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

Department of Veterans Affairs
Department of Defense

QUALIFYING STATEMENTS

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

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

Variations in practice will inevitably and appropriately occur when providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DoD policies. Further, inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 4.0 – 2023

Prepared by

Management of Posttraumatic Stress Disorder and Acute Stress Disorder Work Group

With support from

Office of Quality and Patient Safety, Veterans Health Administration

and

Clinical Quality Improvement Program, Defense Health Agency

Version 4.0 – 2023[a]

Based on evidence reviewed through May 4, 2022

[a] VA/DoD Clinical Practice Guideline. (2023). Management of Posttraumatic Stress Disorder and Acute Stress Disorder Work Group. Washington, DC: U.S. Government Printing Office.

Table of Contents

I. Introduction

The VA and DoD Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the VA/DoD Health Executive Committee "on the use of clinical and epidemiological evidence to improve the health of the population . . ." across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of CPGs for the VA and DoD populations.(1) Development and update of VA/DoD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and wellbeing.

In 2017, VA and DoD published a CPG for Management of Posttraumatic Stress Disorder and Acute Stress Disorder (2017 VA/DoD PTSD CPG), which was based on evidence reviewed through March 2016. Since the release of that CPG, the evidence base on PTSD has expanded. Consequently, the EBPWG initiated the update of the 2017 VA/DoD PTSD CPG in 2022. This updated CPG's use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach reflects a more rigorous application of the methodology than previous iterations.(2) Therefore, the strength of some recommendations might have been modified because of the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

This CPG provides an evidence-based framework for evaluating and managing care for individuals with posttraumatic stress disorder (PTSD) or acute stress disorder (ASD) toward improving clinical outcomes. Successful implementation of this CPG will:

- Assess the patient's condition and collaborate with the patient, family, and caregivers to determine optimal management of patient care;
- Emphasize the use of patient-centered care and shared decision making;
- Minimize preventable complications and morbidity; and
- Optimize individual health outcomes and quality of life (QoL).

II. Background

A. Definition of Traumatic Events

A traumatic event is defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) 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, including (1) transient, non-debilitating symptoms; (2) transient, acute stress response (ASR); (3) acute, time-limited, and clinically significant ASD; and (4) persistent disorder (PTSD) that might become chronic, if untreated.

The DSM-5-TR definition of a traumatic event is the same for both ASD and PTSD, and one can meet the trauma definition with any one of four criteria (see A1–A4 in 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; manmade and natural disasters; accidents; incarceration; exposure to war-zone, urban, and domestic violence), or sexual violence or assault. Criterion A2 is witnessing such events and includes people who directly observe an event but are unharmed. Criterion A3 is indirect exposure, such as learning that a loved one was exposed to or died during a traumatic event. Criterion A3 would be met only if the death were violent or accidental. Criterion A4 applies to exposure to repeated or extreme details of the 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

Acute Stress Reaction is defined by the World Health Organization in ICD-10 as a transient, normal reaction to traumatic stress.[a] Though ASR is not a DSM-5-TR diagnosis, symptoms might be temporarily debilitating. ASR can present with a broad group of physical, mental, behavioral, and emotional symptoms and signs (e.g., confusion; sadness; depression; fatigue; anxiety; social withdrawal; decreased concentration, memory, or both; hyperarousal; dissociation).(3) Onset of stress-related signs and symptoms might be simultaneous or within minutes of the traumatic event or might 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.(4) When symptoms of ASR create social or occupational impairment for greater than 72 hours, a diagnosis of ASD is often warranted, along with evidence-based interventions for this disorder.

Combat and operational stress reaction (COSR) is the military analog of ASR. DoD Instruction 6490.05 defines COSR as "physical, emotional, cognitive, or behavioral reactions, adverse consequences, or psychological injuries of service members who have been exposed to stressful or traumatic events in combat or military operations."[b] COSR might create significant risks to individual and unit safety in combat and operational environments, particularly when active duty Service members are engaged in high-threat situations. Identification of COSR is based on observation of behavior and functioning as well as on clinical assessments because insufficient evidence exists to recommend a specific screening tool. Individuals who experience COSR should receive a comprehensive assessment of their symptoms or behavioral signs to include details about the onset, frequency, course, severity, level of distress, work performance, functional impairment, and safety risks based on the individual's occupational responsibilities. Additionally, the individual should be assessed for medical causes of

[a] https://icd.who.int/browse10/2019/en#/F43.0
[b] https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/649005p.pdf

acute changes in behavior (e.g., traumatic brain injury (TBI), substance use, toxic exposures). Evaluation of active duty Service members with COSR should be informed by collateral information from unit leaders, coworkers, and peers.

Interventions to address COSR emphasize the principles of proximity, immediacy, expectancy, and simplicity. This approach includes actions to promptly restore basic physiology (sleep, nutrition, hydration) while maintaining individuals within their units whenever possible, leveraging peer and command support systems, and reminding the individual and unit leadership that COSRs are common reactions in combat and operational environments that typically resolve promptly with basic supportive interventions.(5) Military policy indicates that active duty Service members with COSR who fail to respond to initial supportive interventions might warrant referral or evacuation, particularly in situations that involve ongoing or worsening threats to the safety of the affected individual or other unit members. Further, suppose ASR/COSR resulting from exposure to trauma continues beyond 3 days with persistent limitations; In that case, evaluating the active duty Service member for the development of ASD or other psychological disorders is necessary.

ASD, a diagnosis defined by DSM-5-TR (see Table 1 for full criteria), can also occur after exposure to a traumatic event. For an individual to meet the criteria for this diagnosis, symptoms must last at least 3 days but less than 1 month after exposure to the traumatic event.

Individuals with ASD must have been exposed to a traumatic stressor (Criteria A1–A4). In addition, they must exhibit at least 9 of 14 possible symptoms nested within five diagnostic clusters shown in Table 1. Symptoms must cause significant distress or functional impairment.

Table 1. DSM-5-TR Diagnostic Criteria for Acute Stress Disorder*(6)

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

DSM-5-TR Diagnostic Criteria for Acute Stress Disorder
Criterion B. Presence of nine (or more) of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal, beginning or worsening after the traumatic event(s) occurred: **Intrusion Symptoms** 1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s). 3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) 4. Intense or prolonged psychological distress or marked physiological reactions in response to internal or external cues that symbolize or resemble an aspect of the traumatic event(s). **Negative Mood** 5. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings). **Dissociative Symptoms** 6. An altered sense of the reality of one's surroundings or oneself (e.g., seeing oneself from another's perspective, being in a daze, time slowing). 7. Inability to remember an important aspect of the event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs). **Avoidance Symptoms** 8. Efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s). 9. Efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s). **Arousal Symptoms** 10. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep). 11. Irritable behavior and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects. 12. Hypervigilance. 13. Problems with concentration. 14. Exaggerated startle response.
Criterion C. Duration of the disturbance (symptoms in Criterion B) is 3 days to 1 month after trauma exposure. **Note:** Symptoms typically begin immediately after the trauma, but persistence for at least 3 days and up to 1 month is needed to meet disorder criteria.
Criterion D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Criterion E. The disturbance is not attributable to the physiological effects of a substance (e.g., medication or alcohol) or another medical condition (e.g., mild traumatic brain injury) and is not better explained by a brief psychotic disorder.

C. Diagnosis of Posttraumatic Stress Disorder

Posttraumatic Stress Disorder 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 have caused significant distress or impairment in social, occupational, or

other important areas of functioning. Table 2 lists the full criteria. Criterion A for PTSD is the same as Criterion A for ASD; however, ASD can be diagnosed only within the first month after the traumatic event. In contrast, PTSD can be diagnosed only when symptoms have persisted for at least one month. Individuals with PTSD must exhibit specific 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 have a delayed expression where full diagnostic criteria are unmet until at least six months after exposure to the traumatic event. PTSD can appear as a sole diagnosis or, more commonly, with another co-occurring DSM-5-TR disorder, such as a substance use disorder (SUD), mood disorder, or anxiety disorder. PTSD is strongly associated with functional difficulties, reduced QoL, and adverse physical health outcomes.

Table 2. DSM-5-TR Diagnostic Criteria for Posttraumatic Stress Disorder*(6)

DSM-5-TR Diagnostic Criteria for PTSD
Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways: 1. Directly experiencing the traumatic event(s). 2. Witnessing, in person, the event(s) as it occurred to others. 3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental. 4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse). **Note:** Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures unless this exposure is work related.
Criterion B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred: 1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s). 3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings) 4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s). 5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
Criterion C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following: 1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s). 2. Avoidance or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

DSM-5-TR Diagnostic Criteria for PTSD
Criterion D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Inability to recall an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs). 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad.", "No one can be trusted,", "The world is completely dangerous,", "My whole nervous system is permanently ruined"). 3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame themself or others. 4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, shame). 5. Markedly diminished interest or participation in significant activities. 6. Feeling of detachment or estrangement from others. 7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
Criterion E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects. 2. Reckless or self-destructive behavior. 3. Hypervigilance. 4. Exaggerated startle response. 5. Problems with concentration. 6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).
Criterion F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.
Criterion G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
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 meet the criteria for posttraumatic stress disorder, 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 or of 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 6 months after the event (although the onset and expression of some symptoms may be immediate).

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 exhibits depersonalization or derealization.
- Also shown in Table 2, **PTSD with delayed expression** is diagnosed if full diagnostic criteria are unmet until at least six months after exposure to the traumatic event.
- **Subthreshold PTSD** (sometimes called **partial PTSD** or **subsyndromal PTSD**) is a diagnosis clinicians use 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-TR diagnosis for such individuals is **Other Specified Trauma and Stress-Related Disorder (309.89)**. However, DSM-5-TR does not include standardized criteria for subthreshold PTSD. Individuals designated as such in one research study might have met different criteria in another study. Furthermore, most participants in the clinical trials cited in this CPG were diagnosed with full rather than subthreshold PTSD. As a result, the Work Group cannot be certain how well the recommendations for the treatment of PTSD apply to individuals with subthreshold PTSD. Providers 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.

D. Epidemiology and Impact

Estimates of the prevalence of PTSD depend on both sample characteristics and study methods. Sample characteristics include the population of the study (e.g., general population, Veterans, active duty Service members; United States (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, service branch, time since deployment, combat exposure, military sexual trauma [MST]), demographic factors (e.g., age, , race, ethnicity), and type and amount of trauma exposure.

a. General Population

The Wave 3 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III) study found a lifetime PTSD prevalence according to DSM-5-TR criteria of 6.1% overall in a sample of more than 36,000 U.S. adults.(7) These participants were surveyed during 2012–2013 as a representative sample that reflected the population based on regional characteristics, age, sex, race, and ethnicity. Lifetime PTSD prevalence was higher in women (8.0%) than in men (4.1%). Past 12-month prevalence was 4.7%, and like lifetime prevalence, more elevated in women (6.1%) than in men
(3.2%). Whites had higher lifetime and current prevalence than Blacks, Asians and

Pacific Islanders, and Hispanics. Whites also had lower lifetime and current prevalence than Native Americans.(8, 9) The differences between Whites versus Blacks and Hispanics were very small (e.g., current PTSD prevalence was 4.8% in Whites and 4.7% in Blacks).

b. Active Duty U.S. Service Members

Several reviews have examined PTSD prevalence estimates among active duty Service members deployed to Iraq, Afghanistan, or both.(10-13) Many of the studies in the reviews, however, are based on data collected relatively early during the wars and might not reflect the changes in the population that have occurred since. Early during the wars, Richardson et al. (2010) reported estimates for current PTSD in U.S. Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) Veterans ranging from 4% to 17%.(13) Kok et al. (2012) reported a weighted post-deployment PTSD prevalence of 13.2% in OEF and OIF infantry units and 6% in the overall population post-deployment.(11) These early data are based on studies that used DSM-IV definitions of PTSD. More recent data from the 2018 Health Related Behavior Survey, a representative survey of active duty Service members, showed that 10.4% of the active component and 9.3% of reserve component active duty Service members report probable PTSD in the past 30 days based on the Primary Care PTSD Screen for DSM-5-TR.(14, 15) Rates of probable PTSD were higher among those serving in the Army, Navy, and Marine Corps compared with the Coast Guard; enlisted active duty Service members and warrant officers compared with junior, mid-grade, and senior officers; women compared with men; older compared with younger active duty Service members; and those who identify as lesbian, gay, or bisexual (LGB) compared with non-LGB peers.(15)

Research reviews show combat is one of the exposures commonly associated with PTSD.(16-18) Additionally, MST is associated with PTSD and other mental health disorders in both men and women.(19-22)

c. Users of Care in the DoD Health Care System

DoD estimates of incidence and prevalence are derived from administrative medical data of active duty Service members who receive care within the DoD direct care system. The data are based on individuals reporting PTSD symptoms and who are assessed or treated for PTSD but might underestimate actual PTSD rates. In 2021, 2.1% of active duty Service members had a PTSD diagnosis.(23) Combat exposure was associated with higher rates of PTSD diagnosis.(24-26) Incidence of PTSD diagnosis was higher in women; however, these sex differences appeared small and were more pronounced before the wars in Iraq and Afghanistan.(25, 27, 28) Rates of PTSD in active duty Service members changed over time, perhaps reflecting in part the changing nature of the conflicts.(27, 28) PTSD incidence increased from 1.2 per 1,000 in 2002 to 12.9 per 1,000 in 2016, with spikes corresponding to increased troop deployments in 2008 and 2012.(28) Following 2016, PTSD incidence decreased until

2018 and increased again from 2018 to 2020.(29) In 2021, annual episode incidence of PTSD (incidence of PTSD among individuals who had no record of PTSD in the 180 days before their diagnosis) among active duty Service members was 1.4%.(23)

d. U.S. Veterans

According to the NESARC-III, which included more than 3,100 Veterans among the total participants, the lifetime prevalence of PTSD among Veterans is 6.9%. Lifetime prevalence in Veterans was higher among women (13.2%) than men (6.2.%). Lifetime prevalence also was higher among Veterans younger than 65 (ages 18–29: 15.3%; ages 30–44: 9.7%; and ages 45–64: 8.6%) than Veterans 65 or older (3.75%). Past-year prevalence of PTSD was higher in women (11.4%) than men (5.2%).(8) In another nationally representative sample of more than 4,000 U.S. Veterans surveyed during 2020–2021, the National Health and Resilience in Veterans Study (NHRVS), the past-month prevalence of PTSD according to DSM-5-TR was 5.0% overall and higher among women (11.2%) than men (4.3%).(30) Lifetime PTSD prevalence was higher in non-Hispanic Blacks (16.7%) and Hispanics (17.8%) relative to non-Hispanic Whites (11.1%), and current PTSD prevalence was higher in non-Hispanic Blacks (10.1%) than in non-Hispanic Whites (5.9%).(31)

e. Veteran Service Era

In the NHRVS sample, both current and lifetime prevalence of PTSD were lower in WWII/Korean War and Vietnam War Veterans relative to Persian Gulf War and OEF/OIF Veterans.(32) For WWII/Korean War, Vietnam War, Persian Gulf War, and OEF/OIF, the current prevalence was 1.6%, 5.0%, 14.4%, and 14.7%, respectively. The lifetime prevalence was 3.2%, 9.7%, 20.9%, and 29.3%, respectively. The estimates are likely affected by differential mortality across cohorts and should be interpreted cautiously. However, despite the lower prevalence of PTSD in older Veterans, these data indicate some Veterans continue to experience PTSD into old age. Other data, less recent than the NHRVS data, suggest a higher prevalence of PTSD in Vietnam Veterans. Approximately 40 years after the Vietnam War, a follow-up of the historic National Vietnam Veterans Readjustment Study, 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-TR (CAPS-5).(33) Prevalence of lifetime war-zone-related PTSD was 17% in men and 15.2% in women.(34) Among theater Veterans, the prevalence of current PTSD from any cause was estimated as 12.2% for men and 8.5% for women.(34) A national survey conducted during 2016–2017 estimated the prevalence of current PTSD in Vietnam Theater Veterans to be even higher (18.2%), but the estimate is not comparable to the NVVLS estimate, which used the CAPS-5 gold-standard interview, because the survey used a brief screening questionnaire.(35) The Health of Vietnam-Era Women's Study examined the prevalence of PTSD in Vietnam-era women Veterans.(36) The prevalence of current PTSD, according to DSM-5-TR, 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. Why the estimates of current and lifetime PTSD are higher in this study than in the NVVLS is unclear, but methodologic differences between studies (e.g., use of clinician interviews in the NVVLS and lay interview in the all-women's study) might account for the difference. One of the most telling findings was that sexual discrimination or harassment, which is not considered war zone exposure, was higher among deployed women and significantly associated with the development of PTSD.

f. Users of Care in the Veterans Health Administration

Estimates of PTSD prevalence are higher among Veterans who use VA health care relative to Veterans in the general population. According to the NHRVS national survey of Veterans, the prevalence of lifetime PTSD was 23.1% in VA users and 7.4% in Veterans who do not use VA.(30) The prevalence of current PTSD was 12.8% in VA users and 3.6% in Veterans who do not use VA.

The VA's Northeast Program Evaluation Center produces an annual data sheet that provides an overview of the PTSD patient population receiving health care in VA. Veterans are defined as meeting a diagnosis of PTSD if they have received at least two visits, or one inpatient/residential stay, with a diagnosis of PTSD in the prior year. Of the 6,087,351 Veterans who used VA health care in fiscal year 2020, 11.1% were diagnosed with PTSD: 11.2% of men and 19.0% of women.(37) Prevalence data in 2020 were much higher among those Veterans who served in Iraq, Afghanistan, or both: 25.6% overall, and 25.7% and 25.5% in men and women, respectively.(38) National data on PTSD prevalence in racial and ethnic minorities and other Veterans subgroups are unavailable, but recent findings show that trans-identifying Veterans are 1.6-1.7 times more likely than cisgender Veterans to have PTSD.(39)

g. Impact

PTSD can affect all aspects of a person's functioning and wellbeing. For example, in the NESARC-III study, PTSD was associated with a greater likelihood of comorbid substance use, mood, anxiety, and personality disorders.(7) PTSD was also associated with greater impairment of functioning. There are specific increased risks of co-occurring depression and SUD (see Patients with Co-occurring Conditions section).(7) In addition, PTSD is associated with poorer perceived physical health, increased morbidity, and greater health care use for physical problems.(40) Findings on mortality are mixed but generally show PTSD is associated with increased overall mortality and mortality because of accidental causes and suicide.(41)

III. Scope of This Guideline

This CPG is based on published clinical evidence and related information available through May 4, 2022. It is intended to provide general guidance on best evidence-based practices (see Appendix A for additional information on the evidence review methodology). Although the CPG is intended to improve the quality of care and clinical

outcomes (see Introduction), it is not intended to define a standard of care (i.e., mandated or strictly required care).

A. Guideline Audience

This CPG is intended for use by providers and others involved in the care of active duty Service members and Veterans with PTSD.

B. Guideline Population

The patient population of interest for this CPG is adults with PTSD or ASD caused by any type of trauma who are eligible for care in VA or DoD health care delivery systems.

IV. Highlighted Features of This Guideline

A. Highlights in this Guideline

The 2023 VA/DoD PTSD CPG reflects a more rigorous application of the GRADE methodology than the 2017 VA/DoD PTSD CPG. This approach has resulted in the exclusion or downgrading of studies included in previous versions of this CPG and has impacted the strength of some recommendations (e.g., *Strong for* downgraded to *Weak for*), despite a similar evidence base. For additional information on GRADE or CPG methodology, see Appendix A.

In the 2017 VA/DoD PTSD CPG, trauma-focused psychotherapies were evaluated as a class that included Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing (EMDR), and Prolonged Exposure (PE). In the 2023 CPG, the evidence on trauma-focused psychotherapies was reviewed for each treatment individually, rather than as a class, for comparison with medications. This review, combined with the more rigorous application of GRADE and accumulated new evidence, resulted in the downgrading of some specific treatments.

Significant changes to the strength of the recommendations include the following.

- Downgrading of some trauma-focused psychotherapies that previously received a *Strong for* recommendation (Brief Eclectic Psychotherapy and Narrative Exposure Therapy [NET] were downgraded to *Neither for nor against* [Recommendation 10], and Ehlers' Cognitive Therapy [CT] for PTSD and written narrative exposure, now called Written Exposure Therapy [WET], was downgraded to *Weak for* [Recommendation 9]).
- Downgrading of some non-trauma-focused psychotherapies that previously received a *Weak for* recommendation (Stress Inoculation Training [SIT] and Interpersonal Psychotherapy [IPT] were downgraded to *Neither for nor against* [Recommendation 10]).

- Downgrading of one medication that previously received a *Strong for* recommendation (Fluoxetine was downgraded to *Neither for nor against* [Recommendation 16]).
- Downgrading of some medications that previously received a *Weak for* recommendation (Nefazodone, phenelzine, and imipramine were downgraded to *Neither for nor against* [Recommendation 16]).
- Adding *Weak for* recommendations for prazosin for nightmares (Recommendation 32) and Mindfulness-Based Stress Reduction® (MBSR) for overall PTSD symptoms (Recommendation 26).

Other changes in the CPG include the following.

- Updated algorithm for screening and treatment of ASD and PTSD
- Greater attention to discussing the generalizability of evidence to subgroups based on sex identity, sexuality, race, ethnicity, age, and other patient characteristics and clearer delineation of complementary, integrative, and alternative health treatment
- Updated recommendations on research needed to strengthen future guidelines

B. Components of This Guideline

This CPG provides clinical practice recommendations for the care of patients with PTSD (see Recommendations). In addition, the Algorithm incorporates the recommendations in the context of the flow of patient care. This CPG also includes Research Priorities, which list areas the Work Group identified as requiring additional research.

To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, a patient summary, and a quick reference guide, which can be found at https://www.healthquality.va.gov/index.asp.

C. Racial and Ethnic Demographic Terminology in This Guideline

Demographic terms referring to an individual's race or ethnicity (e.g., Hispanic, Latino or Latina, Asian, Native American, Black, African American, White, Caucasian) can be ambiguously defined and understood, reflecting diverse geographies, histories, cultures, and experiences. Aligned with the recent Executive Order on Further Advancing Racial Equity and Support for Underserved Communities through the Federal Government,[c] the Work Group used terms such as Black rather than African American and White rather than Caucasian to avoid presumptions about ancestry and to promote inclusivity, clarity, and consistency. However, to represent accurately the evidence on which this CPG is based, the Work Group generally deferred to racial and ethnic terminology as reported in the published SRs, clinical trials, and other studies comprising that evidence

[c] Executive Order on Further Advancing Racial Equity and Support for Underserved Communities Through The Federal Government | The White House

when summarizing or otherwise referring to those studies. Consequently, usage of demographic terms in this CPG might appear inconsistent.

V. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, Defense Health Agency, identified the following four providers to serve as Champions (i.e., leaders) of this CPG's Work Group: Paula Schnurr, PhD, and Jessica Hamblen, PhD, from VA; and Jonathan Wolf, MD, and Marija Kelber, PhD, from DoD.

The Work Group comprised individuals with the following areas of expertise: internal medicine, neurology, nursing, pharmacy, psychiatry, psychology, social work and surgery. Table 3 lists the Work Group and Guideline Development Team members.

This CPG Work Group, led by the Champions, was tasked with

- Determining the scope of the CPG;
- Crafting clinically relevant key questions (KQ) to guide the systematic evidence review;
- Identifying discussion topics for the patient focus group and considering the patient perspective;
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

The Lewin Team, including The Lewin Group, ECRI, Sigma Health Consulting, and Duty First Consulting, was contracted by VA to help develop this CPG.

