divided doses	▪ Avoid TCAs within three months of an acute MI ▪ TCAs are relatively contraindicated in patients with coronary artery disease or prostatic enlargement ▪ TCAs side effects include dry mouth, dry eyes, constipation, orthostatic hypotension, tachycardia, ventricular arrhythmias, weight gain, and drowsiness Photosensitivity may occur
▪ Phenelzine±	15 mg 3 times daily	15 mg daily; 90 mg in divided doses	▪ Phenelzine considerations include drug-drug and drug-food interactions, risk of hypertensive crisis, hypotension, and anticholinergic effects

Abbreviations: FDA: Food and Drug Administration; IR: immediate release; LFT: liver function tests; mg: milligram; MI: myocardial infarction; PTSD: posttraumatic stress disorder; SIADH: syndrome of inappropriate anti-diuretic hormone; SIT: Stress Inoculation Training; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: serotonin reuptake inhibitors; TCA: tricyclic antidepressant; XR: extended release

*Strong For recommendation

±Weak For recommendation

Appendix D: Evidence Table

Recommendation	2010 Grade[1]	Evidence[2]	Strength of Recommendation[3]	Recommendation Category[4]
1. We recommend engaging patients in shared decision making (SDM), which includes educating patients about effective treatment options.	None	**Additional References:** [43-46]	Strong For	Not Reviewed, Amended
2. For patients with posttraumatic stress disorder (PTSD) who are treated in primary care, we suggest collaborative care interventions that facilitate active engagement in evidence-based treatments.	None	[48-54] **Additional References:** [47,55]	Weak For	Reviewed, New-replaced
3. We suggest periodic screening for PTSD using validated measures such as the Primary Care PTSD Screen (PC-PTSD) or the PTSD Checklist (PCL).	B, I	[60] **Additional References:** [10,51,56-59]	Weak For	Not Reviewed, Amended
4. For patients with suspected PTSD, we recommend an appropriate diagnostic evaluation that includes determination of DSM criteria, acute risk of harm to self or others, functional status, medical history, past treatment history, and relevant family history. A structured diagnostic interview may be considered.	B, I	[70-72] **Additional References:** [2,29,61-69]	Strong For	Not Reviewed, Amended

[1] The 2010 VA/DoD PTSD CPG used the USPSTF evidence grading system (http://www.uspreventiveservicestaskforce.org). Inclusion of more than one 2010 Grade indicates that more than one 2010 CPG recommendation is covered under the 2017 recommendation. The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. "None" indicates that the 2017 PTSD CPG recommendation replaced or amended a 2010 PTSD CPG recommendation for which there was no grade. "N/A" indicates that the 2017 PTSD CPG recommendation was a new recommendation, and therefore does not have an associated 2010 Grade.

[2] The evidence column indicates studies that support each recommendation. For new recommendations, developed by the 2017 guideline Work Group, the literature cited corresponds directly to the 2016 evidence review. For recommendations that have been carried over from the 2010 VA/DoD PTSD CPG, slight modifications were made to the language in order to better reflect the current evidence and/or the change in grading system used for assigning the strength of each recommendation (USPSTF to GRADE). For these "modified" recommendations, the evidence column indicates "additional evidence," which can refer to either 1) studies that support the recommendation and which were identified through the 2016 evidence review, or 2) relevant studies that support the recommendation, but which were not systematically identified through a literature review.

[3] Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.

[4] Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Recommendation	2010 Grade[1]	Evidence[2]	Strength of Recommendation[3]	Recommendation Category[4]
5. For patients with a diagnosis of PTSD, we suggest using a quantitative self-report measure of PTSD severity, such as the PTSD Checklist for DSM-5 (PCL-5), in the initial treatment planning and to monitor treatment progress.	None	**Additional References:** [73,74]	Weak For	Not Reviewed, Amended
6. For the selective prevention of PTSD, there is insufficient evidence to recommend the use of trauma-focused psychotherapy or pharmacotherapy in the immediate post-trauma period.	D, I	[76-91]	N/A	Reviewed, New-replaced
7. For the indicated prevention of PTSD in patients with acute stress disorder (ASD), we recommend an individual trauma-focused psychotherapy that includes a primary component of exposure and/or cognitive restructuring.	A, D, I	[77,89]	Strong For	Reviewed, New-replaced
8. For the indicated prevention of PTSD in patients with ASD, there is insufficient evidence to recommend the use of pharmacotherapy.	D, I	[77,89-91]	N/A	Reviewed, New-replaced
9. We recommend individual, manualized trauma-focused psychotherapy (see Recommendation 11) over other pharmacologic and non-pharmacologic interventions for the primary treatment of PTSD.	N/A	[92,93] **Additional References:** [46,94,95]	Strong For	Reviewed, New-added
10. When individual trauma-focused psychotherapy is not readily available or not preferred, we recommend pharmacotherapy (see Recommendation 17) or individual non-trauma-focused psychotherapy (see Recommendation 12). With respect to pharmacotherapy and non-trauma-focused psychotherapy, there is insufficient evidence to recommend one over the other.	N/A	[92,93]	Strong For	Reviewed, New-added
11. For patients with PTSD, we recommend individual, manualized trauma-focused psychotherapies that have a primary component of exposure and/or cognitive restructuring to include Prolonged Exposure (PE), Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing (EMDR), specific cognitive behavioral therapies for PTSD, Brief Eclectic Psychotherapy (BEP), Narrative Exposure Therapy (NET), and written narrative exposure.	A	[92,93,97-118] **Additional References:** [96]	Strong For	Reviewed, New-replaced

Recommendation	2010 Grade[1]	Evidence[2]	Strength of Recommendation[3]	Recommendation Category[4]
12. We suggest the following individual, manualized non-trauma-focused therapies for patients diagnosed with PTSD: Stress Inoculation Training (SIT), Present-Centered Therapy (PCT), and Interpersonal Psychotherapy (IPT).	A	[117-119,121-123] **Additional References:** [120]	Weak For	Reviewed, New-replaced
13. There is insufficient evidence to recommend for or against psychotherapies that are not specified in other recommendations, such as Dialectical Behavior Therapy (DBT), Skills Training in Affect and Interpersonal Regulation (STAIR), Acceptance and Commitment Therapy (ACT), Seeking Safety, and supportive counseling.	None	[103-105,124,125,128-132] **Additional References:** [126,127]	N/A	Reviewed, New-replaced
14. There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over or in addition to the full therapy protocol.	N/A	[97,106,108,116,118,119,130] **Additional References:** [133]	N/A	Reviewed, New-added
15. We suggest manualized group therapy over no treatment. There is insufficient evidence to recommend using one type of group therapy over any other.	C, I	[117,134,136,137] **Additional References:** [135]	Weak For	Reviewed, New-replaced
16. There is insufficient evidence to recommend for or against trauma-focused or non-trauma-focused couples therapy for the primary treatment of PTSD.	I	[138,139]	N/A	Reviewed, Amended
17. We recommend sertraline, paroxetine, fluoxetine, or venlafaxine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy.	A	[92,93,140]	Strong For	Reviewed, New-replaced
18. We suggest nefazodone, imipramine, or phenelzine as monotherapy for the treatment of PTSD if recommended pharmacotherapy (see Recommendation 17), trauma-focused psychotherapy (see Recommendation 11), or non-trauma-focused psychotherapy (see Recommendation 12) are ineffective, unavailable, or not in accordance with patient preference and tolerance. (NOTE: Nefazodone and phenelzine have potentially serious toxicities and should be managed carefully.)	B	[92,93,141-144]	Weak For	Reviewed, New-replaced

Recommendation	2010 Grade[1]	Evidence[2]	Strength of Recommendation[3]	Recommendation Category[4]
19. We suggest against treatment of PTSD with quetiapine, olanzapine, and other atypical antipsychotics (except for risperidone, which is a Strong Against, see Recommendation 20), citalopram, amitriptyline, lamotrigine, or topiramate as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks.	D	[92,93,140,146-152] **Additional References:** [145]	Weak Against	Reviewed, New-replaced
20. We recommend against treating PTSD with divalproex, tiagabine, guanfacine, risperidone, benzodiazepines, ketamine, hydrocortisone, or D-cycloserine, as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks.	D, I	[92,93,153-158,160-166]	Strong Against	Reviewed, New-replaced
21. We recommend against treating PTSD with cannabis or cannabis derivatives due to the lack of evidence for their efficacy, known adverse effects, and associated risks.	N/A	**Additional References:** [167-170]	Strong Against	Reviewed, New-added
22. There is insufficient evidence to recommend for or against monotherapy or augmentation therapy for the treatment of PTSD with eszopiclone, escitalopram, bupropion, desipramine, doxepin, D-serine, duloxetine, desvenlafaxine, fluvoxamine, levomilnacipran, mirtazapine, nortriptyline, trazodone, vilazodone, vortioxetine, buspirone, hydroxyzine, cyproheptadine, zaleplon, and zolpidem.	I	[92,93,140,171-175]	N/A	Reviewed, New-replaced
23. We suggest against the use of topiramate, baclofen, or pregabalin as augmentation treatment of PTSD due to insufficient data and/or known adverse effect profiles and associated risks.	D	[92,93,140,177,178] **Additional References:** [176]	Weak Against	Reviewed, New-replaced
24. We suggest against combining exposure therapy with D-cycloserine in the treatment of PTSD outside of the research setting.	N/A	[161,179]	Weak Against	Reviewed, New-added
25. We recommend against using atypical antipsychotics, benzodiazepines, and divalproex as augmentation therapy for the treatment of PTSD due to low quality evidence or the absence of studies and their association with known adverse effects.	D, I	[92,93,163,164,180,182] **Additional References:** [181]	Strong Against	Reviewed, New-replaced

Recommendation	2010 Grade[1]	Evidence[2]	Strength of Recommendation[3]	Recommendation Category[4]
26. There is insufficient evidence to recommend the combination of exposure therapy with hydrocortisone outside of the research setting.	N/A	[183]	N/A	Reviewed, New-added
27. There is insufficient evidence to recommend for or against the use of mirtazapine in combination with sertraline for the treatment of PTSD.	B	[184]	N/A	Reviewed, New-replaced
28a. For global symptoms of PTSD, we suggest against the use of prazosin as mono- or augmentation therapy.	I	[92,149,185-188,190] **Additional References:** [189]	Weak Against	Reviewed, New-replaced
28b. For nightmares associated with PTSD, there is insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy.	B	[92,149,185-188,190] **Additional References:** [189]	N/A	Reviewed, New-replaced
29. In partial- or non-responders to psychotherapy, there is insufficient evidence to recommend for or against augmentation with pharmacotherapy.	None	[191-194]	N/A	Reviewed, New-replaced
30. In partial- or non-responders to pharmacotherapy, there is insufficient evidence to recommend for or against augmentation with psychotherapy.	None	[191-194]	N/A	Reviewed, New-replaced
31. There is insufficient evidence to recommend for or against starting patients with PTSD on combination pharmacotherapy and psychotherapy.	N/A	[191-194]	N/A	Reviewed, New-added
32. There is insufficient evidence to recommend for or against the following somatic therapies: repetitive transcranial magnetic stimulation (rTMS), electroconvulsive therapy (ECT), hyperbaric oxygen therapy (HBOT), stellate ganglion block (SGB), or vagal nerve stimulation (VNS).	B, D	[195-198] **Additional References:** [199-203]	N/A	Reviewed, New-replaced
33. There is insufficient evidence to recommend acupuncture as a primary treatment for PTSD.	B	[204-206]	N/A	Reviewed, New-replaced
34. There is insufficient evidence to recommend any complementary and integrative health (CIH) practice, such as meditation (including mindfulness), yoga, and mantram meditation, as a primary treatment for PTSD.	C, I	[207-215]	N/A	Reviewed, New-replaced

Recommendation	2010 Grade[1]	Evidence[2]	Strength of Recommendation[3]	Recommendation Category[4]
35. We suggest internet-based cognitive behavioral therapy (iCBT) with feedback provided by a qualified facilitator as an alternative to no treatment.	C, I	[216-222]	Weak For	Reviewed, New-replaced
36. We recommend using trauma-focused psychotherapies that have demonstrated efficacy using secure video teleconferencing (VTC) modality when PTSD treatment is delivered via VTC.	C, I	[223-227]	Strong For	Reviewed, Amended
37. We recommend that the presence of co-occurring disorder(s) not prevent patients from receiving other VA/DoD guideline-recommended treatments for PTSD.	N/A	[122,127,228-232,234]	Strong For	Reviewed, New-added
38. We recommend VA/DoD guideline-recommended treatments for PTSD in the presence of co-occurring substance use disorder (SUD).	I	[127,237-242] **Additional References:** [235,236]	Strong For	Reviewed, New-replaced
39. We recommend an independent assessment of co-occurring sleep disturbances in patients with PTSD, particularly when sleep problems pre-date PTSD onset or remain following successful completion of a course of treatment.	None	[248-251,254-257] **Additional References:** [243-247,252,253]	Strong For	Reviewed, New-replaced
40. We recommend Cognitive Behavioral Therapy for Insomnia (CBT-I) for insomnia in patients with PTSD unless an underlying medical or environmental etiology is identified or severe sleep deprivation warrants the immediate use of medication to prevent harm.	None	[248-251,254-257] **Additional References:** [243-247,252,253]	Strong For	Reviewed, Amended

Appendix E: 2010 Recommendation Categorization Table

2010 Module[1]	2010 Section	2010 Number	2010 Recommendation Text[2]	2010 Grade[3]	Category[4]	2017 Recommendation[5]
CORE	1	A	In high-risk occupations, for which the probability of trauma exposure is moderate or high, efforts should be undertaken to increase the psychological resilience of workers to the negative effects of trauma exposure	None	Not reviewed, Deleted	
CORE	2	B	Persons exposed to trauma should be assessed for the type, frequency, nature, and severity of the trauma. [B] a. Assessment should include a broad range of potential trauma exposures in addition to the index trauma. b. Trauma Exposure Assessment Instruments may assist in evaluating the nature and severity of the exposure. c. Assessment of existing social supports and ongoing stressors is important.	B	Not reviewed, Amended	Recommendation 3
CORE	3	C	All new patients should be screened for symptoms of PTSD initially and then on an annual basis or more frequently if clinically indicated due to clinical suspicion, recent trauma exposure (e.g., major disaster), or history of PTSD. [B]	B	Not reviewed, Amended	Recommendation 3
CORE	3	C	Patients should be screened for symptoms of PTSD using paper-and-pencil or computer-based screening tools. [B]	B	Not reviewed, Amended	Recommendation 3

[1] The first three columns indicate the location of each recommendation within the 2010 PTSD CPG.
[2] The 2010 Recommendation Text column contains the wording of each recommendation from the 2010 PTSD CPG.
[3] The 2010 VA/DoD PTSD CPG used the U.S. Preventive Services Task Force (USPSTF) evidence grading system. http://www.uspreventiveservicestaskforce.org The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. "None" indicates there was no grade assigned to the recommendation in the 2010 PTSD CPG.
[4] The Category column indicates the way in which each 2010 PTSD CPG recommendation was updated.
[5] For recommendations that were carried forward to the 2010 PTSD CPG, this column indicates the new recommendation(s) to which they correspond.

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
CORE	3	C	There is insufficient evidence to recommend one PTSD screening tool versus another. However, the following screening tools have been validated and should be considered for use. For example: (See Appendix C) ▪ Primary Care PTSD Screen (PC-PTSD) ▪ PTSD Brief Screen ▪ Short Screening Scale for DSM IV PTSD. ▪ PTSD Checklist (PCL)	I	Not reviewed, Amended	Recommendation 3
CORE	3	C	There is insufficient evidence to recommend special screening for members of any cultural or racial group or gender. [I]	I	Not reviewed, Deleted	
CORE	3	D	Individuals who are presumed to have symptoms of PTSD or who are positive for PTSD on the initial screening should receive a more detailed assessment of their symptoms.	None	Not reviewed, Amended	Recommendation 4
CORE	3	D	Useful symptom-related information may include details, such as time of onset, frequency, course, severity, level of distress, and degree of functional impairment.	None	Not reviewed, Deleted	
CORE	3	D	The elapsed time since the exposure to trauma should be considered when assessing the risk of developing PTSD and determining the diagnosis and appropriate intervention.	None	Not reviewed, Deleted	
CORE	3	E	Pre- and post-trauma education should include helping the asymptomatic trauma survivor or responder understand that the acute stress reactions of other people are common and probably transient and do not indicate personal failure or weakness, mental illness, or health problems.	None	Not reviewed, Deleted	
CORE	3	E	Education should include sufficient review of the many ways that post-traumatic problems can present, including symptoms in the ASD/PTSD spectrum, behavioral problems with family and friends, occupational problems, and the potential impact of alcohol or other substance misuse/abuse.	None	Not reviewed, Deleted	
CORE	3	E	Education should also include positive messages by identifying and encouraging positive ways of coping, describing simple strategies to resolve or cope with developing symptoms and problems, and setting expectations for mastery and/or recovery.	None	Not reviewed, Deleted	
CORE	3	E	Provide contact information, should post-traumatic symptoms emerge later.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
CORE	3	E	Routine debriefing or formal psychotherapy is not beneficial for asymptomatic individuals and may be harmful. [D]	D	Not reviewed, Deleted	
A	1	B	Identification of a patient with ASR symptoms is based on observation of behavior and function; there is insufficient evidence to recommend a specific screening tool.	None	Not reviewed, Deleted	
A	1	B	Individuals exhibiting the following responses to trauma should be screened for ASR: a. Physical: exhaustion, hyperarousal, somatic complaints (GI, GU, MS, CV, Resp, NS), or symptoms of conversion disorder b. Emotional: anxiety, depression, guilt/hopelessness c. Cognitive/mental: amnestic or dissociative symptoms, hypervigilance, paranoia, intrusive re-experiencing d. Behavioral: avoidance, problematic substance use.	None	Not reviewed, Deleted	
A	1	B	Individuals who experience ASR should receive a comprehensive assessment of their symptoms to include details about the time of onset, frequency, course, severity, level of distress, functional impairment, and other relevant information.	None	Not reviewed, Deleted	
A	1	B	Assess for capability to perform routine functions.	None	Not reviewed, Deleted	
A	1	B	Assess service member's functional status, to include: a. Any changes in productivity b. Co-worker or supervisor reports of recent changes in appearance, quality of work, or relationships c. Any tardiness/unreliability, loss of motivation, or loss of interest d. Forgetful or easily distracted e. Screening for substance use.	None	Not reviewed, Deleted	
A	1	B	Document symptoms of COSR and obtain collateral information from unit leaders, coworkers, or peers about stressors, function, medical history, and absence or impairment in operation or mission.	None	Not reviewed, Deleted	
A	1	B	Consider the service member's role and functional capabilities and the complexity and importance of his/her job.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	1	C	Address acute medical/behavioral issues to preserve life and avoid further harm by: a. Providing appropriate medical/surgical care or referring to stabilize b. Evaluating the use of prescribed medications c. Preventing possible biological or chemical agent exposure d. Managing substance intoxication or withdrawal e. Stopping self-injury or mutilation f. Addressing inability to care for oneself.	None	Not reviewed, Deleted	
A	1	C	Arrange a safe, private, and comfortable environment for continuation of the evaluation: a. Assess danger to self or others (e.g., suicidal, or homicidal behavior) b. Establish a working treatment alliance with the patient c. Maintain a supportive, non-blaming, non-judgmental stance throughout the evaluation d. Assist with the removal of any ongoing exposure to stimuli associated with the traumatic event e. Minimize further traumas that may arise from the initial traumatic event f. Assess and optimize social supports g. Secure any weapons and explosives.	None	Not reviewed, Deleted	
A	1	C	Legal mandates should be followed: a. Reporting of violence, assault b. Confidentiality for the patient c. Mandatory testing d. Attending to chain of evidence in criminal cases (e.g., rape, evaluation) e. Involuntary Commitment procedures if needed.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	1	C	Carefully consider the following potential interventions to secure safety: a. Find safe accommodation and protect against further trauma b. Voluntary admission if suicidal c. Restraint/seclusion only if less restrictive measures are ineffective d. Provide medications managing specific symptoms as needed (e.g., sleep, pain).	None	Not reviewed, Deleted	
A	1	C	Educate and "normalize" observed psychological reactions to the chain of command.	None	Not reviewed, Deleted	
A	1	C	Evacuate to next level of care if unmanageable, if existing resources are unavailable, or if reaction is outside of the scope of expertise of the care provider.	None	Not reviewed, Deleted	
A	1	D	Acute intervention should ensure that the following needs are met: a. Safety/security/survival b. Food, hydration, clothing, hygiene, and shelter c. Sleep d. Medications (i.e., replace medications destroyed/lost) e. Education as to current status f. Communication with family, friends, and community g. Protection from ongoing threats/toxins/harm. If indicated, reduce use of alcohol, tobacco, caffeine, and illicit psychoactive substances.	None	Not reviewed, Deleted	
A	1	D	Provide Psychological First Aid to: a. Protect survivors from further harm b. Reduce physiological arousal c. Mobilize support for those who are most distressed d. Keep families together and facilitate reunion with loved ones e. Provide information and foster communication and education f. Use effective risk communication techniques.	None	Not reviewed, Deleted	
A	1	D	Treat according to member's prior role and not as a "patient."	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	1	D	Assure or provide the following, as needed: a. Reunion or ongoing contact with group/unit b. Promote continuity with established relationships (e.g., primary group) c. Respite from intense stress d. Comfortable environment (e.g., thermal comfort) e. Consider psychoeducation and discussion in a group format f. Assign job tasks and recreational activities that will restore focus and confidence and reinforce teamwork (limited duty).	None	Not reviewed, Deleted	
A	1	E	Acutely traumatized people, who meet the criteria for diagnosis of ASD, and those with significant levels of post-trauma symptoms after at least two weeks post-trauma, as well as those who are incapacitated by acute psychological or physical symptoms, should receive further assessment and early intervention to prevent PTSD.	None	Not reviewed, Amended	Recommendation 4
A	1	E	Trauma survivors, who present with symptoms that do not meet the diagnostic threshold for ASD, or those who have recovered from the trauma and currently show no symptoms, should be monitored and may benefit from follow-up and provision of ongoing counseling or symptomatic treatment.	None	Not reviewed, Deleted	
A	1	E	Service members with COSR who do not respond to initial supportive interventions may warrant referral or evacuation.	None	Not reviewed, Deleted	
A	1	F	Medical status should be obtained for all persons presenting with symptoms to include: a. History, physical examination, and a neurological examination b. Use of prescribed medications, mood or mind-altering substances, and possible biological or chemical agent exposure c. A mini-mental status examination (MMSE) to assess cognitive function if indicated.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	1	F	The history and physical examination findings should lead the provider to other assessments as clinically indicated. Based on the clinical presentation, assessment may include: a. Screen for toxicology if the symptom presentation indicates b. Radiological assessment of patients with focal neurological findings or possible head injury c. Appropriate laboratory studies to rule out medical disorders that may cause symptoms of acute stress reactions (e.g., complete blood count [CBC], chemistry profile, thyroid studies, HCG, EKG, EEG).	None	Not reviewed, Deleted	
A	1	F	A focused psychosocial assessment should be performed to include assessment of active stressors, losses, current social supports, and basic needs (e.g., housing, food, and financial resources).	None	Not reviewed, Deleted	
A	1	F	A brief assessment of function should be completed to evaluate: 1) objectively impaired function based on general appearance and behavior; 2) subjectively impaired function; 3) baseline level of function (LOF) vs. current LOF; and 4) family and relationship functioning.	None	Not reviewed, Deleted	
A	1	G	Assess patients for pre-existing psychiatric conditions to identify high-risk individuals and groups.	None	Not reviewed, Deleted	
A	1	G	Assure access and adherence to medications that the patient is currently taking.	None	Not reviewed, Deleted	
A	1	G	Refer patients with pre-existing psychiatric conditions to mental health specialty when indicated or emergency hospitalization if needed.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	1	H	Trauma survivors who exhibit symptoms or functional impairment should be screened for the following risk factors for developing ASD/PTSD: Pre-traumatic factors 1. Ongoing life stress 2. Lack of social support 3. Young age at time of trauma 4. Pre-existing psychiatric disorders, or substance misuse 5. History of traumatic events (e.g., MVA) 6. History of post-traumatic stress disorder (PTSD). 7. Other pre-traumatic factors, including: female gender, low socioeconomic status, lower level of education, lower level of intelligence, race (Hispanic, African-American, American Indian, and Pacific Islander), reported abuse in childhood, report of other previous traumatization, report of other adverse childhood factors, family history of psychiatric disorders, and poor training or preparation for the traumatic event. Peri-traumatic or trauma-related factors 1. Severe trauma 2. Physical injury to self or others 3. Type of trauma (combat, interpersonal traumas such as killing another person, torture, rape, or assault convey high risk of PTSD) 4. High perceived threat to life of self or others 5. Community (mass) trauma 6. Other peri-traumatic factors, including: history of peri-traumatic dissociation. Post-traumatic factors 1. Ongoing life stress 2. Lack of positive social support 3. Bereavement or traumatic grief 4. Major loss of resources 5. Negative social support (shaming or blaming environment) 6. Poor coping skills 7. Other post-traumatic factors, including: children at home and a distressed spouse.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	2	I	All survivors should be given educational information to help normalize common reactions to trauma, improve coping, enhance self-care, facilitate recognition of significant problems, and increase knowledge of and access to services. Such information can be delivered in many ways, including public media, community education activities, and written materials.	None	Not reviewed, Deleted	
A	2	J	Continue providing psychoeducation and normalization.	None	Not reviewed, Deleted	
A	2	J	Treatment should be initiated after education, normalization, and Psychological First Aid has been provided and after basic needs following the trauma have been made available.	None	Not reviewed, Deleted	
A	2	J	There is insufficient evidence to recommend for or against the use of Psychological First Aid to address symptoms beyond 4 days following trauma. [I]	I	Not reviewed, Deleted	
A	2	J	Survivors who present symptoms that do not meet the diagnostic threshold of ASD or PTSD should be monitored and may benefit from follow-up and provision of ongoing counseling or symptomatic treatment.	None	Not reviewed, Deleted	
A	2	J	Recommend monitoring for development of PTSD using validated symptom measures (e.g., PTSD Checklist, other screening tools for ASD/PTSD).	None	Not reviewed, Amended	Recommendation 3

