

Clinical Guidelines for the Management of PTSD and Acute Stress Disorder

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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
<p>Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:</p> <ol style="list-style-type: none"> 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 <p>Note: In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.</p> <ol style="list-style-type: none"> 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) <p>Note: This does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.</p>
<p>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:</p> <p>Intrusion Symptoms</p> <ol style="list-style-type: none"> 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) <p>Negative Mood</p> <ol style="list-style-type: none"> 5. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, loving feelings) <p>Dissociative Symptoms</p> <ol style="list-style-type: none"> 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) <p>Avoidance Symptoms</p> <ol style="list-style-type: none"> 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) <p>Arousal Symptoms</p> <ol style="list-style-type: none"> 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
<p>Criterion C. Duration of the disturbance (symptoms in Criterion B) is three days to one month after trauma exposure.</p> <p>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.</p>
<p>Criterion D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.</p>
<p>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.</p>

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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
<p>Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:</p> <ol style="list-style-type: none"> 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 <p>Note: In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.</p> <ol style="list-style-type: none"> 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) <p>Note: This does not apply to exposure through electronic media, television, movies or pictures unless this exposure is work-related.</p>

DSM-5 Diagnostic Criteria for PTSD
<p>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.</p> <ol style="list-style-type: none">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)
<p>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:</p> <ol style="list-style-type: none">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)
<p>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:</p> <ol style="list-style-type: none">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 others4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, shame)5. Markedly diminished interest or participation in significant activities6. Feeling of detachment or estrangement from others7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, loving feelings)
<p>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:</p> <ol style="list-style-type: none">1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects2. Reckless or self-destructive behavior3. Hypervigilance4. Exaggerated startle response5. Problems with concentration6. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep)
<p>Criterion F. Duration of the disturbance (symptoms in Criteria B, C, D, and E) is more than one month.</p>
<p>Criterion G. The disturbance causes clinically significant distress or impairment in social, occupation, or other important areas of functioning.</p>

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 individual's 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 Disorder²).
3. Providers should assess and carefully monitor suicide risk (see the VA/DoD CPG for Assessment and Management of Patients at Risk for Suicide³).
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 SUD⁴).
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/mTBI⁵ and VA/DoD CPG for the Management of Chronic Multisymptom Illness⁶ [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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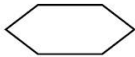

*Additional contributor contact information is available in [Appendix F: Participant List](#).