Table 3. Guideline Work Group and Guideline Development Team

Organization	Names*
Department of Veterans Affairs	**Paula P. Schnurr, PhD (Champion)**
	Jessica L. Hamblen, PhD (Champion)
	Claire Collie, PhD
	Matthew A. Fuller, PharmD, FASHP, BCPP
	Paul E. Holtzheimer, MD, MS
	Ursula Kelly, PhD, APRN, ANP-BC, PMHNP-BC, FAANP, FAAN
	Ariel Lang, PhD, MPH
	Sonya Norman, PhD
	Katie Papke, LMSW, CAADC, CCTP, CHTVSP
	Ismene Petrakis, MD

Organization	Names*
Department of Veterans Affairs (cont.)	Brian Shiner, MD, MPH
	Ilse Wiechers, MD, MPP, MHS
Department of Defense	**Marija Kelber, PhD (Champion)**
	Jonathan Wolf, MD (Champion)
	Rachael Coller, PharmD
	Kate McGraw, PhD
	CAPT Joshua Morganstein, MD
	David Riggs, PhD
VA Evidence Based Practice, Office of Quality and Patient Safety Veterans Health Administration	James Sall, PhD, FNP-BC
	René Sutton, BS, HCA
	Jennifer Ballard-Hernandez, DNP, RN, FNP-BC
Clinical Quality Improvement Program Defense Health Agency	Elaine P. Stuffel, MHA, BSN, RN
	Cynthia F. Villareal, BSN, RN
	Isabella Alvarez, MA, BSN, RN
The Lewin Group	Clifford Goodman, PhD
	Jennifer Weil, PhD
	Erika Beam, MS
	Charlie Zachariades, MSc
	Peter Baroff, BA
	Annie Zhang, BA
ECRI	Jim Reston, PhD, MPH
	Amy Tsou, MD, MSc
	Rebecca Rishar, BA, MLIS
Sigma Health Consulting	Frances M. Murphy, MD, MPH
	James G. Smirniotopoulos, MD
Duty First Consulting	Kate Johnson, BS
	Rachel Piccolino, BA

*Additional contributor contact information is available in Appendix F.

VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the *Guideline for Guidelines*, an internal document of the VA/DoD EBPWG updated in January 2019 that outlines procedures for developing and submitting VA/DoD CPGs.(1) The *Guideline for Guidelines* is available at http://www.healthquality.va.gov/policy/index.asp. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of SR and external review).(42) Appendix A provides a detailed description of the CPG development methodology.

A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see Determining Recommendation Strength and Direction).(43)

1. Confidence in the quality of the evidence
2. Balance of desirable and undesirable outcomes
3. Patient values and preferences
4. Other considerations, as appropriate (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong* or *Weak*). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(43) A *Strong* recommendation generally indicates *High* or *Moderate* confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The manner in which this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice although it is unsupported by clinical evidence and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text as shown in Table 4.

Table 4. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend . . .
Weak for	We suggest . . .
Neither for nor against	There is insufficient evidence to recommend for or against . . .
Weak against	We suggest against . . .
Strong against	We recommend against . . .

That a recommendation's strength (i.e., *Strong* versus *Weak*) is distinct from its clinical importance (e.g., a *Weak* recommendation is evidence based and still important to clinical care) is important to note. The strength of each recommendation is shown in Recommendations.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations; the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making. The confidence in the quality of the evidence is assessed using an objective, systematic approach independent of the clinical topic of interest. Therefore, recommendations on topics for which designing and conducting rigorous studies might be inherently more difficult (e.g., randomized controlled trials [RCT]) are typically supported by lower quality evidence and, in turn, *Weak* recommendations. Recommendations on topics for which rigorous studies can be designed and conducted might more often be *Strong* recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2, 44) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

B. Categorization of Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(45) For example, the U.S. Preventive Services Task Force (USPSTF) has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every five years for either an update or reaffirmation.(46) Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(47, 48) Table 5 lists these categories, which are based on whether the evidence supporting a recommendation was systematically reviewed, the

degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in Recommendation Categorization. The 2023 CPG recommendation categories can be found in Recommendations. Appendix E outlines the 2017 VA/DoD PTSD CPG's recommendation categories.

Table 5. Recommendation Categories and Definitions[a]

Evidence Reviewed	Recommendation Category	Definition
Reviewed[b]	New-added	New recommendation
	New-replaced	Recommendation from previous CPG was carried forward and revised
	Not changed	Recommendation from previous CPG was carried forward but unchanged
	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted
Not Reviewed[c]	Not changed	Recommendation from previous CPG was carried forward but unchanged
	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted

[a] Adapted from the NICE guideline manual (2012)(47) and Garcia et al. (2014)(48)

[b] The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.

[c] The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.

Abbreviation: CPG: clinical practice guideline

C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the *Guideline for Guidelines*.(49) Further, the *Guideline for Guidelines* refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care)(50) as well as to disclosure statements (i.e., standard disclosure form completed at least twice by CPG Work Group members and the guideline development team).(49) The disclosure form inquires regarding relevant financial and intellectual interests or other relationships with, for example, manufacturers of commercial products, providers of commercial services, or other commercial interests. The disclosure form also inquires regarding any other relationships or activities that could be perceived to have influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were subject to random web-

based identification via standard electronic means (e.g., Centers for Medicare & Medicaid Services Open Payments, ProPublica).

Potential COIs were reported to VA and DoD program offices and reviewed with the Champions. VA and DoD program offices and the Champions determined further action as appropriate (e.g., clarify role as Champion or Work Group member, recusing Work Group members from selected relevant deliberations). Disclosure forms are on file with the VA Office of Quality and Patient Safety and are available on request.

D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers.(44, 51) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DoD Leadership arranged a virtual patient focus group on February 23, 2022. The focus group aimed to gain insights into patients with PTSD of potential relevance and incorporate these insights into the CPG, as appropriate. Topics discussed included the patients' priorities, challenges they have experienced, information they have received regarding their care, and impacts of their care on their lives.

The patient focus group comprised a convenience sample of five people. There were three males and two females. All five participants were Veterans who received care from the VA health system. Two participants received care from both VA and DoD health systems. The Work Group acknowledges this convenience sample is not representative of all patients with PTSD within the VA and DoD health care systems and, thus, findings are ungeneralizable and do not comprise evidence. For more information on the patient focus group methods and findings, see Appendix C. The patient focus group participants were provided the opportunity to review the final draft and provide additional feedback.

E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see Drafting and Finalizing the Guideline. Once the Work Group members completed a near-final draft, they identified experts from VA and DoD health care systems and outside organizations generally viewed as experts in the respective field to review it. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

F. Implementation

This CPG and algorithm are designed for adaptation by individual health care providers with respect to unique patient considerations and preferences, local needs, and

resources. The algorithm serves as a tool to prompt providers to consider key decision points in the care for a patient with PTSD. The Work Group submits suggested performance metrics for VA and DoD to use when assessing the implementation of this CPG. Robust implementation is identified in VA and DoD internal implementation plans and policies. Additionally, implementation would entail wide dissemination through publication in the medical literature, online access, educational programs, and, ideally, electronic medical record programming in the form of clinical decision support tools at the point of care.

VII. Approach to Care in the Department of Veterans Affairs and the Department of Defense

A. Patient-Centered Care

Intended to consider patient needs and preferences, guideline recommendations represent a whole/holistic health approach to care that is patient centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities. VA/DoD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs, characteristics, and preferences). This approach aims to treat the particular condition while also optimizing the individual's overall health and wellbeing.

Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence.(52, 53) A whole/holistic health approach (https://www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and wellbeing goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other differences.

B. Shared Decision Making

This CPG encourages providers to practice shared decision making, a process in which providers, patients, and patient care partners (e.g., family, friends, caregivers) consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(54) Shared decision making is emphasized in *Crossing the Quality Chasm,* an Institute of Medicine, now NAM, report in 2001 (55) and is inherent within the whole/holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels or settings of care or both, especially where patient heterogeneity in weighing risks and benefits might exist. VHA and MHS have embraced shared decision making. Providers are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

C. Patients with Co-occurring Conditions

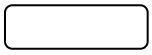
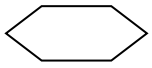
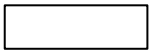
Co-occurring conditions can modify the degree of risk, impact diagnosis, influence patient and provider treatment priorities and clinical decisions, and affect the overall approach to managing PTSD. Many Veterans, active duty Service members, and their families have one or more co-occurring conditions. Because PTSD is sometimes accompanied by co-occurring conditions, managing PTSD collaboratively with other care providers is often best. Some co-occurring conditions might require early specialist consultation to determine necessary changes in treatment or to establish a common understanding of how care will be coordinated. This approach might entail reference to other VA/DoD CPGs (e.g., Suicide Risk, Substance Use Disorder, Major Depressive Disorder).[d]

VIII. Algorithm

This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in managing patients with PTSD. This algorithm format represents a simplified flow of the management of patients with PTSD and helps foster efficient decision making by providers. It includes

- Steps of care in an ordered sequence,
- Decisions to be considered,
- Decision criteria recommended, and
- Actions to be taken.

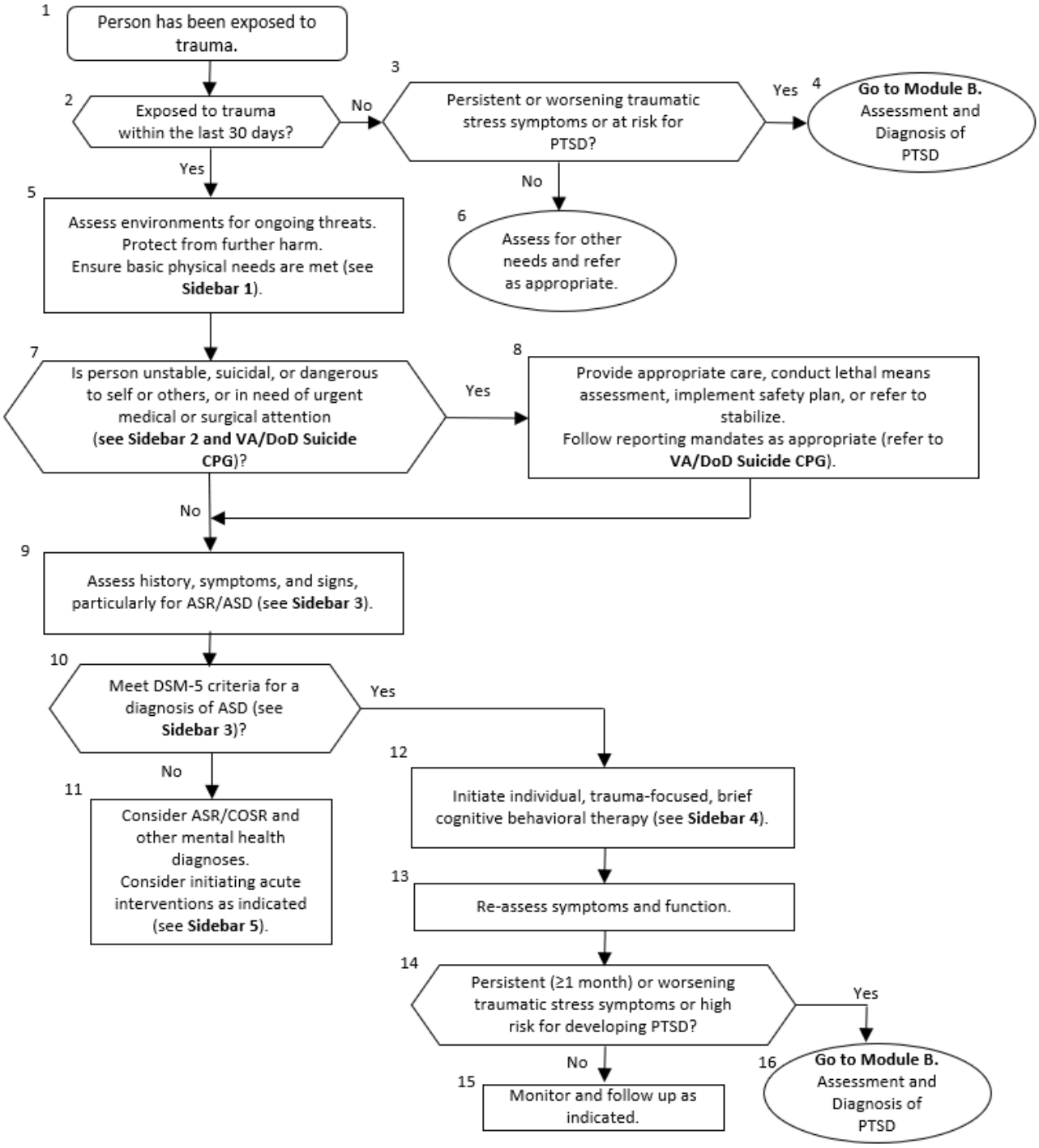
The algorithm is a step-by-step decision tree. Standardized symbols display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.(56) Sidebars 1–11 provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the process of care, formulated as a question that can be answered "Yes" or "No."
	Rectangles represent an action in the process of care.
	Ovals represent a link to another section within the algorithm.

Appendix H contains alternative text descriptions of the algorithms.

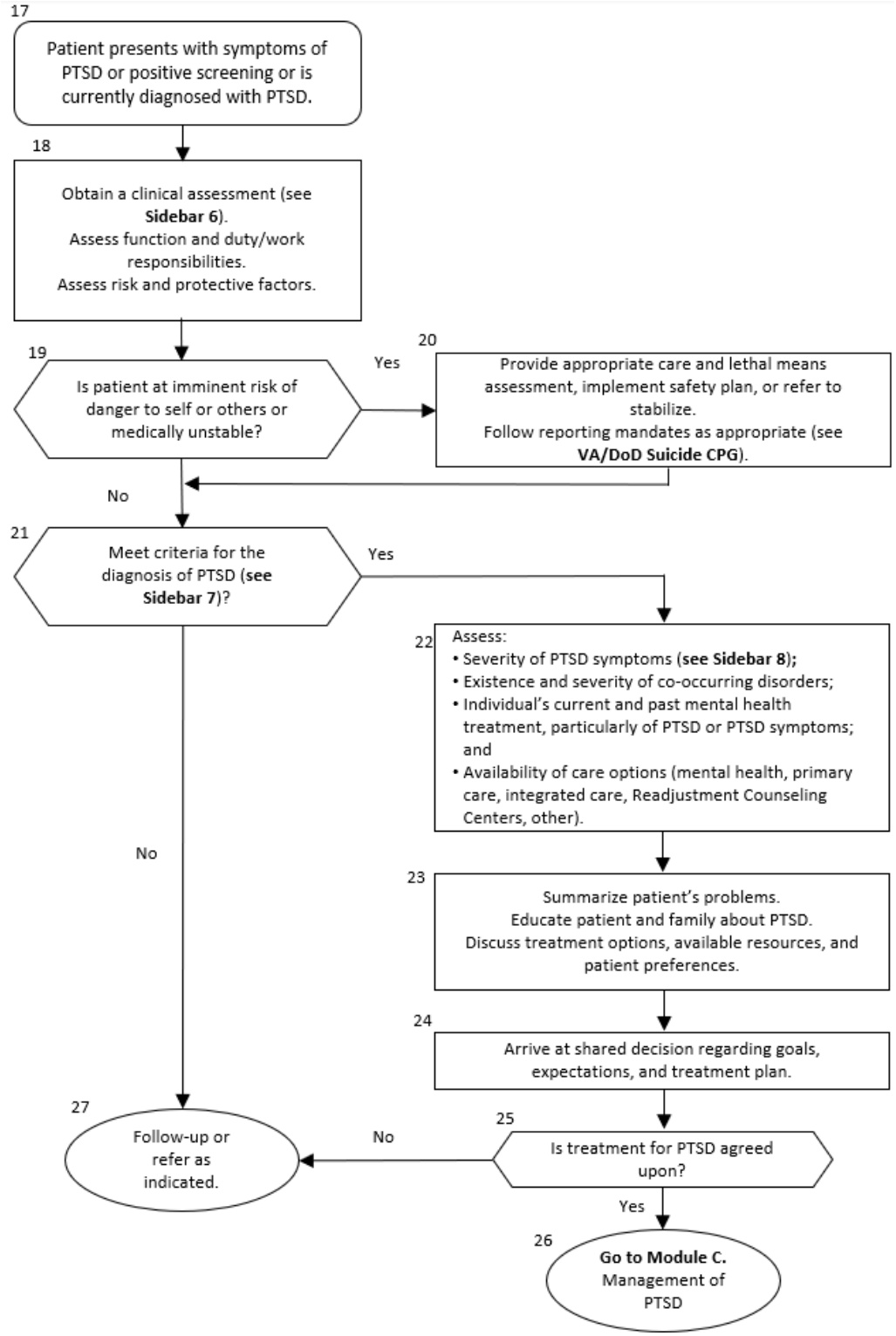
[d] The VA/DoD Clinical Practice Guidelines are available at: https://www.healthquality.va.gov/

A. Module A: Acute Stress Reaction/Disorder



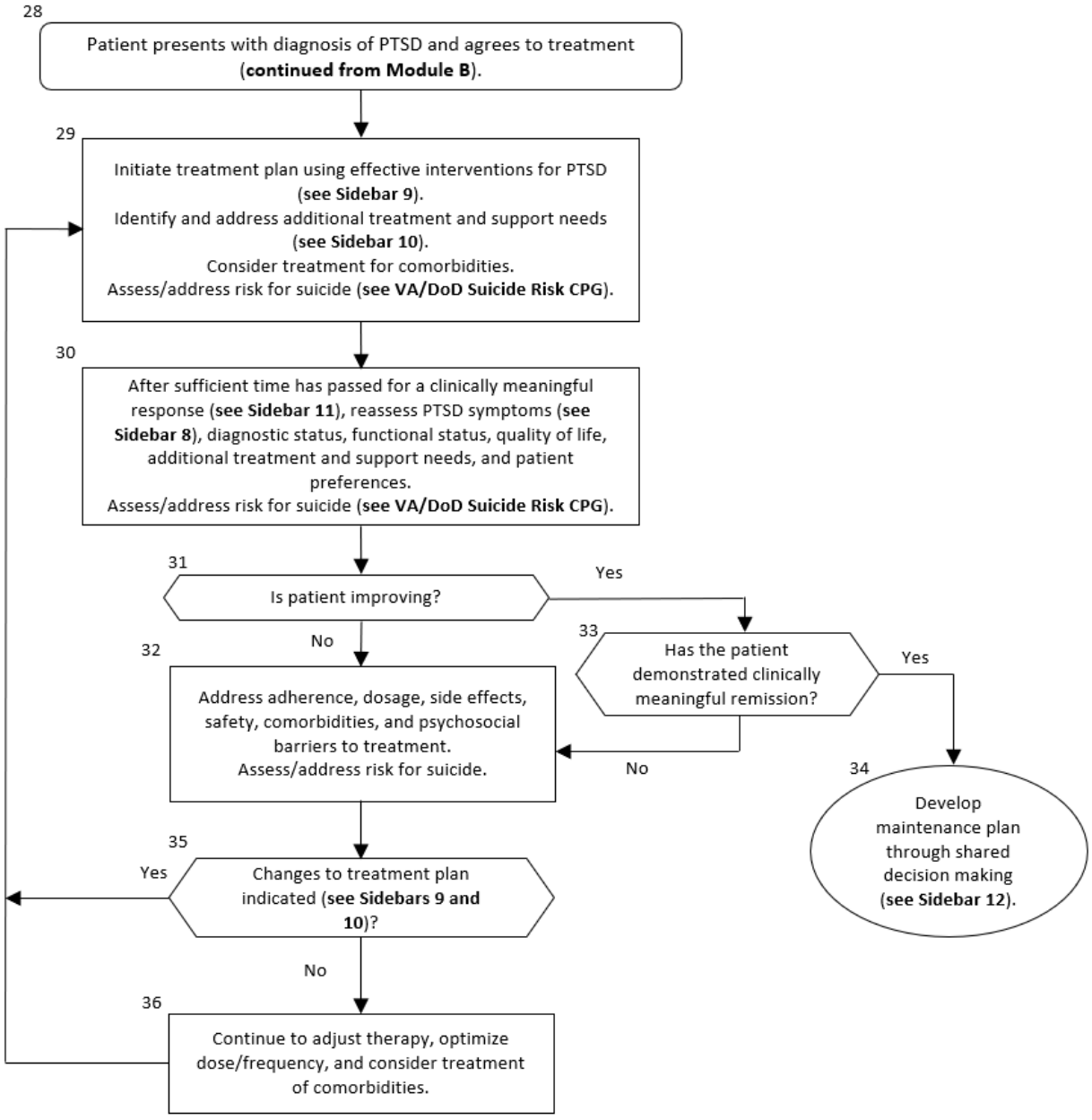
Abbreviations: ASR: Acute Stress Reaction; COSR: Combat and Operational Stress Reaction; CPG: clinical practice guideline; DSM: Diagnostic and Statistical Manual of Mental Disorders; PTSD: Posttraumatic stress disorder; VA: Veteran Affairs; DoD: Department of Defense.

B. Module B: Assessment and Diagnosis of Posttraumatic Stress Disorder



Abbreviations: CPG: clinical practice guideline; PTSD: Posttraumatic stress disorder; VA: Veteran Affairs; DoD: Department of Defense.

C. Module C: Management of Posttraumatic Stress Disorder



Abbreviations: CPG: clinical practice guideline; PTSD: Posttraumatic stress disorder; VA: Veteran Affairs; DoD: Department of Defense.

Sidebar 1: Immediate Needs

- Survival (including first aid and stabilizing physical condition), safety, and security
- Food, hydration, shelter, and clothing
- Sleep
- Orientation
- Communication with unit, family, friends, and community
- Education and normalization of reactions to trauma

Sidebar 2: Assessment

- History of trauma and mental health concerns
- Symptoms
- Consider screening for PTSD symptoms using the PC-PTSD-5 (Recommendation 1)
- Medical status
- Mental status, including suicidality (consult VA/DoD CPG for Assessment and Management of Patients at Risk for Suicide,[a] as needed)
- Functional status
- Psychosocial status, including intimate and family relationships; financial problems; legal issues
- Occupational performance
- Substance use
- Strengths, coping skills, and protective factors

[a] See the VA/DoD CPG for the Assessment and Management of Patients at Risk for Suicide, available at https://www.healthquality.va.gov/.

Abbreviations: PC-PTSD-5: Primary Care PTSD Screen for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; PTSD: posttraumatic stress disorder; VA: Veteran Affairs; DoD: Department of Defense.

Sidebar 3: DSM-5-TR Diagnostic Criteria for Acute Stress Disorder(6)

Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:

1. Directly experiencing the traumatic event(s).
2. Witnessing, in person, the event(s) as it occurred to others.
3. Learning that the event(s) occurred to a close family member or close friend.
   Note: In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse).

Note: This does not apply to exposure through electronic media, television, movies, or pictures unless this exposure is work-related.

Sidebar 3: DSM-5-TR Diagnostic Criteria for Acute Stress Disorder(6)

Criterion B. Presence of nine (or more) of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal, beginning or worsening after the traumatic event(s) occurred:

Intrusion Symptoms

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.)
4. Intense or prolonged psychological distress or marked physiological reactions in response to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

Negative Mood

5. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).

Dissociative Symptoms

6. An altered sense of the reality of one's surroundings or oneself (e.g., seeing oneself from another's perspective, being in a daze, time slowing).
7. Inability to remember an important aspect of the event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).

Avoidance Symptoms

8. Efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
9. Efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

Arousal Symptoms

10. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep).
11. Irritable behavior and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects.
12. Hypervigilance.
13. Problems with concentration.
14. Exaggerated startle response.

Criterion C. Duration of the disturbance (symptoms in Criterion B) is 3 days to 1 month after trauma exposure.

Note: Symptoms typically begin immediately after the trauma, but persistence for at least 3 days and up to 1 month is needed to meet disorder criteria.

Criterion D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Criterion E. The disturbance is not attributable to the physiological effects of a substance (e.g., medication or alcohol) or another medical condition (e.g., mild traumatic brain injury) and is not better explained by a brief psychotic disorder.