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	2	J	Psychotherapy: a. Consider early brief intervention (4 to 5 sessions) of cognitive-based therapy (CBT) that includes exposure-based therapy, alone or combined with a component of cognitive re-structuring therapy for patients with significant early symptom levels, especially those meeting diagnostic criteria for ASD. [A] b. Routine formal psychotherapy intervention for asymptomatic individuals is not beneficial and may be harmful. [D] c. Strongly recommend against individual Psychological Debriefing as a viable means of reducing acute stress disorder (ASD) or progression to post-traumatic stress disorder (PTSD). [D] d. The evidence does not support a single session group Psychological Debriefing as a viable means of reducing acute stress disorder (ASD) or progression to post-traumatic stress disorder, but there is no evidence of harm (Note: this is not a recommendation pertaining to Operational Debriefing). [D] e. Groups may be effective vehicles for providing trauma-related education, training in coping skills, and increasing social support, especially in the context of multiple group sessions. [I] f. Group participation should be voluntary.	A, D, I	Reviewed, New-replaced	Recommendation 7
A	2	J	Pharmacotherapy: a. There is no evidence to support a recommendation for use of a pharmacological agent to prevent the development of ASD or PTSD. [I] b. Strongly recommend against the use of benzodiazepines to prevent the development of ASD or PTSD [D]	D, I	Reviewed, New-replaced	Recommendation 6 Recommendation 8
A	2	K	Symptom-specific treatment should be provided after education, normalization, and basic needs are met.	None	Not reviewed, Deleted	
A	2	K	Consider a short course of medication (less than 6 days), targeted for specific symptoms in patients post-trauma a. Sleep disturbance/insomnia b. Management of pain c. Irritation/excessive arousal/anger.	None	Reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	2	K	Provide non-pharmacological intervention to address specific symptoms (e.g., relaxation, breathing techniques, avoiding caffeine) to address both general recovery and specific symptoms (sleep disturbance, pain, hyperarousal, or anger).	None	Reviewed, Deleted	
A	2	L1	Ensure patient access to spiritual care when sought.	None	Not reviewed, Deleted	
A	2	L1	Assess for spiritual needs.	None	Not reviewed, Deleted	
A	2	L1	Provide opportunities for grieving for losses (providing space and opportunities for prayers, mantras, rites, and rituals and end-of-life care, as determined important by the patient).	None	Not reviewed, Deleted	
A	2	L2	Immediately after trauma exposure, preserve an interpersonal safety zone protecting basic personal space (e.g., privacy, quiet, personal effects).	None	Not reviewed, Deleted	
A	2	L2	As part of Psychological First Aid, reconnect trauma survivors with previously supportive relationships (e.g., family, friends, unit members) and link with additional sources of interpersonal support.	None	Not reviewed, Deleted	
A	2	L2	Assess for impact of PTSD on social functioning.	None	Not reviewed, Deleted	
A	2	L2	Facilitate access to social support and provide assistance in improving social functioning, as indicated.	None	Not reviewed, Deleted	
A	3	M	Assessment of the response to the acute intervention should include an evaluation for the following risk factors: a. Persistent or worsening traumatic stress symptoms (e.g., dissociation, panic, autonomic arousal, cognitive impairment) b. Significant functional impairments (e.g., role/work, relationships) c. Dangerousness (suicidal or violent ideation, plan, and/or intent) d. Severe psychiatric co-morbidity (e.g., psychotic spectrum disorder, substance use disorder or abuse) e. Maladaptive coping strategies (e.g., pattern of impulsivity, social withdrawal, or other reactions under stress) f. New or evolving psychosocial stressors g. Poor social supports.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	3	M	Follow-up after acute intervention to determine patient status should include the following: a. Patient does not improve or status worsens – continue management of PTSD (See Module B) in consultation or referral to PTSD specialty care or mental health provider. Recommend involvement of the primary care provider in the treatment. Patients with multiple problems may benefit from a multi-disciplinary approach to include occupational therapy, spiritual counseling, recreation therapy, social work, psychology, and/or psychiatry. b. Patient demonstrates partial improvement (e.g., less arousal, but no improvement in sleep) – consider augmentation or adjustment of the acute intervention and follow up within 2 weeks. c. Patient recovers from acute symptoms – provide education about acute stress reaction and contact information with instructions for available follow-up if needed.	None	Not reviewed, Deleted	
A	4	N	Individuals who fail to respond to early interventions should be referred for PTSD treatment when they have: a. Worsening of stress-related symptoms b. High potential or new-onset potential for dangerousness c. Development of ASD/PTSD d. Maladaptive coping with stress (e.g., social withdrawal, alcohol use) e. Exacerbation of pre-existing psychiatric conditions f. Deterioration in function g. New onset stressors h. Poor social supports.	None	Not reviewed, Deleted	
A	4	N	Primary Care provider should consider initiating therapy pending referral or if the patient is reluctant or unable to obtain specialty services.	None	Not reviewed, Deleted	
A	4	N	Primary Care provider should continue evaluating and treating co-morbid physical illnesses and addressing any other health concerns, as well as educating and validating the patient regarding his/her illness.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
A	4	O	Follow-up should be offered to individuals who request it or to those at high risk of developing adjustment difficulties following exposure to major incidents and disasters, including individuals who: a. Have acute stress disorder or other clinically significant symptoms stemming from thetrauma b. Are bereaved c. Have a pre-existing psychiatric disorder d. Require medical or surgical attention e. Were exposed to a major incident or disaster that was particularly intense and of long duration.	None	Not reviewed, Deleted	
A	4	O	Primary Care providers should follow-up with patients about issues related to trauma in an ongoing way. Patients with initial sub-threshold presentation are at increased risk of developing PTSD and may need symptom-specific management.	None	Not reviewed, Deleted	
B	1	A	Patients who are presumed to have symptoms of PTSD or who are positive for PTSD on the initial screening should receive a thorough assessment of their symptoms that includes details such as time of onset, frequency, course, severity, level of distress, functional impairment, and other relevant information to guide accurate diagnosis and appropriate clinical decision- making.	None	Not reviewed, Amended	Recommendation 4
B	1	A	Consider use of a validated, self-administered checklist to ensure systematic, standardized, and efficient review of the patient's symptoms and history of trauma exposure. Routine ongoing use of these checklists may allow assessment of treatment response and patient progress (see Appendix C: PCL-C).	None	Not reviewed, Amended	Recommendation 5
B	1	A	Diagnosis of PTSD should be obtained based on a comprehensive clinical interview that assesses all the symptoms that characterize PTSD. Structured diagnostic interviews, such as the Clinician-Administered PTSD scale (CAPS), may be considered.	None	Not reviewed, Amended	Recommendation 4

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	1	B	Assessment of the trauma exposure experience should include: a. History of exposure to traumatic event(s) b. Nature of the trauma c. Severity of the trauma d. Duration and frequency of the trauma e. Age at time of trauma f. Patient's reactions during and immediately following trauma exposure (e.g., helplessness, horror, and fear) g. Existence of multiple traumas.	None	Not reviewed, Deleted	
B	1	B	If trauma exposure is recent (<1 month), particular attention should be given to the following: a. Exposure to/Environment of trauma b. Ongoing traumatic event exposure c. Exposure, perhaps ongoing, to environmental toxins d. Ongoing perceived threat.	None	Not reviewed, Deleted	
B	1	B	When assessing trauma exposure, the clinician must consider the patient's ability to tolerate the recounting of traumatic material, since it may increase distress and/or exacerbate PTSD symptoms.	None	Not reviewed, Deleted	
B	1	C	All patients with PTSD should be assessed for safety and dangerousness, including current risk to self or others, as well as historical patterns of risk: a. Suicidal or homicidal ideation, intent (plan), means (e.g., weapon, excess medications), history (e.g. violence or suicide attempts), behaviors (e.g., aggression, impulsivity), co-morbidities (substance abuse, medical conditions) [B] b. Family and social environment – including domestic or family violence, risks to the family [B] c. Ongoing health risks or risk-taking behavior [B] d. Medical/psychiatric co-morbidities or unstable medical conditions [B] e. Potential to jeopardize mission in an operational environment. [I]	B, I	Not reviewed, Amended	Recommendation 4

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	1	D	All patients should have a thorough assessment of medical and psychiatric history, with particular attention paid to the following: a. Baseline functional status b. Baseline mental status c. Medical history: to include any injury (e.g., mild-TBI) d. Medications: to include medication allergies and sensitivities; prescription medications; herbal or nutritional supplements; and over-the- counter (OTC) medications (caffeine, energy drinks or use of other substances) e. Past psychiatric history: to include prior treatment for mental health and substance use disorder, and past hospitalization for depression or suicidality f. Current life stressors.	None	Not reviewed, Deleted	
B	1	D	All patients should have a thorough physical examination. On physical examination, particular attention should be paid to the neurological exam and stigmata of physical/sexual abuse, self-mutilation, or medical illness. Note distress caused by, or avoidance of, diagnostic tests/examination procedures.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	1	D	All patients, particularly the elderly, should have a Mental Status Examination (MSE) to include assessment of the following: a. Appearance and behavior b. Language/speech c. Thought process (loose associations, ruminations, obsessions) and content (delusions, illusions and hallucinations) d. Mood (subjective) e. Affect (to include intensity, range, and appropriateness to situation and ideation) f. Level of Consciousness (LOC) g. Cognitive function h. All patients should have routine laboratory tests as clinically indicated, such as TSH, Complete Metabolic Panel, Hepatitis, HIV, and HCG (for females). Also consider CBC, UA, Tox/EtoH panel, and other tests i. Other assessments may be considered (radiology studies, ECG, and EEG), as clinically indicated j. All patients should have a narrative summary of psychosocial assessments to include work/school, family, relationships, housing, legal, financial, unit/community involvement, and recreation, as clinically appropriate.	None	Not reviewed, Deleted	
B	1	E	Assessment of function should be obtained through a comprehensive narrative assessment, and the use of standardized, targeted, and validated instruments designed to assess family/relationship, work/school, and/or social functioning.	None	Not reviewed, Amended	Recommendation 4
B	1	E	The determination of when to return to work/duty should take into consideration the complexity and importance of the patient's job role and functional capabilities.	None	Not reviewed, Deleted	
B	1	E	The continuing presence of symptoms of PTSD should not be considered in itself as sufficient justification for preventing a return to work/duty.	None	Not reviewed, Deleted	
B	1	F	Patients should be assessed for risk factors for developing PTSD. Special attention should be given to post-traumatic factors (i.e., social support, ongoing stressors, and functional incapacity) that may be modified by intervention.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	1	F	When evaluating risk factors for PTSD, the clinician should keep in mind that PTSD is defined as occurring only after four weeks have elapsed following a traumatic event. PTSD symptoms, however, may not appear until a considerable time has passed—sometimes surfacing years later.	None	Not reviewed, Deleted	
B	2	G	A diagnosis of stress-related disorder consistent with the DSM IV criteria for PTSD should be formulated before initiating treatment.	None	Not reviewed, Deleted	
B	2	G	Diagnosis of PTSD should be obtained based on a comprehensive clinical interview that assesses all the symptoms that characterize PTSD. Structured diagnostic interviews, such as the Clinician-Administered PTSD scale (CAPS), may be considered.	None	Reviewed, Amended	Recommendation 4
B	2	G	When a diagnostic work up cannot be completed, primary care providers should consider initiating treatment or referral based on a working diagnosis of stress-related disorder.	None	Not reviewed, Deleted	
B	2	G	Patients with difficult or complicated presentation of the psychiatric component should be referred to PTSD specialty care for diagnosis and treatment.	None	Not reviewed, Deleted	
B	2	G	Patients with partial or sub-threshold PTSD should be carefully monitored for deterioration of symptoms.	None	Not reviewed, Deleted	
B	2	H	Providers should recognize that medical disorders/symptoms, mental health disorders, and psychosocial problems commonly coexist with PTSD and should screen for them during the evaluation and treatment of PTSD.	None	Not reviewed, Deleted	
B	2	H	Because of the high prevalence of psychiatric co-morbidities in the PTSD population, screening for depression and other psychiatric disorders is warranted (see also VA/DoD Clinical Practice Guidelines for the Management of Major Depressive Disorder [MDD] and for Bipolar Disorder).	None	Not reviewed, Deleted	
B	2	H	Patterns of current and past use of substance by persons with trauma histories or PTSD should be routinely assessed to identify substance misuse or dependency (alcohol, nicotine, prescribed drugs, and illicit drugs) (see also VA/DoD Clinical Practice Guideline for Substance Use Disorders).	None	Not reviewed, Deleted	
B	2	H	Pain (acute and chronic) and sleep disturbances should be assessed in all patients with PTSD.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	2	H	Generalized physical and cognitive health symptoms - also attributed to concussion/mild traumatic brain injury (mTBI) and many other causes - should be assessed and managed in patients with PTSD and co-occurring diagnosis of mTBI (see also VA/DoD CPG for Concussion/mild-TBI, and the CPG for Post-Deployment Health).	None	Not reviewed, Deleted	
B	2	H	Associated high-risk behaviors (e.g., smoking, alcohol/drug abuse, unsafe weapon storage, dangerous driving, HIV and hepatitis risks) should be assessed in patients with PTSD.	None	Not reviewed, Deleted	
B	2	H	Providers should consider the existence of co-morbid conditions when deciding whether to treat patients in the primary care setting or refer them for specialty mental healthcare (See Annotation J).	None	Not reviewed, Deleted	
B	2	H	Patients with complicated co-morbidity may be referred to mental health or PTSD specialty care for evaluation and diagnosis (see Annotation J).	None	Not reviewed, Deleted	
B	2	I	Trauma survivors and their families should be educated about PTSD symptoms, other potential consequences of exposure to traumatic stress, practical ways of coping with traumatic stress symptoms, co-morbidity with other medical health concerns, processes of recovery from PTSD, and the nature of treatments. [C]	C	Not reviewed, Deleted	
B	2	I	Providers should explain to all patients with PTSD the range of available and effective options for PTSD treatment.	None	Not reviewed, Deleted	
B	2	I	Patient preferences along with provider recommendations should drive the selection of treatment interventions in a shared and informed decision-making process.	None	Not reviewed, Deleted	
B	2	J1	PTSD and co-morbid mental health conditions should be treated concurrently for all conditions through an integrated treatment approach, which considers patient preferences, provider experience, severity of the conditions, and the availability of resources.	None	Reviewed, Deleted	
B	2	J1	Patients with PTSD and severe co-morbid mental health conditions should be treated either through referral or in consultation with a provider that is experienced in treating the co-morbid conditions.	None	Reviewed, Deleted	

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B	2	J1	Because of the profound social impairment of PTSD (caused, for example, by the patient's anger and avoidance symptoms), close friends and family members in the patient's immediate daily environment (e.g., parents, spouse, or children) should be provided with education and advised to consider assistance from specialty care, both for individual treatment and couples/family treatment.	None	Not reviewed, Deleted	
B	2	J1	Factors to consider when determining the optimal setting for treatment include: a. Severity of the PTSD or co-occurring disorders b. Local availability of service options (specialized PTSD programs, evidence-based treatments, behavioral health specialty care, primary care, integrated care for co-occurring disorders, Vet Centers, other) c. Level of provider comfort and experience in treating psychiatric co-morbidities d. Patient preferences e. The need to maintain a coordinated continuum of care for chronic co-morbidities f. Availability of resources and time to offer treatment.	None	Not reviewed, Deleted	