V. Algorithm

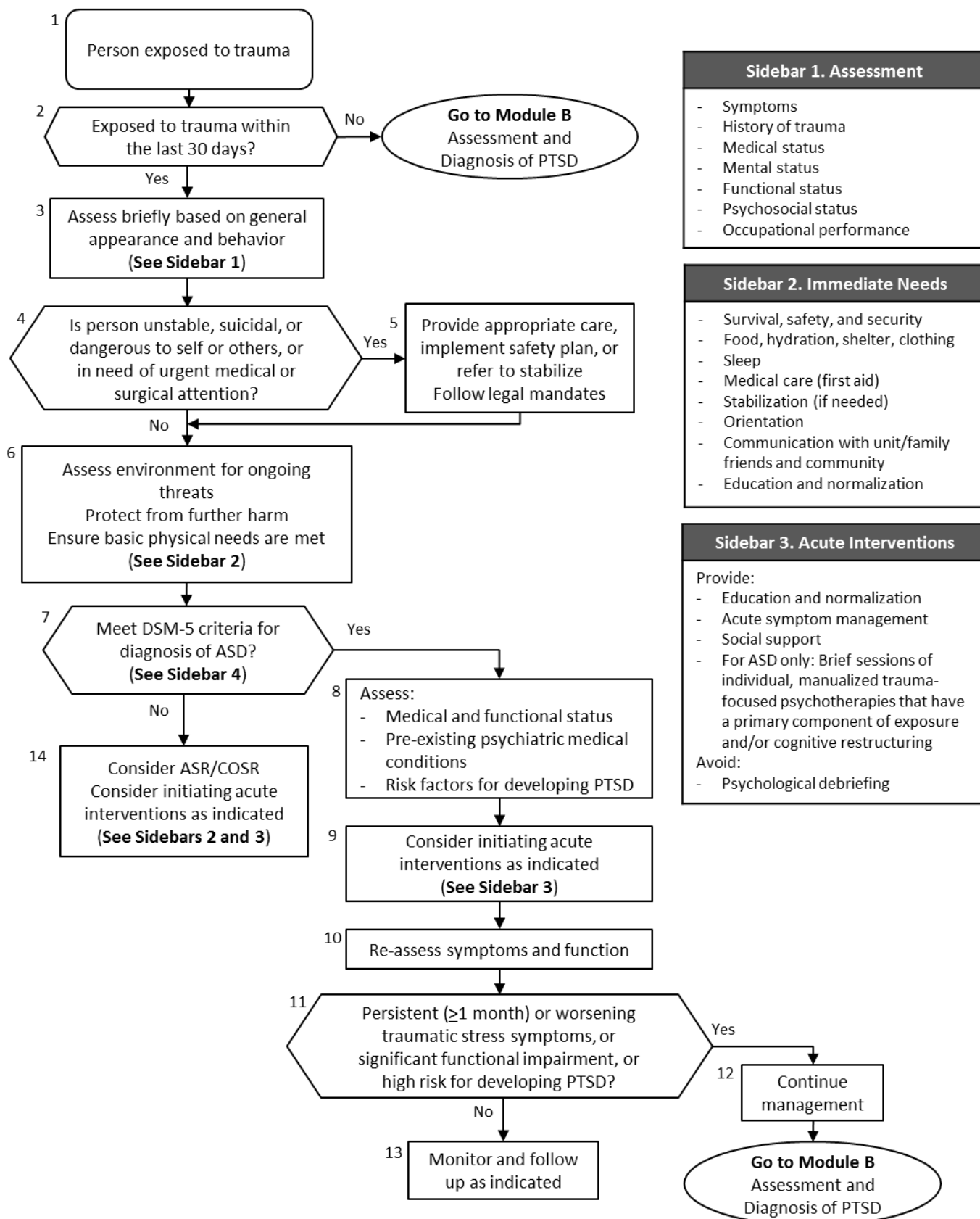
This CPG includes an algorithm that is designed to facilitate understanding of the clinical pathway and decision making process used in management of PTSD. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more 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



Sidebar 1. Assessment

- Symptoms
- History of trauma
- Medical status
- Mental status
- Functional status
- Psychosocial status
- Occupational performance

Sidebar 2. Immediate Needs

- Survival, safety, and security
- Food, hydration, shelter, clothing
- Sleep
- Medical care (first aid)
- Stabilization (if needed)
- Orientation
- Communication with unit/family friends and community
- Education and normalization

Sidebar 3. Acute Interventions

Provide:

- Education and normalization
- Acute symptom management
- Social support
- For ASD only: Brief sessions of individual, manualized trauma-focused psychotherapies that have a primary component of exposure and/or cognitive restructuring