Sidebar 4: Acute Interventions for Acute Stress Disorder

- Individual, manualized trauma-focused cognitive behavioral psychotherapy
- Consider: Collaborative care or wellness-oriented activities

Sidebar 5: Acute Interventions for Acute Stress Response/Combat and Operational Stress Reaction

- Education and normalization, acute symptom management, social support
- Suggest: Brief cognitive behavioral psychotherapy

Sidebar 6: General Assessment

- Complete comprehensive clinical assessment of presenting complaints and comorbid conditions
- Perform safety, lethal means, and environmental assessment
- Consider history and presenting complaints: mental health, medical, military, marital, family, substance use, social and spiritual life, functional status
- Identify lifetime trauma history and duration of exposure
- Record current and past medications (including over-the-counter drugs and herbals) and psychosocial treatment
- Consider, with patient consent, obtaining an additional history from family, significant other, or both
- Perform mental status exam
- Consider, in cases of diagnostic uncertainty, use of validated structured clinical interviews for PTSD (i.e., CAPS-5, PSSI) (see Recommendation 2)

Abbreviations: CAPS-5: Clinician-Administered Posttraumatic Stress Disorder Scale for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision; PSSI: PTSD Symptom Scale - Interview Version

Sidebar 7: DSM-5-TR Diagnostic Criteria for PTSD(6)

Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:

1. Directly experiencing the traumatic event(s).
2. Witnessing, in person, the event(s) as it occurred to others.
3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse).

Note: Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures unless this exposure is work related.

Criterion B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings)
4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

Sidebar 7: DSM-5-TR Diagnostic Criteria for PTSD(6)
Criterion C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following: 1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s). 2. Avoidance or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
Criterion D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Inability to recall an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs). 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad.", "No one can be trusted,", "The world is completely dangerous,", "My whole nervous system is permanently ruined"). 3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame themself or others. 4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, shame). 5. Markedly diminished interest or participation in significant activities. 6. Feeling of detachment or estrangement from others. 7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
Criterion E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects. 2. Reckless or self-destructive behavior. 3. Hypervigilance. 4. Exaggerated startle response. 5. Problems with concentration. 6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).
Criterion F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.
Criterion G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Criterion H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.

Sidebar 7: DSM-5-TR Diagnostic Criteria for PTSD(6)

***Specify* whether:**

With dissociative symptoms: The individual's symptoms meet the criteria for posttraumatic stress disorder, 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 or of 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 6 months after the event (although the onset and expression of some symptoms may be immediate).

Sidebar 8: Assessment of PTSD Symptoms

- Assess PTSD symptoms using validated instruments, such as the PTSD Checklist for DSM-5 (PCL-5), or a structured clinician-administered interview (e.g., CAPS-5) (see Recommendation 3).

Abbreviations: CAPS-5: Clinician-Administered PTSD Scale for DSM-5; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; PCL-5: PTSD Checklist for DSM-5; PTSD: posttraumatic stress disorder

Sidebar 9: Treatment Selection

1. Initiate recommended individual, manualized psychotherapy (see Recommendation 8) according to patient preference.
2. If individual psychotherapy is unavailable or not preferred, initiate recommended pharmacotherapy (see Recommendation 15).
3. If options 1 and 2 are infeasible or are not preferred, offer suggested psychotherapy (see Recommendation 9) or suggested CIH (see Recommendation 26).
4. If options 1, 2, and 3 are infeasible or are not preferred, consider other psychotherapies (see Recommendation 10, Recommendation 12, and Recommendation 14), other pharmacotherapy (see Recommendation 16), complementary, integrative, or alternative approaches (see Recommendation 27 and Recommendation 28) based on availability, patient preference, and review of current evidence.
5. If none of the options above are acceptable to the patient, consider treating other disorders, issues, or both and reevaluating for PTSD treatment later.

Abbreviations: CIH: complementary and integrative health; PTSD: posttraumatic stress disorder

Sidebar 10: Additional Treatment and Support Needs

- Consider treatment for comorbidities and other identified problems (see Recommendation 34 as well as other relevant VA/DoD CPGs*).
- Consider symptom-specific management (e.g., sleep, pain).
- Facilitate social support.
- Address Whole Health by offering CIH, alternative approaches, health and wellbeing coaching, recreation therapy, etc.

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

Abbreviations: CIH: complementary and integrative health

Sidebar 11: Clinically Meaningful Response Time

- Psychotherapies require an adequate dosage to be fully effective in reducing PTSD symptoms; some effects might also not become apparent until some period has elapsed after treatment is initiated. For the indicated psychotherapies for PTSD (see Recommendation 8), it is generally accepted that initial treatment effects will be noticeable after 4–8 sessions typically delivered over 8-12 weeks. Psychotherapies might have an attenuated effect if delivered less than weekly.
- The pharmacological management of PTSD requires the SSRI (e.g., sertraline) or SNRI (e.g., venlafaxine) be given at an appropriate dosage for an adequate time to allow for the full therapeutic effects before moving to alternative or augmentative treatment options. These medications should be initiated at the recommended starting dose and titrated based on clinical response and tolerability (see Appendix B). The duration of the trial should be 8–12 weeks.

Abbreviations: PTSD: posttraumatic stress disorder; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor

Sidebar 12: Maintenance Plan

- Terminate PTSD treatment or taper based on clinician judgment and patient preference, normalize fluctuations in symptoms, discuss self-monitoring for symptoms that warrant future attention, and provide resources for seeking care in the future.
- Before termination of psychopharmacology, discuss the risks and benefits of discontinuing medication, including possible side effects and return of symptoms. Make a schedule to taper based on patient preference with a discussion of the length of time required and consideration of anticipated life events and stressors. Discuss the plan for monitoring during and post taper, including steps needed to reinitiate pharmacology.
- Should the patient wish to continue pharmacotherapy, investigate, and discuss continuing medications with behavioral health or primary care.
- Refer the patient for treatment of other disorders or functional issues (e.g., relationship distress).
- If desired, facilitate referral to health and wellbeing programs as a part of a Whole Health approach to care.

Abbreviations: PTSD: posttraumatic stress disorder

IX. Recommendations

The evidence-based clinical practice recommendations listed (in Table 6) were made using a systematic approach considering four domains as per the GRADE approach (see Summary of Guideline Development Methodology). These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

Table 6. Evidence-Based Clinical Practice Recommendations with Strength and Category

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Assessment and Diagnosis of PTSD		1.	When screening for PTSD, we suggest using the Primary Care PTSD Screen for DSM-5.	Weak for	Reviewed, New-replaced
		2.	For confirmation of the diagnosis of PTSD, we suggest using a validated structured clinician-administered interview, such as the Clinician-Administered PTSD Scale or PTSD Symptom Scale - Interview Version.	Weak for	Reviewed, New-replaced
		3.	To detect changes in PTSD symptom severity over time, we suggest the use of a validated instrument, such as the PTSD Checklist for DSM-5, or a structured clinician-administered interview, such as the Clinician-Administered PTSD Scale.	Weak for	Reviewed, New-replaced
Prevention of PTSD	*Selective Prevention of PTSD*	4.	For the prevention of PTSD among individuals who have been exposed to trauma, there is insufficient evidence to recommend for or against psychotherapy or pharmacotherapy in the immediate post-trauma period.	Neither for nor against	Not Reviewed, Amended
	Indicated Prevention of PTSD	5.	For the prevention of PTSD among patients diagnosed with acute stress disorder, we suggest trauma-focused cognitive behavioral psychotherapy.	Weak for	Reviewed, New-replaced
		6.	For the prevention of PTSD among patients diagnosed with acute stress reaction/acute stress disorder, there is insufficient evidence to recommend for or against any pharmacotherapy.	Neither for nor against	Reviewed, New-replaced
Treatment of PTSD	*Treatment Selection*	7.	We recommend individual psychotherapies, listed in Recommendation 8, over pharmacologic interventions for the treatment of PTSD.	Strong for	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Treatment of PTSD (cont.)	*Psychotherapy*	8.	We recommend the individual, manualized trauma-focused psychotherapies for the treatment of PTSD: Cognitive Processing Therapy, Eye Movement Desensitization and Reprocessing, or Prolonged Exposure.	Strong for	Reviewed, New-replaced
		9.	We suggest the following individual, manualized psychotherapies for the treatment of PTSD: Ehlers' Cognitive Therapy for PTSD, Present-Centered Therapy, or Written Exposure Therapy.	Weak for	Reviewed, New-replaced
		10.	There is insufficient evidence to recommend for or against the following individual psychotherapies for the treatment of PTSD: Accelerated Resolution Therapy, Adaptive Disclosure, Acceptance and Commitment Therapy, Brief Eclectic Psychotherapy, Dialectical Behavior Therapy, Emotional Freedom Techniques, Impact on Killing, Interpersonal Psychotherapy, Narrative Exposure Therapy, Prolonged Exposure in Primary Care, psychodynamic therapy, psychoeducation, Reconsolidation of Traumatic Memories, Seeking Safety, Stress Inoculation Training, Skills Training in Affective and Interpersonal Regulation, Skills Training in Affective and Interpersonal Regulation in Primary Care, supportive counseling, Thought Field Therapy, Trauma-Informed Guilt Reduction, or Trauma Management Therapy.	Neither for nor against	Reviewed, New-replaced
		11.	There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over, or in addition to, the full therapy protocol for the treatment of PTSD.	Neither for nor against	Reviewed, Not Changed
		12.	There is insufficient evidence to recommend for or against any specific manualized group therapy for the treatment of PTSD.	Neither for nor against	Reviewed, New-replaced
		13.	There is insufficient evidence to recommend using group therapy as an adjunct for the primary treatment of PTSD.	Neither for nor against	Reviewed, New-replaced
		14.	There is insufficient evidence to recommend for or against the following couples therapies for the treatment of PTSD: Behavioral Family Therapy, Structured Approach Therapy, or Cognitive Behavioral Conjoint Therapy.	Neither for nor against	Reviewed, Not Changed

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Treatment of PTSD (cont.)	*Pharmacotherapy*	15.	We recommend paroxetine, sertraline, or venlafaxine for the treatment of PTSD.	Strong for	Reviewed, New-replaced
		16.	There is insufficient evidence to recommend for or against amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.	Neither for nor against	Reviewed, New-replaced
		17.	There is insufficient evidence to recommend for or against psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.	Neither for nor against	Reviewed, New-added
		18.	We suggest against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.	Weak against	Reviewed, New-replaced
		19.	We recommend against benzodiazepines for the treatment of PTSD.	Strong against	Reviewed, New-replaced
		20.	We recommend against cannabis or cannabis derivatives for the treatment of PTSD.	Strong against	Reviewed, Amended
	Augmentation Therapy	21.	There is insufficient evidence to recommend for or against the combination or augmentation of psychotherapy (see Recommendation 8 and Recommendation 9) or medications (see Recommendation 15) with any psychotherapy or medication for the treatment of PTSD (see Recommendation 22 for antipsychotic medications and Recommendation 23 for 3,4-methylenedioxymethamphetamine).	Neither for nor against	Reviewed, New-replaced
		22.	We suggest against aripiprazole, asenapine, brexpiprazole, cariprazine, iloperidone, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone for augmentation of medications for the treatment of PTSD.	Weak against	Reviewed, New-replaced
		23.	There is insufficient evidence to recommend for or against 3,4-methylenedioxymethamphetamine assisted psychotherapy for the treatment of PTSD.	Neither for nor against	Reviewed, New-added
	Non-pharmacologic Biological Treatments	24.	There is insufficient evidence to recommend for or against the following somatic therapies for the treatment of PTSD: capnometry-assisted respiratory therapy, hyperbaric oxygen therapy, neurofeedback, NightWare©, repetitive transcranial magnetic stimulation, stellate ganglion block, or transcranial direct current stimulation.	Neither for nor against	Reviewed, New-replaced
		25.	We suggest against electroconvulsive therapy or vagus nerve stimulation for treatment of PTSD.	Weak against	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Treatment of PTSD (cont.)	*Complementary, Integrative, and Alternative Approaches*	26.	We suggest Mindfulness-Based Stress Reduction for the treatment of PTSD.	Weak for	Reviewed, New-replaced
		27.	There is insufficient evidence to recommend for or against the following mind-body interventions for the treatment of PTSD: acupuncture, Cognitively Based Compassion Training Veteran version, creative arts therapies (e.g., music, art, dance), guided imagery, hypnosis or self-hypnosis, Loving Kindness Meditation, Mantram Repetition Program, Mindfulness-Based Cognitive Therapy, other mindfulness trainings (e.g., integrative exercise, Mindfulness-Based Exposure Therapy, brief mindfulness training), relaxation training, somatic experiencing, tai chi or qigong, Transcendental Meditation®, and yoga.	Neither for nor against	Reviewed, New-replaced
		28.	There is insufficient evidence to recommend for or against the following interventions for the treatment of PTSD: recreational therapy, aerobic or non-aerobic exercise, animal-assisted therapy (e.g., canine, equine), and nature experiences (e.g., fishing, sailing).	Neither for nor against	Reviewed, New-replaced
	Technology-based Treatment	29.	We recommend secure video teleconferencing to deliver treatments in Recommendation 8 and Recommendation 9 when that therapy has been validated for use with video teleconferencing or when other options are unavailable.	Strong for	Reviewed, New-replaced
		30.	There is insufficient evidence to recommend for or against mobile apps or other self-help-based interventions for the treatment of PTSD.	Neither for nor against	Reviewed, New-added
		31.	There is insufficient evidence to recommend for or against facilitated internet-based cognitive behavioral therapy for the treatment of PTSD.	Neither for nor against	Reviewed, New-replaced
Treatment of Nightmares		32.	We suggest prazosin for the treatment of nightmares associated with PTSD.	Weak for	Reviewed, Amended
		33.	There is insufficient evidence to recommend for or against the following treatments for nightmares associated with PTSD: Imagery Rehearsal Therapy, Exposure Relaxation and Rescripting Therapy, Imaging Rescripting and Reprocessing Therapy, or NightWare.	Neither for nor against	Reviewed, New-added
Treatment of PTSD with Co-Occurring Conditions		34.	We suggest that the presence of co-occurring substance use disorder and/or other disorder(s) not preclude treatments in Recommendation 8 and Recommendation 9 for PTSD.	Weak for	Reviewed, New-replaced

[a] For additional information, see Determining Recommendation Strength and Direction.

[b] For additional information, see Recommendation Categorization.

A. Assessment and Diagnosis of PTSD

Recommendation

1. When screening for PTSD, we suggest using the Primary Care PTSD Screen for DSM-5.
   (Weak for | Reviewed, New-replaced)

Discussion

The Primary Care PTSD Screen (PC-PTSD-5) for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) is a five-item questionnaire that performs well in detecting a DSM-5 PTSD diagnosis.(57, 58) Initial validation of the PC-PTSD-5 suggested a score of three was optimal. However, a definitive validation of the scale in a sample of more than 400 VA primary care patients found a score of four was optimal for detecting a diagnosis according to the CAPS-5.(58) A second study identified a score of three as maximally sensitive and four as maximally efficient.(57) Both studies comprised predominantly White male Veteran samples. One study reported analyses for women specifically and found that although a score of four was still an optimal cutoff point, it performed less well than it did for men.(57) Studies with other populations (e.g., women and individuals of other sexes, active duty Service members, samples with greater racial or ethnic diversity) are necessary to ensure cutoff scores are appropriate for the population. Therefore, no screening measure or cutoff point should be the sole basis for diagnosis.

Patient preferences vary regarding whether the patient wants to be screened, and there might be variations in cut scores among different subpopulations. Therefore, the applicability of the measure and the cut score to the population that will be screened should be considered.

The Work Group systematically reviewed evidence related to this recommendation.(57, 58) The systematic evidence review conducted for the 2017 VA/DoD PTSD CPG identified no studies of the PC-PTSD-5. Therefore, the recommendation is categorized as *Reviewed, New-replaced.* The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including few studies and validation only with predominantly White male Veterans such that little is known about psychometric characteristics and appropriate cutoffs for other populations. No potential harms were identified in the systematic evidence review. Patient values and preferences varied because a small number of patients do not like completing screening measures. Thus, the Work Group made the following recommendation: When screening for PTSD, we suggest using the Primary Care PTSD Screen for DSM-5.

Recommendation

2. For confirmation of the diagnosis of PTSD, we suggest using a validated structured clinician-administered interview, such as the Clinician-Administered PTSD Scale or PTSD Symptom Scale - Interview Version.
   (Weak for | Reviewed, New-replaced)

Discussion

Evidence supports the use of validated structured clinician-administered interviews, such as the CAPS-5 to diagnose PTSD.(59) Jackson et al. (2022) found high diagnostic agreement (95.1%) among the DSM-IV version, CAPS-IV, and CAPS-5.(59) These findings are consistent with another study that found correspondence between CAPS-IV and CAPS-5 and demonstrated good convergent validity and discriminant validity for CAPS-5.(60) Overall, these findings show CAPS-5 is a valid measure of DSM-5 PTSD diagnosis. Additionally, Foa et al. (2016) (not included in the systematic evidence review nor impacting the strength of this recommendation) found good convergent validity between PTSD Symptom Scale - Interview Version (PSSI-5) and CAPS-5 total scores and moderate correspondence between CAPS-5 and PSSI-5 diagnoses.(61) Though the studies included in the evidence base were conducted with predominantly White male Veterans, other studies not included in the systematic evidence review nor impacting the strength of this recommendation have demonstrated that CAPS and PSSI perform well in more diverse samples.(62)

Assessing patients for a PTSD diagnosis can result in a temporary increase in symptoms related to describing traumatic events or distressing symptoms. Patient preferences varied for undergoing a structured clinician-administered interview. Structured clinician-administered interviews can be resource intensive and time consuming and often require specialized training and competency. However, the benefits of getting an accurate diagnosis outweigh these harms.

The Work Group systematically reviewed evidence related to this recommendation.(59, 60) The systematic evidence review conducted for the 2017 VA/DoD PTSD CPG did not review evidence related to these measures. Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including a small number of studies conducted on the validity of clinician-administered interviews for DSM-5 and a lack of diversity in patient samples. The benefits of conducting clinician-administered interviews outweighed the potential harm. Patient values and preferences varied because some patients might find assessments inconvenient or invasive. Thus, the Work Group made the following recommendation: For confirmation of the diagnosis of PTSD, we suggest using a validated structured clinician-administered interview, such as the Clinician-Administered PTSD Scale or PTSD Symptom Scale - Interview Version.

Recommendation

3. To detect changes in PTSD symptom severity over time, we suggest the use of a validated instrument, such as the PTSD Checklist for DSM-5, or a structured clinician-administered interview, such as the Clinician-Administered PTSD Scale.
   (Weak for | Reviewed, New-replaced)

Discussion

Evidence supports the use of validated instruments, such as the PTSD Checklist for DSM-5 (PCL-5), or a structured clinician-administered interview (e.g., CAPS-5) to detect change in PTSD symptom severity over time.(63, 64) Lee et al. (2022) found the CAPS-5 and PCL-5 scores changed in a similar manner over time; however, at 12-month posttreatment assessment, CAPS-5 scores exhibited greater improvement since baseline compared with PCL-5 scores.(63) This body of evidence is further supported by prior research (not included in the systematic evidence review nor impacting the strength of this recommendation) that found correspondence in longitudinal scores in the DSM-IV versions of these two instruments.(65) Although no studies on sensitivity to change for the PSSI-5 were found in the evidence review, prior research (not included in the systematic evidence review) supports its validity and applicability for measuring symptom change.(61)

Assessing PTSD symptoms can be distressing for some patients. Patients might vary in their preferences for completing assessments. Assessment can be resource intensive and time consuming. However, failure to assess change in PTSD symptoms can result in administering or persisting with ineffective treatment. Thus, the benefits of evaluating for change outweigh these potential harms. Further, the studies included samples that consisted predominantly of White male Veterans. The applicability of these instruments to more diverse samples should be considered.

The Work Group systematically reviewed evidence related to this recommendation.(63, 64). The systematic evidence review conducted for the 2017 VA/DoD PTSD CPG did not review evidence related to these measures. Therefore, the recommendation is categorized as *Reviewed, New-replaced.* The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including a few studies examining change in PTSD symptoms over time and studies that included primarily male Veterans.(63, 64) The benefits of monitoring symptom change outweighed the potential harm. Patient values and preferences varied because some patients might find assessments inconvenient or invasive. Thus, the Work Group made the following recommendation: To detect changes in PTSD symptom severity over time, we suggest the use of a validated instrument, such as the PTSD Checklist for DSM-5, or a structured clinician-administered interview, such as the Clinician-Administered PTSD Scale.

B. Prevention of PTSD

a. Selective Prevention of PTSD

Recommendation

4. For the prevention of PTSD among individuals who have been exposed to trauma, there is insufficient evidence to recommend for or against psychotherapy or pharmacotherapy in the immediate post-trauma period. **(Neither for nor against | Not reviewed, Amended)**

Discussion

Studies examining the use of individual trauma-focused psychotherapy in the immediate post-trauma period for the selective prevention of PTSD are limited, with no high-quality studies demonstrating that any intervention is effective at preventing PTSD, particularly in the target population. Rothbaum et al. (2012) completed a study in which individuals who experienced a Criterion A trauma were assigned to a modified PE group or a waitlist group within 72 hours of the event.(66) Compared with waitlist controls, brief trauma-focused cognitive behavioral therapy (CBT) significantly reduced the severity of PTSD symptoms as assessed by the PTSD Symptom Scale-I (PSS-I) at 4 and 12 weeks follow-up.

An SR of individual psychological debriefing studies included two blinded RCTs using Critical Incident Stress Debriefing (CISD) in civilian trauma samples.(67) CISD administered immediately after trauma exposure did not reduce the incidence of PTSD at 6-month follow-up compared with groups that received no debriefing.

One RCT compared the early administration of propranolol with placebo in individuals with trauma exposure who were treated in an emergency department.(68) Findings indicated no difference in the likelihood of developing PTSD between those who received propranolol and those who received placebo.(68)

Included in an SR from Amos et al. (2014) was an RCT that compared the early administration of temazepam (within 3 weeks of trauma) with placebo in individuals with trauma exposure and found no benefit.(69) Another RCT also included in the SR compared the early administration of gabapentin (within 48 hours of trauma) with placebo, which also found no benefit.

Four RCTs, included in Amos et al. (2014) compared hydrocortisone with placebo for the prevention of PTSD in various acute inpatient medical settings, such as the intensive care unit, cardiac surgery, emergency department, and trauma center. Compared with placebo, hydrocortisone administration during life-threatening medical illnesses was associated with significantly fewer PTSD symptoms at 3 months.(69) However, it is unclear whether these findings can be generalized to non-medical traumatic events or are generalizable to a population without 100% medical comorbidity. 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.

Fewer than 10 RCTs evaluated five different medication types, and wide variation occurred in the administration and dosage of medications and the 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.(67, 70)

Patient preferences vary regarding these treatments for prophylaxis of a potential disorder. The patient focus group noted psychotherapy and pharmacotherapy are often helpful in the treatment of PTSD, but information on the benefits of using these modalities in preventing the development of PTSD following trauma is not well studied. Anticipating that most individuals would tolerate moderate short-term side effects is reasonable if they effectively prevented PTSD.

The Work Group considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(66-70) Therefore, this recommendation is categorized as *Not Reviewed, Amended*. The Work Group's confidence in the quality of the evidence overall was very low. The body of evidence had some limitations, including very few studies, smaller sample sizes, limited follow-up, and confounders in the analyses. In addition, most studies were not performed in active duty Service member and Veteran populations, increasing uncertainty about the generalizability of the findings. For psychotherapy, PE benefits outweighed harms and burdens, albeit in a single study, although for other psychotherapies the harms and burdens slightly outweighed the benefits, and for pharmacotherapy the harms and burdens outweighed the benefits. Patient values and preferences varied largely because of time commitments, the potential for adverse effects (e.g., worsening traumatic symptoms during psychotherapy, side effects from pharmacotherapy), and frequent delays in the onset of symptom improvement. Thus, the Work Group made the following recommendation: For the prevention of PTSD among individuals who have been exposed to trauma, there is insufficient evidence to recommend for or against psychotherapy or pharmacotherapy in the immediate post-trauma period.

b. Indicated Prevention of PTSD

Recommendation

5. For the prevention of PTSD among patients diagnosed with acute stress disorder, we suggest trauma-focused cognitive behavioral psychotherapy. **(Weak for | Reviewed, New-replaced)**

Discussion

One SR found that individuals with ASD who received brief trauma-focused CBT, with components of cognitive restructuring and exposure, compared with supportive counseling or waitlist had significantly reduced PTSD symptom severity at 3- to 6-month follow-up.(71) Within the SR, nine studies evaluated multiple session trauma-focused

psychotherapy as an intervention for individuals diagnosed with ASD, four of which had methodologic limitations and non-significant findings. The remaining five studies were conducted by an Australian team who compared 5–6 weeks of trauma-focused CBT with supportive counseling or waitlist in a combined total of 195 civilian survivors of mixed trauma with ASD; four of the studies used the critical outcome of clinician-rated PTSD,(72-75) and one study used a self-report measure.(76) Participants with trauma from motor vehicle or industrial accidents 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, waitlist, or both. Brief trauma-focused CBT significantly reduced clinician-rated PTSD severity post-treatment and the incidence of PTSD at 6 months.