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B	2	J1	Considerations related to possible referral: Complicated severe PTSD: Some patients with PTSD have complicated, challenging presentations. These patients warrant referral to specialty PTSD care that includes access to cognitive-behavioral evidence-based treatments (see Module I-2: Treatment for PTSD). Co-occurring major depressive disorder (MDD) in the absence of significant suicidality, panic, or generalized anxiety often shows reduction in intensity when the PTSD is treated. Depression of mild severity may not require referral to specialty care or additional treatments outside those targeting PTSD. Patients should be carefully monitored for changes in symptoms. A reduction of PTSD symptoms that is not accompanied by reduction of symptoms in depression or anxiety would justify a more formally targeted treatment (refer to the VA/DoD guideline for MDD). Co-occurring mild to moderate disorders, such as substance use, pain disorders, and sleep problems, can frequently be effectively treated in the context of PTSD treatment and do not require a referral to specialty care. Consultation, to integrate adjunctive interventions, may be considered (see the respective VA/DoD CPGs). Co-occurring severe psychiatric disorders, while not precluding concurrent PTSD treatment, typically justify referral to specialty care for evaluation and treatment. These disorders may include: Severe Major Depression or Major Depression with suicidality, Unstable Bipolar Disorder, Severe Personality Disorders, Psychotic Disorders, Significant TBI, and Severe Substance Use Disorder (SUD) or substance abuse of such intensity that PTSD treatment components are likely to be difficult to implement. Persistent Post-Concussion Symptoms in patients who present with PTSD and a history of concussion/mTBI may be best managed within either primary care or polytrauma rehab settings that utilize a multidisciplinary team approach. Providers should recognize that mTBI/concussion is one of numerous possible etiologies of co-morbid post-deployment symptoms occurring in Veterans and Service Members with PTSD, and it is often difficult to precisely attribute symptoms to concussive events that occurred months or years earlier. From a treatment standpoint, physical or cognitive symptoms, such as headaches or memory problems, or other persistent post-concussive symptoms should be treated symptomatically whether or not concussion/mTBI is thought to be one of the causal factors. Clinicians should not get caught up in debating causation but maintain focus on identifying and treating the symptoms that are contributing to the most impairment. There is no evidence to support withholding PTSD treatments while addressing post-concussive symptoms.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	2	J2	All patients diagnosed with PTSD should receive comprehensive assessment for SUD, including nicotine dependence (as recommended by the separate Clinical Practice Guideline).	None	Not reviewed, Deleted	
B	2	J2	Recommend and offer cessation treatment to patients with nicotine dependence. [A]	A	Reviewed, Deleted	
B	2	J2	Patients with SUD and PTSD should be educated about the relationships between PTSD and substance abuse. The patient's prior treatment experience and preference should be considered since no single intervention approach for the co- morbidity has yet emerged as the treatment of choice.	None	Not reviewed, Deleted	
B	2	J2	Treat other concurrent Substance Use Disorders consistent with VA/DoD clinical practice guidelines including concurrent pharmacotherapy: a. Addiction-focused pharmacotherapy should be discussed, considered, available and offered, if indicated, for all patients with alcohol dependence and/or opioid dependence. b. Once initiated, addiction-focused pharmacotherapy should be monitored for adherence and treatment response.	None	Reviewed, New-replaced	Recommendation 38
B	2	J2	Provide multiple services in the most accessible setting to promote engagement and coordination of care for both conditions. [I]	I	Not reviewed, Deleted	
B	2	J2	Reassess response to treatment for SUD periodically and systematically, using standardized and valid self-report instrument(s) and laboratory tests. Indicators of SUD treatment response include ongoing substance use, craving, side effects of medication, emerging symptoms, etc.	None	Not reviewed, Deleted	
B	2	J2	There is insufficient evidence to recommend for or against any specific psychosocial approach to addressing PTSD that is co-morbid with SUD. [I]	I	Reviewed, New-replaced	Recommendation 38

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	2	J3	Primary care providers should routinely provide the following services for all patients with trauma-related disorders, especially those who are reluctant to seek specialty mental healthcare: ▪ Education about the disorder and importance of not letting stigma and barriers to care interfere with specialty treatment if needed ▪ Provision of evidence-based treatment within the primary Care or through referral ▪ Regular follow-up and monitoring of symptoms ▪ Regular follow-up and monitoring of co-morbid health concerns.	None	Not reviewed, Deleted	
B	2	J3	Primary care providers should consider consultation with mental health providers for patients with PTSD who warrant a mental health referral but refuse it or seem reluctant to talk to a mental health provider.	None	Not reviewed, Deleted	
B	2	J3	Primary care providers should take leadership in providing a collaborative multi-disciplinary treatment approach. Team members may include the primary care providers, mental health specialists, other medical specialists (e.g., neurology, pain management), chaplains, pastors, social workers, occupational or recreational therapists, Vet Center staff members, staff of family support centers, exceptional family member programs, VA benefits counselors, vocational rehabilitation specialists, peer counselors, and others.	None	Reviewed, New-replaced	Recommendation 2
B	2	J3	When an integrated behavioral health clinician is available (e.g., collaborative care model, or Post-Deployment Care clinics) evidence-based treatment should be provided.	None	Reviewed, New-replaced	Recommendation 2
B	2	J3	Primary care providers should continue to be involved in the treatment of patients with acute or chronic stress disorders. All patients with PTSD should have a specific primary care provider assigned to coordinate their overall healthcare.	None	Not reviewed, Deleted	
B	3	K	A supportive and collaborative treatment relationship or therapeutic alliance should be developed and maintained with patients with PTSD.	None	Not reviewed, Deleted	
B	3	K	Evidence-based psychotherapy and/or evidence-based pharmacotherapy are recommended as first-line treatment options.	None	Reviewed, Deleted	
B	3	K	Specialized PTSD psychotherapies may be augmented by additional problem-specific methods/services and pharmacotherapy.	None	Reviewed, New-replaced	Recommendation 29

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	3	K	Consider referral for alternative care modalities (Complementary Alternative Medicine) for patient symptoms, consistent with available resources and resonant with patient belief systems. [See Module I-2]	None	Reviewed, Deleted	
B	3	K	Patients with PTSD who are experiencing clinically significant symptoms, including chronic pain, insomnia, anxiety, should receive symptom-specific management interventions. [See Module I-3]	None	Not reviewed, Deleted	
B	3	K	Management of PTSD or related symptoms may be initiated based on a presumptive diagnosis of PTSD. Long-term pharmacotherapy will be coordinated with other intervention.	None	Reviewed, Deleted	
B	4	N	At a minimum, providers should perform a brief PTSD symptom assessment at each treatment visit. The use of a validated PTSD symptom measure, such as the PTSD Checklist, should be considered (see Appendix C).	None	Not reviewed, Deleted	
B	4	N	Comprehensive re-assessment and evaluation of treatment progress should be conducted at least every 90 days, perhaps with greater frequency for those in active treatment, and should include a measure of PTSD symptomatology (e.g., PCL) and strongly consider a measure of Depression symptomatology (e.g., PHQ9).	None	Not reviewed, Deleted	
B	4	N	Other specific areas of treatment focus (e.g., substance abuse) should also be reevaluated and measured by standardized measures of outcome.	None	Not reviewed, Deleted	
B	4	N	Assessment of functional impairment should also be made, at a minimum, by asking patients to rate to what extent their symptoms make it difficult to engage in vocational, parental, spousal, familial, or other roles.	None	Not reviewed, Deleted	
B	4	N	Consider continued assessment of: ▪ Patient preferences ▪ Treatment adherence ▪ Adverse treatment effects.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	4	O	If patient does not improve or status worsens, consider one of the following treatment modification options: a. Continue application of the same modality at intensified dose and/or frequency b. Change to a different treatment modality c. Apply adjunctive therapies d. Consider a referral to adjunctive services for treatment of co-morbid disorders or behavioral abnormalities (e.g., homelessness, domestic violence, or aggressive behavior). e. For patient with severe symptoms or coexisting psychiatric problems consider referrals to: • Specialized PTSD programs • Specialized programs for coexisting problems and conditions • Partial psychiatric hospitalization or "day treatment" programs • Inpatient psychiatric hospitalization.	None	Reviewed, New-replaced	Recommendation 29 Recommendation 30

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	4	O	If patient demonstrates partial (insufficient) remission, consider one of the following treatment modification options: a. Before making any therapeutic change, ensure that "treatment non-response" is not due to one or more of the following: not keeping psychotherapy appointments, not doing prescribed homework, not taking prescribed medications, still using alcohol or illicit substances, still suffering from ongoing insomnia or chronic pain, not experiencing any new psychosocial stressors, the original assessment did not overlook a co-morbid medical or psychiatric condition b. Continue the present treatment modality to allow sufficient time for full response c. Continue application of the same modality at intensified dose and/or frequency d. Change to a different treatment modality e. Apply adjunctive therapies f. Increase level of care (e.g., referral facility, partial hospitalization, inpatient hospitalization, residential care) g. Consider a referral to adjunctive services for treatment of co-morbid disorders or behavioral abnormalities (e.g., homelessness or domestic violence).	None	Reviewed, New-replaced	Recommendation 29 Recommendation 30
B	4	O	If patient demonstrates improved symptoms and functioning but requires maintenance treatment: a. Continue current course of treatment b. Consider stepping down the type, frequency, or dose of therapy c. Consider: • Transition from intensive psychotherapy to case management contacts • Transition from individual to group treatment modalities • Transition to as-needed treatment d. Discuss patient status and need for monitoring with the primary care provider e. Consider a referral to adjunctive services for treatment of co-morbid disorders or behavioral abnormalities (e.g., homelessness or domestic violence).	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
B	4	O	If patient demonstrates remission from symptoms and there are no indications for further therapy: a. Discontinue treatment b. Educate the patient about indications for and route of future care access c. Monitor by primary care for relapse/exacerbation.	None	Not reviewed, Deleted	
B	4	O	Evaluate psychosocial function and refer for psychosocial rehabilitation, as indicated. Available resources include, but are not limited to: chaplains, pastors, Family Support Centers, Exceptional Family Member Programs, VA benefits counselors, occupational or recreational therapists, Vet Centers, and peer-support groups (see Module I-2 D: Psychosocial Rehabilitation).	None	Not reviewed, Deleted	
B	4	O	Provide case management, as indicated, to address high utilization of medical resources.	None	Reviewed, Deleted	
I	1	-	Continue providing psychoeducation and normalization.	None	Not reviewed, Deleted	
I	1	-	Treatment should be initiated after education, normalization, and Psychological First Aid has been provided and after basic needs following the trauma have been made available.	None	Not reviewed, Deleted	
I	1	-	There is insufficient evidence to recommend for or against the use of Psychological First Aid to address symptoms beyond 4 days following trauma. [I]	I	Not reviewed, Deleted	
I	1	-	Survivors who present with symptoms that do not meet the diagnostic threshold of ASD or PTSD should be monitored and may benefit from follow-up and provision of ongoing counseling or symptomatic treatment.	None	Not reviewed, Deleted	
I	1	-	Recommend monitoring for development of PTSD using validated symptom measures (e.g., PTSD Checklist, other screening tools for ASD/PTSD).	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	1	-	Psychotherapy: a. Consider early brief intervention (4 to 5 sessions) of cognitive-based therapy (CBT) that includes exposure-based therapy, alone or combined with a component of cognitive re-structuring therapy for patients with significant early symptom levels, especially those meeting diagnostic criteria for ASD. [A] b. Routine formal psychotherapy intervention for asymptomatic individuals is not beneficial and may be harmful. [D] c. Strongly recommend against individual Psychological Debriefing as a viable means of reducing acute stress disorder (ASD) or progression to post-traumatic stress disorder (PTSD). [D] d. The evidence does not support a single session group Psychological Debriefing as a viable means of reducing acute stress disorder (ASD) or progression to post-traumatic stress disorder, but there is no evidence of harm (Note: this is not a recommendation pertaining to Operational Debriefing). [D] e. Groups may be effective vehicles for providing trauma-related education, training in coping skills, and increasing social support, especially in the context of multiple group sessions. [I] f. Group participation should be voluntary.	A, D, I	Reviewed, New-replaced	Recommendation 7
I	1	-	Pharmacotherapy: a. There is no evidence to support a recommendation for use of a pharmacological agent to prevent the development of ASD or PTSD. [I] b. Strongly recommend against the use of benzodiazepines to prevent the development of ASD or PTSD [D]	D, I	Reviewed, New-replaced	Recommendation 6 Recommendation 8
I	2	A	Providers should explain to all patients with PTSD the range of available and effective therapeutic options for PTSD.	None	Not reviewed, Amended	Recommendation 1
I	2	A	Patient education is recommended as an element of treatment of PTSD for all patients and the family members. [C]	C	Not reviewed, Deleted	
I	2	A	Patient and provider preferences should drive the selection of evidence-based psychotherapy and/or evidence-based pharmacotherapy as the first line treatment.	None	Not reviewed, Amended	Recommendation 1

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	2	A	Psychotherapies should be provided by practitioners who have been trained in the particular method of treatment.	None	Reviewed, Deleted	
I	2	A	A collaborative care approach to therapy administration, with care management, may be considered, although supportive evidence is lacking specifically for PTSD.	None	Reviewed, Amended	Recommendation 2
I	2	B	Strongly recommend that patients who are diagnosed with PTSD should be offered one of the evidence-based trauma-focused psychotherapeutic interventions that include components of exposure and/or cognitive restructuring; or stress inoculation training. [A] The choice of a specific approach should be based on the severity of the symptoms, clinician expertise in one or more of these treatment methods and patient preference, and may include an exposure-based therapy (e.g., Prolonged Exposure), a cognitive-based therapy (e.g., Cognitive Processing Therapy), Stress management therapy (e.g., SIT) or Eye Movement Desensitization and Reprocessing (EMDR).	A	Reviewed, New-replaced	Recommendation 11 Recommendation 12
I	2	B	Relaxation techniques should be considered as a component of treatment approaches for ASD or PTSD in alleviating symptoms associated with physiological hyper-reactivity. [C]	C	Reviewed, Deleted	
I	2	B	Imagery Rehearsal Therapy [IRT] can be considered for treatment of nightmares and sleep disruption. [C]	C	Reviewed, Deleted	
I	2	B	Brief Psychodynamic Therapy can be considered for patients with PTSD. [C]	C	Reviewed, Deleted	
I	2	B	Hypnotic Techniques can be considered, especially for symptoms associated with PTSD, such as pain, anxiety, dissociation, and nightmares, for which hypnosis has been successfully used. [C]	C	Not reviewed, Deleted	
I	2	B	There is insufficient evidence to recommend for or against Dialectical Behavioral Therapy (DBT) as first-line treatment for PTSD [I] ▪ Dialectical Behavioral Therapy can be considered for patients with a borderline personality disorder typified by parasuicidal behaviors. [B]	B, I	Reviewed, Deleted	
I	2	B	There is insufficient evidence to recommend for or against Family or Couples Therapy as first-line treatment for PTSD; Family or Couples therapy may be considered in managing PTSD-related family disruption or conflict, increasing support, or improving communication. [I]	I	Reviewed, Amended	Recommendation 16

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	2	B	Group Therapy may be considered for treatment of PTSD [C] ▪ There is insufficient evidence to favor any particular type of group therapy over other types ▪ Patients being considered for group therapy should exhibit acceptance for the rationale for trauma work, and willingness to self-disclose in a group.	C, I	Reviewed, New-replaced	Recommendation 15
I	2	B	Consider augmenting with other effective evidence-based interventions for patients who do not respond to a single approach.	None	Reviewed, New-replaced	Recommendation 29 Recommendation 30
I	2	B	Supportive psychotherapy is not considered to be effective for the treatment of PTSD. However, multiple studies have shown that supportive interventions are significantly more helpful than no treatment, and they may be helpful in preventing relapse in patients who have reasonable control over their symptoms and are not in severe and acute distress.	None	Reviewed, New-replaced	Recommendation 13
I	2	B	Telemedicine interventions that involve person-to-person individual treatment sessions appear to have similar efficacy and satisfaction clinically as a direct face-to-face interaction, though data are much more limited than for face-to-face encounters. [C] a. Telemedicine interventions are recommended when face-to-face interventions are not feasible due to geographic distance between patient and provider or other barriers to patient access (e.g., agoraphobia, physical disability); when the patient would benefit from more frequent contact than is feasible with face-to-face sessions; or when the patient declines more traditional mental health interventions. b. Providers using telemedicine interventions should endeavor to maintain and strengthen the therapeutic relationship, build patient rapport, stress practice and assignment completion, and ensure adequacy of safety protocols using similar techniques as they do in a face-to-face session. c. Providers using technology-assisted interventions should take steps to ensure that their work complies with the regulations and procedures of the organization in which they are employed, legal standards, and the ethical standards of their professions. Patient confidentiality and safety should be monitored closely.	C	Reviewed, Amended	Recommendation 35 Recommendation 36

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	2	B	There is insufficient evidence to recommend for or against Web-based interventions as a stand-alone intervention or as an alternative to standard mental health treatment for PTSD. [I] If used: a. Clinicians should carefully review the content of any web-based materials to ensure their accuracy and ethical application before recommending use to patients. b. Web-based approach may be used where face-to-face interventions are not feasible (e.g., geography limits access to other forms of treatment) or when patients decline more traditional mental health interventions. It has also been suggested that web-based interventions may provide more confidentiality than more traditional approaches. c. Providers should regularly encourage patients to complete the intervention and endeavor to maintain and strengthen the therapeutic relationship, build patient rapport, stress practice and assignment completion, and ensure adequacy of safety protocols. Availability of telephone contact for initial assessment or other reasons (e.g. emergencies, suicidality/homicidality, or follow-up of specific problems) should be considered. d. Providers using technology-assisted interventions should take steps to ensure that their work complies with the regulations and procedures of the organization in which they are employed, legal standards, and the ethical standards of their professions. Patient confidentiality and safety should be monitored closely.	I	Reviewed, New-replaced	Recommendation 35 Recommendation 36
I	2	C	Risks and benefits of long-term pharmacotherapy should be discussed prior to starting medication and should be a continued discussion item during treatment.	None	Reviewed, Deleted	
I	2	C	Monotherapy therapeutic trial should be optimized before proceeding to subsequent strategies by monitoring outcomes, maximizing dosage (medication or psychotherapy), and allowing sufficient response time (for at least 8 weeks). [C]	C	Reviewed, Deleted	
I	2	C	If there is some response and patient is tolerating the drug, continue for at least another 4 weeks.	None	Reviewed, Deleted	
I	2	C	If the drug is not tolerated, discontinue the current agent and switch to another effective medication.	None	Reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	2	C	If no improvement is observed at 8 weeks consider: a. Increasing the dose of the initial drug to maximum tolerated b. Discontinuing the current agent and switching to another effective medication	None	Reviewed, Deleted	
I	2	C	Recommend assessment of adherence to medication at each visit.	None	Reviewed, Deleted	
I	2	C	Recommend assessment of side effects and management to minimize or alleviate adverse effects.	None	Reviewed, Deleted	
I	2	C	Assess for treatment burden (e.g., medication adverse effects, attending appointments) after initiating or changing treatment when the patient is non-adherent to treatment or when the patient is not responding to treatment.	None	Reviewed, Deleted	
I	2	C	Since PTSD is a chronic disorder, responders to pharmacotherapy may need to continue medication indefinitely; however, it is recommended that maintenance treatment should be periodically reassessed.	None	Reviewed, Deleted	
I	2	C	Providers should give simple educational messages regarding antidepressant use (e.g., take daily, understand gradual nature of benefits, continue even when feeling better, medication may cause some transient side effects, along with specific instructions on how to address issues or concerns, and when to contact the provider) in order to increase adherence to treatment in the acute phase. [B]	B	Reviewed, Deleted	
I	2	C	Strongly recommend that patients diagnosed with PTSD should be offered selective serotonin reuptake inhibitors (SSRIs), for which fluoxetine, paroxetine, or sertraline have the strongest support, or serotonin norepinephrine reuptake inhibitors (SNRIs), for which venlafaxine has the strongest support, for the treatment of PTSD. [A]	A	Reviewed, New-replaced	Recommendation 17
I	2	C	Recommend mirtazapine, nefazodone, tricyclic antidepressants (TCAs), amitriptyline and imipramine, or monoamine oxidase inhibitors (phenelzine) for the treatments for PTSD. [B]	B	Reviewed, New-replaced	Recommendation 18 Recommendation 19 Recommendation 20 Recommendation 22
I	2	C	Recommend against the use of guanfacine, anticonvulsants (tiagabine, topiramate, or valproate) as monotherapy in the management of PTSD. [D]	D	Reviewed, New-replaced	Recommendation 19 Recommendation 20