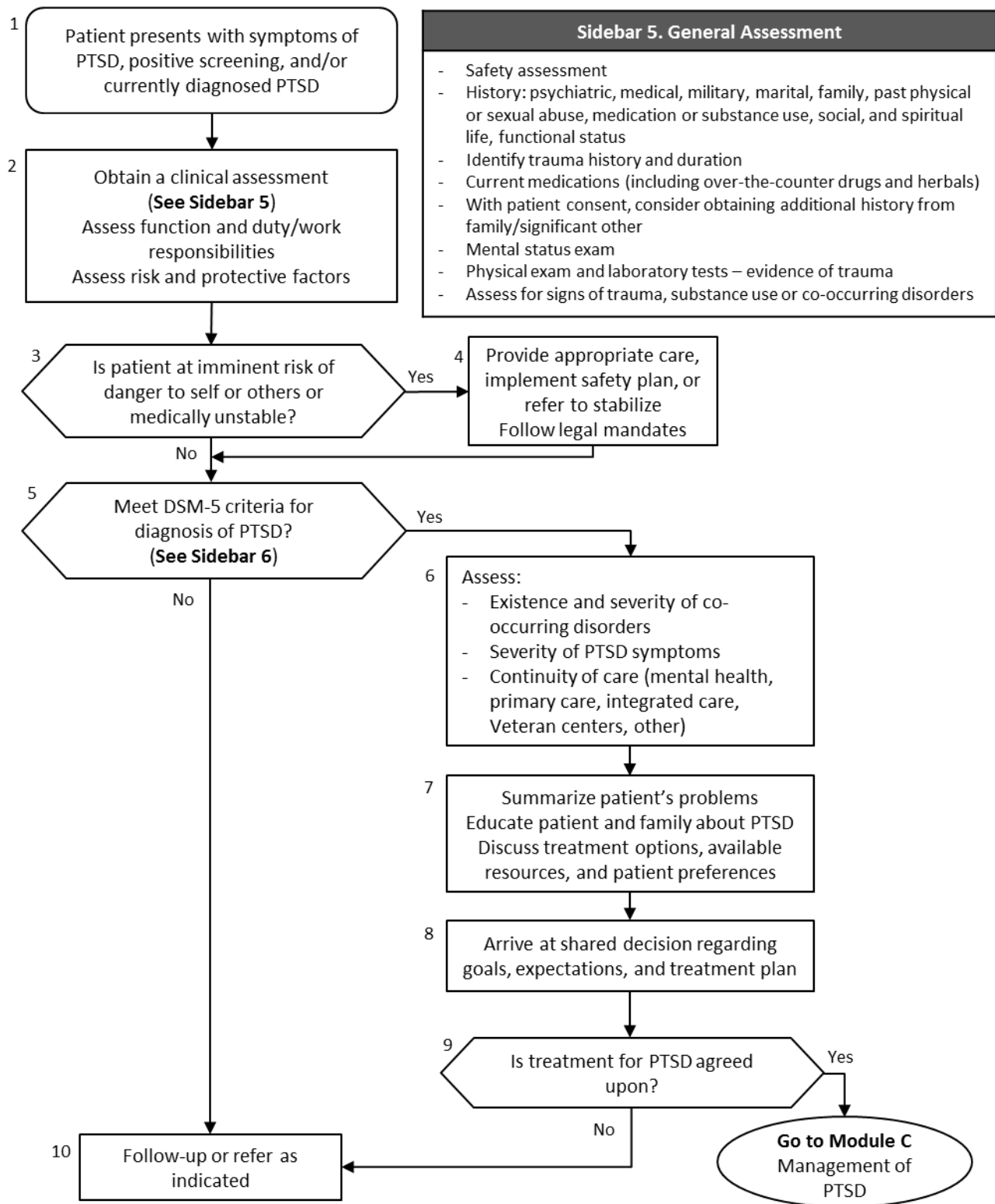
Avoid:

- Psychological debriefing

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	<p>Exposure to actual or threatened death, serious injury or sexual violation in one (or more) of the following way(s):</p> <ol style="list-style-type: none"> 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	<p>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:</p> <p>The traumatic event is persistently re-experienced, in the following way(s):</p> <ol style="list-style-type: none"> 1. Intrusive thoughts 2. Nightmares 3. Flashbacks 4. Emotional distress or physical reactivity after exposure to traumatic reminders <p>Negative mood</p> <ol style="list-style-type: none"> 5. Difficulty experiencing positive affect <p>Dissociative symptoms</p> <ol style="list-style-type: none"> 6. Altered sense of reality 7. Inability to recall key aspects of the trauma <p>Avoidance of trauma-related stimuli after the trauma, in the following way(s):</p> <ol style="list-style-type: none"> 8. Trauma-related thoughts or feelings 9. Trauma-related reminders <p>Arousal symptoms</p> <ol style="list-style-type: none"> 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