The Work Group also reviewed the literature from the 2017 VA/DoD PTSD CPG, including a meta-analysis and an SR.(67, 70) Within the SR and meta-analysis, studies relevant to this recommendation were already included in the Bisson et al. (2021) SR that was part of the literature review for the current CPG.(71) One additional study from the 2017 VA/DoD PTSD CPG included 242 individuals who experienced motor vehicle accidents (MVA), workplace or other accidents, or terrorist attacks and met the criteria for ASD; they were subsequently randomized to receive either trauma-focused CBT (immediate or delayed PE or CT), escitalopram, placebo, or waitlist. The authors reported a significant reduction in PTSD symptoms for those who received trauma-focused CBT compared with the other groups.(77)

The Work Group found no additional studies of interventions to prevent PTSD among individuals with ASR or ASD, including other types of psychotherapy and system-level interventions such as stepped collaborative care. Overall, no studies in the literature review for the present CPG evaluated interventions to prevent progression to PTSD in patients who present with ASR, which is a significant gap in the evidence base.

Patient preferences vary regarding this treatment. However, most patients with ASD will want to receive an intervention that is likely to relieve symptoms, even if it causes transient distress. Further, implications for resource use, equity, acceptability, feasibility, and subgroup considerations arise. Offering trauma-focused CBT requires extra training by providers and support staff. Some patients might find therapy unacceptable, infeasible (i.e., they might not have the time to engage in psychotherapy), or both. Whether results from these studies derived from community samples are applicable to active duty Service members and Veterans is also unclear.

The Work Group systematically reviewed evidence related to this recommendation(71) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(67, 70, 77) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including small sample sizes and risk of bias. The extent

to which the results of these studies generalize to active duty Service member and Veteran populations is unclear given most of the research reviewed was in civilian patients.(71) The benefits of trauma-focused CBT in the treatment of individuals with ASD (e.g., reduced symptoms severity and lower rates of subsequent diagnosis of PTSD) outweighed the potential harms and burdens (e.g., transient distress related to reexamining of the trauma in therapy, time and energy required to attend psychotherapy sessions) and seem most significant for those diagnosed with ASD following an MVA. Thus, the Work Group made the following recommendation: For the prevention of PTSD among patients diagnosed with acute stress disorder, we suggest trauma-focused cognitive behavioral psychotherapy.

Recommendation

6. For the prevention of PTSD among patients diagnosed with acute stress reaction/acute stress disorder, there is insufficient evidence to recommend for or against any pharmacotherapy.
   (Neither for nor against | Reviewed, New-replaced)

Discussion

An SR by Bisson et al. (2021) examined 12 studies of pharmacotherapy, including propranolol, oxytocin, hydrocortisone, docosahexaenoic acid, and gabapentin.(71) Only 6 of the studies used the critical outcome of clinician-rated PTSD. However, none of the patients included in these studies was diagnosed with ASR or ASD. Another study of paroxetine versus placebo used pharmacotherapy prophylactically in patients following exposure to a traumatic event who were not diagnosed with ASR or ASD.(78) Therefore, the results of these studies cannot be used to determine the extent to which pharmacotherapy for patients with ASR or ASD prevents progression to PTSD.

The 2017 VA/DoD PTSD CPG reviewed 2 studies that examined the efficacy of escitalopram versus placebo for the prevention of PTSD.(77, 79) An RCT by Suliman et al. (2015) randomized individuals who met full DSM-IV criteria or intrusion and hyper-arousal criteria for ASD to escitalopram or placebo fewer than 4 weeks after a traumatic exposure. It found a significant reduction in PTSD symptoms for both escitalopram and placebo groups at 24 weeks follow-up, with a significantly greater reduction in clinician-rated PTSD using the CAPS in the placebo group.(79) A five-armed trial by Shalev et al. (2012) compared escitalopram with placebo, waitlist, prolonged exposure, and non-trauma-focused CBT in a sample of individuals who experienced a life-threatening trauma from terrorist activity, MVAs, or other accidents and who met criteria for ASD.(77) It found individuals who received PE and CBT had a significantly lower incidence of PTSD at the 5-month follow-up using the critical outcome of clinician-rated PTSD compared with individuals who received waitlist, escitalopram, or placebo.(77)

No studies in the literature review evaluated the role of pharmacotherapy in preventing the progression to PTSD in patients who present with ASR, revealing a gap in the literature base.

Patient preferences vary regarding this treatment. The patient focus group noted variable benefits and perceptions of the utility of pharmacotherapy that can result in significant side effects well before clinical benefits are realized. Medications, particularly those newer to the market, can be costly for some patients. Clinicians also differ in their opinions and approach to the use of pharmacotherapy, particularly when used off-label for the prevention of PTSD in patients with ASR or ASD.

The Work Group systematically reviewed evidence related to this recommendation(71, 78) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(77, 79) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had limitations, including small sample sizes, frequent use of only patient rating scales, and lack of formal diagnosis of ASR or ASD in participants. The benefits of hydrocortisone, propranolol, oxytocin, paroxetine, and escitalopram range from being balanced to being outweighed by their potential harm. Patient values and preferences varied largely because some patients strongly oppose the use of medications whereas others have a strong preference for their use. Thus, the Work Group made the following recommendation: For the prevention of PTSD among patients diagnosed with acute stress reaction/acute stress disorder, there is insufficient evidence to recommend for or against any pharmacotherapy.

C. Treatment of PTSD

a. Treatment Selection

Recommendation

7. We recommend individual psychotherapies, listed in Recommendation 8, over pharmacologic interventions for the treatment of PTSD.
   (Strong for | Reviewed, New-replaced)

Discussion

Both psychotherapy (see Recommendation 8) and pharmacotherapy (see Recommendation 15) are effective in treating PTSD. When both treatment modalities are available and feasible, the Work Group recommends the use of the indicated psychotherapies over the indicated pharmacotherapies. Feasibility determinations should consider the time demands placed on both clinicians and patients.

The Work Group's recommendation to use specific individual trauma-focused psychotherapy over pharmacotherapy reflects the current state of research on PTSD treatment. A small, but growing, body of literature is directly comparing specific psychotherapy protocols with specific pharmacologic agents. An SR by Merz et al. (2019) concluded the studies they reviewed that included pharmacological and psychotherapeutic treatment modalities tended to favor psychotherapy over pharmacotherapy.(80) Two additional meta-analyses, included in the 2017 VA/DoD PTSD CPG systematic evidence review, compare the treatment effects of

psychotherapies and pharmacotherapies.(81-83) The results of these meta-analyses provided support for a similar recommendation in the 2017 VA/DoD PTSD CPG. They indicate that trauma-focused psychotherapies impart greater change on core PTSD symptoms than pharmacotherapies do and that these improvements persist for longer time periods. This finding appears to hold true even when restricting the meta-analyses to studies that used active comparison treatments, such as Present-Centered Therapy (PCT) as control groups for psychotherapy studies, as opposed to waitlists or treatment as usual (TAU). Notably, one recent RCT directly compared PE, sertraline, and the combination for treating PTSD and found no difference among the groups over the 24 weeks that medication was provided.(84)

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, although the risks for negative side effects or negative reactions vary across individual patients, they are generally more likely to occur with pharmacologic treatments than with psychotherapies (see Recommendation 15 and Appendix B). Second, the positive effects of medication treatment diminish over time and are lost when medications are stopped.(81)

Large variation occurs in patient preferences for psychotherapy or pharmacotherapy. Patients often express a strong preference for one modality or the other. However, a small body of literature, including Simiola et al. (2015), Swift et al. (2015), and Zoellner et al. (2019) (these three studies are not included in the evidence base nor do they impact the strength of the recommendation), as well as Watts et al. (2015) indicate more patients prefer psychotherapy over pharmacotherapy.(83, 85-87) These studies are limited by sampling issues and the specific treatments for which preferences are examined. However, comments from participants in the patient focus group also suggest this preference and support the recommendation to use psychotherapies when available. The Work Group noted that the delivery of psychotherapy is more resource intensive than pharmacologic treatment because of the need for frequent therapy appointments (typically 10–15 appointments held weekly or more frequently). These additional requirements might make offering psychotherapy in some settings more challenging.

The Work Group systematically reviewed evidence related to this recommendation(80) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(81-83) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including a small number of direct comparison studies with small sample sizes.(80) The benefits of using psychotherapy over pharmacotherapy slightly outweighed the potential harm of doing so, which was considered minimal. Patient values and preferences varied largely, with some patients expressing a strong preference for one modality or the other, but most patients appear to prefer psychotherapy, even when it includes a trauma focus. Thus, the Work Group

made the following recommendation: We recommend individual psychotherapies, listed in Recommendation 8, over pharmacologic interventions for the treatment of PTSD.

b. Psychotherapy

Recommendation

8. We recommend the individual, manualized trauma-focused psychotherapies for the treatment of PTSD: Cognitive Processing Therapy, Eye Movement Desensitization and Reprocessing, or Prolonged Exposure.
   (Strong for | Reviewed, New-replaced)

Discussion

The 2017 VA/DoD PTSD CPG included a *Strong for* recommendation on trauma-focused therapies that used 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. In contrast, recommendations for medications were made for specific drugs and not drug classes. For comparability in the review of psychotherapies and medications for this revised guideline, the Work Group reviewed the evidence for specific psychotherapies, rather than classes such as trauma-focused psychotherapies.

The systematic evidence review identified three trauma-focused psychotherapies with the strongest evidence of efficacy for improving the critical outcome of clinician-rated PTSD symptoms according to a structured clinical interview: CPT (with or without a trauma account: CPT and CPT-A, respectively), EMDR, and PE.(88-96) A network meta-analysis found all three treatments were superior to waitlist, and CPT and PE outperformed active controls, although PE did not outperform psychoeducation.(88) However, other reviews found that EMDR also outperformed active controls.(92-94)

Individual RCTs included in the SRs also found these treatments improved important outcomes, such as self-reported PTSD symptoms, depression, functioning, and QoL, in addition to the critical outcome of clinician-rated PTSD symptoms.(97-100) The SR by Cusack et al. (2016) reported moderate quality evidence for CPT and EMDR and high-quality evidence for exposure therapy for improving depression.(96) Regarding dropout, an SR that included studies with military samples found dropout was higher in trauma-focused treatments (including CPT, EMDR, and PE) relative to non-trauma-focused treatments.(101) Studies of massed protocols in which treatment is delivered in 2–3 weeks have found lower dropout.(98)

None of the SRs included in the systematic evidence review reported on adverse events. Some adverse events were reported in included RCTs, but relatively few overall. The SR by Cusack et al. (2016) found that some included studies did not report on adverse events, although of those that did, the reports were low.(96) Increases in symptoms might occur during trauma processing, but these increases are typically transitory and not severe. Thus, the recommended treatments were found to have a low risk of harm.

Patient preferences varied regarding these treatments. Perceived benefit varied among focus group participants who had tried one of the treatments. Some studies not included in the systematic evidence review supporting this recommendation found a preference for CPT over PE(102, 103) and CPT over EMDR.(102) However, a recent RCT of more than 900 Veterans found equivalent preference for PE and CPT.(97) Treatments like CPT, EMDR, and PE typically require 10–12 weekly 60- or 90-minute sessions. In DoD and in some VA settings, challenges can occur in delivering any treatment requiring weekly individual sessions; furthermore, in DoD, treatment can be interrupted by deployment. In settings where treatment could be delivered daily or multiple times per week, massed protocols could enhance the feasibility of delivering a full course of treatment (not included in the evidence base nor impacting the strength of this recommendation).(104) All three treatments require therapist training and supervision to achieve proficiency. EMDR-trained therapists are not widely available in VA or DoD, in large part because EMDR is a proprietary treatment managed by outside organizations with their own certification processes and, as a result, is poorly integrated into standard graduate educational training structures.

The Work Group systematically reviewed evidence related to this recommendation(88-94, 98, 101) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(95, 96) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including no studies of EMDR in active duty Service members and few studies of EMDR in Veterans. The benefits of CPT, EMDR, and PE in improving the critical outcome of clinician-rated PTSD symptoms and other important outcomes outweighed the potential harms (e.g., adverse events), which were small. Patient values and preferences varied because some patients might prefer one modality for trauma processing over another. Thus, the Work Group made the following recommendation: We recommend the individual, manualized trauma-focused psychotherapies for the treatment of PTSD: Cognitive Processing Therapy, Eye Movement Desensitization and Reprocessing, or Prolonged Exposure.

Recommendation

9. We suggest the following individual, manualized psychotherapies for the treatment of PTSD: Ehlers' Cognitive Therapy for PTSD, Present-Centered Therapy, or Written Exposure Therapy.
   (Weak for | Reviewed, New-replaced)

Discussion

As noted in the discussion of Recommendation 8, the 2017 VA/DoD PTSD CPG included a *Strong for* recommendation for trauma-focused therapies that use cognitive, emotional, or behavioral techniques to facilitate processing a traumatic experience in which the trauma focus is a central component of the therapeutic process. In contrast, recommendations for medications were made for specific drugs and not drug classes.

For comparability in the review of psychotherapies and medications for this revised guideline, the Work Group reviewed the evidence for specific psychotherapies rather than classes, such as trauma-focused psychotherapies. This approach resulted in downgrading the recommendations for Ehlers' CT and WET from *Strong for* in the 2017 VA/DoD PTSD CPG to *Weak for*; WET had been included as a type of trauma-focused written narrative exposure.

The Work Group decided on a *Weak for* recommendation for Ehlers' CT, PCT, and WET based on evidence from two SRs and their included studies.(88, 105) An SR of 4 studies examining Ehlers' CT included 2 studies with the critical outcome of clinician-rated PTSD (92). Although there were only 2 studies, there were six relevant comparisons. One study compared CT with both waitlist and psychoeducation, and the other compared weekly CT and daily CT with both waitlist and emotional supportive therapy. CT was superior to control in all six comparisons.(106, 107)

An SR of PCT that included 12 studies and 1,837 participants found PCT was superior to waitlist and not non-inferior to trauma-focused psychotherapy for improving clinician-rated PTSD, with additional analyses showing a small effect for trauma-focused psychotherapy as superior to PCT.(105) An SR that included 2 studies of WET found that WET was superior to waitlist and non-inferior to CPT, for improving the critical outcome of clinician-rated PTSD.(88) An additional RCT found that WET was non-inferior to CPT in a sample of active duty Service members.(89) (Note that the Jericho et al. [2022] SR incorrectly categorized a study of a three-session written exposure protocol as WET.)

Individual RCTs of Ehlers' CT, included in the Jericho et al. (2022) SR, also found this treatment improved important outcomes such as self-reported PTSD symptoms, depression, functioning, and QoL for comparisons with waitlist and active controls.(88) Individual RCTs of PCT, included in the Belsher et al. (2019) SR, reported similar findings on the important outcomes for comparisons with waitlist.(105) One of the RCTs of WET reported that the treatment was non-inferior to CPT for the important outcome of depression.(90)

None of the SRs included in the evidence base reported on adverse events. Some were reported in the included RCTs, but relatively few overall. Thus, the suggested treatments were found to have a low risk of harm.

Patient preferences vary regarding these treatments. Generally, PCT might be more acceptable, relative to trauma-focused treatments, because it does not require talking about trauma. In addition, PCT has lower dropout relative to trauma-focused treatments. Treatments like Ehlers' CT and PCT typically require 10–12 weekly 60- to 90-minute sessions. In DoD, and in some VA settings, challenges can occur in delivering any treatment requiring weekly individual sessions; furthermore, in DoD, treatment can be interrupted by deployment. When these potential barriers exist, WET might be more

feasible because it requires fewer and briefer sessions. Ehlers' CT also has demonstrated efficacy in a weekly compressed format. There are no studies of Ehlers' CT in military populations and all studies were conducted in England or Northern Ireland. Only one of the three trials of WET focused exclusively on a military population, with one other including Veterans in a mixed sample. In contrast, 10 of the 12 studies in the SR of PCT were in U.S. Veteran or active duty Service member populations.(105) All three treatments require therapist training and supervision to achieve proficiency. VA or DoD have limited availability of therapists trained in Ehlers' CT.

The Work Group systematically reviewed evidence related to this recommendation(88, 105) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(95, 96) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including no studies of Ehlers' CT and only 1 study of WET in military populations. All studies of CT and WET were conducted by the respective treatment developers, which might limit generalizability of findings because of the potential of allegiance bias. No studies compared PCT with an active control, although there were multiple comparisons with active treatment. The benefits of Ehlers' CT, PCT, and WET in improving the critical outcome of clinician-rated PTSD symptoms and other important outcomes outweighed the potential harms (e.g., of adverse events), which were minimal. Patient values and preferences varied because some patients might prefer talking about, versus not talking about, their trauma. Thus, the Work Group made the following recommendation: We suggest the following individual, manualized psychotherapies for the treatment of PTSD: Ehlers' Cognitive Therapy for PTSD, Present-Centered Therapy, or Written Exposure Therapy.

Recommendation

10. There is insufficient evidence to recommend for or against the following individual psychotherapies for the treatment of PTSD: Accelerated Resolution Therapy, Adaptive Disclosure, Acceptance and Commitment Therapy, Brief Eclectic Psychotherapy, Dialectical Behavior Therapy, Emotional Freedom Techniques, Impact on Killing, Interpersonal Psychotherapy, Narrative Exposure Therapy, Prolonged Exposure in Primary Care, psychodynamic therapy, psychoeducation, Reconsolidation of Traumatic Memories, Seeking Safety, Stress Inoculation Training, Skills Training in Affective and Interpersonal Regulation, Skills Training in Affective and Interpersonal Regulation in Primary Care, supportive counseling, Thought Field Therapy, Trauma-Informed Guilt Reduction, or Trauma Management Therapy, or Virtual Reality Exposure Therapy. **(Neither for nor against | Reviewed, New-replaced)**

Discussion

Two network meta-analyses, Jericho et al. (2022) and Mavranezouli et al. (2020), a meta-analysis by Lewis et al. (2020), an RCT from Litz et al. (2021), and an RCT from Norman

et al. (2022), combined with evidence from the 2017 VA/DoD PTSD CPG (Roberts et al. [2015]), suggest there are a number of psychotherapies that might have a positive benefit but for which the evidence is insufficient.(88, 108-112) Two trauma-focused treatments, NET and BEP, which were given *Strong for* recommendations in the 2017 VA/DoD PTSD CPG, were determined to have insufficient evidence in this guideline. The change is primarily due to considering the treatments on their own rather than as members of a class of trauma-focused psychotherapies, in addition to the new focus on the critical outcome of clinician-rated PTSD symptoms. Four RCTs of NET in the SR by Jericho et al. (2022) included the critical outcome of clinician-administered PTSD measures (Hensel-Dittman et al. [2011], Jacob et al. [2014], Lely et al. [2019], and Morath et al. [2014]).(88) The two waitlist control studies in refugees found support for NET, but studies comparing NET to active controls were mixed. One found support for NET over SIT but had methodologic flaws that precluded interpretation. The other found that PCT was superior to NET. With respect to BEP, only one very small RCT by Lindauer et al. (2008) in Jericho et al. (2022) included a critical outcome.(113, 114) Additionally, neither treatment has been studied in Veterans or active duty Service members.

Several other trauma-focused treatments also had insufficient evidence. A meta-analysis found Virtual Reality Exposure Therapy (VRET) was superior to waitlist but not compared with active control.(115) When VRET was compared with active controls, findings were mixed; no differences were found in five RCTs (Botella et al. [2010], GaMito et al. [2010], McLay et al. [2010], McLay et al. [2017], and Ready et al. [2010]), one RCT found VRET was superior to a non-specific non-trauma-focused treatment (van Gelderen et al. [2020]), and in a final study VRET was found to be inferior to PE at follow-up (Reger et al. [2016]).(116-122) No RCTs tested the effectiveness of Trauma Management Therapy (TMT). In one low-quality RCT of TMT (Beidel et al. [2019]) included in the Jericho et al. (2022) network meta-analysis, the exposure component of TMT was delivered virtually to both groups.(88) Both received VRET followed by either the group component of TMT focused on social interactions, depression, and anxiety or on group psychoeducation. There were no differences in clinician-rated PTSD in either group.

There was also insufficient evidence to recommend for or against Accelerated Resolution Therapy (ART) and Reconsolidation of Traumatic Memories (RTM). No RCTs of ART included the critical outcome of clinician-rated PTSD. The evidence for RTM comes from two waitlist-controlled RCTs included in the meta-analysis by Lewis et al. (2020). Although the data were positive, the evidence was judged to be very low quality.(108)

Similarly, there were too few trials to determine the effect of treatments intended to target PTSD as well as moral injury and guilt. One low-quality trial of Adaptive Disclosure (110) and one moderate quality trial of Trauma-Informed Guilt Reduction (TrIGR) included the critical outcome of clinician-rated PTSD.(111) Another RCT evaluating Impact on Killing (included in the Jericho et al. [2022] network meta-analysis) did not include the critical outcome.(123)

A number of non-trauma-focused treatments were also determined to have insufficient evidence because of either having only one or two RCTs on the specific treatment or having a relatively small number of total participants across all RCTs. As was the case with NET and BEP, SIT and IPT, which were given *Strong for* recommendations in the 2017 VA/DoD PTSD CPG, were determined to have insufficient evidence in this guideline. As reported in Jericho et al. (2022) and Mavranezouli et al. (2020), two RCTs of SIT included the critical outcome of clinician-reported PTSD.(88, 109) In one, SIT was superior to waitlist (Foa et al. [1999]), and in the other it was inferior to NET (Hensel-Dittman et al. [2011]). As reported in Jericho (2022), there is only one study of IPT that included the critical outcome of clinician-reported PTSD (Markowitz et al, 2015). In that three arm study, IPT was noninferior to PE, but not superior to relaxation therapy. Additionally, as reported in Jericho et al. (2022) and Mavranezouli et al. (2020), there were no studies of standalone STAIR; single studies of Dialectical Behavior Therapy, Acceptance and Commitment Therapy, Thought Field Therapy, and Emotional Freedom Techniques; and no studies of psychodynamic psychotherapy.(88, 109) No new studies of Seeking Safety were identified, but an SR included in the 2017 VA/DoD PTSD CPG, Roberts et al. (2015), found that Seeking Safety was not more effective than TAU for reducing PTSD symptoms in patients with PTSD and SUD.(112)

Some studies were evaluating psychoeducation and supportive therapy. Jericho et al. (2022) and Mavranezouli et al. (2020) found RCTs of psychoeducation did not differ from waitlist, and another network meta-analysis by Melton et al. (2020) found RCTs of supportive therapy also did not differ from waitlist.(88, 109, 124)

Other than WET (see Recommendation 9), insufficient evidence existed to recommend for or against the use of the brief interventions, defined as therapies with a maximum of six 60-minute sessions. These therapies included Prolonged Exposure for Primary Care (PE-PC) and STAIR-PC. There was only a single trial of PE-PC in the evidence review, Cigrang et al. (2017), which compared PE-PC with a minimal contact control at post-treatment and found no difference for the critical outcome of clinician-rated PTSD symptoms.(125) Conducted in a military population, the study showed a significantly greater reduction in the important outcome of patient-reported PTSD in PE-PC compared with the control condition. No studies of STAIR-PC included the critical outcome of clinician-rated PTSD symptoms.

In general, the SRs and network meta-analyses did not report on other outcomes of interest, such as depression, functioning, treatment dropout, or adverse events.

Across these treatments, patient preferences varied. Some patients prefer a non-trauma-focused treatment, even if they understand the most effective treatments are trauma focused (see Recommendation 8). PCT is the non-trauma-focused treatment with the most evidence (see Recommendation 9), but patients might be interested in other treatments, as well. For example, patients might prefer a treatment focused on a specific symptom (e.g., TrIGR for guilt), or they might desire a more general approach (e.g., supportive counseling). In addition, many of these treatments require specific training that is not widely available.