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	2	C	The existing evidence does not support the use of bupropion, buspirone, and trazodone, anticonvulsants (lamotrigine or gabapentin) or atypical antipsychotics as monotherapy in the management of PTSD. [I]	I	Reviewed, New-replaced	Recommendation 22
I	2	C	There is evidence against the use of benzodiazepines in the management of PTSD. [D]	D	Reviewed, Amended	Recommendation 20
I	2	C	There is insufficient evidence to support the use of prazosin as monotherapy in the management of PTSD. [I]	I	Reviewed, New-replaced	Recommendation 28a
I	2	C	Recommend against the use of risperidone as adjunctive therapy [D]. There is insufficient evidence to recommend the use of any other atypical antipsychotic for treatment of PTSD. [I]	D, I	Reviewed, New-replaced	Recommendation 20 Recommendation 22 Recommendation 25
I	2	C	Recommend adjunctive treatment with prazosin for sleep/nightmares. [B]	B	Reviewed, New-replaced	Recommendation 28b
I	2	C	There is insufficient evidence to recommend a sympatholytic or an anticonvulsant as an adjunctive therapy for the treatment of PTSD. [I]	I	Reviewed, Deleted	
I	2	D	Consider psychosocial rehabilitation techniques once the client and clinician identify the following kinds of problems associated with the diagnosis of PTSD: persistent high-risk behaviors, lack of self-care/independent living skills, homelessness, interactions with a family that does not understand PTSD, socially inactive, unemployed, and encounters with barriers to various forms of treatment/rehabilitation services.	None	Not reviewed, Deleted	
I	2	D	Patient and clinician should determine whether such problems are associated with core symptoms of PTSD and, if so, ensure that rehabilitation techniques are used as a contextual vehicle for alleviating PTSD symptoms.	None	Not reviewed, Deleted	
I	2	D	Psychosocial rehabilitation should occur concurrently or shortly after a course of treatment for PTSD, since psychosocial rehabilitation is not trauma-focused.	None	Not reviewed, Deleted	
I	2	E	There is insufficient evidence to recommend the use of any of the Biomedical Somatic Therapies for first-line treatment of PTSD. [D]	D	Reviewed, New-replaced	Recommendation 32
I	2	E	ECT and rTMS may be considered as an alternative in chronic, severe, medication- and psychotherapy-resistant PTSD. [B]	B	Reviewed, New-replaced	Recommendation 32
I	2	E2	Acupuncture may be considered as treatment for patients with PTSD. [B]	B	Reviewed, Amended	Recommendation 33

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	2	F	There is insufficient evidence to recommend CAM approaches as first line treatments for PTSD. [I]	I	Reviewed, New-replaced	Recommendation 34
I	2	F	CAM approaches that facilitate a relaxation response (e.g. mindfulness, yoga, acupuncture, massage, and others) may be considered for adjunctive treatment of hyperarousal symptoms, although there is no evidence that these are more effective than standard stress inoculation techniques. [I]	I	Reviewed, New-replaced	Recommendation 34
I	2	F	CAM approaches may be considered as adjunctive approaches to address some co- morbid conditions (e.g. acupuncture for pain). [C]	C	Reviewed, New-replaced	Recommendation 34
I	2	F	CAM may facilitate engagement in medical care and may be considered in some patients who refuse evidence-based treatments. However, providers should discuss the evidence for effectiveness and risk-benefits of different options, and ensure that the patient is appropriately informed.	None	Reviewed, Deleted	
I	3	A	Encourage patients to practice good sleep hygiene, including: ▪ Restricting the night-time sleep period to about eight hours ▪ Waking at a regular time ▪ Arising from bed at a regular time ▪ Avoiding going to bed too early ▪ Avoiding alcohol ▪ Avoiding stimulants, caffeinated beverages, power/energy drinks, nicotine, and over-the-counter medications ▪ Avoiding stimulating activities, light, noise, and temperature extremes before bedtime (e.g., exercise, video games, T.V.) or in the sleeping area ▪ Reducing (to less than 30 minutes), or abolishing, daytime naps ▪ Practicing relaxation techniques ▪ Engaging in moderate exercise, but not immediately before bedtime	None	Not reviewed, Deleted	
I	3	A	Offer Cognitive Behavioral Therapy for Insomnia, which may include: ▪ Educating about proper sleep habits and sleep needs ▪ Correcting false and unrealistic beliefs/concerns about sleep ▪ Identifying and addressing anxious, automatic thoughts which disrupt sleep	None	Reviewed, Amended	Recommendation 40
I	3	A	Consider adjunctive therapy for nightmares using prazosin. [B]	B	Reviewed, New-replaced	Recommendation 28b

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	3	A	Any significant change in sleep patterns should trigger clinical reassessment in order to rule out worsening or new onset of co-morbid conditions	None	Reviewed, Deleted	
I	3	A	Monitor symptoms to assess improvement or deterioration and reassess accordingly.	None	Not reviewed, Deleted	
I	3	A	Explore cause(s) for insomnia, including co-morbid conditions.	None	Reviewed, New-replaced	Recommendation 39
I	3	A	Begin treatment for insomnia with non-pharmacological treatments, including sleep hygiene and cognitive behavioral treatment (see recommendation for Sleep Disturbances).	None	Reviewed, New-replaced	Recommendation 40
I	3	A	The selection of sleep agents for the treatment of insomnia in PTSD patients may be impacted by other treatment decisions (e.g., medications already prescribed for the treatment of PTSD, depression, TBI, pain, or concurrent substance abuse/withdrawal) and social/environmental/logistical concerns associated with deployment. a. Trazodone may be helpful in management of insomnia and may also supplement the action of other antidepressants. b. Hypnotics are a second-line approach to the management of insomnia and should only be used for short periods of time. Should hypnotic therapy be indicated, the newer generation of non-benzodiazepines (e.g., zolpidem, eszopiclone, ramelteon) may have a safety advantage by virtue of their shorter half-life and lower risk of dependency. Patients should be warned of and monitored for the possibility of acute confusional states/bizarre sleep behaviors associated with hypnotic use. Benzodiazepines can be effective in chronic insomnia but may have significant adverse effects (confusion, sedation, intoxication) and significant risk of dependency. c. Atypical antipsychotics should be avoided due to potential adverse effects but may be of value when agitation or other symptoms are severe. d. If nightmares remain severe, consider adjunctive treatment with prazosin [B] e. If symptoms persist or worsen, refer for evaluation and treatment of insomnia	B, None	Reviewed, Deleted	
I	3	B	Recommend pain assessment using a '0 to 10' scale.	None	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	3	B	Obtain a thorough biopsychosocial history and assess for other medical and psychiatric problems, including risk assessment for suicidal and homicidal ideation and misuse of substances, such as drugs or alcohol and over-the-counter and prescription drugs or narcotics.	None	Not reviewed, Deleted	
I	3	B	Assessment should include questions about the nature of the pain and likely etiology (i.e., musculoskeletal and neuropathic), locations, quality, quantity, triggers, intensity, and duration of the pain, as well as aggravating and relieving factors.	None	Not reviewed, Deleted	
I	3	B	Assessment should include evaluation of the impact of pain on function and activities, pain-related disability, or interference with daily activities.	None	Not reviewed, Deleted	
I	3	B	Assessment should include the identification of avoidance behaviors that contribute to emotional distress and/or impaired functioning.	None	Not reviewed, Amended	Recommendation 4
I	3	B	Management of pain should be multidisciplinary, addressing the physical, social, psychological, and spiritual components of pain in an individualized treatment plan that is tailored to the type of pain. [C]	C	Reviewed, Deleted	
I	3	B	Selection of treatment options should balance the benefits of pain control with possible adverse effects (especially sedating medications) on the individual's ability to participate in, and benefit from, PTSD treatment. [I]	I	Not reviewed, Deleted	
I	3	B	Musculoskeletal pain syndromes can respond to correcting the underlying condition and treatment with non-steroidal anti-inflammatory drugs (NSAIDs).	None	Not reviewed, Deleted	
I	3	B	When appropriate, recommend use of non-pharmacological modalities for pain control, such as biofeedback, massage, imaging therapy, physical therapy, and complementary alternative modalities (yoga, meditation, acupuncture). [C]	C	Not reviewed, Deleted	
I	3	B	Centrally acting medications should be used in caution in patients with PTSD, as they may cause confusion and deterioration of cognitive performance and interfere with the recovery process. a. If required, lower doses of opioid therapy or other centrally acting analgesics should be used for short duration with transition to the use of NSAIDs. [C]	C	Not reviewed, Deleted	

2010 Module	2010 Section	2010 Number	2010 Recommendation Text	2010 Grade	Category	2017 Recommendation
I	3	B	Consider offering Cognitive Behavioral Therapy, which may include: a. Encouraging increasing activity by setting goals b. Correcting false and unrealistic beliefs/concerns about pain c. Teaching cognitive and behavioral coping skills (e.g., activity pacing) d. Practicing and consolidation of coping skills and reinforcement of use	None	Not reviewed, Deleted	
I	3	C	Assess the nature of symptoms, severity, and dangerousness. Consider using standardized Anger Scales, such as Spielberger's State-Trait Anger Expression Inventory, to quantify.	None	Not reviewed, Deleted	
I	3	C	Explore for cause of symptoms and follow-up to monitor change.	None	Not reviewed, Deleted	
I	3	C	Consider referral to specialty care for counseling or for marital or family counseling as indicated. Offer referral for: a. Anger Management therapy b. Training in exercise and relaxation techniques	None	Not reviewed, Deleted	
I	3	C	Promote participation in enjoyable activities - especially with family/ loved ones.	None	Not reviewed, Deleted	
I	3	C	Promote sleep and relaxation.	None	Not reviewed, Deleted	
I	3	C	Avoid stimulants and other substances (caffeine, alcohol).	None	Not reviewed, Deleted	
I	3	C	Address pain (see pain management).	None	Not reviewed, Deleted	
I	3	C	Avoid benzodiazepines.	None	Reviewed, Amended	Recommendation 20
I	3	C	Consider SSRIs/SNRIs a. If not responding to SSRIs/SNRIs and other non-pharmacological interventions, consider low-dose anti-adrenergics or low-dose atypical antipsychotics (risperidone, quetiapine). b. If not responding or worsening, refer to specialty care.	None	Reviewed, New-replaced	Recommendation 17

Appendix F: Participant List

Nancy C. Bernardy, PhD (Champion) Director, PTSD Mentoring Program Associate Director for Clinical Networking, VA National Center for PTSD Associate Professor of Psychiatry Geisel School of Medicine at Dartmouth White River Jct, VT	**Kathleen M. Chard, PhD** Associate Chief of Staff for Research Director, Trauma Recovery Center Cincinnati VA Medical Center Professor of Psychiatry and Behavioral Neuroscience University of Cincinnati Cincinnati, OH
Lori Davis, MD Associate Chief of Staff for Research and Development Tuscaloosa VA Medical Center Clinical Professor of Psychiatry The University of Alabama at Birmingham Tuscaloosa, AL	**Megan J. Ehret, PharmD, MS, BCPP** Behavioral Health Clinical Pharmacy Specialist Fort Belvoir Community Hospital Fort Belvoir, VA
Bradford Felker, MD Director, Telemental Health Program VA Puget Sound Health Care System Professor, Department of Psychiatry and Behavioral Sciences University of Washington Seattle, WA	**Joel T. Foster, PhD** Maj, USAF, BSC Psychologist Chief, Air Force Deployment Mental Health Defense Health Agency Headquarters Falls Church, VA
Matthew J. Friedman, MD, PhD (Champion) Senior Advisor, VA National Center for PTSD Professor of Psychiatry Geisel School of Medicine at Dartmouth White River Jct, VT	**Jessica Hamblen, PhD** Acting Deputy Executive Director, VA National Center for PTSD Associate Professor, Department of Psychiatry Geisel School of Medicine at Dartmouth White River Jct, VT
Charles W. Hoge, MD (Champion) Senior Scientist, Walter Reed Army Institute of Research Neuropsychiatry Consultant, Office of the Army Surgeon General Attending Psychiatrist, Walter Reed National Military Medical Center Bethesda, MD	**Matthew Jeffreys, MD** Telehealth Psychiatrist VA Texas Valley Coastal Bend Healthcare System Associate Professor of Psychiatry University of Texas Health Science Center San Antonio, TX
Shawn F. Kane, MD, FAAFP, FACSM COL, MC, MFS, DMO Commander, Special Warfare Medical Group (Airborne) Dean, Joint Special Operations Medical Training Center Family Medicine Consultant to The Surgeon General United States Army Special Operations Command Fort Bragg, NC	**Kate McGraw, PhD** Interim Director, Deployment Health Clinical Center Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury Silver Spring, MD

Jeffrey Millegan, MD, MPH, FAPA CDR MC USN Director, Naval Center for Combat & Operational Stress Control Bureau of Medicine and Surgery (M3) San Diego, CA	**Sonya Norman, PhD** Director, PTSD Consultation Program VA National Center for PTSD VA San Diego Healthcare System Professor, University California San Diego School of Medicine San Diego, CA
Mary Jo Pugh, RN, PhD, FACMPH National Quality Assurance Director, VA Epilepsy Centers of Excellence Research Health Scientist, Veterans Evidence-based Research, Dissemination, and Implementation Center Professor, Department of Epidemiology and Biostatistics Co-Director, Research to Advance Community Health (ReACH) Center University of Texas Health Science Center San Antonio, TX	**Sheila A.M. Rauch, PhD, ABPP** Director, Mental Health Research and Program Evaluation Atlanta VAMC Clinical Director, Emory Healthcare Veterans Program Associate Professor of Psychiatry and Behavioral Sciences Emory University School of Medicine Atlanta, GA
David S. Riggs, PhD (Champion) Professor and Chair, Department of Medical and Clinical Psychology Executive Director, Center for Deployment Psychology Uniformed Services University of the Health Sciences Bethesda, MD	**Todd P. Semla, MS, PharmD, BCPS, FCCP, AGSF** National PBM Clinical Pharmacy Program Manager Mental Health & Geriatrics National Pharmacy Benefits Management Services US Department of Veterans Affairs Feinberg School of Medicine Northwestern University Chicago, IL
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Lisa A. Teegarden, PsyD COL, MS, USA Director for Behavioral Health Walter Reed National Military Medical Center Bethesda, MD	**Meena Vythilingam, MD** CDR, USPHS Deputy Director of Psychological Health Head Quarters Marine Corps, Health Services Arlington, VA
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Appendix G: Literature Review Search Terms and Strategy

A. Topic-specific Search Terms

The search strategies employed combinations of free-text keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. Strategies for each bibliographic database follow this table.

EMTREE, Medical Subject Headings (MeSH), PsycInfo, and Keywords

Concept	Controlled Vocabulary	Keywords
Acute Stress Disorders/Reactions & PTSD	**Embase (EMTREE)** 'acute stress disorder'/de 'posttraumatic stress disorder'/de **Medline (MeSH)** Combat Disorders/ Stress Disorders, Post-Traumatic/ Stress Disorders, Traumatic, Acute/ **PsycINFO** Acute Stress Disorder/ Posttraumatic Stress Disorder/ Stress Reactions/	acute stress disorder* acute stress reaction* "Combat and operational stress reaction" "combat disorder" "combat disorders" "combat fatigue" "combat stress" "post-traumatic neurosis" "post-traumatic psychic" "post-traumatic psychoses" "post-traumatic psychosis" "post-traumatic stress" "post-traumatic syndrome" "post-traumatic syndromes" "posttraumatic neurosis" "posttraumatic psychic" "posttraumatic psychoses" "posttraumatic psychosis" "posttraumatic stress" "posttraumatic syndrome" "posttraumatic syndromes" PTSD "stress disorder" "stress disorders" "trauma syndrome" "trauma syndromes" "traumatic stress" "war neuroses" "war neurosis"

Concept	Controlled Vocabulary	Keywords
Biological Treatments	**Embase (EMTREE)** 'electroconvulsive therapy'/de 'hyperbaric oxygen'/de 'stellate ganglion block'/de 'transcranial magnetic stimulation'/de **Medline (MeSH)** Electroconvulsive Therapy/ Hyperbaric Oxygenation/ Transcranial Magnetic Stimulation/ **PsycINFO** Electroconvulsive Shock Therapy/ Transcranial Magnetic Stimulation/	convulsive therapy ECS ECT electric shock therapy electroconvulsive therapy electroconvulsant therapy electroconvulsive shock therapy electroconvulsive treatment electroshock therapy electroshock treatment “high pressure o” “high pressure oxygen” hyperbaric medicine hyperbaric o2 hyperbaric oxygen therapy hyperbaric oxygenation hyperbaric oxygen shock therapy stellate ganglion block stellate ganglion blockade stellate ganglion blocking rTMS TMS transcranial magnetic stimulation

Concept	Controlled Vocabulary	Keywords
CAM	**Embase (EMTREE)** 'acupuncture'/exp 'alternative medicine'/exp 'animal assisted therapy'/exp 'art therapy'/de 'dance therapy'/de 'diet supplementation'/de 'exercise'/exp 'herbal medicine'/de 'homeopathic agent'/de 'integrative medicine'/de 'meditation'/de 'mindfulness'/de 'music therapy'/de 'phytotherapy'/de 'Psychodrama'/de 'recreational therapy'/de 'Tai Chi'/de 'transcendental meditation'/de 'yoga'/de **Medline (MeSH)** Acupuncture/ Acupuncture Therapy/ Animal Assisted Therapy/ Art Therapy/ Dance Therapy/ Dietary Supplements/ exp Exercise/ Herbal Medicine/ Homeopathy/ Integrative Medicine/ Meditation/ exp Mind-Body Therapies/ Music Therapy/ Plants, Medicinal/ Psychodrama/ Recreation Therapy/ Relaxation/ Relaxation Therapy/ Tai Ji/ yoga/ **PsycINFO** Acupuncture/ exp Alternative Medicine/ Art Therapy/ Animal Assisted Therapy/ exp Creative Arts Therapy/ Dietary Supplements/ exp Exercise/	acupuncture alternative medicine animal-assisted therapy art therapy complementary medicine creative arts therapy dance therapy dietary supplements drama therapy exercise fishing herbs herbal Homeopath* integrative medicine mantram meditation mind-body mindfulness Movement Therapy music therapy phytotherapy progressive muscle relaxation Psychodrama recreational therapy relaxation Tai Chi Tai Ji yoga

Concept	Controlled Vocabulary	Keywords
	Holistic Health/ Martial Arts/ exp "medicinal herbs and plants"/ Mind Body Therapy/ Mindfulness/ Meditation/ Movement Therapy/ Music Therapy/ Progressive Relaxation Therapy/ Psychodrama/ Recreation Therapy/ Relaxation/ Relaxation Therapy/ Yoga/	
Collaborative Care	**Embase (EMTREE)** 'integrated health care system'/de **Medline (MeSH)** Delivery of Health Care, Integrated/	CALM Care management Collaborative care Collaborative mental health "Coordinated Anxiety Learning and Management" Coordinated care Embedded behavioral health IMPACT Integrated mental health Mental health integration PCMHI "Primary Care Mental Health Integration" "Re-Engineering Systems of Primary Care Treatment in the Military" "re-engineering systems for the primary care treatment of PTSD" "RESPECT MIL" "RESPECT PTSD" Stepped care "Stepped Enhancement of PTSD Services Using Primary Care" "STEPS UP" TIDES "Translating Initiatives for Depression into Effective Solutions"

Concept	Controlled Vocabulary	Keywords
Group / Peer Support	**Embase (EMTREE)** 'group therapy'/de 'peer group'/de 'social support'/de **Medline (MeSH)** Exp Peer Group/ Exp Psychotherapy, Group/ Exp Self-Help Groups/ Social Support/ **PsycINFO** Exp Encounter Group Therapy/ Group Counseling/ Group Intervention/ Exp Group Psychotherapy/ Peer Counseling/ Peer Relations/ Peers/ Social Group Work/ Social Support/ Support Groups/ Supportive Psychotherapy/	community therapy community treatment encounter group group psychotherapy Group setting Group therapy group treatment peer group Peer support Self-help Support group Supportive Psychotherapy Supportive therapy
Pharmacotherapy – Alpha Adrenergic Antagonists	**Embase (EMTREE)** 'alpha adrenergic receptor blocking agent'/mj **Medline (MeSH)** exp Adrenergic alpha-Antagonists/ Doxazosin/ Prazosin/ Sympatholytics/ **PsycINFO** Adrenergic Blocking Drugs/	adrenergic alpha-Antagonist* adrenergic receptor block* alpha adrenergic antagonist* alpha block* antiadrenergic* doxazosin prazosin sympatholytic* terazosin