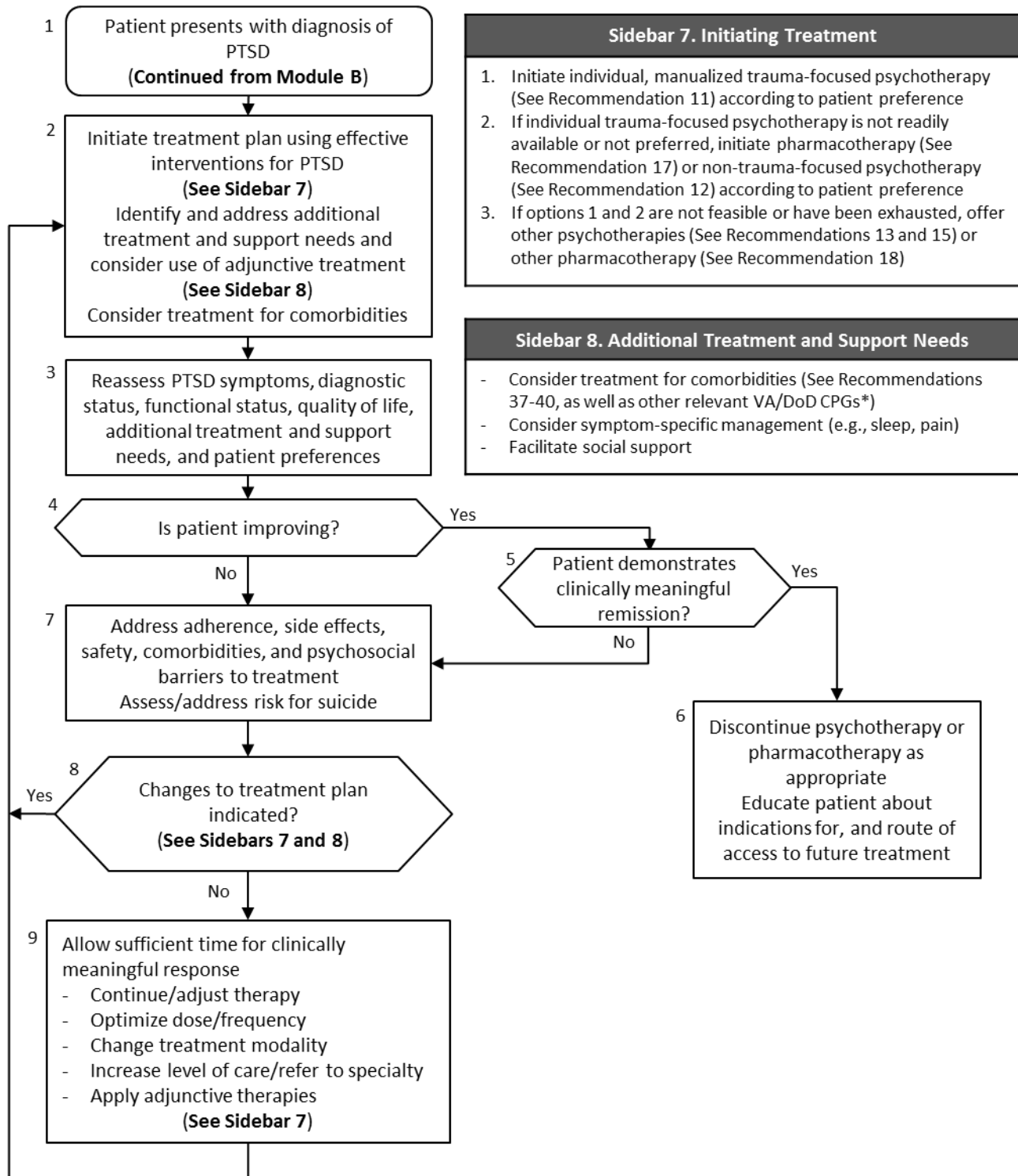
Module B: Assessment and Diagnosis of Posttraumatic Stress Disorder



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): <ol style="list-style-type: none"> 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): <ol style="list-style-type: none"> 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): <ol style="list-style-type: none"> 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): <ol style="list-style-type: none"> 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): <ol style="list-style-type: none"> 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 conferencing (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, Spont 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. Spont 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] Spont 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 of 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 ginkgo 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 conferencing (VTC) modality when PTSD treatment is delivered via VTC.
(Strong For | Reviewed, Amended)

Discussion

An initial study in 2009 demonstrated the non-inferiority of VTC to in-person treatment of anger management in combat Veterans with PTSD.[\[223\]](#) Since then, additional studies have been completed that support the delivery of exposure therapies, anger treatment, and CPT 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 confidentiality and 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

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