Several factors influenced the confidence in the quality of evidence ratings, including a lack of RCTs with Veteran and active duty Service member populations and study size (some treatments had relatively few RCTs or a small number of patients who received the treatment). Additionally, there were not enough studies of any specific treatment to have evaluated the treatments in diverse populations.

The Work Group systematically reviewed evidence related to this recommendation(88, 108-111, 115, 124, 125) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(112) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low to low. The body of evidence had some limitations, including single studies, small sample sizes, treatments tested only outside the U.S., and failure to include Veterans and active duty Service members. In general, the benefits of these individual manualized psychotherapies slightly outweighed any potential harms. Across the psychotherapies, patient values and preferences varied. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the following individual psychotherapies for the treatment of PTSD: Accelerated Resolution Therapy, Adaptive Disclosure, Acceptance and Commitment Therapy, Brief Eclectic Psychotherapy, Dialectical Behavior Therapy, Emotional Freedom Techniques, Impact on Killing, Interpersonal Psychotherapy, Narrative Exposure Therapy, Prolonged Exposure in Primary Care, psychodynamic therapy, psychoeducation, Reconsolidation of Traumatic Memories, Seeking Safety, Stress Inoculation Training, Skills Training in Affective and Interpersonal Regulation, Skills Training in Affective and Interpersonal Regulation in Primary Care, supportive counseling, Thought Field Therapy, Trauma-Informed Guilt Reduction, or Trauma Management Therapy, or Virtual Reality Exposure Therapy.

Recommendation

11. There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over, or in addition to, the full therapy protocol for the treatment of PTSD.
    (Neither for nor against | Reviewed, Not Changed)

Discussion

The 2017 VA/DoD PTSD CPG found insufficient evidence to recommend for or against the use of individual components of a manualized psychotherapy protocol over, or in addition to, a full protocol. The systematic evidence review performed for the 2023 PTSD CPG identified two meta-analyses of patients with complex trauma histories that examined different treatment components.(124, 126) However, these analyses did not specifically address the question of whether components of a protocol, such as CPT or PE, were similar in effectiveness to the full protocol. The populations studied were patients with complex trauma histories, including some Veterans, but in general did not focus on PTSD populations. Therefore, given the lack of new evidence, the Work Group decided to carry forward the previous recommendation unchanged.

Relatively few studies have examined whether modifying psychotherapy protocols by adding components of other effective psychotherapies is beneficial, or conversely, whether the individual components of a multicomponent 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 unaware of studies conducted in Veterans or active duty Service members. In addition, insufficient evidence exists 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(72, 75) and two studies finding no benefit.(127, 128) An SR of these studies found no additional benefit of adding cognitive restructuring for PTSD symptom severity, loss of PTSD diagnosis, and depression symptoms.(96) An additional study examined the benefits of SIT, with the addition of PE relative to SIT alone and PE alone, and found all three treatments superior to waitlist and similar to one another.(129)

A dismantling study of CPT, which initially included both a written trauma narrative as well as CT, examined full CPT versus the separate narrative and cognitive components.(130) 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 the written narrative is optional. CPT with the account is now referred to as CPT-A, and the standard protocol, now referred to as CPT, includes the cognitive component only.(131) Although insufficient evidence exists to make a general recommendation regarding dismantling psychotherapy protocols, both CPT and CPT-A are included in the evidence base for psychotherapies that received a *Strong for* recommendation (see Recommendation 8).

Patient preferences might vary regarding the use of components versus full protocols. If components require less time than a full protocol, they might have enhanced feasibility in settings with limited resources. If modifications to an established protocol (e.g., PE, CPT, EMDR) are clinically necessary, the modifications should be empirically and theoretically guided, with an understanding of the core components of trauma-focused psychotherapies considered most therapeutically active.

The Work Group systematically reviewed evidence related to this recommendation(124, 126) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(72, 75, 96, 127-130). The Work Group determined the new evidence was insufficient to alter the recommendation; therefore, the recommendation is categorized as *Reviewed, Not changed*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including few overall studies and none in Veterans or active duty Service members. The benefits of using components versus full protocols or adding components to full protocols were balanced with potential harms. Patient values and preferences varied because some patients

might prefer a briefer treatment as opposed to a full protocol. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over, or in addition to, the full therapy protocol for the treatment of PTSD.

Recommendation

12. There is insufficient evidence to recommend for or against any specific manualized group therapy for the treatment of PTSD.
    (Neither for nor against | Reviewed, New-replaced)

13. There is insufficient evidence to recommend using group therapy as an adjunct for the primary treatment of PTSD.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Following the recommendations in the 2017 VA/DoD PTSD CPG, the Work Group members first considered the effectiveness of group therapy as a primary treatment modality. They then considered the effectiveness of group therapy as adjunctive treatment and of specific types of group therapy as primary treatment.

An SR of group therapy by Schwartze et al. (2019) contained 13 RCTs with no treatment controls and 8 RCTs with active treatment controls that included cognitive behavioral therapies, trauma-focused cognitive behavioral therapies, IPT, stabilization groups, psychoeducation, and a resilience intervention.(132) Although the SR found some types of manualized group therapy appeared more effective than no treatment, it failed to identify any specific type of manualized group therapy as more or less effective than another and failed to find efficacy for group therapy as an adjunctive treatment. Findings were mixed for group treatments compared with no treatment controls and included the critical outcome of clinician-rated PTSD symptoms. The Schwartze et al. (2019) SR included three different trauma-focused treatment studies, two of which had significant effect sizes that differed from no treatment, Beck et al. (2009) and Castillo et al. (2016), and 1 RCT, Falsetti et al. (2008), which did not.(133-135) All 3 RCTs included in the Schwartze et al. (2019) SR of non-trauma-focused treatments had non-significant effect sizes.(136-138) The Work Group did not look at studies that compared group therapy with active controls because the SR did not find that treatment modality to be superior to other active treatments. One additional RCT found individual CPT was more effective than group CPT.(139)

Schwartze et al. (2019) also did not find a benefit for group therapy as an adjunctive treatment.(132) Five RCTs in this SR compared adjunctive group treatment with no treatment in patients receiving one or more types of primary therapy. Only two of these studies included the critical outcome of clinician-rated PTSD symptoms and neither had effect sizes that differed from no treatment, indicating that in people who are already getting treatment, group therapy did not enhance PTSD outcomes.

Limited evidence existed to address whether any type of group therapy was superior to another. Several RCTs in Schwartze et al. (2019) compared trauma-focused treatments with PCT and included the critical outcome of clinician-rated PTSD.(132) Resick et al. (2015) studied group CPT, while Classen et al. (2001) and Schnurr et al. (2003) studied trauma-focused group therapy.(140-142) None of the effect sizes for the trauma-focused treatments was statistically significant for the critical outcome of clinician-rated PTSD. This finding is consistent with the results of another RCT (not included in the systematic evidence review nor impacting the strength of this recommendation) that also failed to find a difference between a trauma-focused group therapy and PCT.(143)

An SR on dropout from psychotherapies found the dropout rate of group treatments did not differ from individual psychological treatments for PTSD.(108) Consistent with findings based on the critical outcome, Schwartze et al. (2019) reported group therapy was more effective than no treatment for the important outcomes of anxiety, depression, and remission.(132) Although the Schwartze et al. (2019) SR did not consider adverse events, Resick et al. (2017) reported a similar number of adverse events in the group and individual conditions (not included in the evidence base nor impacting the strength of this recommendation).(131)

The rationale for group therapy stems from the idea patients desire and benefit from sharing common experiences. However, patient preferences vary regarding group treatment. Although some patients prefer a group setting, others prefer their treatment delivered in private. Other factors influencing ratings were the limited number of studies on a specific treatment that included Veterans and active duty Service members. Two RCTs, Castillo et al. (2016) and Resick et al. (2017), focused exclusively on Veterans and active duty Service members, and a third (not included in the systematic evidence review nor impacting the strength of this recommendation), Sloan et al. (2018), also targeted Veterans.(131, 134, 143)

The Work Group systematically reviewed evidence related to these recommendations (108, 132, 144) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(134, 140, 145, 146) Therefore, these recommendations are categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some significant limitations, such as only a few studies of any specific treatment, missing intention-to-treat (ITT) analyses, missing details related to treatment protocols, and lack of representative subject populations. The benefits of manualized group therapy slightly outweighed the potential harm of no treatment; however, insufficient evidence exists to recommend one type of specific group therapy over another and insufficient evidence to recommend group therapy as an adjunct treatment. Additionally, group therapy would be of reduced benefit if it is being offered in lieu of, or if it is delaying, more effective treatment. Patient values and preferences varied because some patients prefer individual therapy over group therapy. Thus, the Work Group made the following recommendations: There is insufficient evidence to recommend for or against any specific manualized group therapy for the

treatment of PTSD. There is insufficient evidence to recommend using group therapy as an adjunct for the primary treatment of PTSD.

Recommendation

14. There is insufficient evidence to recommend for or against the following couples therapies for the treatment of PTSD: Behavioral Family Therapy, Structured Approach Therapy, or Cognitive Behavioral Conjoint Therapy.
    (Neither for nor against | Reviewed, Not Changed)

Discussion

Although two SRs and one RCT reported promising findings, insufficient evidence exists to recommend for or against couples therapy for the treatment of PTSD.(109, 147, 148) An SR by Suomi et al. (2019) identified two small RCTs of couples' therapy, Monson et al. (2012) and Sautter et al. (2015), that included the critical outcome of clinician-rated PTSD.(147, 149, 150) A trial by Glynn et al. (1999), included in Suomi et al. (2019), did not include the critical outcome of clinician-rated PTSD.(151) The RCT by Sautter et al. (2015) randomized Veterans and their partners to Structured Approach Therapy (SAT) or family education.(150) SAT is a 12-session manualized treatment that includes education about PTSD and how it affects relationships, emotion activation, and disclosure-based exposures. The second RCT in the SR, Monson et al. (2012), randomized Veteran couples to either CBCT or waitlist.(149) CBCT is a 15-session, manualized treatment for PTSD that focuses on reducing avoidance and challenging core beliefs maintaining PTSD and relationship difficulties. The RCT by Morland et al. (2022) randomized Veteran couples to either a brief 8-session version of CBCT delivered in person, the same treatment offered by video telehealth, or in-person family education.(148)

All three trials found that the couples treatments were more effective than control treatments in reducing clinician-rated PTSD in the identified Veterans with PTSD. The two RCTs in the Suomi et al. (2019) SR also found the couples treatments to be more effective for reducing anxiety and depression in the primary patient.(147) However, the trials found no support for dyadic adjustment or the mental health benefits for their partners.(147) Similarly, no statistical differences were found between the two CBCT arms and the active control on relationship satisfaction or functional impairment in the standalone RCT.(148)

An SR by Lewis et al. (2020) on dropout from psychotherapies found the dropout rate of couples therapy, 22%, to be similar to the pooled dropout rate of psychotherapies for PTSD, 16%.(108) However, data from an outpatient VA PTSD clinic (not included in the systematic evidence review nor impacting the strength of this recommendation) suggested almost half of the couples dropped out of treatment.(152) The recent study from Morland et al. (2022) found 26% to 30% dropout rates in the two CBCT arms, suggesting the briefer version of CBCT might be more acceptable to couples.(148)

Patients' preferences for couples therapy vary. In some cases, patients might prefer PTSD treatment that includes attention focused on their intimate relationships. In other cases, they might not want to share their traumatic experiences with their partners or have their partners involved in their recovery. One barrier to couples therapy is that some people have no intimate partner. CBCT addresses this situation by allowing the involvement of another close person, such as a parent. There is national training in VA for CBCT, making the treatment more widely available than it would be otherwise. However, the high dropout rate in VA suggests feasibility might be an issue, at least with the original 15-session version. Acceptability was higher with the briefer protocol.

The Work Group systematically reviewed evidence related to this recommendation(108, 109, 147, 148) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(149, 150) Therefore, the recommendation is categorized as *Reviewed, Not Changed*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had limitations; there was only a single study of SAT, and the two studies of CBCT used different protocols. The benefits of couples therapies slightly outweighed the harms because some patients might prefer an approach that also focuses on their relationships, and some might not. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the following couples therapies for the treatment of PTSD: Behavioral Family Therapy, Structured Approach Therapy, or Cognitive Behavioral Conjoint Therapy.

c. Pharmacotherapy

Recommendation

15. We recommend paroxetine, sertraline, or venlafaxine for the treatment of PTSD. **(Strong for | Reviewed, New-replaced)**

Discussion

Evidence from one SR, Williams et al. (2022), indicates that paroxetine, sertraline, or venlafaxine compared with placebo improves clinician-rated PTSD scores at 10 weeks or more.(153) Two RCTs within the SR found that venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI), provided benefit in clinician-rated PTSD scores at 12–24 weeks follow-up.(153) Six industry-sponsored RCTs within the SR found sertraline, a selective serotonin reuptake inhibitor (SSRI), provided a clinically significant benefit in clinician-rated PTSD scores at 10–12 weeks follow-up.(153) Only two trials were conducted in a Veteran population, both of which demonstrated no benefit in clinician-rated PTSD scores. Six industry-sponsored RCTs demonstrated paroxetine, when compared with placebo, decreased PTSD severity on the primary outcome of clinician-rated PTSD at 12 weeks–36 weeks. Three of the trials demonstrated a beneficial effect, although three trials did not, resulting in an overall positive benefit for paroxetine when compared with placebo. Considerable heterogeneity (I^2=77%) was found among the trials for paroxetine. Three studies demonstrated a benefit in the critical outcome, Clinical Global Impressions –

Improvement scale at 12–22 weeks.(153). Although the SR reviewed antidepressants as a class, higher quality evidence of benefit was found for paroxetine, venlafaxine, and sertraline individually compared with other SSRIs and SNRIs.(153) This finding is a change from the recommendations in the 2017 VA/DoD PTSD CPG, which also recommended fluoxetine based on older SRs by Lee et al. (2015) and Hoskins et al. (2016).(81, 154) The more recent SR by Williams et al. (2022) found no benefit with fluoxetine (see Recommendation 16).(153)

Patient preference varies regarding the treatment of PTSD with paroxetine, sertraline, or venlafaxine. Some patients might prefer to take medication, although others might strongly oppose taking any medication for their PTSD because of side effects, stigma, or perceived lack of benefit. Individuals diagnosed with PTSD and treated with paroxetine were more likely to withdraw from treatment because of treatment-related adverse events. In five of the six RCTs in the Williams et al. (2022) SR, paroxetine was associated with more side effects than placebo. Patients who are active duty Service members might be concerned about how taking these medications would affect their duty status. The Work Group determined 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 or fatigue. A Black Box warning by the Food and Drug Administration (FDA) states that compared with placebo, antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults; however, there appears to be no increase in the risk of suicidality in adults beyond age 24, and there might be a reduced risk in adults age 65 and older. Venlafaxine shares these potential harms and can increase blood pressure at higher dosages.

The Work Group systematically reviewed evidence related to this recommendation(153) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(81, 154) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had limitations, including the risk of bias and concerns regarding study quality and high heterogeneity. The study population was not limited to Veterans or in-combat related trauma, which might limit the generalizability to individuals who have PTSD from unrelated trauma or from prior active duty service.(153) The benefits of treatment with paroxetine, sertraline, and venlafaxine outweighed the potential harm of adverse events, which was small. Patient values and preferences variedmainly because some patients prefer to avoid medications, whereas others might prefer medication to any other treatment. Thus, the Work Group made the following recommendation: We recommend paroxetine, sertraline, or venlafaxine for the treatment of PTSD.

Recommendation

16. There is insufficient evidence to recommend for or against amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone,

olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.
(Neither for nor against | Reviewed, New-replaced)

Discussion

This group of medications with insufficient evidence includes several changes from the 2017 VA/DoD PTSD CPG, reflecting the current application of the GRADE standard and new SRs, rather than new clinical trial data.(153, 155) Most notably, fluoxetine previously carried a *Strong for* recommendation, the antipsychotics olanzapine and quetiapine previously carried *Weak against* recommendations, and the MAOI antidepressant phenelzine carried a *Weak for* recommendation. Across these medications, confidence in the quality of evidence was found to be very low.

Patient values and preferences vary considerably regarding these medications. Different concerns are present for each medication, including the level of evidence, side effect profiles, and potential benefit for alternative uses. Quetiapine and olanzapine have aroused additional concerns about significant side effects and stigma associated with use. Given the very low evidence for these medications in treating PTSD symptoms, patient preferences should be strongly considered when prescribing medication from this list. Clinicians should strongly consider adverse effects, including but not limited to, the potential for overdose in the case of amitriptyline and imipramine; seizure in the case of bupropion, amitriptyline, and imipramine; QT interval prolongation in the case of citalopram, amitriptyline, and imipramine; metabolic derangements such as weight gain in the case of mirtazapine, phenelzine, olanzapine, and quetiapine; hepatic failure in the case of nefazodone; abuse in the case of eszopiclone and pregabalin; toxic epidermal necrolysis (Stevens-Johnson syndrome) in the case of lamotrigine; and cognitive side effects in the case of topiramate.

The Work Group systematically reviewed evidence related to this recommendation(153, 155) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(81, 154) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. For treating PTSD, the benefits of monotherapy with amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine were balanced with the potential harms. Patient values and preferences varied because some patients might not want to use medication for their PTSD, and different considerations must be made for each medication. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.

Recommendation

17. There is insufficient evidence to recommend for or against psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.
    (Neither for nor against | Reviewed, New-added)

Discussion

The Work Group found no studies meeting the search criteria that assessed the effects of psychedelics (e.g., psilocybin, ayahuasca, dimethyltryptamine [DMT], lysergic acid diethylamide [LSD]) for the treatment of PTSD. Recommendations for other specific psychedelic agents (ketamine, cannabis and cannabis derivatives, 3,4-methylenedioxymethamphetamine [MDMA] assisted psychotherapy) are addressed in Recommendation 18, Recommendation 20, and Recommendation 23. Of note, these agents cannot be legally prescribed in the U.S. outside a research study. Additionally, given the lack of evidence, these agents might have adverse effects, risks, or both that are currently unknown (and adverse events have been anecdotally reported). Therefore, insufficient evidence exists to recommend for or against these specific psychedelic agents as a treatment for PTSD.

Patient preferences vary largely regarding treatment with these interventions because some individuals might be unwilling to engage with them or others might request them specifically. Further, resource use and feasibility concerns are due to the number of trained providers as well as to issues related to access and equity because of the legality of these interventions in the U.S.

The Work Group systematically reviewed evidence related to this recommendation. Given the lack of evidence in the systematic evidence review, the Work Group concluded harm slightly outweighed any potential benefit. Therefore, the recommendation is categorized as *Reviewed, New-added.* Patient values and preferences varied because some patients might want to try psychedelics, but others may not. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.

Recommendation

18. We suggest against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.
    (Weak against | Reviewed, New-replaced)

Discussion

This recommendation encompasses several changes in guidance on specific medications from the 2017 VA/DoD PTSD CPG. Changes reflect the current application of the GRADE approach and the publication of new SRs and clinical trials. The

evidence base for this recommendation consists of SRs by Dunlop et al. (2021), Hoskins et al. (2021), Williams et al. (2022), and Yan et al. (2022).(153, 155-157) The 2017 VA/DoD PTSD CPG included a *neither for nor against* recommendation on vortioxetine. The *Weak against* recommendation on ketamine was maintained, reflecting findings of recently published clinical trials.(158) These medications are known to be effective for other conditions, and providers should refer to Recommendation 34 when addressing comorbid conditions.

Patient preferences vary largely regarding these medications. Differing considerations are associated with each, including the side effect profiles and balance of harms and benefits. The Work Group notes that this *Weak against* recommendation covers prazosin when used as monotherapy for PTSD. Please see Recommendation 32 for information on using prazosin to treat nightmares associated with PTSD.

The Work Group systematically reviewed evidence related to this recommendation(153, 155-158) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(81, 159) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of the evidence had some limitations, which included a lack of strong evidence for the efficacy of these medications for the treatment of PTSD. The benefits of treating PTSD using divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine as monotherapy were outweighed by the potential harm. Patient values and preferences varied mainly because of the different considerations for each medicine, including the level of evidence for an effect on PTSD symptoms, side effect profiles, and potential benefits for alternative uses. Thus, the Work Group made the following recommendation: We suggest against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.

Recommendation

19. We recommend against benzodiazepines for the treatment of PTSD. **(Strong against | Reviewed, New-replaced)**

Discussion

The evidence base for this recommendation includes the SR by Williams et al. (2022).(153) A paucity of evidence evaluating the effectiveness of benzodiazepines on PTSD symptoms exists. Included in the Williams et al. (2022) SR was an RCT (one null trial conducted in 1990 randomizing 32 patients to alprazolam or placebo). It, along with evidence from the 2017 VA/DoD PTSD CPG (Guina et al. [2015]), found that benzodiazepines are associated with misuse, decreased effectiveness of recommended PTSD treatments, and cognitive changes, especially in the elderly.(153, 160)

Patient preferences vary considerably regarding this treatment. The patient focus group noted interest in using benzodiazepines because they are effective for short-term anxiety relief. However, these medications are ineffective in the long term and can be

harmful. Concerns surrounding co-occurring SUD and elderly patients in VA should also be strongly considered if prescribing these medications.

The Work Group systematically reviewed evidence related to this recommendation (153) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(160) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The confidence in the quality of the evidence was very low. The potential harms of these medications (e.g., cognitive changes, misuse) outweighed the benefits because no evidence of long-term benefit was found. Patient values and preferences varied largely. Thus, the Work Group made the following recommendation: We recommend against benzodiazepines for the treatment of PTSD.

Recommendation

20. We recommend against cannabis or cannabis derivatives for the treatment of PTSD.
    (Strong against | Reviewed, Amended)

Discussion

The Work Group recommends against the use of cannabis or cannabis derivatives in treating patients with PTSD because of the lack of well-designed RCTs evaluating the efficacy of cannabis derivatives in large samples of individuals with PTSD and the serious side effects associated with their use.(161-164) Evidence from one randomized, double-blind, crossover study (not included in the systematic evidence review nor impacting the strength of this recommendation) found no significant difference in change in PTSD symptom severity between active cannabis concentrations and placebo.(165)

Evidence from the 2017 VA/DoD PTSD CPG indicates significant harm associated with cannabis use. Wilkinson et al. (2016) reported that marijuana impairs attention, memory, IQ, and driving ability, and early and persistent use has been associated with the emergence of psychosis.(163) Steenkamp et al. (2017) noted the adverse psychiatric outcomes associated with marijuana use in patients with PTSD—including depression, anxiety, psychosis, and substance misuse.(161) Kansagara et al. (2017) reported possible treatment-related serious events, such as suicide attempts, paranoia, and agitation.(162)

Patient preferences vary significantly regarding this treatment. The patient focus group described the benefits of cannabis and encouraged VA to consider this treatment. Other patients might be unwilling to try cannabis. However, significant unknowns are related to resource use, acceptability, and feasibility regarding cannabis use (e.g., CBD or THC ratio, cost, dose, dosage form, route of administration, legality).

The Work Group found no new evidence related to this recommendation in the current systematic evidence review and used the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(161-164) Therefore, the recommendation is categorized as

Reviewed, Amended. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had significant limitations, including a lack of randomized, controlled, methodologically sound clinical trials; small sample sizes, and selection bias.(161-164) The benefits of cannabis were outweighed by the potential serious adverse effects. Patient values and preferences varied largely because some patients seek new, novel treatments although others might be unwilling to use cannabis or cannabis derivatives. Thus, the Work Group made the following recommendation: We recommend against cannabis or cannabis derivatives for the treatment of PTSD.

d. Augmentation Therapy

Recommendation

21. There is insufficient evidence to recommend for or against the combination or augmentation of psychotherapy (see Recommendation 8 and Recommendation 9) or medications (see Recommendation 15) with any psychotherapy or medication for the treatment of PTSD (see Recommendation 22 for antipsychotic medications and Recommendation 23 for 3,4-methylenedioxymethamphetamine).
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Combination treatment involves combining two or more evidence-based treatments for PTSD to improve outcomes. The combination can occur at the initiation of treatment or following a period of monotherapy to address partial or nonresponse. With augmentation, an intervention that has not demonstrated efficacy for PTSD in and of itself is added to evidence-based treatment to enhance its effect.