Concept	Controlled Vocabulary	Keywords
Pharmacotherapy – Antidepressants	**Embase (EMTREE)** 'antidepressant agent'/exp/mj 'serotonin noradrenalin reuptake inhibitor'/exp/mj 'serotonin uptake inhibitor'/exp/mj 'tricyclic antidepressant agent'/exp/mj 'triple reuptake inhibitor'/exp/mj **Medline (MeSH)** amitriptyline/ amoxapine/ exp Antidepressive Agents/ Antidepressive Agents, Tricyclic/ citalopram/ clomipramine/ desipramine/ Desvenlafaxine Succinate/ doxepin/ Duloxetine Hydrochloride/ fluoxetine/ fluvoxamine/ imipramine/ maprotiline/ nortriptyline/ paroxetine/ protriptyline/ Serotonin and Noradrenaline Reuptake Inhibitors/ exp serotonin uptake inhibitors/ sertraline/ trazodone/ trimipramine/ Venlafaxine Hydrochloride/ Vilazodone Hydrochloride/ **PsycINFO** exp Antidepressant Drugs/ exp Serotonin Norepinephrine Reuptake Inhibitors/ exp Serotonin Reuptake Inhibitors/ exp Tricyclic Antidepressant Drugs/	amitriptyline amoxapine bupropion anti-depressant* antidepressant* citalopram clomipramine desipramine desvenlafaxine doxepin duloxetine escitalopram fluoxetine fluvoxamine hydroxizine imipramine levomilnacipran maprotiline milnacipran mirtazapine nefazodone nortriptyline paroxetine protriptyline selective serotonin reuptake inhibitor* serotonin–noradrenaline reuptake inhibitor* Serotonin–norepinephrine reuptake inhibitor* sertraline SNRI* SSRI* trazodone tricyclic antidepressant* trimipramine venlafaxine vilazodone vortioxetine

Concept	Controlled Vocabulary	Keywords
Pharmacotherapy – Antipsychotics	**Embase (EMTREE)** 'neuroleptic agent'/mj **Medline (MeSH)** Antipsychotic Agents/ chlorpromazine/ fluphenazine/ haloperidol/ loxapine/ perphenazine/ pimozide/ thioridazine/ thiothixene/ trifluoperazine/ **PsycINFO** exp Neuroleptic Drugs/	anti-psychotic* antipsychotic* chlorpromazine fluphenazine haloperidol loxapine neuroleptic perphenazine pimozide thioridazine thiothixene trifluoperazine

Concept	Controlled Vocabulary	Keywords
Pharmacotherapy – Atypical antipsychotics	**EMBASE (EMTREE)** 'atypical antipsychotic agent'/de **MEDLINE(MeSH)** Antipsychotic Agents/ aripiprazole/ clozapine/ lurasidone hydrochloride/ paliperidone palmitate/ quetiapine fumarate/ risperidone/ **PsycINFO** aripiprazole/ exp Neuroleptic Drugs/	aripiprazole asenapine atypical antipsychotic* brexpiprazole cariprazine clozapine iloperidone lurasidone olanzapine paliperidone quetiapine risperidone ziprasidone
Pharmacotherapy - Benzodiazepines	**Embase (EMTREE)** 'benzodiazepine derivative'/exp **Medline (MeSH)** alprazolam/ exp benzodiazepines/ Clorazepate Dipotassium/ diazepam/ estazolam/ flurazepam/ lorazepam/ midazolam/ oxazepam/ temazepam/ triazolam/ **PsycINFO** exp Benzodiazepines/	Alprazolam benzodiazepine* benzodiazepinone* chlordiazepoxide clonazepam clorazepate diazepam estazolam flurazepam lorazepam midazolam oxazepam quazepam temazepam triazolam
Pharmacotherapy - Cannabinoids	**Embase (EMTREE)** 'cannabidiol'/de 'cannabinoid'/exp/mj 'cannabis'/de 'dronabinol'/de 'medical cannabis'/de 'tetrahydrocannabinol'/de **Medline (MeSH)** Cannabidiol/ Exp Cannabinoids/ Cannabis/ Dronabinol/ Medical Marijuana/ **PsycINFO** Exp Cannabinoids/ Exp Cannabis/ Marijuana/ Tetrahydrocannabinol/	Cannabidiol Cannabinoid* CBD Dronabinol Marijuana Tetrahydrocannabinol THC

Concept	Controlled Vocabulary	Keywords
Pharmacotherapy - General	**Embase (EMTREE)** 'drug therapy'/de/mj **Medline (MeSH)** Drug Therapy/ dt.fs **PsycINFO** exp Drug Therapy/	drug therap* drug treatment* pharmacological pharmaco-therap* pharmacotherap*
Pharmacotherapy – Monoamine oxidase inhibitor (MAOIs)	**EMBASE (EMTREE)** 'monoamine oxidase inhibitor'/de **MEDLINE (MeSH)** Isocarboxazid/ Monoamine Oxidase Inhibitors/ phenelzine/ selegiline/ tranylcypromine/ **PsycINFO** exp Monoamine Oxidase Inhibitors/	isocarboxazid monoamine oxidase inhibitor* MAO MAOI* "MAO inhibitor" "MAO inhibitors" monoamine oxidase A inhibitor monoamine oxidase B inhibitor phenelzine selegiline tranylcypromine
Pharmacotherapy – Mood Stabilizers	**Embase (EMTREE)** 'anticonvulsive agent'/de **Medline (MeSH)** carbamazepine/ clonidine/ lithium/ pregabalin/ valproic acid/ **PsycINFO** anticonvulsive drugs/ Carbamazepine/ exp Lithium/ Mood Stabilizers/ Valproic Acid/	anticonvuls* carbamazepine divalproex gabapentin lamotrigine lithium mood stabilizer* oxcarbazepine pregabalin tiagabine topiramate valproate valproic acid
Pharmacotherapy - Other	**Medline (MeSH)** ketamine/ propranolol/	Propranolol "D-cycloserine" ketamine

Concept	Controlled Vocabulary	Keywords
Pharmacotherapy - Psychostimulants	**Embase (EMTREE)** '3,4 methylenedioxymethamphetamine'/de 'amphetamine plus dexamphetamine'/de 'amphetamine'/de 'atomoxetine'/de 'dexamphetamine'/de 'dexmethylphenidate'/de 'lisdexamfetamine'/de 'methamphetamine'/de 'methylphenidate'/de 'psychostimulant agent'/exp/mj **Medline (MeSH)** N-Methyl-3,4-methylenedioxyamphetamine/ Exp Amphetamine/ Atomoxetine Hydrochloride/ Dexmethylphenidate Hydrochloride/ Dextroamphetamine/ Methamphetamine/ Methylphenidate/ **PsycINFO** Amphetamine/ Atomoxetine/ cns stimulating drugs/ Dextroamphetamine/ Methamphetamine/ Methylenedioxymethamphetamine/ Methylphenidate/	"3,4-methylenedioxymethamphetamine" Adderall Amphetamine Armodafanil Atomoxetine Dexmethylphenidate Dextroamphetamine Lisdexamphetamine MDMA Methamphetamine Methylphenidate Modafanil Psychostimulant*
Pharmacotherapy - Sedatives	**Embase (EMTREE)** 'hypnotic sedative agent'/exp/mj 'sedative agent'/de/mj **Medline (MeSH)** anti-anxiety agents/ buspirone/ diphenhydramine/ eszopiclone/ guanfacine/ Hypnotics and Sedatives/ **PsycINFO** exp sedatives/	anti-anxiety antianxiety buspirone clonidine diphenhydramine eszopiclone guanfacine hydroxizine hypnotic* ramelteon sedative* suvorexant tasimelteon zaleplon zolpidem zopiclone

Concept	Controlled Vocabulary	Keywords
Pharmacotherapy - Steroids	**Embase (EMTREE)** 'hydrocortisone'/de 'mifepristone'/de 'prasterone'/de 'steroid'/exp/mj **Medline (MeSH)** Exp Dehydroepiandrosterone/ Hydrocortisone/ Mifepristone/ Steroids/ **PsycINFO** Hydrocortisone/ Steroids/	Dehydroepiandrosterone DHEA Hydrocortisone Mifepristone Steroid*

Concept	Controlled Vocabulary	Keywords
Psychotherapy - Brief	**Medline (MeSH)** Psychotherapy, Brief/ **PsycINFO** Brief Psychotherapy/	Brief CBT Brief counsel* Brief intervention* Brief Psychotherap* Brief therap* Brief treatment* Short term CBT Short term counsel* Short term intervention* Short term Psychotherap* Short term therap* Short term treatment* Time limited CBT Time limited counsel* Time limited intervention* Time limited Psychotherap* Time limited therap* Time limited treatment*

Concept	Controlled Vocabulary	Keywords
Psychotherapy - Non-Trauma-focused	**Embase (EMTREE)** 'acceptance and commitment therapy'/mj 'family therapy'/mj 'marital therapy'/mj 'mindfulness'/mj 'psychodynamic psychotherapy'/mj psychotherapy/exp/mj **Medline (MeSH)** Acceptance and Commitment Therapy/ Family Therapy/ exp Mind-Body Therapies/ mindfulness/ Neurolinguistic Programming/ exp psychotherapy/ Psychotherapy, Psychodynamic/ px.fs Relaxation Therapy/ exp Socioenvironmental Therapy/ th.fs **PsycINFO** Acceptance and Commitment Therapy/ Brief Psychotherapy/ exp Cognitive Behavior Therapy/ Cognitive Therapy/ Conjoint Therapy/ Couples Therapy/ Emotion Focused Therapy/ exp Family Therapy/ Interpersonal Psychotherapy/ exp Marriage Counseling/ Meditation/ mindfulness/ Neurolinguistic Programming/ exp Psychoanalysis/ Psychodynamic Psychotherapy/ Psychotherapy/ Relaxation/ exp Relaxation Therapy/	acceptance and commitment therapy behavioral activation couples therapy emotion focused couples therapy family therapy interpersonal therapy IPT marital therapy marriage therapy meditation mindfulness Neurolinguistic programming PCT Present Centered Therapy Problem Solving Therapy Psychoanalysis psychodynamic* psychotherap* relaxation Seeking Safety SIT Socioenvironmental Therapy Stress Inoculation Therapy supportive counseling

Concept	Controlled Vocabulary	Keywords
Psychotherapy – Trauma-focused	**Embase (EMTREE)** 'behavior therapy'/exp 'cognitive therapy'/exp 'narrative therapy'/de 'virtual reality exposure therapy'/de **Medline (MeSH)** exp Cognitive Therapy/ Eye Movement Desensitization Reprocessing/ Virtual Reality Exposure Therapy/ **PsycINFO** exp Behavior Therapy/ exp Cognitive Behavior Therapy/ Cognitive Therapy/ Eclectic Psychotherapy/ exp Exposure Therapy/ Eye Movement Desensitization Therapy/ Virtual Reality/	Accelerated Resolution Therapy ART behavior therapy behaviour therapy BEP-TG brief eclectic psychotherapy CBCT CBT "cognitive behavioral conjoint therapy" cognitive behavioral therapy Cognitive Processing Therapy cognitive therapy Ehlers[tiab] EMDR emotional freedom technique* exposure therapy Eye Movement Desensitization imagery rehearsal therapy Mindfulness based exposure therapy Narrative Therapy Prolonged Exposure Therapy thought field therapy "trauma focused" virtual reality exposure Written Exposure Therapy

Concept	Controlled Vocabulary	Keywords
Technology	**Embase (EMTREE)** 'mobile application'/de 'mobile phone'/exp 'telecommunication'/exp 'teleconference'/de 'teleconsultation'/de 'telehealth'/exp 'telemedicine'/exp 'telephone'/de 'telepsychiatry'/de 'virtual reality'/de **Medline (MeSH)** Exp Cell Phones/ Remote Consultation/ Smartphone/ exp Telemedicine/ exp Telephone/ **PsycINFO** Cellular Phones/ Exp Mobile Devices/ Teleconferencing/ telemedicine/ exp Telephone Systems/ Virtual Reality/	"clinical video teleconferencing" CVT Ehealth e-health mobile device* Mobile phone* Mobile application* Mobile app* Smartphone* Tele-communication* Tele-conferenc* Tele-health* Tele-medicine Tele-monitor* Tele-psych* Telecommunication* Teleconferenc* Teleconsultation* Telehealth* Telemedicine Telemonitor* Telephone Telepsych* telephone care management video conferenc* Video tele-conferencing Video teleconferencing Virtual reality

B. Search Strategies

MEDLINE/PSYCINFO (presented in OVID syntax)

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Pharmacotherapy – General	dt.fs or exp Drug Therapy/ OR (drug* ADJ2 (therap* OR treatment*)).ti,ab. or pharmacological.ti,ab. or pharmaco-therap*.ti,ab. or pharmacotherap*.ti,ab.
3	Pharmacotherapy – Alpha Adrenergic Antagonists	exp Adrenergic alpha-Antagonists/ or Sympatholytics/ or Adrenergic Blocking Drugs/ or Doxazosin/ or Prazosin/ or (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.

Set Number	Concept	Search statement
4	Pharmacotherapy – Antipsychotics	Antipsychotic Agents/ OR chlorpromazine/ OR fluphenazine/ OR haloperidol/ OR loxapine/ OR perphenazine/ OR pimozide/ OR thioridazine/ OR thiothixene/ OR trifluoperazine/ OR exp Neuroleptic Drugs/ OR (anti-psychotic* OR antipsychotic* OR chlorpromazine OR fluphenazine OR haloperidol OR loxapine OR neuroleptic OR perphenazine OR pimozide OR thioridazine OR thiothixene OR trifluoperazine).ti,ab.
5	Pharmacotherapy – Atypical antipsychotics	Antipsychotic Agents/ OR aripiprazole/ OR clozapine/ OR lurasidone hydrochloride/ OR paliperidone palmitate/ OR quetiapine fumarate/ OR risperidone/ OR aripiprazole/ OR exp Neuroleptic Drugs/ OR (aripiprazole OR asenapine OR brexpiprazole OR cariprazine OR clozapine OR iloperidone OR lurasidone OR olanzapine OR paliperidone OR quetiapine OR risperidone OR ziprasidone).ti,ab.
6	Pharmacotherapy – Benzodiazepines	alprazolam/ OR exp benzodiazepines/ OR Clorazepate Dipotassium/ OR diazepam/ OR estazolam/ OR flurazepam/ OR lorazepam/ OR midazolam/ OR oxazepam/ OR temazepam/ OR triazolam/ OR exp Benzodiazepines/ OR (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.
7	Pharmacotherapy – MAOIs	Isocarboxazid/ OR Monoamine Oxidase Inhibitors/ OR phenelzine/ OR selegiline/ OR tranylcypromine/ OR exp Monoamine Oxidase Inhibitors/ OR (monoamine oxidase inhibitor* or ((MAO* OR "monoamine oxidase") ADJ2 inhibitor*) or MAOI* or isocarboxazid OR phenelzine OR selegiline OR tranylcypromine).ti,ab.
8	Pharmacotherapy – Mood Stablizers	carbamazepine/ OR clonidine/ OR lithium/ OR pregabalin/ OR valproic acid/ OR anticonvulsive drugs/ OR Carbamazepine/ OR exp Lithium/ OR Mood Stabilizers/ OR Valproic Acid/ OR (anticonvuls* OR carbamazepine OR divalproex OR gabapentin OR lamotrigine OR lithium OR (mood ADJ2 stabiliz*) OR oxcarbazepine OR pregabalin OR tiagabine OR topiramate OR valproate OR valproic acid).ti,ab.
9	Pharmacotherapy – Sedatives	anti-anxiety agents/ OR buspirone/ OR diphenhydramine/ OR eszopiclone/ OR guanfacine/ OR Hypnotics and Sedatives/ OR exp sedatives/ OR (buspirone OR clonidine 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.
10	Pharmacotherapy – Antidepressants	amitriptyline/ OR amoxapine/ OR exp Antidepressive Agents/ OR Antidepressive Agents, Tricyclic/ OR citalopram/ OR clomipramine/ OR desipramine/ OR Desvenlafaxine Succinate/ OR doxepin/ OR Duloxetine Hydrochloride/ OR fluoxetine/ OR fluvoxamine/ OR imipramine/ OR maprotiline/ OR nortriptyline/ OR paroxetine/ OR protriptyline/ OR Serotonin and Noradrenaline Reuptake Inhibitors/ OR exp serotonin uptake inhibitors/ OR sertraline/ OR trazodone/ OR trimipramine/ OR Venlafaxine Hydrochloride/ OR Vilazodone Hydrochloride/ OR exp Antidepressant Drugs/ OR exp Serotonin Norepinephrine Reuptake Inhibitors/ OR exp Serotonin Reuptake Inhibitors/ OR exp Tricyclic Antidepressant Drugs/ OR (amitriptyline OR amoxapine OR bupropion OR anti-depressant* OR antidepressant* 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 selective serotonin reuptake inhibitor* OR serotonin noradrenaline reuptake inhibitor* OR Serotonin norepinephrine reuptake inhibitor* OR sertraline OR SNRI* OR SSRI* OR trazodone OR tricyclic antidepressant* OR trimipramine OR venlafaxine OR vilazodone OR vortioxetine).ti,ab.
11	Pharmacotherapy – Psychostimulants	*N-Methyl-3,4-methylenedioxyamphetamine/ OR *Amphetamine/ OR *Atomoxetine Hydrochloride/ OR *Dexmethylphenidate Hydrochloride/ OR *Dextroamphetamine/ OR *Methamphetamine/ OR *Methylphenidate/ OR *Amphetamine/ OR *Atomoxetine/ OR *cns stimulating drugs/ OR *Dextroamphetamine/ OR *Methamphetamine/ OR *Methylenedioxymethamphetamine/ OR *Methylphenidate/ OR ("3,4-methylenedioxymethamphetamine" OR Adderall OR Amphetamine OR Armodafanil OR Atomoxetine OR Dexmethylphenidate OR Dextroamphetamine OR Lisdexamphetamine OR MDMA OR Methamphetamine OR Methylphenidate OR Modafanil OR Psychostimulant*).ti,ab.

Set Number	Concept	Search statement
12	Pharmacotherapy – Steroids	exp Dehydroepiandrosterone/ or *Hydrocortisone/ or *Mifepristone/ or *Steroids/ or *Hydrocortisone/ or *Steroids/ or (Dehydroepiandrosterone or DHEA or Hydrocortisone or Mifepristone or Steroid*).ti,ab.
13	Pharmacotherapy – Cannabinoids	*Cannabidiol/ OR Exp Cannabinoids/ OR *Cannabis/ OR *Dronabinol/ OR *Medical Marijuana/ OR Exp Cannabinoids/ OR Exp Cannabis/ OR *Marijuana/ OR *Tetrahydrocannabinol/ OR (Cannabidiol OR Cannabinoid* OR CBD OR Dronabinol OR Marijuana OR Tetrahydrocannabinol OR THC).ti,ab.
14	Pharmacotherapy – Other	ketamine/ OR propranolol/ OR (propranolol OR "D-cycloserine" OR ketamine).ti,ab.
15	Combine Pharmacotherapies	Or/2-14
16	Combine PTSD & Pharmacotherapies	1 and 15
17	English Language	limit 16 to english language
18	Human	limit 17 to human
19	Date	limit 18 to yr="2009 -Current"
20	Humans	limit 19 to humans [Limit not valid in PsycINFO; records were retained]
21	Systematic Reviews	20 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
22	RCTs	20 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
23	Combine Systematic Reviews & RCTs	21 or 22
24	Remove Selected Publication Types	23 not (letter/ or editorial/ or news/ or comment/ or case report or case reports/ or note/ or conference paper/ or (letter or editorial or news or comment or case reports or conference abstract$).pt.)
25	Deduplication	remove duplicates from 24

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Psychotherapy – Trauma-Focused	exp Cognitive Therapy/ OR Eye Movement Desensitization Reprocessing/ OR Virtual Reality Exposure Therapy/ OR exp Behavior Therapy/ OR exp Cognitive Behavior Therapy/ OR Cognitive Therapy/ OR Eclectic Psychotherapy/ OR exp Exposure Therapy/ OR Eye Movement Desensitization Therapy/ OR Virtual Reality/ OR (Accelerated Resolution Therapy OR ART OR (Behavior* ADJ2 therap*) OR (behaviour* ADJ2 therap*) OR BEP-TG OR Brief eclectic psychotherapy OR CBCT OR CBT OR cognitive behavioral conjoint therapy OR cognitive behavioral therapy OR Cognitive Processing Therapy OR (cognitive ADJ2 therap*) OR Ehlers OR EMDR OR emotional freedom OR exposure therapy OR Eye Movement Desensitization OR imagery rehearsal OR Mindfulness OR Narrative Therapy OR Prolonged Exposure Therapy OR thought field therapy OR trauma focused OR virtual reality exposure OR Written Exposure Therapy).ti,ab.

Set Number	Concept	Search statement
3	Psychotherapy – Non-trauma-focused	Acceptance and Commitment Therapy/ OR Family Therapy/ OR exp Mind-Body Therapies/ OR mindfulness/ OR Neurolinguistic Programming/ OR exp psychotherapy/ OR Psychotherapy, Psychodynamic/ OR px.fs OR Relaxation Therapy/ OR exp Socioenvironmental Therapy/ OR th.fs OR Acceptance and Commitment Therapy/ OR Brief Psychotherapy/ OR exp Cognitive Behavior Therapy/ OR Cognitive Therapy/ OR Conjoint Therapy/ OR Couples Therapy/ OR Emotion Focused Therapy/ OR exp Family Therapy/ OR Interpersonal Psychotherapy/ OR exp Marriage Counseling/ OR Meditation/ OR mindfulness/ OR Neurolinguistic Programming/ OR exp Psychoanalysis/ OR Psychodynamic Psychotherapy/ OR Psychotherapy/ OR Relaxation/ OR exp Relaxation Therapy/ OR (acceptance and commitment therapy OR behavioral activation OR couples therapy OR emotion focused couples therapy OR family therapy OR interpersonal therapy OR IPT OR marital therapy OR marriage therapy OR meditation OR mindfulness OR Neurolinguistic programming OR PCT OR Present Centered Therapy OR Problem Solving Therapy OR Psychoanalysis OR psychodynamic* OR psychotherap* OR relaxation OR Seeking Safety OR SIT OR Socioenvironmental Therapy OR Stress Inoculation Therapy OR supportive counseling).ti,ab.
4	Combine Psychotherapies	2 or 3
5	PTSD & Psychotherapies	1 and 4
6	Remove Publication Types & Non-Adult Subjects	5 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
7	Systematic Reviews	6 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
8	RCTs	6 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
9	Combine SRs & RCTs	7 or 8
10	English	limit 9 to english language
11	Date	limit 10 to yr="2009 - 2016"

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Interventions	Electroconvulsive Therapy/ OR Hyperbaric Oxygenation/ OR Transcranial Magnetic Stimulation/ OR Electroconvulsive OR Shock Therapy/ OR Transcranial Magnetic Stimulation/ OR (((convulsive or "electric shock" or electroconvuls* or electroshock or shock) adj2 (therap* or treatment*)) or (ECS or ECT or rTMS or TMS or "transcranial magnetic stimulation") or (("high pressure" or hyperbaric) adj2 (o or oxygen or oxygenation)) or ("stellate ganglion" adj2 block*)).ti,ab.
3	Combine	1 and 2

Set Number	Concept	Search statement
4	Systematic Reviews	3 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
5	RCTs	3 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
6	Combine	4 or 5
7	Remove Selected Publication Types	6 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
8	Deduplication	remove duplicates from 7

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	CAM Interventions – Controlled Vocabulary	Acupuncture/ OR Acupuncture Therapy/ OR Animal Assisted Therapy/ OR Art Therapy/ OR Dance Therapy/ OR Dietary Supplements/ OR exp Exercise/ OR Herbal Medicine/ OR Homeopathy/ OR Integrative Medicine/ OR Meditation/ OR exp Mind-Body Therapies/ OR Music Therapy/ OR Plants, Medicinal/ OR Psychodrama/ OR Recreation Therapy/ OR Relaxation/ OR Relaxation Therapy/ OR Tai Ji/ OR yoga/ OR Acupuncture/ OR exp Alternative Medicine/ OR Art Therapy/ OR Animal Assisted Therapy/ OR exp Creative Arts Therapy/ OR Dietary Supplements/ OR exp Exercise/ OR Holistic Health/ OR Martial Arts/ OR exp "medicinal herbs and plants"/ OR Mind Body Therapy/ OR Mindfulness/ OR Meditation/ OR Movement Therapy/ OR Music Therapy/ OR Progressive Relaxation Therapy/ OR Psychodrama/ OR Recreation Therapy/ OR Relaxation/ OR Relaxation Therapy/ OR Yoga/
3	CAM Interventions – Keywords/ Phrases	Acupuncture.ti,ab. OR (("animal assisted" OR art OR "creative art" OR "creative arts" OR dance OR drama OR movement OR music OR recreational) ADJ2 therap*).ti,ab. OR ((alternative OR complementary OR integrative) ADJ2 medicine).ti,ab. OR (dietary ADJ2 supplement*).ti,ab. OR exercise.ti,ab. OR fishing.ti,ab. OR herbs.ti,ab. OR herbal.ti,ab. OR Homeopath*.ti,ab. OR mantram.ti,ab. OR meditation.ti,ab. OR meditate*.ti,ab. OR mind-body.ti,ab. OR mindfulness.ti,ab. OR phytotherapy.ti,ab. OR "progressive muscle relaxation".ti,ab. OR Psychodrama.ti,ab. OR relaxation.ti,ab. OR "Tai Chi".ti,ab. OR "Tai Ji".ti,ab. OR Yoga.ti,ab.
4	Combine Interventions	2 or 3
5	Combine PTSD & Intervention	1 and 4
6	Systematic Reviews	5 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
7	RCTs	5 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
8	Combine	6 or 7
9	Remove Selected Publication Types	8 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
10	Deduplication	remove duplicates from 9
11	English	limit 10 to english language
12	Human	limit 11 to human
13	Date	limit 12 to yr="2009 - 2016"
14	Humans	limit 13 to humans [Limit not valid in PsycINFO; records were retained]

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Group/Peer Interventions	Exp Peer Group/ OR Exp Psychotherapy, Group/ OR Exp Self-Help Groups/ OR *Social Support/ OR Exp Encounter Group Therapy/ OR *Group Counseling/ OR *Group Intervention/ OR Exp Group Psychotherapy/ OR *Peer Counseling/ OR *Peer Relations/ OR Peers/ OR *Social Group Work/ OR *Social Support/ OR *Support Groups/ OR *Supportive Psychotherapy/ OR ((community OR group* OR peer* OR “self-help” OR support*) ADJ2 (group* OR psychotherap* OR setting OR support* OR therap* OR treatment*)).ti,ab. OR “encounter group”.ti,ab.
3	Combine PTSD & Interventions	1 and 2
4	Systematic Reviews	3 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
5	RCTs	3 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
6	Combine	4 or 5
7	Remove Selected Publication Types	6 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
8	Deduplication	remove duplicates from 7
9	English	limit 8 to english language
10	Human	limit 9 to human
11	Date	limit 10 to yr="2009 - 2016"
12	Humans	limit 11 to humans [Limit not valid in PsycINFO; records were retained]

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Collaborative Care	Delivery of Health Care, Integrated/ OR (“Care management” OR “Collaborative care” OR “Coordinated Anxiety Learning and Management” OR “Coordinated care” OR “Embedded behavioral health” OR “Mental health integration” OR PCMHI OR “Primary Care Mental Health Integration” OR “Re-Engineering Systems of Primary Care Treatment in the Military” OR “re-engineering systems for the primary care treatment of PTSD” OR “RESPECT MIL” OR “RESPECT PTSD” OR “Stepped care” OR “STepped Enhancement of PTSD Services Using Primary Care” OR “STEPS UP” OR TIDES OR “Translating Initiatives for Depression into Effective Solutions”).ti,ab.
3	Combine PTSD & Collaborative Care	1 and 2
4	Systematic Reviews	3 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
5	RCTs	3 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
6	Combine	4 or 5
7	Remove Selected Publication Types	6 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
8	Deduplication	remove duplicates from 7
9	English	limit 8 to english language
10	Human	limit 9 to human
11	Date	limit 10 to yr="2009 - 2016"
12	Humans	limit 11 to humans [Limit not valid in PsycINFO; records were retained]

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Technologies	Exp Cell Phones/ OR Remote Consultation/ OR Smartphone/ OR exp Telemedicine/ OR exp Telephone/ OR Cellular Phones/ OR Exp Mobile Devices/ OR Teleconferencing/ OR telemedicine/ OR exp Telephone Systems/ OR Virtual Reality/ OR ("clinical video teleconferencing" or CVT or Ehealth or "e-health" or (mobile adj2 (application* or app or apps or device* or phone*)) or Smartphone* or Tele-communication* or Tele-conferenc* or Tele-health* or Tele-medicine or Tele-monitor* or Tele-psych* or Telecommunication* or Teleconferenc* or Teleconsultation* or Telehealth* or Telemedicine or Telemonitor* or Telephone or Telepsych* or "telephone care management" or (video adj2 (conferenc* or tele-conferenc* or teleconference*)) or Virtual reality).ti,ab.
3	Combine PTSD & Technologies	1 and 2
4	Systematic Reviews	3 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
5	RCTs	3 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
6	Combine	4 or 5
7	Remove Selected Publication Types	6 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
8	Deduplication	remove duplicates from 7
9	English	limit 8 to english language
10	Human	limit 9 to human
11	Date	limit 10 to yr="2009 - 2016"
12	Humans	limit 11 to humans [Limit not valid in PsycINFO; records were retained]

Set Number	Concept	Search statement
1	PTSD	*Posttraumatic Stress Disorder/ or *Combat Disorders/ or *Stress Disorders, Post-Traumatic/ or *Acute Stress Disorder/ OR *Stress Reactions/ OR * Stress Disorders, Traumatic, Acute/ OR ((combat or war) adj2 (disorder* or fatigue or neuros* stress*)).ti,ab. or (("post-traumatic" or posttraumatic) adj2 (neurosis or psych* or stress* or syndrome*)).ti,ab. or PTSD.ti,ab. or (stress* adj2 (disorder* or reaction*)).ti,ab. or (trauma* adj2 (stress or syndrome*)).ti,ab.
2	Brief	Psychotherapy, Brief/ or Brief Psychotherapy/ or ((brief or "short term" or "time limited") adj2 (CBT or intervention* or psychotherap* or therap* or counsel* or treatment*)).ti,ab.
3	Combine PTSD & Brief	1 and 2

Set Number	Concept	Search statement
4	Remove Publication Types & Non-Adult Subjects	3 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
5	Systematic Reviews	4 and (research synthesis or pooled or systematic review/ or meta analysis/ or meta-analysis/ or ((evidence base$ or methodol$ or systematic or quantitative$ or studies or search$).mp. and (review/ or review.pt. or literature review/)))
6	RCTs	4 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies).de. or placebo$.mp. or random$.ti,ab. or crossover$.mp. or cross over.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (blind$ or mask$ or sham$)).mp. or latin square.mp. or ISRTCN or ACTRN$ or (NCT$ not NCT) or (clinical trials/ and random$.ti,ab.))
7	Combine SRs & RCTs	5 or 6
8	English	limit 7 to english language
9	Human	limit 8 to human
10	Date	limit 9 to yr="2009 - 2016"
11	Humans	limit 10 to humans [Limit not valid in PsycINFO; records were retained]
12	Dedupe	remove duplicates from 11

OVID syntax:

$ or *	=	truncation character (wildcard)
ADJ*n*	=	search terms within a specified number (*n*) of words from each other in any order
/	=	search as a subject heading (note that terms preceded by an asterisk are searched as a major subject headings)
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

Embase/MEDLINE

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	Pharmacotherapy – General	'drug therapy'/exp OR ((drug* OR pharma*) NEAR/2 (therap* OR treatment*)) OR pharmacological OR "pharmaco-therapy" OR "pharmaco-therapies" OR pharmacotherap*
3	Pharmacotherapy – Alpha Adrenergic Antagonists	'alpha adrenergic receptor blocking agent'/mj OR antiadrenergic* OR doxazosin OR prazosin OR terazosin OR ((adrenergic OR alpha*) NEAR/2 (antagonist* OR block*))
4	Pharmacotherapy – Antipsychotics	'neuroleptic agent'/exp OR 'anti psychotic' OR 'anti psychotics' OR antipsychotic* OR chlorpromazine OR fluphenazine OR haloperidol OR loxapine OR neuroleptic OR perphenazine OR pimozide OR thioridazine OR thiothixene OR trifluoperazine
5	Pharmacotherapy – Atypical antipsychotics	'atypical antipsychotic agent'/mj OR aripiprazole OR asenapine OR brexpiprazole OR clozapine OR iloperidone OR lurasidone OR olanzapine OR paliperidone OR quetiapine OR risperidone OR ziprasidone
6	Pharmacotherapy - Benzodiazepines	'benzodiazepine derivative'/mj OR 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
7	Pharmacotherapy - MAOIs	'monoamine oxidase inhibitor'/mj OR ((MAO* OR "monoamine oxidase") NEAR/2 inhibit*) OR isocarboxazid OR monoamine oxidase A inhibitor OR monoamine oxidase B inhibitor OR phenelzine OR selegiline OR tranylcypromine
8	Pharmacotherapy – Mood Stablizers	'anticonvulsive agent'/mj OR anticonvuls* OR carbamazepine OR divalproex OR gabapentin OR lamotrigine OR lithium OR mood stabilizer* OR oxcarbazepine OR pregabalin OR tiagabine OR topiramate OR valproate OR valproic acid
9	Pharmacotherapy - Sedatives	'hypnotic sedative agent'/mj OR 'sedative agent'/mj OR anti-anxiety OR antianxiety OR buspirone OR clonidine OR diphenhydramine OR eszopiclone OR guanfacine OR hydroxizine OR hypnotic* OR ramelteon OR sedative* OR suvorexant OR tasimelteon OR zaleplon OR zolpidem OR zopiclone
10	Pharmacotherapy - Antidepressants	'antidepressant agent'/exp/mj OR 'serotonin noradrenalin reuptake inhibitor'/exp/mj OR 'serotonin uptake inhibitor'/exp/mj OR 'tricyclic antidepressant agent'/exp/mj OR 'triple reuptake inhibitor'/exp/mj OR amitriptyline OR amoxapine OR bupropion OR 'anti-depressant' OR 'anti-depressants' OR antidepressant* 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 'selective serotonin reuptake inhibitor' OR 'selective serotonin reuptake inhibitors' OR 'serotonin noradrenaline reuptake inhibitor' OR 'serotonin noradrenaline reuptake inhibitors' OR 'serotonin norepinephrine reuptake inhibitor' OR 'serotonin norepinephrine reuptake inhibitors' OR sertraline OR snri* OR ssri* OR trazodone OR trimipramine OR venlafaxine OR vilazodone OR vortioxetine OR tricyclic NEAR/2 antidepressant*
11	Pharmacotherapy – Other	propranolol OR "D-cycloserine" OR ketamine
12	Combine Pharmacotherapies	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

Set Number	Concept	Search statement
13	Combine PTSD & Pharmacotherapies	#1 AND #12
14	Systematic Reviews & Meta Analyses	#13 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
15	RCTs	#13 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
16	Systematic Reviews & RCTs	#14 OR #15
17	Humans, English, & Date Limits	#14 OR #15 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
18	Remove Selected Publication Types	#17 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
19	Embase Only Records	#18 AND [embase]/lim NOT [medline]/lim

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	Antipsychotic	Cariprazine:ti,ab
3	Psychostimulants	'3,4 methylenedioxymethamphetamine'/mj OR 'amphetamine plus dexamphetamine'/mj OR 'amphetamine'/mj OR 'atomoxetine'/mj OR 'dexamphetamine'/mj OR 'dexmethylphenidate'/mj OR 'lisdexamfetamine'/mj OR 'methamphetamine'/mj OR 'methylphenidate'/mj OR 'psychostimulant agent'/exp/mj OR "3,4-methylenedioxymethamphetamine":ti,ab OR Adderall:ti,ab OR Amphetamine:ti,ab OR Armodafanil:ti,ab OR Atomoxetine:ti,ab OR Dexmethylphenidate:ti,ab OR Dextroamphetamine:ti,ab OR Lisdexamphetamine:ti,ab OR MDMA:ti,ab OR Methamphetamine:ti,ab OR Methylphenidate:ti,ab OR Modafanil:ti,ab OR Psychostimulant*:ti,ab
4	Steroids	'hydrocortisone'/mj OR 'mifepristone'/mj OR 'prasterone'/mj OR 'steroid'/exp/mj OR Dehydroepiandrosterone:ti,ab OR DHEA:ti,ab OR Hydrocortisone:ti,ab OR Mifepristone:ti,ab OR Steroid*:ti,ab
5	Cannabinoids	'cannabidiol'/mj OR 'cannabinoid'/exp/mj OR 'cannabis'/mj OR 'dronabinol'/mj OR 'medical cannabis'/mj OR 'tetrahydrocannabinol'/mj OR Cannabidiol;ti,ab OR Cannabinoid*:ti,ab OR CBD:ti,ab OR Dronabinol:ti,ab OR Marijuana:ti,ab OR Tetrahydrocannabinol:ti,ab OR THC:ti,ab
6	Other	'cycloserine'/mj OR "D-cycloserine":ti,ab
7	Combine Pharmacotherapies	#2 OR #3 OR #4 OR #5 OR #6
8	Combine PTSD & Pharmacotherapies	#1 AND #7

Set Number	Concept	Search statement
9	Systematic Reviews & Meta Analyses	#8 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
10	RCTs	#8 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
11	Systematic Reviews & RCTs	#9 OR #10
12	Humans, English, & Date Limits	#9 OR #10 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
13	Remove Selected Publication Types	#12 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
14	Embase Only Records	#13 AND [embase]/lim NOT [medline]/lim
15	Remove Non-Adult Abstracts	#14 NOT (adolescen*:ti OR antenatal:ti OR babies:ti OR baby:ti OR birth:ti OR child*:ti OR infan*:ti OR kid:ti OR kids:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR perinatal:ti OR prenatal:ti OR teen*:ti OR toddler*:ti OR young*:ti OR youth*:ti)

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	Brief Therapies	((Brief OR “short term” OR “time limited”) NEAR/2 (CBT OR counsel* OR intervention* OR therap* OR treatment*)):ti,ab
3	Combine PTSD & Brief Interventions	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
5	RCTs	#3 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
6	Combine	#4 OR #5
7	Humans, English, & Date Limits	#6 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
8	Remove Selected Publication Types	#7 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
9	Embase Only Records	#8 AND [embase]/lim NOT [medline]/lim

Set Number	Concept	Search statement
10	Remove Non-Adult Citations	#9 NOT (adolescen*:ti OR antenatal:ti OR babies:ti OR baby:ti OR birth:ti OR child*:ti OR infan*:ti OR kid:ti OR kids:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR perinatal:ti OR prenatal:ti OR teen*:ti OR toddler*:ti OR young*:ti OR youth*:ti)

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	Psychotherapy – Trauma-focused	'behavior therapy'/exp OR 'cognitive therapy'/exp OR 'narrative therapy'/mj OR 'virtual reality exposure therapy'/mj OR 'accelerated resolution therapy':ab,ti OR art:ab,ti OR "behavior therapy":ti,ab OR "behaviour therap":ti,ab OR "behavioral therapy":ti,ab OR "behavioural therapy":ti,ab OR 'bep tg':ab,ti OR cbct:ab,ti OR cbt:ab,ti OR 'cognitive behavioral conjoint therapy':ab,ti OR 'cognitive behavioral therapy':ab,ti OR 'cognitive behavioural therapy':ab,ti OR 'cognitive processing therapy':ab,ti OR 'cognitive therapy':ab,ti OR eclectic:ab,ti OR ehlers:ab,ti OR emdr:ab,ti OR 'emotional freedom':ab,ti OR 'exposure therapy':ab,ti OR 'eye movement desensitization':ab,ti OR 'imagery rehearsal therapy':ab,ti OR 'implosive therapy':ab,ti OR mindfulness:ab,ti OR 'narrative therapy':ab,ti OR 'prolonged exposure therapy':ab,ti OR 'thought field therapy':ab,ti OR 'trauma focused':ab,ti OR 'virtual reality':ab,ti OR 'written exposure therapy':ab,ti
3	Psychotherapy – Non-trauma-focused	'acceptance and commitment therapy'/exp OR 'family therapy'/exp OR 'marital therapy'/exp OR 'mindfulness'/exp OR 'psychodynamic psychotherapy'/exp OR psychotherapy/exp OR "acceptance and commitment therapy":ti,ab OR ACT:ti,ab OR "behavioral activation":ti,ab OR "behavioural activation":ti,ab OR "couples counseling":ti,ab OR "couples therapy":ti,ab OR "emotion focused couples therapy":ti,ab OR "family therapy":ti,ab OR "interpersonal therapy":ti,ab OR IPT:ti,ab OR "marital therapy":ti,ab OR "marriage therapy":ti,ab OR Mindfulness:ti,ab OR "Neurolinguistic programming":ti,ab OR PCT:ti,ab OR "Present Centered Therapy":ti,ab OR "Problem Solving Therapy":ti,ab OR Psychoanalysis:ti,ab OR psychodynamic*:ti,ab OR psychotherap*:ti,ab OR relaxation:ti,ab OR "Seeking Safety":ti,ab OR SIT:ti,ab OR "Socioenvironmental Therapy":ti,ab OR "Stress Inoculation Therapy":ti,ab OR "supportive counseling":ti,ab
4	Combine Psychotherapies	#2 or #3
5	PTSD & Psychotherapies	#1 AND #4
6	Systematic Reviews & Meta Analyses	#5 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
7	RCTs	#5 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
8	Combine	#6 OR #7