Evidence is inconclusive on whether combining effective medications or psychotherapies enhances treatment outcomes in PTSD.(84, 166) Several studies have tested PE in combination with either paroxetine or sertraline. A very small study of survivors of the attacks on September 11, 2001, found the combination of paroxetine and PE more effective than PE alone at post-treatment, but the advantage disappeared at follow-up.(167) However, 2 more extensive studies failed to find that medication enhances the effects of PE. A study of survivors of MVAs found no difference between the combination of paroxetine and PE versus PE or paroxetine alone.(168) In addition, a placebo-controlled trial in Veterans found no difference between sertraline versus placebo when added to PE.(84) Two studies examined partial responders. A study of sertraline versus placebo for patients with partial response to PE found no added benefit of sertraline.(169) Another study found no additional benefits of adding PE after 8 weeks of treatment with sertraline versus placebo, although a post-hoc analysis found that PE (versus continued sertraline monotherapy) improved response among partial medication responders.(170)

Moreover, insufficient evidence exists to support augmenting effective psychotherapy or medication with other medications to reduce PTSD symptoms. Two SRs by Hoskins et al. (2021a and 2021b) examined the evidence for augmentation of psychotherapy (2021a) and of medication (2021b) using several different medications.(157, 166) A total of 4 studies were included in the SR that evaluated d-cycloserine augmentation of psychotherapy (PE in 2 studies and VRET in 2 studies).(166) No overall effect of d-cycloserine augmentation was found. In the SR that evaluated medication augmentation, 30 studies were identified that compared an active medication with placebo, but none of these studies ensured that the primary treatment being augmented was an evidence-based medication for PTSD. Also, many studies were small, did not assess a primary PTSD outcome, or both.(157) Several studies assessed prazosin or MDMA-assisted psychotherapy; these agents are addressed in Recommendation 18, Recommendation 23, and Recommendation 32. Other studies assess augmentation with an antipsychotic medication; these agents are addressed in Recommendation 22.(157)

An additional protocol mentioned in the SR by Hoskins et al. (2021a), which used propranolol with trauma memory reactivation, is neither a combination nor augmentation treatment.(166) A placebo-controlled trial described by Hoskins et al. (2021a) found the protocol was effective.(171) However, because this trial was a single study, Hoskins et al. (2021a) did not formally report meta-analytic findings for it, and the Work Group was unable to recommend it because of serious imprecision.(166)

Other considerations about combination and augmentation strategies include side effect profile and acceptability. Treatment considerations are also related to subgroups, such as those with depression, mild traumatic brain injury (mTBI), and co-occurring alcohol use disorder, where more evidence exists to support the use of medication to treat the co-occurring condition. These conditions are prevalent in the Veteran population and relevant for both Veterans and active duty Service members.

The Work Group systematically reviewed evidence related to this recommendation(84, 157, 166) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(167-169, 172) Therefore, the recommendation is categorized as *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including few studies for each medication and, in the SR by Hoskins et al. (2021), randomization and allocation procedures and modified ITT.(157) The benefits of using medications in combination or for treatment augmentation were balanced with the potential harms. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the combination or augmentation of psychotherapy (see Recommendation 8 and Recommendation 9) or medications (see Recommendation 15) with any psychotherapy or medication for the treatment of PTSD (see Recommendation 22 for antipsychotic medications and Recommendation 23 for 3,4-methylenedioxymethamphetamine).

Recommendation

22. We suggest against aripiprazole, asenapine, brexpiprazole, cariprazine, iloperidone, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone for augmentation of medications for the treatment of PTSD.
    (Weak against | Reviewed, New-replaced)

Discussion

Risperidone, aripiprazole, and olanzapine are the only atypical antipsychotics studied for the augmentation of other medications in treating PTSD found by the 2022 systematic evidence review. An SR by Hoskins et al. (2021) included three RCTs examining the effects of risperidone augmentation.(157) VA Cooperative Study #504 randomized Veterans with military-related PTSD deemed resistant to SSRI treatment to either risperidone augmentation or placebo.(173) Changes in the critical outcome of clinician-rated PTSD subscales for reexperiencing and hyperarousal statistically favored risperidone at 24 weeks, but overall changes in PTSD were not statistically significant. A small study not mentioned in Hoskins et al. (2021b) demonstrated a statistically significant reduction in CAPS scores at 9 months for patients treated with adjunctive risperidone, whereas two small studies of patients with treatment-resistant PTSD also found no statistically significant changes to clinician-rated PTSD when compared with placebo.(170, 174)

Aripiprazole was studied as an augmentation to SSRI medication in a very small study of Veterans with PTSD.(175) Improvement in clinician-rated PTSD scores was not statistically significant. In the sole study of olanzapine augmentation, Veterans with chronic military-related PTSD were compared with placebo. PTSD changes on clinician-administered scales did not significantly differ between the groups.(176)

The sole study of olanzapine augmentation is a study in which 19 Veterans with chronic military-related PTSD were compared with placebo. Although sleep and depressive symptoms improved, PTSD changes on clinician-rated scales did not differ significantly between the groups.(176)

Atypical antipsychotics (other than risperidone, aripiprazole, and olanzapine) have not been studied for the augmentation of different medications for the treatment of PTSD. Although not included in the systematic evidence review, the risks of these medications include weight gain, hyperlipidemia, diabetes mellitus, QTc prolongation, and extrapyramidal side effects are well established and outweigh the unknown benefits.(177)

Patient preferences vary considerably regarding these treatments. The patient focus group did not comment directly on this class of medications, though they did express interest in a broader range of pharmacological options. Patients' preferences on

antipsychotic treatment have varied mainly because of concern for weight gain and other health effects, the stigma around treatment with antipsychotic medication, and perceived potential for adverse impact on a military career.

The Work Group systematically reviewed evidence related to this recommendation(157) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(170, 173-176) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, which included few studies of antipsychotic augmentation and small sample sizes. The well-established, significant potential harms outweighed the uncertain, small potential benefits. Patient values and preferences varied mainly because of concern for weight gain and other health effects, the stigma around treatment with antipsychotic medication, and perceived potential for adverse impact on a military career. Thus, the Work Group made the following recommendation: We suggest against aripiprazole, asenapine, brexpiprazole, cariprazine, iloperidone, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone for augmentation of medications for the treatment of PTSD.

Recommendation

23. There is insufficient evidence to recommend for or against 3,4-methylenedioxymethamphetamine assisted psychotherapy for the treatment of PTSD.
    (Neither for nor against | Reviewed, New-added)

Discussion

MDMA-assisted psychotherapy involves an individual taking MDMA before 2 – 3 eight hour psychotherapy sessions. Typically, 3 preparatory sessions occur before the first MDMA-assisted psychotherapy session, and up to 3 "integration" sessions occur after each MDMA-assisted psychotherapy session (for a total of 12–15 sessions). The type of psychotherapy provided is not strictly prescribed, although the manual provides several options to be considered. Additionally, MDMA sessions are provided by two therapists, typically a man and a woman. Five small to moderately sized RCTs (including a total of 176 participants) have found this form of MDMA-assisted psychotherapy to benefit individuals with PTSD.(157) However, these studies have differed notably in the control condition used. Some have used low-dose MDMA as the control condition, whereas others have used an inactive placebo. Studies using low-dose MDMA as the control condition generally demonstrated much better blinding. Differences in the adequacy of blinding could have potentially biased outcomes.(157) Additionally, these studies included few Veterans and no active duty Service members, limiting generalizability to VA and DoD population of interest.

It would be challenging to implement MDMA-assisted psychotherapy in current VA and DoD health care systems. The treatment protocol requires a high investment of resources

(e.g., two therapists committed for 8 hours during each therapy MDMA session in addition to 12 standard psychotherapy sessions and extensive therapist training requirements). Allocation of staff to conduct MDMA-assisted psychotherapy could have negative impacts on access for other patients. The success of MDMA-assisted psychotherapy might also require discontinuing SSRI use by the patient. Additionally, patients' willingness to engage in this intervention would likely vary significantly.

The Work Group systematically reviewed evidence related to this recommendation. (157) Therefore, the recommendation is categorized as a *Reviewed, New-added* recommendation. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations, including relatively few participants, including few Veterans and no Service members, studied and differing control conditions that impacted adequacy of blinding and could have biased the outcomes.(157) Additionally, relatively few Veterans or active duty Service members were included. The benefits of MDMA are balanced with the potential harms, which include worsening symptoms and an increase in suicidal ideation (study not included in the evidence base nor impacting the strength of the recommendation).(178) Patient values and preferences varied mainly because of comfort with psychedelic treatment. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against 3,4-methylenedioxymethamphetamine assisted psychotherapy for the treatment of PTSD.

e. Non-pharmacologic Biological Treatments

Recommendation

24. There is insufficient evidence to recommend for or against the following somatic therapies for the treatment of PTSD: capnometry-assisted respiratory therapy, hyperbaric oxygen therapy, neurofeedback, NightWare, repetitive transcranial magnetic stimulation, stellate ganglion block, or transcranial direct current stimulation.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Repetitive transcranial magnetic stimulation (rTMS) is an intervention that uses magnetic pulses to create electrical currents in the brain, leading to neuronal depolarization. rTMS can be delivered to any part of the cortex using high (≥5 Hz) or low (≤1 Hz) frequency stimulation. The location of the stimulation on the cortex determines which neural systems are impacted. Further, high- versus low-frequency stimulations are thought to have different neurophysiological and potentially behavioral effects. Therefore, to interpret the rTMS literature, one must know how rTMS was delivered (e.g., left versus right side of the brain, dorsolateral versus dorsomedial cortex, high frequency versus low frequency).

Two SRs included 11 and 7 RCTs, respectively, with the critical outcome of clinician-rated PTSD reporting the benefits for the use of rTMS in treating PTSD; 7 of the RCTs were included in both SRs.(179, 180) rTMS is well tolerated and has very low risk when

established safety guidelines are followed. However, a significant challenge in interpreting these SRs is that the individual trials use significantly different treatment parameters (e.g., left dorsolateral prefrontal cortex versus right dorsolateral prefrontal cortex, high frequency versus low frequency). Additionally, the individual studies within the two SRs generally have small sample sizes, making generalizing from each study difficult.(179, 180) Therefore, concluding which type of rTMS is most effective in treating PTSD is impossible currently, even though rTMS, in general, is beneficial. Based on this fact, the Work Group concluded there is insufficient evidence to recommend for or against the use of rTMS using any specific parameter set for the treatment of PTSD.

Neurofeedback is a biofeedback approach that helps individuals control specific aspects of brain activity, typically using functional magnetic resonance or electroencephalography. Two RCTs and one RCT from an SR with the critical outcome of clinician-rated PTSD found benefit for neurofeedback as a treatment for PTSD.(181-183) Neurofeedback is very low risk and well tolerated. However, each neurofeedback paradigm studied varied, so inconclusive evidence exists for any particular neurofeedback approach to recommend for or against it as an intervention for PTSD.

Two RCTs have assessed stellate ganglion block (SGB) as a treatment for PTSD.(184, 185) An RCT by Hanling et al. (2016) randomized active duty Service members with PTSD to receive either a single injection of anesthetic near the SGB or a saline injection (sham).(184) No difference was found between the SGB and sham groups in the critical outcome of provider-rated PTSD at 1 week, 1 month, or 3 months after the intervention. (184) In an RCT by Olmstead et al. (2020), active duty Service members with PTSD were randomized to receive either SGB or sham.(185) In this study, the SGB group received two injections of anesthetic 2 weeks apart near the stellate ganglion. The sham group received two saline injections into muscles in the region of the stellate ganglion. Six weeks after the second injection, this study found a benefit for SGB versus sham for improving provider-rated PTSD severity. A significant limitation of this study is the nature of the sham condition, which allowed the individuals administering the treatment to be unblinded and possibly caused unblinding among participants. Additionally, the follow-up period of only 6 weeks is too brief to provide information on the durability of this intervention. Therefore, when these results are considered with the prior negative RCT, the Work Group concluded the current evidence is insufficient to recommend for or against SGB as a treatment for PTSD.

An RCT by Doenyas-Barak et al. (2022) evaluated hyperbaric oxygen therapy (HBOT) versus a waitlist control condition specifically in patients with PTSD.(186) Although this study suggested a benefit for HBOT on the critical outcome of clinician-rated PTSD, the absence of an adequate control condition significantly limits the confidence in these results. A waitlist controlled trial of capnometry-assisted respiratory therapy (CART) by Jamison et al. (2022) failed to identify any benefit of CART for hyperarousal symptoms in

PTSD or overall PTSD severity.(187) No RCTs with a clinician-rated outcome were identified to inform on the efficacy of NightWare for treating PTSD.

None of the studies relating to transcranial direct current stimulation (tDCS) assessed its ability to decrease PTSD severity using the critical outcome of clinician-rated PTSD. Two small RCTs found mixed results using a patient-rated measure of PTSD severity, and the confidence in the data quality for these studies was low to very low.(188, 189) However, tDCS is low risk and associated with very few side effects or adverse events. Therefore, it was concluded there is insufficient evidence to recommend for or against tDCS for the treatment of PTSD.

Patient preferences vary considerably across the various treatment modalities included in this recommendation. rTMS protocols can be time burdensome given the frequent visits required and might be difficult for patients facing challenges with distance to the treatment sites or with transportation. HBOT protocols have similar burdens for patients, but some patients are very vocal in requesting access to this treatment. Also, some patients are vocal advocates of SGB, although others might be highly reluctant to engage in treatment involving neck injections. Further, significant inequities exist regarding access to the treatments included in this recommendation. HBOT and SGB are available in a few places, and both require substantial resources to implement, including specially trained interventional providers for SGB. rTMS has wider availability but still requires important resources to stand up and maintain a clinical service. Acceptability of rTMS might be decreased in some patients because of tolerability issues. Neurofeedback also requires specific resources to implement, which might be unavailable in some health care settings.

The Work Group systematically reviewed evidence related to this recommendation (179-189) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(190, 191) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low to very low. The evidence had limitations, including a small sample size and concerns surrounding blinding in RCTs.(179-189) The benefits of these treatment modalities were balanced with the potential harms. Patient values and preferences varied mainly because of the different considerations for each treatment modality, such as time burden and accessibility. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the following somatic therapies for the treatment of PTSD: capnometry-assisted respiratory therapy, hyperbaric oxygen therapy, neurofeedback, NightWare, repetitive transcranial magnetic stimulation, stellate ganglion block, or transcranial direct current stimulation.

Recommendation

25. We suggest against electroconvulsive therapy or vagus nerve stimulation for treatment of PTSD.
    (Weak against | Reviewed, New-replaced)

Discussion

No studies were identified in the 2022 systematic evidence review to support the efficacy of either electroconvulsive therapy (ECT) or vagus nerve stimulation (VNS) for the treatment of PTSD. However, the VA/DoD CPG for the Management of Major Depressive Disorder (MDD CPG) recommends ECT to treat some patients with severe major depressive disorder (MDD).[f] Because PTSD is highly comorbid with MDD in both Veterans and active duty Service members, ECT might be considered for certain patients with both conditions. Therefore, this *Weak against* recommendation for using ECT to treat PTSD should not be interpreted as a recommendation against using ECT if it is otherwise clinically indicated for another condition (e.g., in some cases of MDD).

Patient preferences vary significantly given the historical stigma associated with ECT and the invasive nature of surgical procedures involved with VNS. Both interventions require general anesthesia, and VNS also requires minor surgery. Additionally, these interventions are resource intensive for staff, space, and equipment. Further, they are not readily available across health care systems, which raises equity of access issues.

Because the 2022 systematic evidence review uncovered no new evidence, the Work Group considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(190-192) Therefore, this recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. A lack of published studies limited the body of evidence. The potential harms of ECT and VNS outweighed the potential benefits. Patient values and preferences varied widely because of the associated risk and stigma with the interventions. Thus, the Work Group made the following recommendation: We suggest against electroconvulsive therapy or vagus nerve stimulation for treatment of PTSD.

f. Complementary, Integrative, and Alternative Approaches

Recommendation

26. We suggest Mindfulness-Based Stress Reduction for the treatment of PTSD. **(Weak for | Reviewed, New-replaced)**

Discussion

MBSR is a comprehensive mindfulness training program typically considered to be a Complementary and Integrative Health (CIH) intervention, meaning it is a non-mainstream approach that might be used in conjunction with conventional medical care.[g] Evidence from an SR of MBSR, which included five RCTs that employed the critical outcome of clinician-rated PTSD, suggests that MBSR improves PTSD symptoms relative to any comparator.(193) Three of these RCTs involved Veterans and showed that MBSR outperformed Present-Centered Group Therapy (PCGT)(194, 195)

[f] For additional information, see the VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder (MDD CPG). Available at: https://www.healthquality.va.gov/.

[g] Complementary, Alternative, or Integrative Health: What's In a Name? | NCCIH (nih.gov)

or TAU.(196) A fourth RCT in civilians found that MBSR+TAU outperformed PCGT+TAU.(197) One Veteran trial showed no difference from PCGT on the critical outcome of clinician-rated PTSD but did find an advantage for MBSR in terms of self-reported PTSD symptoms.(198) One trial of brief mindfulness training, an abbreviated form of MBSR, did not outperform TAU.(199) Additional strengths of the evidence for MBSR include the large number of Veteran trials and implementation by multiple research groups.

Patient preferences about mindfulness vary, with some patients strongly preferring CIH interventions and other patients strongly preferring conventional interventions. MBSR does require provider certification; such training is widely available, although the cost of and prerequisites for (e.g., personal meditation practice) training might limit the number of available providers. The intervention is typically delivered in eight 2.5-hour sessions plus a full-day retreat and requires regular practice, so the burden for participants is similar to psychotherapy. Although briefer classes are available, their efficacy is currently unknown.

The Work Group systematically reviewed evidence related to this recommendation (193, 200) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(200) Therefore, the recommendation is categorized as *Reviewed, New-replaced* recommendation. The Work Group's confidence in the quality of the evidence was moderate. The benefits of MBSR outweighed the potential harms, which were minimal. MBSR might have other benefits regarding anxiety reduction and overall wellbeing and should be supported among interested individuals (not included in the systematic evidence review nor impacting the strength of this recommendation).(201, 202) Thus, the Work Group made the following recommendation: We suggest Mindfulness-Based Stress Reduction for the treatment of PTSD.

Recommendation

27. There is insufficient evidence to recommend for or against the following mind-body interventions for the treatment of PTSD: acupuncture, Cognitively Based Compassion Training Veteran version, creative arts therapies (e.g., music, art, dance), guided imagery, hypnosis or self-hypnosis, Loving Kindness Meditation, Mantram Repetition Program, Mindfulness-Based Cognitive Therapy, other mindfulness trainings (e.g., integrative exercise, Mindfulness-Based Exposure Therapy, brief mindfulness training), relaxation training, somatic experiencing, tai chi or qigong, Transcendental Meditation, and yoga.
    (Neither for nor against | Reviewed, New-replaced)

Discussion

Mind-body practices are a diverse group of techniques taught or administered by a trained practitioner and involve mental and physical aspects. They are a subgroup of CIH. The mind-body practices reviewed herein were typically evaluated as standalone interventions, in lieu of or in conjunction with other treatments; to the extent that they

were applied in the context of other interventions (e.g., for individuals on stable pharmacotherapy), adjunctive effects were not evaluated.

Evidence from an SR that included three RCTs that employed the critical outcome of clinician-rated PTSD suggests acupuncture improves PTSD symptoms relative to TAU, sham, and paroxetine.(203) Additional evidence comes from an RCT that used a self-report measure of PTSD. Little evidence exists of harm from acupuncture, aside from discomfort with needles and mild local reactions (e.g., bleeding). Concerns related to acupuncture include low study quality, use of different acupuncture styles (e.g., whole body versus auricular), and limitations of comparison conditions (e.g., failure to control for nonspecific aspects of acupuncture).

Three studies, all of which used critical outcome of clinician-rated PTSD and involved Veteran samples, evaluated Transcendental Meditation (TM) for the treatment of PTSD symptoms. The most extensive study demonstrated that TM was non-inferior to PE and outperformed a health education control.(204) An additional study found that TM was superior to TAU,(205, 206) although a third study found that TM did not differ from PCGT on clinician-rated outcomes but outperformed PCGT on patient-rated outcomes.(205) The limited number of studies, mixed results, and very low to low quality evidence led to an insufficient evidence recommendation for TM.

Two studies with the critical outcome of clinician-rated PTSD evaluated the Mantram Repetition Program (MRP) for the treatment of PTSD in Veterans. In a two-site VA trial, MRP outperformed PCT in change in PTSD symptoms and insomnia.(207) Additional evidence for MRP comes from its demonstrated added benefit over TAU alone for Veterans with PTSD.(208) Low-quality evidence, a limited number of studies, and concerns about allegiance bias preclude a recommendation for or against MRP.

A single study showed Loving Kindness Meditation was not inferior to CPT regarding change in clinician-rated PTSD symptoms.(209) This study was of good quality, but more than a single study is needed to support a recommendation.

One study of yoga included the critical outcome of clinician-rated PTSD. That RCT found that a holistic yoga program was more effective than a wellness lifestyle program in terms of reducing PTSD symptoms.(210) Evidence from an SR including seven RCTs suggests that yoga is associated with more improvement in self-reported PTSD symptoms than no treatment, TAU, or psychoeducation control.(210-212) The single study with the critical outcome, low evidence quality, and variability in practices precludes a recommendation for or against yoga.

Single, low-quality studies exist for the following practices: Cognitively Based Compassion Training Veteran version,(213) Integrative Exercise (214), Mindfulness-Based Exposure Therapy and progressive muscle relaxation,(215) somatic experiencing,(216) and visual art therapy.(217)

No evidence was identified evaluating exercise, guided imagery, hypnosis and self-hypnosis, tai chi, or qigong for the treatment of PTSD.

Patient preferences about mind-body practices vary, with some patients strongly preferring CIH interventions and other patients strongly preferring conventional interventions. The patient focus group reported benefits from engaging in acupuncture, creative arts therapy, meditation, tai chi, qigong, and yoga.

There are varied considerations in offering mind-body approaches practiced in settings that provide care to active duty Service members and Veterans. As with other protocols and specializations, CIH approaches require providers to meet minimum standards of training and to have that approach within their scope of practice. The training and degree of personal practice required among providers varies in relation to the type of approach being delivered. Mind-body practices vary in burden for participants, including the length and frequency of instructional sessions, the amount of time they are expected to practice to see results, and the degree of physical demand. Providers should consider these differences when discussing options with active duty Service members and Veterans. Providers might also want to consider potential benefits to overall health when discussing mind-body practices with Veterans and active duty Service members interested in incorporating such practices into their lives.

The Work Group systematically reviewed evidence related to this recommendation (203-217) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(200, 218) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including few studies for each intervention and studies with small sample sizes or other methodological problems. The benefits of mind-body interventions outweighed the potential harms, which were minimal. Patient values and preferences varied because patients differ in their views about mind-body practices. These practices might have other benefits regarding overall wellbeing and should be supported among interested individuals. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the following mind-body interventions for the treatment of PTSD: acupuncture, Cognitively Based Compassion Training Veteran version, creative arts therapies (e.g., music, art, dance), guided imagery, hypnosis or self-hypnosis, Loving Kindness Meditation, Mantram Repetition Program, Mindfulness-Based Cognitive Therapy, other mindfulness trainings (e.g., integrative exercise, Mindfulness-Based Exposure Therapy, brief mindfulness training), relaxation training, somatic experiencing, tai chi or qigong, Transcendental Meditation, and yoga.