Set Number	Concept	Search statement
9	Humans, English, & Date Limits	#8 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
10	Remove Selected Publication Types	#9 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
11	Embase Only Records	#10 AND [embase]/lim NOT [medline]/lim

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	Interventions	'electroconvulsive therapy'/de OR 'hyperbaric oxygen'/de OR 'stellate ganglion block'/de OR 'transcranial magnetic stimulation'/de OR “convulsive therapy”:ti,ab OR ECS:ti,ab OR ECT:ti,ab OR “electric shock therapy”:ti,ab OR “electroconvulsive therapy”:ti,ab OR “electroconvulsant therapy”:ti,ab OR “electroconvulsive shock therapy”:ti,ab OR “electroconvulsive treatment”:ti,ab OR “electroshock therapy”:ti,ab OR “electroshock treatment”:ti,ab OR “high pressure o”:ti,ab OR “high pressure oxygen”:ti,ab OR “hyperbaric medicine”:ti,ab OR “hyperbaric o2”:ti,ab OR “hyperbaric oxygen therapy”:ti,ab OR “hyperbaric oxygenation”:ti,ab OR “hyperbaric oxygen”:ti,ab OR “shock therapy”:ti,ab OR “stellate ganglion block”:ti,ab OR “stellate ganglion blockade”:ti,ab OR “stellate ganglion blocking”:ti,ab OR rTMS:ti,ab OR TMS:ti,ab OR “transcranial magnetic stimulation”:ti,ab
3	Combine	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
5	RCTs	#3 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
6	Combine	#4 or #5
7	Humans, English, & Date Limits	#6 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
8	Remove Selected Publication Types	#7 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
9	Embase Only Records	#8 AND [embase]/lim NOT [medline]/lim

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	CAM Controlled vocabulary	'acupuncture'/exp OR 'alternative medicine'/exp OR 'animal assisted therapy'/exp OR 'art therapy'/de OR 'dance therapy'/de OR 'diet supplementation'/de OR 'exercise'/exp OR 'herbal medicine'/de OR 'homeopathic agent'/de OR 'integrative medicine'/de OR 'meditation'/de OR 'mindfulness'/de OR 'music therapy'/de OR 'phytotherapy'/de OR 'psychodrama'/de OR 'recreational therapy'/de OR 'tai chi'/de OR 'transcendental meditation'/de OR 'yoga'/de
3	CAM Keywords / Phrases	Acupuncture:ti,ab OR (("animal assisted" OR art OR "creative art" OR "creative arts" OR dance OR drama OR movement OR music OR recreational) NEAR/2 therap*):ti,ab OR ((alternative OR complementary OR integrative) NEAR/2 medicine):ti,ab OR (dietary NEAR/2 supplement*):ti,ab OR exercise:ti,ab OR fishing:ti,ab OR herbs:ti,ab OR herbal:ti,ab OR Homeopath*:ti,ab OR mantram:ti,ab OR meditation:ti,ab OR meditate*:ti,ab OR mindbody:ti,ab OR "mind body":ti,ab OR mindfulness:ti,ab OR phytotherapy:ti,ab OR "progressive muscle relaxation":ti,ab OR Psychodrama:ti,ab OR relaxation:ti,ab OR "Tai Chi":ti,ab OR "Tai Ji":ti,ab OR Yoga:ti,ab
4	Combine Interventions	#2 or #3
5	Combine PTSD & Interventions	#1 and #4
6	Systematic Reviews & Meta Analyses	#5 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
7	RCTs	#5 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
8	Combine SRs & RCTs	#6 or #7
9	Humans, English, & Date Limits	#8 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
10	Remove Selected Publication Types	#9 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
11	Remove Out of Scope Ages	#10 NOT (adolescen*:ti OR antenatal:ti OR babies:ti OR baby:ti OR birth:ti OR child*:ti OR infan*:ti OR kid:ti OR kids:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR perinatal:ti OR prenatal:ti OR teen*:ti OR toddler*:ti OR young*:ti OR youth*:ti)
12	Embase Only Records	#11 AND [embase]/lim NOT [medline]/lim

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/de OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti
2	Group/Peer Interventions	'group therapy'/mj OR 'peer group'/mj OR 'social support'/mj OR “community therapy”:ti,ab OR “community treatment”:ti,ab OR “encounter group”:ti,ab OR “group psychotherapy”:ti,ab OR “Group setting”:ti,ab OR “Group therapy”:ti,ab OR “group treatment”:ti,ab OR “peer group”:ti,ab OR “peer groups”:ti,ab OR “Peer support”:ti,ab OR “Self-help”:ti,ab OR “Support group”:ti,ab OR “Support groups”:ti,ab OR “Supportive Psychotherapy”:ti,ab OR “supportive psychotherapies”:ti,ab OR “Supportive therapy”:ti,ab OR “supportive therapies”:ti,ab
3	Combine PTSD & Interventions	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
5	RCTs	#3 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
6	Combine SRs & RCTs	#4 OR #5
7	Humans, English, & Date Limits	#6 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
8	Remove Selected Publication Types	#7 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
9	Embase Only Records	#8 AND [embase]/lim NOT [medline]/lim
10	Remove non-Adult Abstracts	#9 NOT (adolescen*:ti OR antenatal:ti OR babies:ti OR baby:ti OR birth:ti OR child*:ti OR infan*:ti OR kid:ti OR kids:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR perinatal:ti OR prenatal:ti OR teen*:ti OR toddler*:ti OR young*:ti OR youth*:ti)

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti

Set Number	Concept	Search statement
2	Collaborative Care Interventions	'integrated health care system'/mj OR "Care management":ti,ab OR "Collaborative care":ti,ab OR "Coordinated Anxiety Learning and Management":ti,ab OR "Coordinated care":ti,ab OR "Embedded behavioral health":ti,ab OR "Mental health integration":ti,ab OR PCMHI:ti,ab OR "Primary Care Mental Health Integration":ti,ab OR "Re-Engineering Systems of Primary Care Treatment in the Military":ti,ab OR "re-engineering systems for the primary care treatment of PTSD":ti,ab OR "RESPECT MIL":ti,ab OR "RESPECT PTSD":ti,ab OR "Stepped care":ti,ab OR "STepped Enhancement of PTSD Services Using Primary Care":ti,ab OR "STEPS UP":ti,ab OR TIDES:ti,ab OR "Translating Initiatives for Depression into Effective Solutions":ti,ab
3	Combine PTSD & Collaborative Care	#1 AND #2
4	Remove Non-Adult Citations	#3 NOT (adolescen*:ti OR antenatal:ti OR babies:ti OR baby:ti OR birth:ti OR child*:ti OR infan*:ti OR kid:ti OR kids:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR perinatal:ti OR prenatal:ti OR teen*:ti OR toddler*:ti OR young*:ti OR youth*:ti)
5	Systematic Reviews & Meta Analyses	#4 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
6	RCTs	#4 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
7	Combine SRs & RCTs	#5 OR #6
8	Humans, English, & Date Limits	#7 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
9	Remove Selected Publication Types	#8 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
10	Embase Only Records	#9 AND [embase]/lim NOT [medline]/lim

Set Number	Concept	Search statement
1	PTSD	'posttraumatic stress disorder'/mj OR 'acute stress disorder'/mj OR 'acute stress disorder':ab,ti OR 'acute stress disorders':ab,ti OR 'acute stress reaction':ab,ti OR 'acute stress reactions':ab,ti OR 'combat and operational stress reaction':ab,ti OR 'combat disorder':ab,ti OR 'combat disorders':ab,ti OR 'combat fatigue':ab,ti OR 'combat stress':ab,ti OR 'post-traumatic neurosis':ab,ti OR 'post-traumatic neuroses':ab,ti OR 'post-traumatic psychoses':ab,ti OR 'post-traumatic psychosis':ab,ti OR 'post-traumatic stress':ab,ti OR 'post-traumatic syndrome':ab,ti OR 'post-traumatic syndromes':ab,ti OR 'posttraumatic neurosis':ab,ti OR 'posttraumatic neuroses':ab,ti OR 'posttraumatic psychoses':ab,ti OR 'posttraumatic psychosis':ab,ti OR 'posttraumatic stress':ab,ti OR 'posttraumatic syndrome':ab,ti OR 'posttraumatic syndromes':ab,ti OR ptsd:ab,ti OR 'stress disorder':ab,ti OR 'stress disorders':ab,ti OR 'trauma syndrome':ab,ti OR 'trauma syndromes':ab,ti OR 'traumatic stress':ab,ti OR 'war neuroses':ab,ti OR 'war neurosis':ab,ti

Set Number	Concept	Search statement
2	Technologies	'mobile application'/de OR 'mobile phone'/exp OR 'telecommunication'/exp OR 'teleconference'/de OR 'teleconsultation'/de OR 'telehealth'/exp OR 'telemedicine'/exp OR 'telephone'/de OR 'telepsychiatry'/de OR 'virtual reality'/de OR 'clinical video teleconferencing':ab,ti OR cvt:ab,ti OR ehealth:ab,ti OR 'e-health':ab,ti OR smartphone*:ab,ti OR 'tele communication*':ab,ti OR 'tele conferenc*':ab,ti OR 'tele health*':ab,ti OR 'tele medicine':ab,ti OR 'tele monitor*':ab,ti OR 'tele psych*':ab,ti OR telecommunication*:ab,ti OR teleconferenc*:ab,ti OR teleconsultation*:ab,ti OR telehealth*:ab,ti OR telemedicine:ab,ti OR telemonitor*:ab,ti OR telephone:ab,ti OR telepsych*:ab,ti OR 'telephone care management':ab,ti OR (video NEAR/2 (conferenc* OR 'tele conferenc*' OR teleconference*)):ab,ti OR (mobile NEAR/2 (application* OR app OR apps OR device* OR phone*)):ab,ti
3	Combine PTSD & Technologies	#1 AND #2
4	Remove non-Adult Abstracts	#3 NOT (adolescen*:ti OR antenatal:ti OR babies:ti OR baby:ti OR birth:ti OR child*:ti OR infan*:ti OR kid:ti OR kids:ti OR neonat*:ti OR newborn*:ti OR paediatric*:ti OR pediatric*:ti OR perinatal:ti OR prenatal:ti OR teen*:ti OR toddler*:ti OR young*:ti OR youth*:ti)
5	Systematic Reviews & Meta Analyses	#4 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR 'meta analysis'/de OR 'meta analysis (topic)'/de OR 'systematic review'/de OR 'systematic review (topic)'/de OR (systematic* NEAR/2 review*):ab,ti OR metaanaly*:ab,ti OR 'meta analysis':ab,ti OR 'meta analyses':ab,ti OR search*:ab)
6	RCTs	#4 AND ('randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR random*:ab,ti OR nct*)
7	Combine SRs & RCTs	#5 OR #6
8	Humans, English, & Date Limits	#7 AND [humans]/lim AND [english]/lim AND [2009-2016]/py
9	Remove Selected Publication Types	#8 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)
10	Embase Only Records	#9 AND [embase]/lim NOT [medline]/lim

EMBASE.com Syntax:

*	=	truncation character (wildcard)
NEAR/*n*	=	search terms within a specified number (*n*) of words from each other in any order
NEXT/*n*	=	search terms within a specified number (*n*) of words from each other in the order specified
/	=	search as a subject heading
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
mj	=	denotes a term that has been searched as a major subject heading
:de	=	search in the descriptors field (controlled terms and keywords)
:lnk	=	floating subheading
:it,pt.	=	source item or publication type
:ti.	=	limit to title
:ti,ab.	=	limit to title and abstract fields

PUBMED (In-Process, Publisher, PubMed Not Medline)

Set Number	Concept	Search statement
1	PTSD	"acute stress disorder"[tiab] OR "acute stress disorders"[tiab] OR "acute stress reaction"[tiab] OR "acute stress reactions"[tiab] OR "combat and operational stress reaction"[tiab] OR "combat disorder"[tiab] OR "combat disorders"[tiab] OR "combat fatigue"[tiab] OR "combat stress"[tiab] OR "post-traumatic neurosis"[tiab] OR "post-traumatic neuroses"[tiab] OR "post-traumatic psychoses"[tiab] OR "post-traumatic psychosis"[tiab] OR "post-traumatic stress"[tiab] OR "post-traumatic syndrome"[tiab] OR "post-traumatic syndromes"[tiab] OR "posttraumatic neurosis"[tiab] OR "posttraumatic neuroses"[tiab] OR "posttraumatic psychoses"[tiab] OR "posttraumatic psychosis"[tiab] OR "posttraumatic stress"[tiab] OR "posttraumatic syndrome"[tiab] OR "posttraumatic syndromes"[tiab] OR ptsd OR "stress disorder"[tiab] OR "stress disorders"[tiab] OR "trauma syndrome"[tiab] OR "trauma syndromes"[tiab] OR "traumatic stress"[tiab] OR "war neuroses"[tiab] OR "war neurosis"[tiab]
2	Pharmacotherapy – General	((drug*[tiab] OR pharma*[tiab]) AND (therap*[tiab] OR treatment*[tiab])) OR pharmacological[tiab] OR "pharmaco-therapy"[tiab] OR "pharmaco-therapies"[tiab] OR pharmacotherap*[tiab]
3	Pharmacotherapy – Alpha Adrenergic Antagonists	antiadrenergic*[tiab] OR doxazosin[tiab] OR prazosin[tiab] OR sympatholytic*[tiab] OR terazosin[tiab] OR ((adrenergic[tiab] OR alpha*[tiab]) AND (antagonist*[tiab] OR block*[tiab]))
4	Pharmacotherapy – Antipsychotics	"anti psychotic"[tiab] OR "anti psychotics"[tiab] OR antipsychotic*[tiab] OR chlorpromazine[tiab] OR fluphenazine[tiab] OR haloperidol[tiab] OR loxapine[tiab] OR neuroleptic[tiab] OR perphenazine[tiab] OR pimozide[tiab] OR thioridazine[tiab] OR thiothixene[tiab] OR trifluoperazine[tiab]
5	Pharmacotherapy – Atypical antipsychotics	aripiprazole[tiab] OR asenapine[tiab] OR brexpiprazole[tiab] OR clozapine[tiab] OR iloperidone[tiab] OR lurasidone[tiab] OR olanzapine[tiab] OR paliperidone[tiab] OR quetiapine[tiab] OR risperidone[tiab] OR ziprasidone[tiab]
6	Pharmacotherapy - Benzodiazepines	Alprazolam[tiab] OR benzodiazepine*[tiab] OR benzodiazepinone*[tiab] OR chlordiazepoxide[tiab] OR clonazepam[tiab] OR clorazepate[tiab] OR diazepam[tiab] OR estazolam[tiab] OR flurazepam[tiab] OR lorazepam[tiab] OR midazolam[tiab] OR oxazepam[tiab] OR quazepam[tiab] OR temazepam[tiab] OR triazolam[tiab]
7	Pharmacotherapy - MAOIs	((MAO*[tiab] OR "monoamine oxidase" [tiab]) AND inhibit*[tiab]) OR isocarboxazid[tiab] OR monoamine oxidase A inhibitor OR monoamine oxidase B inhibitor[tiab] OR phenelzine[tiab] OR selegiline[tiab] OR tranylcypromine[tiab] OR MAOI*[tiab]
8	Pharmacotherapy – Mood Stablizers	'anticonvulsive agent'/mj OR anticonvuls* OR carbamazepine OR divalproex OR gabapentin OR lamotrigine OR lithium OR mood stabilizer* OR oxcarbazepine OR pregabalin OR tiagabine OR topiramate OR valproate OR valproic acid
9	Pharmacotherapy - Sedatives	buspirone[tiab] OR clonidine[tiab] OR diphenhydramine[tiab] OR eszopiclone[tiab] OR guanfacine[tiab] OR hydroxyzine[tiab] OR hypnotic*[tiab] OR ramelteon[tiab] OR sedative*[tiab] OR suvorexant[tiab] OR tasimelteon[tiab] OR zaleplon[tiab] OR zolpidem[tiab] OR zopiclone[tiab]
10	Pharmacotherapy - Antidepressants	amitriptyline[tiab] OR amoxapine[tiab] OR bupropion[tiab] OR "anti-depressant" [tiab] OR "anti-depressants" [tiab] OR antidepressant*[tiab] OR citalopram[tiab] OR clomipramine[tiab] OR desipramine[tiab] OR desvenlafaxine[tiab] OR doxepin[tiab] OR duloxetine[tiab] OR escitalopram[tiab] OR fluoxetine[tiab] OR fluvoxamine[tiab] OR hydroxizine[tiab] OR imipramine[tiab] OR levomilnacipran[tiab] OR maprotiline[tiab] OR milnacipran[tiab] OR mirtazapine[tiab] OR nefazodone[tiab] OR nortriptyline[tiab] OR paroxetine[tiab] OR protriptyline[tiab] OR "selective serotonin reuptake inhibitor"[tiab] OR "selective serotonin reuptake inhibitors"[tiab] OR "serotonin noradrenaline reuptake inhibitor"[tiab] OR "serotonin noradrenaline reuptake inhibitors"[tiab] OR "serotonin norepinephrine reuptake inhibitor"[tiab] OR "serotonin norepinephrine reuptake inhibitors"[tiab] OR sertraline[tiab] OR snri*[tiab] OR ssri*[tiab] OR trazodone[tiab] OR trimipramine[tiab] OR venlafaxine[tiab] OR vilazodone[tiab] OR vortioxetine[tiab] OR (tricyclic[tiab] AND antidepressant*[tiab])
11	Pharmacotherapy – Other	propranolol[tiab] OR "D-cyclcerine"[tiab] OR ketamine[tiab]

Set Number	Concept	Search statement
12	Combine Pharmacotherapies	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
13	Combine PTSD & Pharmacotherapies	#1 AND #12
14	Systematic Reviews & Meta Analyses	#13 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
15	RCTs	#13 AND (random*[tiab] OR nct*[tiab])
16	Systematic Reviews & RCTs	#14 OR #15
17	In-Process Subsets	(#16 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb]))
18	Limits	Filters activated: Publication date from 2009/01/01 to 2016/12/31, English

Set Number	Concept	Search statement
1	PTSD	"acute stress disorder"[tiab] OR "acute stress disorders"[tiab] OR "acute stress reaction"[tiab] OR "acute stress reactions"[tiab] OR "combat and operational stress reaction"[tiab] OR "combat disorder"[tiab] OR "combat disorders"[tiab] OR "combat fatigue"[tiab] OR "combat stress"[tiab] OR "post-traumatic neurosis"[tiab] OR "post-traumatic neuroses"[tiab] OR "post-traumatic psychoses"[tiab] OR "post-traumatic psychosis"[tiab] OR "post-traumatic stress"[tiab] OR "post-traumatic syndrome"[tiab] OR "post-traumatic syndromes"[tiab] OR "posttraumatic neurosis"[tiab] OR "posttraumatic neuroses"[tiab] OR "posttraumatic psychoses"[tiab] OR "posttraumatic psychosis"[tiab] OR "posttraumatic stress"[tiab] OR "posttraumatic syndrome"[tiab] OR "posttraumatic syndromes"[tiab] OR ptsd OR "stress disorder"[tiab] OR "stress disorders"[tiab] OR "trauma syndrome"[tiab] OR "trauma syndromes"[tiab] OR "traumatic stress"[tiab] OR "war neuroses"[tiab] OR "war neurosis"[tiab]
2	Antipychotic	Cariprazine[tiab]
3	Psychostimulants	"3,4-methylenedioxymethamphetamine"[tiab] OR Adderall[tiab] OR Amphetamine[tiab] OR Armodafanil[tiab] OR Atomoxetine[tiab] OR Dexamphetamine[tiab] OR Dexmethylphenidate[tiab] OR Dextroamphetamine[tiab] OR Lisdexamphetamine[tiab] OR MDMA[tiab] OR Methamphetamine[tiab] OR Methylphenidate[tiab] OR Modafanil[tiab] OR Psychostimulant*[tiab]
4	Steroids	Dehydroepiandrosterone[tiab] OR DHEA[tiab] OR Hydrocortisone[tiab] OR Mifepristone[tiab] OR Steroid*[tiab]
5	Cannabinoids	Cannabidiol[tiab] OR Cannabinoid*[tiab] OR CBD[tiab] OR Dronabinol[tiab] OR Marijuana[tiab] OR Tetrahydrocannabinol[tiab] OR THC[tiab]
6	Other	"D-cycloserine"[tiab]
7	Combine Pharmacotherapies	#2 OR #3 OR #4 OR #5 OR #6
8	Combine PTSD & Pharmacotherapies	#1 And #7
9	Systematic Reviews & Meta Analyses	#8 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
10	RCTs	#8 AND (random*[tiab] OR nct*[tiab])
11	Systematic Reviews & RCTs	#8 OR #10
12	In-Process Subsets	(#11 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb]))
13	Remove Non-Adult Abstracts	#12 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])

Set Number	Concept	Search statement
14	Limits	Filters activated: Publication date from 2009/01/01 to 2016/12/31, English

Set Number	Concept	Search statement
1	PTSD	"acute stress disorder"[tiab] OR "acute stress disorders"[tiab] OR "acute stress reaction"[tiab] OR "acute stress reactions"[tiab] OR "combat and operational stress reaction"[tiab] OR "combat disorder"[tiab] OR "combat disorders"[tiab] OR "combat fatigue"[tiab] OR "combat stress"[tiab] OR "post-traumatic neurosis"[tiab] OR "post-traumatic neuroses"[tiab] OR "post-traumatic psychoses"[tiab] OR "post-traumatic psychosis"[tiab] OR "post-traumatic stress"[tiab] OR "post-traumatic syndrome"[tiab] OR "post-traumatic syndromes"[tiab] OR "posttraumatic neurosis"[tiab] OR "posttraumatic neuroses"[tiab] OR "posttraumatic psychoses"[tiab] OR "posttraumatic psychosis"[tiab] OR "posttraumatic stress"[tiab] OR "posttraumatic syndrome"[tiab] OR "posttraumatic syndromes"[tiab] OR ptsd OR "stress disorder"[tiab] OR "stress disorders"[tiab] OR "trauma syndrome"[tiab] OR "trauma syndromes"[tiab] OR "traumatic stress"[tiab] OR "war neuroses"[tiab] OR "war neurosis"[tiab]
2	Trauma-focused Psychotherapy	Accelerated Resolution Therapy[tiab] OR ART[tiab] OR (Behavior*[tiab] AND therap*[tiab]) OR (behaviour*[tiab] AND therap*[tiab]) OR "BEP-TG"[tiab] OR "Brief eclectic psychotherapy"[tiab] OR CBCT[tiab] OR CBT[tiab] OR "cognitive behavioral conjoint therapy"[tiab] OR "cognitive behavioral therapy"[tiab] OR "Cognitive Processing Therapy"[tiab] OR (cognitive[tiab] AND therap*[tiab]) OR Ehlers[tiab] OR EMDR[tiab] OR "emotional freedom"[tiab] OR (exposure[tiab] AND therap*[tiab]) OR "Eye Movement Desensitization"[tiab] OR "imagery rehearsal"[tiab] OR Mindfulness[tiab] OR "Narrative Therapy"[tiab] OR "Prolonged Exposure Therapy"[tiab] OR "thought field therapy"[tiab] OR "trauma focused"[tiab] OR "virtual reality"[tiab] OR "Written Exposure Therapy"[tiab]
3	Non-trauma-focused Psychotherapy	"acceptance and commitment therapy"[tiab] OR "behavioral activation"[tiab] OR ((couples[tiab] OR family[tiab] OR marriage[tiab] OR marital[tiab]) AND (therap*[tiab] OR counsel*[tiab])) OR "emotion focused"[tiab] OR "interpersonal therapy"[tiab] OR IPT[tiab] OR meditation OR mindfulness OR "Neurolinguistic programming"[tiab] OR PCT[tiab] OR "Present Centered Therapy"[tiab] OR "Problem Solving Therapy"[tiab] OR Psychoanalysis[tiab] OR psychodynamic*[tiab] OR psychotherap*[tiab] OR relaxation[tiab] OR "Seeking Safety"[tiab] OR SIT[tiab] OR "Socioenvironmental Therapy"[tiab] OR "Stress Inoculation Therapy"[tiab] OR "supportive counseling"[tiab]
4	Combine Psychotherapies	#2 OR #3
5	PTSD & Psychotherapies	#1 AND #4
6	Systematic Reviews & Meta Analyses	#5 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
7	RCTs	#5 AND (random*[tiab] OR nct*[tiab])
8	Combine SRs & RCTs	#6 OR #7
9	In-Process Subsets	#8 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
10	Limits	Filters activated: Publication date from 2009/01/01 to 2016/12/31, English
11	Remove Age	#10 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])

Set Number	Concept	Search statement
1	PTSD	"acute stress disorder"[tiab] OR "acute stress disorders"[tiab] OR "acute stress reaction"[tiab] OR "acute stress reactions"[tiab] OR "combat and operational stress reaction"[tiab] OR "combat disorder"[tiab] OR "combat disorders"[tiab] OR "combat fatigue"[tiab] OR "combat stress"[tiab] OR "post-traumatic neurosis"[tiab] OR "post-traumatic neuroses"[tiab] OR "post-traumatic psychoses"[tiab] OR "post-traumatic psychosis"[tiab] OR "post-traumatic stress"[tiab] OR "post-traumatic syndrome"[tiab] OR "post-traumatic syndromes"[tiab] OR "posttraumatic neurosis"[tiab] OR "posttraumatic neuroses"[tiab] OR "posttraumatic psychoses"[tiab] OR "posttraumatic psychosis"[tiab] OR "posttraumatic stress"[tiab] OR "posttraumatic syndrome"[tiab] OR "posttraumatic syndromes"[tiab] OR ptsd OR "stress disorder"[tiab] OR "stress disorders"[tiab] OR "trauma syndrome"[tiab] OR "trauma syndromes"[tiab] OR "traumatic stress"[tiab] OR "war neuroses"[tiab] OR "war neurosis"[tiab]
2	Brief Interventions	((Brief[tiab[OR "short term"[tiab] OR "time limited"[tiab]) AND (CBT[tiab] OR counsel*[tiab] OR intervention*[tiab] OR therap*[tiab] OR treatment*[tiab])
3	Combine PTSD & Brief Interventions	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
5	RCTs	#3 AND (random*[tiab] OR nct*[tiab])
6	Combine SRs & RCTs	#4 OR #5
7	In-Process Subsets	#6 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
8	Remove Age	#7 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])
9	Filters	Filters activated: Publication date from 2009/01/01 to 2016/12/31, English

Set Number	Concept	Search statement
1	PTSD	“acute stress disorder”[tiab] OR “acute stress disorders”[tiab] OR “acute stress reaction”[tiab] OR “acute stress reactions”[tiab] OR “combat and operational stress reaction”[tiab] OR “combat disorder”[tiab] OR “combat disorders”[tiab] OR “combat fatigue”[tiab] OR “combat stress”[tiab] OR “post-traumatic neurosis”[tiab] OR “post-traumatic neuroses”[tiab] OR “post-traumatic psychoses”[tiab] OR “post-traumatic psychosis”[tiab] OR “post-traumatic stress”[tiab] OR “post-traumatic syndrome”[tiab] OR “post-traumatic syndromes”[tiab] OR “posttraumatic neurosis”[tiab] OR “posttraumatic neuroses”[tiab] OR “posttraumatic psychoses”[tiab] OR “posttraumatic psychosis”[tiab] OR “posttraumatic stress”[tiab] OR “posttraumatic syndrome”[tiab] OR “posttraumatic syndromes”[tiab] OR ptsd OR “stress disorder”[tiab] OR “stress disorders”[tiab] OR “trauma syndrome”[tiab] OR “trauma syndromes”[tiab] OR “traumatic stress”[tiab] OR “war neuroses”[tiab] OR “war neurosis”[tiab]
2	Interventions	(((convulsive[tiab] or "electric shock"[tiab] or electroconvuls*[tiab] or electroshock[tiab] or shock[tiab]) AND (therap*[tiab] or treatment*[tiab])) or (ECS[tiab] or ECT[tiab] or rTMS[tiab] or TMS[tiab] or "transcranial magnetic stimulation"[tiab]) or (("high pressure"[tiab] or hyperbaric[tiab]) AND (oxygen[tiab] or oxygenation[tiab])) or ("stellate ganglion"[tiab] AND block*[tiab]))
3	Combine	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR “meta analysis”[tiab] OR “meta analyses”[tiab] OR search*[ab])
5	RCTs	#3 AND (random*[tiab] OR nct*[tiab])
6	Combine SRs & RCTs	#4 OR #5
7	In-Process Subsets	#6 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
8	Limits	Filters activated: Publication date from 2009/01/01 to 2016/12/31, English

Set Number	Concept	Search statement
1	PTSD	“acute stress disorder”[tiab] OR “acute stress disorders”[tiab] OR “acute stress reaction”[tiab] OR “acute stress reactions”[tiab] OR “combat and operational stress reaction”[tiab] OR “combat disorder”[tiab] OR “combat disorders”[tiab] OR “combat fatigue”[tiab] OR “combat stress”[tiab] OR “post-traumatic neurosis”[tiab] OR “post-traumatic neuroses”[tiab] OR “post-traumatic psychoses”[tiab] OR “post-traumatic psychosis”[tiab] OR “post-traumatic stress”[tiab] OR “post-traumatic syndrome”[tiab] OR “post-traumatic syndromes”[tiab] OR “posttraumatic neurosis”[tiab] OR “posttraumatic neuroses”[tiab] OR “posttraumatic psychoses”[tiab] OR “posttraumatic psychosis”[tiab] OR “posttraumatic stress”[tiab] OR “posttraumatic syndrome”[tiab] OR “posttraumatic syndromes”[tiab] OR ptsd OR “stress disorder”[tiab] OR “stress disorders”[tiab] OR “trauma syndrome”[tiab] OR “trauma syndromes”[tiab] OR “traumatic stress”[tiab] OR “war neuroses”[tiab] OR “war neurosis”[tiab]
2	CAM Interventions	Acupuncture[tiab] OR ((“animal assisted”[tiab] OR art[tiab] OR “creative art”[tiab] OR “creative arts”[tiab] OR dance[tiab] OR drama[tiab] OR movement[tiab] OR music[tiab] OR recreational[tiab]) AND therap*[tiab]) OR ((alternative[tiab] OR complementary[tiab] OR integrative[tiab]) AND medicine[tiab]) OR (dietary[tiab] AND supplement*[tiab]) OR exercise[tiab] OR fishing[tiab] OR herbs[tiab] OR herbal[tiab] OR Homeopath*[tiab] OR mantram[tiab] OR meditation[tiab] OR meditate*[tiab] OR mindbody[tiab] OR “mind body”[tiab] OR mindfulness[tiab] OR phytotherapy[tiab] OR “progressive muscle relaxation”[tiab] OR Psychodrama[tiab] OR relaxation[tiab] OR “Tai Chi”[tiab] OR “Tai Ji”[tiab] OR Yoga[tiab]
3	Combine PTSD & CAM Interventions	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR “meta analysis”[tiab] OR “meta analyses”[tiab] OR search*[ab])
5	RCTs	#3 AND (random*[tiab] OR nct*[tiab])

Set Number	Concept	Search statement
6	Combine SRs & RCTs	#4 OR #5
7	In-Process Subsets	#6 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
8	Remove Out of Scope Ages	#7 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])
9	Limits	Filters activated: Publication date from 2009/01/01 to 2016/12/31, English

Set Number	Concept	Search statement
1	PTSD	"acute stress disorder"[tiab] OR "acute stress disorders"[tiab] OR "acute stress reaction"[tiab] OR "acute stress reactions"[tiab] OR "combat and operational stress reaction"[tiab] OR "combat disorder"[tiab] OR "combat disorders"[tiab] OR "combat fatigue"[tiab] OR "combat stress"[tiab] OR "post-traumatic neurosis"[tiab] OR "post-traumatic neuroses"[tiab] OR "post-traumatic psychoses"[tiab] OR "post-traumatic psychosis"[tiab] OR "post-traumatic stress"[tiab] OR "post-traumatic syndrome"[tiab] OR "post-traumatic syndromes"[tiab] OR "posttraumatic neurosis"[tiab] OR "posttraumatic neuroses"[tiab] OR "posttraumatic psychoses"[tiab] OR "posttraumatic psychosis"[tiab] OR "posttraumatic stress"[tiab] OR "posttraumatic syndrome"[tiab] OR "posttraumatic syndromes"[tiab] OR ptsd OR "stress disorder"[tiab] OR "stress disorders"[tiab] OR "trauma syndrome"[tiab] OR "trauma syndromes"[tiab] OR "traumatic stress"[tiab] OR "war neuroses"[tiab] OR "war neurosis"[tiab]
2	Group/Peer Interventions	"community therapy"[tiab] OR "community treatment"[tiab] OR "encounter group"[tiab] OR "group counseling"[tiab] OR "group intervention"[tiab] OR "group psychotherapy"[tiab] OR "Group setting"[tiab] OR "Group therapy"[tiab] OR "group treatment"[tiab] OR "peer counseling"[tiab] OR "peer group"[tiab] OR "peer groups"[tiab] OR "Peer support"[tiab] OR "Self-help"[tiab] OR "social group"[tiab] OR "social support"[tiab] OR "Support group"[tiab] OR "Support groups"[tiab] OR "Supportive Psychotherapy"[tiab] OR "supportive psychotherapies"[tiab] OR "Supportive therapy"[tiab] OR "supportive therapies"[tiab]
3	Combine PTSD & Interventions	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
5	RCTs	#3 AND (random*[tiab] OR nct*[tiab])
6	Combine SRs & RCTs	#4 OR #5
7	Remove Non-Adult Abstracts	#6 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])
8	In-Process Subsets	#7 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
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Set Number	Concept	Search statement
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2	Collaborative Care	"Care management"[tiab] OR "Collaborative care"[tiab] OR "Coordinated Anxiety Learning and Management"[tiab] OR "Coordinated care"[tiab] OR "Embedded behavioral health"[tiab] OR "Mental health integration"[tiab] OR PCMHI[tiab] OR "Primary Care Mental Health Integration"[tiab] OR "Re-Engineering Systems of Primary Care Treatment in the Military"[tiab] OR "re-engineering systems for the primary care treatment of PTSD"[tiab] OR "RESPECT MIL"[tiab] OR "RESPECT PTSD"[tiab] OR "Stepped care"[tiab] OR "STepped Enhancement of PTSD Services Using Primary Care"[tiab] OR "STEPS UP"[tiab] OR TIDES[tiab] OR "Translating Initiatives for Depression into Effective Solutions"[tiab]
3	Combine PTSD & Collaborative Care	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
5	RCTs	#3 AND (random*[tiab] OR nct*[tiab])
6	Combine SRs & RCTs	#4 OR #5
7	Remove Non-Adult Abstracts	#6 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])
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Set Number	Concept	Search statement
2	Technologies	"clinical video teleconferencing"[tiab] OR CVT[tiab] OR Ehealth[tiab] OR "e-health"[tiab] OR Smartphone*[tiab] OR Tele-communication*[tiab] OR Tele-conferenc*[tiab] OR Tele-health*[tiab] OR Tele-medicine[tiab] OR Tele-monitor*[tiab] OR Tele-psych*[tiab] OR Telecommunication*[tiab] OR Teleconferenc*[tiab] OR Teleconsultation*[tiab] OR Telehealth*[tiab] OR Telemedicine[tiab] OR Telemonitor*[tiab] OR Telephone[tiab] OR Telepsych*[tiab] OR "telephone care management"[tiab] OR "virtual reality"[tiab] OR (video[tiab] AND (conferenc*[tiab] OR tele-conferenc*[tiab] OR teleconference*[tiab])) OR (Mobile[tiab] AND (application*[tiab] OR app[tiab] OR apps[tiab] OR device*[tiab] OR phone*[tiab]))
3	Combine PTSD & Technologies	#1 AND #2
4	Systematic Reviews & Meta Analyses	#3 AND (Cochrane[tiab] OR (systematic*[tiab] AND review*[tiab]) OR metaanaly*[tiab] OR "meta analysis"[tiab] OR "meta analyses"[tiab] OR search*[ab])
5	RCTs	#3 AND (random*[tiab] OR nct*[tiab])
6	Combine SRs & RCTs	#4 OR #5
7	Remove Non-Adult Citations	#6 NOT (adolescen*[ti] OR antenatal[ti] OR babies[ti] OR baby[ti] OR birth[ti] OR child*[ti] OR infan*[ti] OR kid[ti] OR kids[ti] OR neonat*[ti] OR newborn*[ti] OR paediatric*[ti] OR pediatric*[ti] OR perinatal[ti] OR prenatal[ti] OR teen*[ti] OR toddler*[ti] OR young*[ti] OR youth*[ti])
8	In-Process Subsets	#7 AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])
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PubMed syntax:

[Mesh] = search as a subject heading

[majr] = search as a major subject heading

* = truncation character (wildcard)

[ti] = limit to title field

[tiab] = limit to title and abstract fields

[tw] = text word

Appendix H: Abbreviation List

Abbreviation	Definition
ACT	Acceptance and Commitment Therapy
AHRQ	Agency for Healthcare Research and Quality
Army STARRS	Army Study to Assess Risk and Resilience in Service Members
ASD	Acute stress disorder
ASR	Acute stress reaction
AUD	Alcohol use disorder
AUDIT-C	Alcohol Use Disorders Identification Test—Consumption
BEP	Brief Eclectic Psychotherapy
CAPS	Clinician-Administered PTSD Scale
CAPS-5	Clinician Administered PTSD Scale for DSM-5
CBCT	Cognitive Behavioral Conjoint Therapy
CBT	Cognitive behavioral therapy
CBT-I	Cognitive Behavioral Therapy for Insomnia
CGIC	Clinical Global Impression of Change Scale
CIH	Complementary and integrative health
CISD	Critical Incident Stress Debriefing
COI	Conflict of interest
COPD	Chronic obstructive pulmonary disorder
COR	Contracting officer's representative
COSR	Combat and Operational Stress Reaction
CPG	Clinical practice guideline
CPT	Cognitive Processing Therapy
CS	Comparative study
DLPFC	Dorsolateral prefrontal cortex
DoD	Department of Defense
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EBPWG	Evidence-Based Practice Work Group
ECT	Electroconvulsive therapy
EMDR	Eye Movement Desensitization and Reprocessing
ERRT	Exposure, Relaxation, and Rescripting Therapy
ES	Effect size
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBOT	Hyperbaric oxygen therapy
HealthVIEWS	Health of Vietnam-Era Women's Study
Hz	Hertz
HIV	Human immunodeficiency virus
iCBT	Internet-based cognitive behavioral therapy
IPT	Interpersonal Psychotherapy

Abbreviation	Definition
IR	Immediate release
IRT	Imagery Rehearsal Therapy
IV	Intravenous
KQ	Key question
LFT	Liver function test
MAOIs	Monoamine oxidase inhibitors
MBSR	Mindfulness-based stress reduction
MDD	Major depressive disorder
mg	Milligram
MI	Myocardial infarction
mTBI	Concussion/mild traumatic brain injury
NCS-R	National Comorbidity Survey-Replication
NESARC	National Epidemiologic Survey on Alcohol and Related Conditions
NET	Narrative Exposure Therapy
NICE	National Institute for Health and Care Excellence
NLP	Neurolinguistic programming
NVVLS	National Vietnam Veterans Longitudinal Study
NVVRS	National Vietnam Veterans Readjustment Study
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OND	Operation New Dawn
OUC	Optimized usual care
PC-PTSD	Primary Care PTSD Screen
PCL	PTSD Checklist
PCL-5	DSM-5 PTSD Checklist
PCL-C	PTSD Checklist – Civilian Version
PCT	Present-centered therapy
PDS	Posttraumatic Diagnostic Scale
PE	Prolonged exposure
PHQ-9	Patient Health Questionnaire-9
PICOTS	Population, intervention, comparison, outcome, timing and setting framework
PSSI-I	Posttraumatic Stress Disorder Symptom Scale Interview for DSM-5
PTSD	Posttraumatic stress disorder
QoL	Quality of life
RCT	Randomized controlled trial
rTMS	Repetitive transcranial magnetic stimulation
SCID-5	Structured Clinical Interview for DSM-5
SDM	Shared decision making
SGA	Second generation antipsychotic
SGB	Stellate ganglion block

Abbreviation	Definition
SIADH	Syndrome of inappropriate anti-diuretic hormone
SIT	Stress Inoculation Training
SNRI	Serotonin norepinephrine reuptake inhibitor
SR	Systematic review
SSRI	Selective serotonin reuptake inhibitor
SUD	Substance use disorder
TBI	Traumatic brain injury
TCA	Tricyclic antidepressant
USPSTF	U.S. Preventive Services Task Force
VA	Department of Veterans Affairs
VNS	Vagal nerve stimulation
VTC	Video-teleconferencing
WTU	Warrior Transition Unit
XR	Extended release

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