Recommendation

28. There is insufficient evidence to recommend for or against the following interventions for the treatment of PTSD: recreational therapy, aerobic or non-

aerobic exercise, animal-assisted therapy (e.g., canine, equine), and nature experiences (e.g., fishing, sailing).
(Neither for nor against | Reviewed, New-replaced)

Discussion

No studies were identified in the literature review to allow evaluation of exercise (aerobic and non-aerobic), animal-involved interventions, or nature experiences for the treatment of PTSD. An RCT comparing service dogs with emotional support dogs, published after the evidence review and, therefore, not affecting the strength of this recommendation, found no benefit of service dogs on the critical outcome of clinician-rated PTSD nor on the study's primary outcomes of mental- and physical-health-related QoL and functioning.(219)

Patient preferences varied largely regarding these interventions. Many are niche modalities that appeal to only some patients. The patient focus group reported benefits from engaging in equine therapy specifically. Because these interventions might provide ancillary benefits, such as positive affect, physical activity, and social engagement, these interventions might be encouraged to support overall wellness in Veterans and active duty Service members interested in incorporating such activities into their lives. Some of these activities are provided as part of a Whole Health System of Care or Recreation Therapy Programs.

Resource use is significant for some approaches (e.g., nature experiences), although others require minimal resources (e.g., exercise). Protocols for animal-involved interventions are poorly developed, and their effects on the service animals and family members of the individual with PTSD are poorly understood.

The Work Group found no evidence in the systematic evidence review related to this recommendation. Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was very low based on the lack of studies meeting inclusion standards. Patient values and preferences varied mainly because some patients might have strong allegiances to these programs. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the following interventions for the treatment of PTSD: recreational therapy, aerobic or non-aerobic exercise, animal-assisted therapy (e.g., canine, equine), and nature experiences (e.g., fishing, sailing).

g. Technology-Based Treatment

Recommendation

29. We recommend secure video teleconferencing to deliver treatments in Recommendation 8 and Recommendation 9 when that therapy has been validated for use with video teleconferencing or when other options are unavailable.
(Strong for | Reviewed, New-replaced)

Discussion

Video teleconferencing is a significant advancement with the potential to significantly increase the reach of psychotherapy. Four RCTs reviewed as part of the 2017 VA/DoD PTSD CPG(220-222) plus three additional RCTs identified in the current evidence review that included the critical outcome of clinician-rated PTSD suggest CPT and PE delivered via video teleconferencing (VTC) are not inferior to treatments delivered face-to-face (FTF).(223-225) Two RCTs and an SR demonstrated the non-inferiority of CPT delivered through VTC to FTF treatment.(223-225) One RCT demonstrated the non-inferiority of PE.(221) In addition, building on the prior literature that included some in-office VTC and some in-home VTC, Morland et al. (2020) conducted a study of PE using a superiority design, hypothesizing more significant effects of in-home VTC and in-home FTF as compared with office-based VTC.(224) Although the study failed to find in-home treatment of either type superior, participants in both VTC treatment conditions improved. Across all RCTs, the quality of evidence for the critical outcome was moderate.

Individual RCTs also found that PE and CPT delivered via VTC improved important outcomes, such as self-reported PTSD symptoms, depression, anxiety, QoL, and the critical outcome of clinician-rated PTSD symptoms.(220-222) Morland et al. (2020) reported specifically on dropouts, finding more dropouts in the two VTC conditions than in-home treatment.(224) None of the RCTs reported adverse events. Patient preferences vary regarding VTC. The patient focus group noted they often prefer in-person care, but VTC might be less burdensome and time intensive than in-person treatment. Moreover, VTC can increase access for patients unable to attend treatment in person. However, some patients might not have access to the high-speed internet needed to support VTC. All RCTs were conducted with Veteran samples except one that was a mix of Veterans and non-Veterans. Both men and women were included in the RCTs.

Although this recommendation is specific to the delivery of CPT and PE therapies tested in VTC settings, the Work Group recognizes that VTC policies across VA and DoD take a broad interpretation of the literature in assuming that any evidence-based outpatient modality being delivered in a FTF clinical setting might be considered for VTC delivery. Therefore, this recommendation should not be interpreted to imply that modalities that have not been tested explicitly through VTC are precluded from consideration based on factors such as research literature outside the scope of this guideline, clinical judgment, shared decision making, availability of treatment modalities, and so forth. However, because the recommendations in this guideline are based on empirical evidence, the PTSD Work Group limited the recommendation to treatments that have demonstrated efficacy when delivered by VTC.

The Work Group systematically reviewed evidence related to this recommendation(223-225) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(220-222) Therefore, the recommendation is categorized as *Reviewed, New-*

replaced. The Work Group's confidence in the body of evidence was moderate. The benefits outweighed the potential for harm from lack of treatment if they cannot receive intervention in-person. Secure VTC can increase accessibility for Veterans who travel and have no time to attend weekly in-person appointments. Patient values and preferences vary because some patients might prefer in-person care. Thus, the Work Group decided on a *Strong for r*ecommendation. Thus, the Work Group made the following recommendation: We recommend secure video teleconferencing to deliver treatments in Recommendation 8 and Recommendation 9 when that therapy has been validated for use with video teleconferencing or when other options are unavailable.

Recommendation

30. There is insufficient evidence to recommend for or against mobile apps or other self-help-based interventions for the treatment of PTSD.
(Neither for nor against | Reviewed, New-added)

Discussion

Mobile apps are considered self-help interventions to aid in managing symptoms in the moment. A meta-analysis by Goreis et al. (2020) identified two RCTs evaluating mobile apps or other internet interventions delivered without facilitation.(226) Neither included the critical outcome of clinician-rated PTSD. Both studies compared the PTSD Coach mobile app with waitlist, using the important outcome of self-reported PTSD. Although the smaller feasibility pilot by Miner et al. (2016) did not find that PTSD Coach had an effect on PTSD, the larger RCT by Kuhn et al. (2017), which had participants spend more time using the app, was positive for self-reported PTSD, depression, and functioning.(227, 228) Neither study reported adverse events nor included Veterans or active duty Service members.

Patient preferences vary regarding this treatment. The patient focus group noted that some participants found benefits in using mobile apps or online resources to manage their symptoms, but most patients said they prefer in-person care. However, mobile apps might be less stigmatizing and increase access for patients with low socioeconomic status, elderly populations, and those in rural and deployed settings.

The Work Group systematically reviewed evidence related to this recommendation.(226) Therefore, the recommendation is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence was minimal given there were only two studies, and neither included the critical outcome of clinician-rated PTSD. No evidence of severe adverse events was reported. Patient values and preferences varied because some might prefer using mobile apps or other self-help-based interventions versus in-person interventions. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against mobile apps or other self-help-based interventions for the treatment of PTSD.

Recommendation

31. There is insufficient evidence to recommend for or against facilitated internet-based cognitive behavioral therapy for the treatment of PTSD.
(Neither for nor against | Reviewed, New-replaced)

Discussion

Data from an SR by Simon et al. (2021),which included 11 RCTs of therapist-facilitated internet-based cognitive behavioral therapy (I-CBT), showed that it led to significant improvement in PTSD symptoms.(229) However, only four studies contained the critical outcome of clinician-rated PTSD, and only one of those studies found I-CBT was superior to control. A small RCT included in Simon et al. (2021) found 8 weeks of I-CBT with brief support every other week by a therapist was superior to the waitlist for PTSD and depression and anxiety.(230) Two additional RCTs, included in Simon et al. (2021), compared I-CBT with online non-trauma-focused CBT (i.e., an active control) but failed to find significance.(110, 231) The fourth RCT compared online PE (a trauma-focused CBT) with PCT delivered FTF in a mixed military and Veteran sample.(232) There were no differences between the groups, but the study was underpowered because of recruitment challenges.

Additional studies supporting this recommendation were included in the 2017 VA/DoD PTSD CPG.(233-239)

Patient preferences vary largely regarding this treatment. The focus group participants noted that patients often prefer in-person care, but virtual might be less stigmatizing and burdensome than in-person. Further, virtual visits require internet access; however, eliminating the burden of traveling to seek care might increase access for patients with low socioeconomic status, elderly populations, and those in rural and deployed settings.

The Work group systematically reviewed evidence related to this recommendation (229) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(233-239) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. This recommendation is based on mixed findings and very low confidence in the quality of the evidence. The benefits of I-CBT slightly outweighed the potential harms, which were none, and there might be some benefits compared with no treatment. Facilitated I-CBT programs could be beneficial to those in remote areas, locations where other services are less readily available, or when irregular hours preclude conventional clinical care. Patient values and preferences varied largely for I-CBT. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against facilitated internet-based cognitive behavioral therapy for the treatment of PTSD.

D. Treatment of Nightmares

Recommendation

32. We suggest prazosin for the treatment of nightmares associated with PTSD. **(Weak for | Reviewed, Amended)**

Discussion

Evidence suggests treatment with prazosin improves nightmares related to PTSD, as demonstrated by two SRs and one RCT.(240-242) Treatment with prazosin was associated with a clinically significant improvement in nightmares in an SR with six studies.(240) The other SR, which included seven studies, also found a clinically significant improvement with overlap between the SRs the studies included.(241) One additional RCT, not included in the SRs, found no significant difference in nightmare outcomes between prazosin and placebo; however, the study might have been underpowered because of a small sample size.(242) Included in the SRs was a large, well-designed, VA Cooperative multisite trial with Veterans in which prazosin failed to improve global symptoms of PTSD and nightmares compared with placebo.(243) However, the recent SRs identified by this evidence review determined a benefit with the treatment of prazosin for nightmares even when including the large VA Cooperative trial.

Patient preferences vary regarding this treatment. Some patients might prefer not to use medication to treat nightmares or symptoms of their PTSD. Some patients might experience side effects from prazosin, such as orthostatic hypotension, dizziness, or headaches. However, these side effects might be mitigated by slowly increasing the dose to the desired result. Caution should be used in patients on other medications that affect blood pressure or can cause orthostasis, including the concomitant use of phosphodiesterase type 5 inhibitors. Prazosin is inexpensive and has limited side effects when titrated slowly and, thus, is easily accessible for providers to prescribe in various clinical practice settings. Patients might be more accepting of prazosin because it is classified as a blood pressure medication and has reduced stigma compared with other medications used in mental health.

The Work Group systematically reviewed evidence related to this recommendation (240-242) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(244-248) Therefore, the recommendation is categorized as *Reviewed, Amended*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations, including small sample sizes, high heterogeneity, and risk of bias.(240-242) The benefits of prazosin in improving nightmares slightly outweighed the potential harm of adverse events. Patient values and preferences varied because some patients might prefer medications over non-pharmacologic treatment and vice versa. Thus, the Work Group made the following recommendation: We suggest prazosin for the treatment of nightmares associated with PTSD.

Recommendation

33. There is insufficient evidence to recommend for or against the following treatments for nightmares associated with PTSD: Imagery Rehearsal Therapy, Exposure Relaxation and Rescripting Therapy, Imaging Rescripting and Reprocessing Therapy, or NightWare.
(Neither for nor against | Reviewed, New-added)

Discussion

Insufficient evidence exists to recommend for or against Imagery Rehearsal Therapy (IRT), Exposure Relaxation and Rescripting Therapy, Imaging Rescripting and Reprocessing Therapy, or NightWare. An SR by Yücel et al. (2020) on imagery rehearsal therapies, which included eight RCTs, reported a medium effect favoring IRT, but four of the RCTs were not in PTSD populations.(249) When the RCTs were looked at individually, only one of the four RCTs in a PTSD population (Krakow et al. [2001]) found IRT was better than waitlist for reducing the critical outcome of nightmares and for the important outcome of improving sleep quality.(250) The other three, one of which was a large trial of more than 100 Veterans, found no effect.(251) Similarly, the SR identified five RCTs that reported PTSD symptoms and found a small effect of imagery rehearsal therapies. Still, results were inconsistent in the three RCTs focused on PTSD populations.(249) An additional RCT, Harb et al. (2019), found no additional reductions in nightmare frequency or distress when adding IRT to CBT for insomnia.(252) No information was available on other outcomes of interest, such as depression, functioning, treatment dropout, or adverse events. No RCTs had the critical outcome of clinician-rated PTSD using NightWare for treatment of nightmares associated with PTSD.

Patient preferences vary regarding this treatment. For example, some patients might prefer a treatment focused specifically on their nightmares, although others might prefer to focus on PTSD as the underlying problem. In addition, imagery rehearsal therapies are not widely available in VA or DoD. NightWare is also not widely available.

The Work Group systematically reviewed evidence related to this recommendation.(249, 252) Therefore, the recommendation is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. Limitations in the body of evidence included very few studies, and the findings were imprecise, with some trials finding an effect and others finding none. In general, the benefits slightly outweighed any potential harms. Patient values and preferences varied. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the following treatments for nightmares associated with PTSD: Imagery Rehearsal Therapy, Exposure Relaxation and Rescripting Therapy, Imaging Rescripting and Reprocessing Therapy, or NightWare.

E. Treatment of PTSD with Co-occurring Conditions

Recommendation

34. We suggest that the presence of co-occurring substance use disorder and/or other disorder(s) not preclude treatments in Recommendation 8 and Recommendation 9 for PTSD.
(Weak for | Reviewed, New-replaced)

Discussion

Treatment studies of PTSD among patients with various co-occurring disorders have shown individuals with comorbid conditions can tolerate and benefit from evidence-based individual trauma-focused PTSD treatments such as PE and CPT.(112, 253-267)

Research has also shown that the presence of comorbidities does not appear to alter the effectiveness of these treatments.(253, 254, 263-266) Results of these studies suggest that the presence of comorbidities should not delay PTSD treatment because, for adults diagnosed with PTSD, treatment safety and effectiveness do not appear to be altered by the presence of comorbidities. The studies included in the evidence review for this recommendation ranged from poor to good quality.

The research on treating PTSD with a co-occurring SUD was extensive. Based on two SRs and two RCTs, the Work Group concluded that the presence of an SUD should not prevent treatment with evidence-based, trauma-focused therapy for PTSD.(112, 258, 259, 267) The research that led to these conclusions included both studies where PTSD and SUD were treated concurrently with trauma-focused treatment and SUD treatment and where they were treated within a single integrated protocol that included both.(112) The integrated protocol studied most extensively and shown consistently to improve PTSD is Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE).(112, 258, 259) On the other hand, non-trauma-focused integrated PTSD and SUD therapies (e.g., Seeking Safety) did not improve PTSD symptoms in individuals with a SUD more than SUD treatment alone or TAU and, thus, are not included in this recommendation.(112) One study directly comparing COPE to Seeking Safety found COPE to be more effective in reducing PTSD symptoms than Seeking Safety.(259) Both were comparably effective in reducing alcohol use.(259) Thus, the Work Group does not recommend non-trauma-focused therapies such as Seeking Safety for treating PTSD in the context of a co-occurring SUD. Evidence of improvement in SUD symptoms is mixed as to whether PTSD treatment plus SUD treatment is more effective than SUD treatment alone.(112)

The evidence shows good tolerance and efficacy for trauma-focused PTSD treatments in patients with other common impairing comorbid conditions, including psychotic disorders, personality disorders, severe mental illness, dissociation, anger, suicidal ideation, TBI, and depression.(253, 254, 257-266) These studies included the critical outcome of clinician-rated PTSD. The Work Group did not find any studies meeting the

inclusion criteria that examined the common comorbidity of pain. Although the Work Group did not specifically search for studies of PTSD treatment in the presence of comorbid sleep disorders, the literature (not included in the systematic evidence review nor impacting the strength of this recommendation) suggests trauma-focused PTSD treatment is effective for patients with insomnia.(268) Studies examining whether comorbidities altered the safety or effectiveness of PTSD treatments were reviewed, and several low to very-low-quality SRs were identified. The findings consistently showed that comorbidities, including substance use characteristics and suicidal ideation, did not alter safety or effectiveness of interventions for PTSD. Individuals with comorbidities might start and end treatment with higher symptom severity than those without comorbidities.(261-266)

The Work Group systematically reviewed evidence related to this recommendation (253, 254, 257-266) and considered the assessment of the evidence from the 2017 VA/DoD PTSD CPG.(112, 255, 256, 267) Therefore, the recommendation is categorized as *Reviewed, New-replaced*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had limitations, including small sample sizes and high dropout. The benefits of treating PTSD in patients with comorbidities outweighed the potential harms. Patient values and preferences varied because of variations in if and how patients would like PTSD or the co-occurring condition addressed. Thus, the Work Group made the following recommendation: We suggest that the presence of co-occurring substance use disorder and/or other disorder(s) not preclude treatments in Recommendation 8 and Recommendation 9 for PTSD.

X. Research Priorities

During the development of the 2023 VA/DoD PTSD CPG, the Work Group identified topics needing additional research, including areas requiring stronger evidence to support current recommendations and research exploring new areas to guide future CPGs. In general, the greatest priorities are studies of comparative effectiveness, along with studies that evaluate strategies to enhance treatment outcomes. Also, studies of active duty Service members are needed, especially for medication and complementary, integrative, and alternative health interventions.

A. Assessment

Despite the availability of questionnaires and interviews with strong psychometric properties, additional research is needed to support their use. Most of this research has focused on samples of Veterans and not on active duty Service members.

- Evaluation of existing questionnaires and interviews in DoD samples as well as analyses that examine relevant subgroups (e.g., women, individuals of other sexes, racial and ethnic minorities)
- Validation of categorical indicators of treatment outcome, such as response and remission

B. Prevention

More research is needed in the prevention of PTSD because this topic is particularly important for the DoD population.

- Interventions to be used in the immediate aftermath of a traumatic event to manage acute reactions (e.g., Psychological First-Aid, iCOVER)
- Interventions for prevention of ASD and PTSD (e.g., hydrocortisone)
- Prediction of who needs a preventive intervention

C. Comparative Effectiveness

Given the number of recommended and suggested treatments for PTSD, one of the greatest research priorities is the comparative effectiveness of treatments.

- Head-to-head and meta-analytic comparisons of specific treatments and types of treatment (e.g., MBSR versus CPT, sertraline versus CPT, trauma-focused psychotherapies versus SSRIs and SNRIs)
- Generalizability of findings to subgroups based on sex identity, sexuality, race, ethnicity, age, and other patient characteristics
- Determining the optimal treatment for a given patient using biomarkers, patient characteristics, and social determinants of health

D. Enhancing Treatment Outcome

In addition to determining the optimal treatment strategy for patients, another important research priority is enhancing treatment outcomes using

- Combined treatments, including psychotherapy, medication, devices, and complementary, integrative, and alternative health interventions; and
- Strategies to guide treatment sequencing given partial or non-response (e.g., augmentation, switching).

E. Psychotherapy

In addition to the priorities for comparative effectiveness research and enhancing treatment outcome, research is needed in

- Strategies to enhance the feasibility of delivery, such as brief treatments for primary care or another setting in which 10 to 12 sessions might be infeasible, briefer PE sessions (60 versus 90 minutes), and massed or intensive schedules;
- Strategies to enhance engagement and retention;
- Effectiveness and safety of manualized group therapies versus individualized therapies, both trauma- and non-trauma-focused, and studies of the comparative effectiveness of one type of group therapy over another;
- Couples and family therapy; and

- Evaluation of psychedelic-assisted psychotherapy using active drug controls.

F. Pharmacotherapy

Given the limited number of recommended and suggested medications for PTSD and the recommendation of psychotherapy over medication as a front-line strategy, research is needed to enhance knowledge about effective medications, including

- Novel medications;
- Medication trials of longer than 12 weeks' duration;
- Trials of medications used in combination for the treatment of PTSD;
- Follow-up studies of patients after discontinuation of pharmacology to determine the risk of recurrence of symptoms; and
- Evaluation of psychedelic medications in rigorous studies using active controls.

G. Somatic Treatments

Of the somatic treatments evaluated, additional research is needed in

- Continued development of neuromodulation strategies, both as standalone and adjunctive therapies; and
- Studies of other procedure-based treatments for PTSD (e.g., stellate ganglion block).

H. Complementary, Integrative, and Alternative Health Interventions

In addition to conventional treatments, the number of promising complementary, integrative, and alternative health modalities is growing. Research is needed in

- Comparisons of CIH with active controls;
- Integration of mind-body practices with conventional therapeutic approaches as part of a Whole Health approach to care; and
- Animal-assisted therapy using active controls.

I. Technology

Technological strategies can offer a way to enhance reach and scalability, but research is needed in

- Apps and online self-help, with or without facilitation;
- Effectiveness of apps as standalone treatment or as adjunctive care; and
- VRET.

J. Comorbidity

Although studies have failed to find that comorbid conditions substantially moderate treatment response, more definitive research on comorbidity is needed.

- Studies specifically designed to examine whether comorbidity moderates treatment response
- Studies of integrated treatments for PTSD and comorbidity

K. Process of Care

In addition to the study of specific treatments, research is needed in strategies to enhance outcome by modifying the environment of care.

- Collaborative behavioral health and primary care
- Measurement-based care
- Shared decision making

Appendix A: Guideline Development Methodology

A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 KQs on clinical topics of the highest priority for the VA and DoD populations. The KQs followed the population, intervention, comparison, outcome, timing and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ) (see Table A-1).

Table A-1. PICOTS(269)

PICOTS Element	Description
Population or Patients	Patients of interest. It includes the condition or conditions, populations or subpopulations, disease severity or stage, co-occurring conditions and other patient characteristics or demographics.
Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic /screening test used with the patient or population.
Comparator	Treatment or treatments (e.g., placebo, different drugs) or approach or approaches (e.g., different dose, different frequency, standard of care) being compared with the intervention or exposure of interest described above.
Outcomes	Results of interest (e.g., mortality, morbidity, QoL, complications). Outcomes can include short, intermediate, and long-term outcomes.
Timing, if applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
Setting, if applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or type of practice.

Abbreviations: PICOTS: population, intervention, comparison, outcome, timing, and setting; QoL: quality of life

Because of resource constraints, all KQs of interest to the Work Group could not be included in the systematic evidence review. Thus, the Work Group selected the 12 highest priority KQs for inclusion in the systematic evidence review (see Table A-2).

Using the GRADE approach, the Work Group rated each outcome on a 1–9 scale (7–9, critical for decision making; 4–6, important, but not critical, for decision making; and 1–3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see Outcomes); however, only critical outcomes were used to determine the overall quality of evidence (see Determining Recommendation Strength and Direction).

a. Populations

Key Question	Population
1–4, 6–8	Adults with diagnosed PTSD
5, 11	Adults with diagnosed PTSD; Partial or non-responders to pharmacotherapy or psychotherapy
9	Adults with acute stress disorder or acute stress reaction
10	Adults with diagnosed PTSD with or without co-occurring conditions Any psychiatric or physical conditions (e.g., MDD, SUD, TBI, suicidality, borderline personality disorder, dissociation, psychosis, pain)
12	Adults with suspected or diagnosed PTSD

b. Interventions and Comparators

Key Question	Interventions	Comparators
1 (a–b)	a. Individual drugs (listed in Appendix A) b. Drug classes • SSRIs • SNRIs • Tricyclic antidepressant • Monoamine oxidase inhibitors • Other antidepressants • Mood stabilizer/anticonvulsants • Antipsychotics • Benzodiazepines (antianxiety, sedative/hypnotics) • Nonbenzodiazepine sedative/hypnotics • Antianxiety, nonbenzodiazepines • Antiadrenergics • Other sympatholytics • Psychostimulants • Cannabinoids • Psychedelics	a. Placebo b. Individual drugs within a drug class versus other drugs within that same class c. Placebo or another pharmacotherapy

Key Question	Interventions	Comparators
1 (c)	c. Individual Drugs Intended to Treat Nightmares • Prazosin • Clonidine • Trazodone • Gabapentin • Pregabalin • Gabapentinoids • Atypical antipsychotics • Risperidone • Olanzapine • Quetiapine • Aripiprazole • Thioridazine • Perphenazine • Cyproheptadine • Benzodiazepines • Non-benzodiazepine receptor antagonists (e.g., zolpidem) • SSRIs • Nefazodone • Trazodone • Mirtazapine • Venlafaxine • Cannabis, Nabilone	
2 (a–e)	Psychotherapies • a,b. See list of psychotherapies in Appendix B. • c. Components of psychotherapy • d. Brief intervention (any intervention that includes a maximum of six or fewer sessions with sessions lasting no longer than 60 minutes) • d. Couples therapy • d. Family therapy • e. Psychotherapies for nightmares	a. TAU, waitlist, active control conditions b. Other psychotherapies (psychotherapies for KQ2) c. Full psychotherapy protocol or components of combined psychotherapy protocols
3	Non-pharmacologic Biological Treatments • SGB • HBOT • Rapid Eye Movement (REM) Desensitization (REM-D) • Transcutaneous electrical acupoint stimulation • Transcranial direct current stimulation • Transcranial magnetic stimulation (TMS; including theta burst stimulation, repetitive TMS/rTMS, and MERT) • Neurofeedback • ECT • VNS • Deep brain stimulation • Cranial electrotherapy stimulation • Capnometry (e.g., Freespira) • NightWare©	• TAU • Waitlist • Placebo • Active control conditions (e.g., another psychotherapy or sham) (Active control conditions should be prioritized over waitlist/TAU.)

Key Question	Interventions	Comparators
4	Complementary and Integrative Treatments • Mind-body practices ♦ Acupuncture ♦ Mindfulness (standalone) ♦ Meditation ♦ Relaxation/progressive muscle relaxation ♦ Mantram ♦ Yoga ♦ Tai chi or qigong ♦ Guided imagery ♦ Biofeedback ♦ Somatic experiencing Other Therapies • Hypnosis • Self-hypnosis • Animal-assisted therapy • Creative therapy (e.g., music, art, or drama therapy) • Recreational therapy (e.g., exercise, fishing) • Self-help regardless of delivery platform	• TAU • Waitlist • Placebo • Active control conditions (e.g., another psychotherapy) (Active control conditions or placebo should be prioritized over waitlist/TAU.)
5 (a–d)	See list of interventions for KQs 1 and 2. Augmentation Strategies for 5b • Psychotherapy: Virtual reality • Medication: Oxytocin, MDMA, psilocybin, d-cycloserine, NAC, propranolol, dexamethasone, hydrocortisone, LSD, cannabinoids, ketamine	• TAU • Waitlist • Placebo • Active control conditions (e.g., another psychotherapy) (Active control conditions or placebo should be prioritized over waitlist/TAU.)
6	See list of interventions for KQs 1 and 2.	• For single studies: effective pharmacotherapies, effective psychotherapies • For meta-analyses: placebo, TAU, active psychotherapy control condition
7	• CBT (TFP or non-TFP), psychodynamic therapy, supportive psychotherapy, or peer psychotherapy treatments delivered in a group setting • Group psychotherapy (anger therapy, problem solving, psychoeducation, group EMDR)	• TAU • Waitlist • Placebo • Active control conditions (e.g., another psychotherapy) (Active control conditions or placebo should be prioritized over waitlist/TAU.)

Key Question	Interventions	Comparators
8 (a–d)	• a,b,c. Telehealth, video teleconferencing, telephone-based or web-based tools, mobile apps, secure text messaging • d. Guided internet-based interventions (secure text messaging, web-based tools, mobile apps)	• a. TAU, waitlist, placebo • b, c. Active psychotherapy delivered via different modalities • d. Non-guided internet-based interventions
9	Any intervention in KQs 1–5 plus interventions for secondary prevention (e.g., psychological first aid, other post-trauma interventions)	• TAU • Waitlist • Active control conditions
10	Treatments from KQs 1–4 for patients with PTSD and a co-occurring condition	Same treatment in patients without a co-occurring condition
11	Specific sequence of treatments (taken from KQs 1–4)	Different sequence of treatments
12	Interviews/Questionnaires • Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) • Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) • PTSD Symptom Scale - Interview for DSM-5 (PSSI-5) • Structured Clinical Interview for the DSM-5 Disorders (SCID PTSD Module) • Posttraumatic Diagnostic Scale for DSM-5 (PDS-5) • PTSD Checklist for DSM-5 (PCL-5)	Other interviews/questionnaires

c. Outcomes

Key Question	Critical Outcomes	Important Outcomes
1–11	• Improvement in global PTSD severity based on CAPS, SPRINT, PSS-I, or other validated structured clinical interviews	• Serious adverse events • Retention/dropout rate • Loss of diagnosis/remission (number-needed-to-treat [NNT] measure) • Self-reported PTSD (PCL) • Comorbid symptoms (e.g., depression, anxiety, sleep, aggression) • QoL, including functional status
12	• Diagnostic accuracy • Sensitivity to symptom change for severity measures	No important outcomes

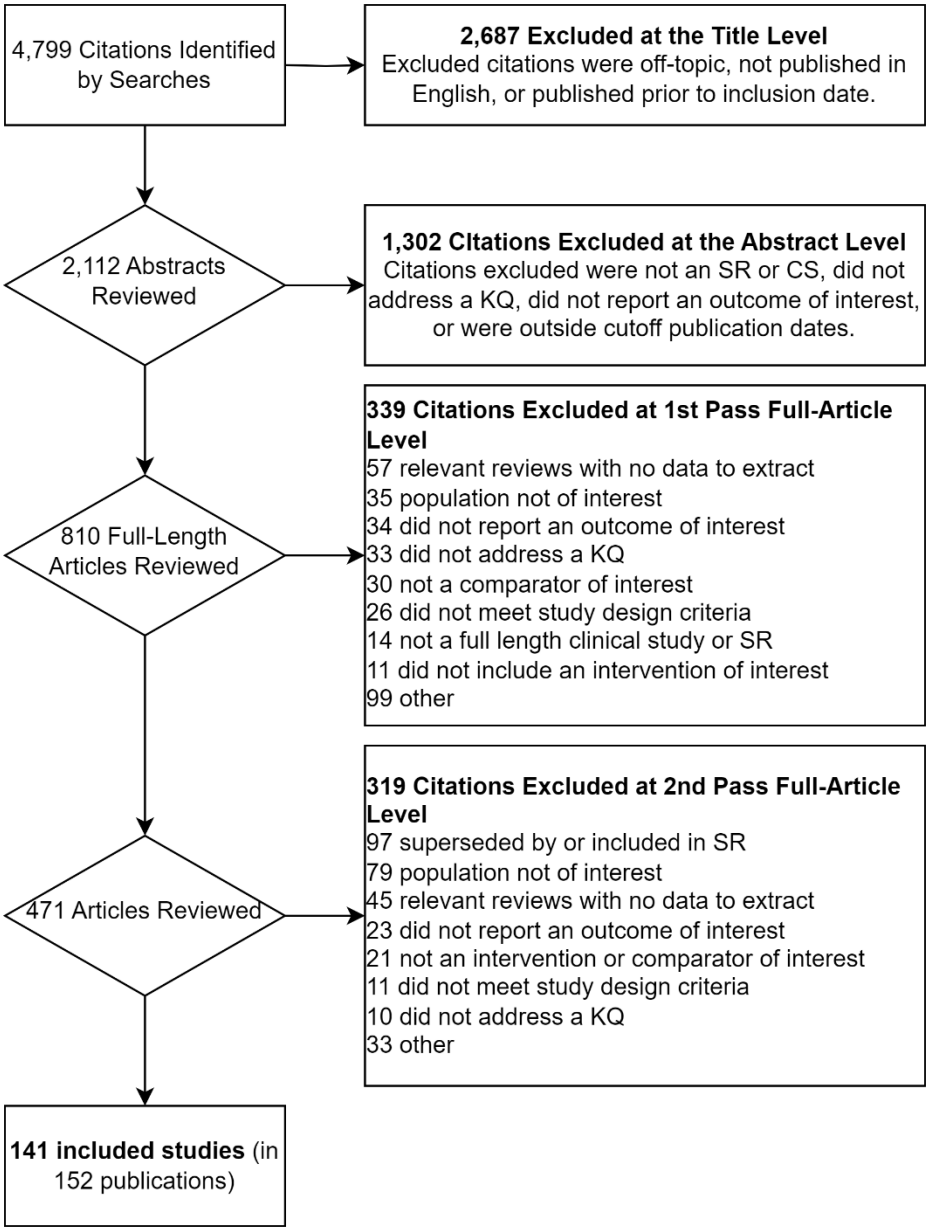
B. Conducting the Systematic Review

Based on the Work Group's decisions regarding the CPG's scope, KQs, and PICOTS statements, the Lewin Team produced a systematic evidence review protocol before conducting the review. The protocol detailed the KQs, PICOTS criteria, methodology to be used during the systematic evidence review and the inclusion and exclusion criteria

to be applied to each potential study, including study type and sample size. The Work Group reviewed and approved the protocol.

Figure A-1 below outlines the systematic evidence review's screening process (see also the General Criteria for Inclusion in Systematic Review and Key Question Specific Criteria). In addition, Table A-2 indicates the number of studies that addressed each of the questions.

Figure A-1. Study Flow Diagram



Abbreviations: CS: clinical study; KQ: key question; SR: systematic review

Alternative Text Description of Study Flow Diagram

Figure A-1. Study Flow Diagram is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion/exclusion process. Arrows point down to boxes that describe the next literature review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

1. Box 1: 4,799 Citations Identified by Searches
    a. Right to Box 2: 2,687 citations excluded at the title level
        i. Citations excluded at this level were off-topic, not published in English, or published prior to inclusion date.
    b. Down to Box 3
2. Box 3: 2,112 Abstracts Reviewed
    a. Right to Box 4: 1,302 citations excluded at the abstract level
        i. Citations excluded at this level were not an SR or CS, did not address a KQ, did not report an outcome of interest, or were outside cutoff publication dates.
    b. Down to Box 5
3. Box 5: 810 Full-Length Articles Reviewed.
    a. Right to Box 6: 339 citations excluded at 1st pass full-article level
        i. 57 relevant reviews with no data to extract, 35 population not of interest, 34 did not report an outcome of interest, 33 did not address a KQ, 30 not a comparator of interest, 26 did not meet study design criteria, 14 not a full length clinical study or SR, 11 did not include an intervention of interest, 99 other
    b. Down to Box 7
4. Box 7: 471 Articles Reviewed
    a. Right to Box 8: 319 citations excluded at 2nd pass full-article level
        i. 97 superseded by or included in SR, 79 population not of interest, 45 relevant reviews with no data to extract, 23 did not report an outcome of interest, 21 not an intervention of comparator of interest, 11 did not meet study design criteria, 10 did not address a KQ, 33 other
    b. Down to Box 9
5. Box 9: 141 Included Studies (in 152 publications)

Table A-2. Evidence Base for KQs

KQ Number	Key Question	Number and Study Type
1	For adults diagnosed with PTSD, what is the effectiveness, comparative effectiveness, and safety of pharmacotherapy treatments for improving PTSD symptoms? a. What is the effectiveness of pharmacotherapy for improving PTSD symptoms? b. What is the comparative effectiveness of pharmacotherapies for improving PTSD symptoms? c. For adults with PTSD, what is the effectiveness, comparative effectiveness, and safety of the treatment of nightmares as a symptom of PTSD?	5 SRs and 2 RCTs
2	For adults diagnosed with PTSD, what is the effectiveness, comparative effectiveness, and safety of psychotherapy treatments for improving PTSD symptoms? a. What is the effectiveness of psychotherapy for improving PTSD symptoms? b. What is the comparative effectiveness of psychotherapy treatments for improving PTSD symptoms? c. For the therapies that are effective, is the efficacy of the components of psychotherapies equivalent to the full therapy protocol or components of combined protocols? d. What is the safety and effectiveness of brief interventions to be delivered in primary care or any setting where full interventions are not feasible for improving PTSD symptoms? e. For adults with PTSD, what is the effectiveness, comparative effectiveness, and safety of psychotherapy treatments of nightmares as a symptom of PTSD?	4 network meta-analyses, 18 SRs, and 23 RCTs (in 31 publications)
3	For adults diagnosed with PTSD, what is the effectiveness and safety of non-pharmacological biological treatments, as primary treatments or adjunctive to standard treatment, for improving PTSD symptoms?	3 SRs and 10 RCTs
4	For adults diagnosed with PTSD, what is the effectiveness and safety of complementary and integrative treatments and other therapies (e.g., recreational therapy, animal-assisted therapy, self-help), as primary treatments or adjunctive to standard treatments, for improving PTSD symptoms?	7 SRs and 9 RCTs
5	For adults diagnosed with PTSD, what combined treatment approaches are safe and effective in enhancing treatment response? a. Combination of two or more medication monotherapies b. Augmenting psychotherapy or medication treatment to enhance outcomes c. Combination of psychotherapy with medication d. Combination of two or more psychotherapies	2 SRs (in 3 publications) and 8 RCTs

KQ Number	Key Question	Number and Study Type
6	For adults diagnosed with PTSD, what is the comparative effectiveness of medication and psychotherapy?	2 SRs and 1 RCT (in 3 publications)
7	For adults diagnosed with PTSD, what is the effectiveness and safety of CBT (TFP or non-TFP), psychodynamic therapy, supportive psychotherapy, or peer psychotherapy treatments delivered in a group therapy setting? a. What is the effectiveness of group therapy versus individual therapy setting? b. What is the effectiveness of group interventions as an adjunct to individual psychotherapy?	4 SRs and 2 RCTs
8	What is the effectiveness, comparative effectiveness, and safety of treatment delivered via technology based modalities as evaluated by the following? a. What is the effectiveness and safety of technology based modalities? b. What is the comparative effectiveness of psychotherapy delivered by a therapist or licensed health professional via video teleconferencing or telephone versus in-person? c. What is the comparative effectiveness of treatment delivered via video-teleconferencing based modalities versus telephone based modalities? d. What is the comparative effectiveness of guided internet-based interventions versus non-guided internet-based interventions?	4 SRs and 8 RCTs
9	What treatments are safe and effective for acute stress disorder or acute stress reaction? a. In adults with acute stress disorder or acute stress reaction, what treatments are effective in preventing development of PTSD?	1 SR and 4 RCTs
10	For adults diagnosed with PTSD and a co-occurring condition, is treatment safety and effectiveness altered by presence of co-morbidities?	1 SR, 11 secondary analyses of RCTs, and 1 retrospective cohort study
11	For adults diagnosed with PTSD, what sequence of treatments is safest and most effective in enhancing treatment response?	1 RCT
12	What is the accuracy of specific interviews/questionnaires for screening, diagnosing, or monitoring symptoms of PTSD?	9 diagnostic studies
	Total Evidence Base	141 studies (in 152 publications)

Abbreviations: RCT: randomized controlled trial; SR: systematic review

a. General Criteria for Inclusion in Systematic Evidence Review

- RCTs or SRs published on or after January 1, 2016, to May 4, 2022. If multiple SRs addressed a key question, we selected the most recent and/or comprehensive review. SRs were supplemented with RCTs published subsequent to the SR.

- Studies had to be published in English.
- Publication must have been a full clinical study or SR; abstracts alone were not included. Similarly, letters, editorials, and other publications that were not full-length clinical studies were not accepted as evidence.
- SRs must have searched MEDLINE or EMBASE for eligible publications, performed a risk of bias assessment of included studies, and assessed the quality of evidence using a recognizable rating system, such as GRADE or something compatible (e.g., the Strength of Evidence grading used by the Evidence-based Practice Centers of the Agency for Healthcare Research and Quality). If an existing review did not assess the overall quality of the evidence, evidence from the review must have been reported in a manner that allowed us to judge the overall risk of bias, consistency, directness, and precision of evidence. We did not use an existing review as evidence if we were unable to assess the overall quality of the evidence in the review.
- Study must have enrolled at least 20 patients (10 per study group for treatment studies, 20 total patients for diagnostic studies); Small sample size is associated with increased risk of bias and we downgrade small studies in the GRADE domain of precision: one downgrade for imprecision of a single study with <200 patients per study arm.
    - Newer Cochrane reviews already take into account small sample-size in their estimation of risk of bias. In these cases, where sample size has already contributed to the assessment of the evidence, we did not downgrade those data a second time.
- Study must have reported on an outcome of interest.
- Study must have enrolled a patient population in which at least 80% of patients were diagnosed with PTSD (or ASD for KQ 9) and were age 18 years or older. If the percentage was less than 80%, then data must have been reported separately for this patient subgroup.

b. Key Question Specific Criteria for Inclusion in Systematic Evidence Review

- For KQs 1–9 and 11, acceptable study designs included SRs of randomized controlled trials (RCT) and individual RCTs not evaluated in SRs. If no relevant studies with these designs were found for a given KQ or sub-question, prospective nonrandomized comparative studies were evaluated for inclusion.
- For KQ 10, acceptable study designs included SRs, RCTs or prospective cohort studies that statistically compared outcomes for patients with PTSD and a co-occurring medical or mental health condition to patients with PTSD without the identified co-occurring medical or mental health condition. Large retrospective database studies (200 patients minimum) that performed multivariate statistical analyses of the effect of co-occurring conditions on patient outcomes were also acceptable.

- For KQ 12, acceptable study designs included SRs, RCTs, non-randomized clinical trials, or observational diagnostic study designs that compared different assessment methods/tools and their diagnostic accuracy for detection or monitoring of PTSD in adults with suspected or diagnosed PTSD.

c. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform/provider can be found in Table A-3. See Appendix G for additional information on the search strategies, including topic-specific search terms and search strategies.

Table A-3. Bibliographic Database Information

Name		Date Limits	Platform/Provider
Bibliographic Databases	Embase (Excerpta Medica) and MEDLINE	January 1, 2016, through May 1, 2022	Elsevier
	PsycINFO	January 1, 2016, through May 1, 2022	OVID
	PubMed (In-process, Publisher, and PubMedNotMedline records)	January 1, 2016, through May 1, 2022	National Library of Medicine
Gray Literature Resources	Agency for Healthcare Research and Quality (AHRQ)	January 1, 2016, through May 1, 2022	AHRQ
	The Evidence-based Synthesis Program (ESP) Reports	January 1, 2016, through May 1, 2022	VA

d. Rating the Quality of Individual Studies and the Body of Evidence

The Lewin Team assessed the methodological risk of bias of individual diagnostic, observational and interventional studies using the USPSTF method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual.(46)

Following this, the Lewin Team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low* and *Very low*.

C. Developing Evidence-Based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, Defense Health Agency, the Lewin Team convened a 4-day virtual recommendation development meeting from September 20–23, 2022, to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Lewin Team finalized the systematic evidence review and distributed the report to the Work Group; findings were also presented during the recommendation development meeting.

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. Where appropriate, the Work Group carried forward and modified recommendations from the 2017 VA/DoD PTSD CPG as necessary (see Reconciliation of 2017 Clinical Practice Guideline Recommendations). The Work Group also developed new recommendations not included in the 2017 VA/DoD PTSD CPG based on the 2022 evidence review. The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences and other implications (see Determining Recommendation Strength and Direction)

a. Determining Recommendation Strength and Direction

Per GRADE, each recommendation's strength and direction is determined by the following four domains.(270)

1. Confidence in the Quality of the Evidence

Confidence in the quality of the evidence reflects the quality of the body of evidence supporting a recommendation (see Rating the Quality of Individual Studies and the Body of Evidence). The options for this domain include *High*, *Moderate*, *Low*, or *Very low*. This is a direct reflection of the GRADE ratings for each relevant critical outcome in the evidence review (see Outcomes). Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2, 44)

The recommendation strength generally aligns with the confidence in the quality of evidence. For example, *Strong* recommendations are typically supported by *High* or *Moderate* quality evidence. However, GRADE permits *Low* or *Very low* quality evidence to support a *Strong* recommendation in certain instances (e.g., life-threatening situation).(270)

2. Balance of Desirable and Undesirable Outcomes

The balance of desirable and undesirable outcomes (i.e., benefits and harms) refers to the relative magnitudes or tradeoffs of anticipated benefits (e.g., increased longevity, reduced morbidity, improved quality of life, decreased resource use) and harms (e.g., decreased longevity, increased complications, impaired quality of life). The options for this domain include *benefits outweigh harms/burdens*, *benefits slightly outweigh harms/burdens*, *benefits and harms/burdens are balanced*, *harms/burdens slightly outweigh benefits*, and *harms/burdens outweigh benefits*. This domain assumes most providers will offer patients an intervention if its advantages exceed the harms. The Work Group's understanding of the benefits and harms associated with the recommendation influenced the recommendation's strength and direction.

3. Patient Values and Preferences

Patient values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations and goals for health and life as they might apply to the intervention's potential benefits, harms, costs, limitations and inconvenience. The options for this domain include *similar values*, *some variation*, or *large variation*. For instance, there might be *some variation* in patient values and preferences for a recommendation on the use of acupuncture, as some patients might dislike needles. When patient values seem homogeneous, this domain might increase the recommendation's strength. Alternatively, when patient values seem heterogeneous, this domain might decrease a recommendation's strength. As part of this domain, the Work Group considered the findings from the patient focus group carried out as part of this CPG update (see Appendix C).

4. Other Implications

Other implications encompass the potential consequences or other impacts that might affect the strength or direction of the recommendation. Questions to consider, listed in Table A-4, help guide decision making in this regard. The options for this domain include, for example, resource use, equity, acceptability, feasibility, and subgroup considerations. The following are example implications related to equity and subgroup considerations, respectively; some of the indicated population might be geographically remote from an intervention (e.g., complex radiological equipment); a drug might be contraindicated in a subgroup of patients.

Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgment
Confidence in the quality of the evidence	Among the designated critical outcomes, what is the lowest quality of relevant evidence? How likely is further research to change the confidence in the estimate of effect?	High Moderate Low Very low
Balance of desirable and undesirable outcomes	What is the magnitude of the anticipated desirable outcomes? What is the magnitude of the anticipated undesirable outcomes? Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?	Benefits outweigh harms/burdens Benefits slightly outweigh harms/burdens Benefits and harms/burdens are balanced Harms/burdens slightly outweigh benefits Harms/burdens outweigh benefits
Patient values and preferences	What are the patients' values and preferences? Are values and preferences similar across the target population? Are you confident about typical values and preferences?	Similar values Some variation Large variation

Decision Domain	Questions to Consider	Judgment
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	What are the costs per resource unit? Is this intervention generally available? What is the variability in resource requirements across the target population and settings? Are the resources worth the expected net benefit from the recommendation? Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?	Various considerations

b. Recommendation Categorization

A summary of the recommendation categories and definitions is available in Table 5.

1. Categorizing Recommendations with an Updated Review of the Evidence

Reviewed refers to recommendations on topics included in this CPG's systematic evidence review. *Reviewed*, *New-added* recommendations are original, new recommendations (i.e., not included in the previous CPG). These recommendations are based entirely on evidence included in the current CPG's systematic evidence review.

Reviewed, *New-replaced* recommendations were in the previous CPG but revised based on the updated evidence review. These recommendations might have clinically relevant edits. *Reviewed*, *Not changed* recommendations were carried forward from the previous CPG unchanged. *Reviewed*, *Amended* recommendations were carried forward from the previous CPG with a nominal change. This allowed for the recommendation language to reflect GRADE approach and any other not clinically meaningful edits deemed necessary. These recommendations can be based on a combination of evidence included in the current CPG's systematic evidence review and the evidence base that supported the recommendation in the previous CPG.

Reviewed, *Deleted* refers to recommendations from the previous CPG that were deleted after a review of the evidence. This might occur if the evidence supporting the recommendation is outdated (e.g., there is no longer a basis to recommend use of an intervention and/or new evidence suggests a shift in care), rendering the recommendation obsolete.

2. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous CPG without an updated review of the evidence. Given time and resource constraints, the systematic evidence review carried out for this CPG update could not cover all available evidence on PTSD; therefore, its KQs focused on new or updated research or areas not covered in the previous CPG.

For areas in which the relevant evidence was not changed and for which recommendations made in the previous CPG were still relevant, recommendations could have been carried forward to the updated CPG without an updated review of the evidence. The evidence supporting these recommendations was thus also carried forward from the previous CPG. These recommendations were categorized as *Not reviewed*. If evidence had not been reviewed, recommendations could have been categorized as *Not changed*, *Amended*, or *Deleted*. *Not reviewed*, *Not changed* recommendations were carried forward from the previous CPG unchanged. *Not reviewed*, *Amended* recommendations were carried forward from the previous CPG with a nominal change. *Not reviewed*, *Deleted* recommendations were determined by the Work Group to not be relevant. A recommendation might be irrelevant if it, for example, pertained to a topic (e.g., population, care setting, treatment) outside of the updated CPG's scope or if it was determined to be common practice.

The recommendation categories for the current CPG are noted in the Recommendations. The recommendation categories from the 2017 VA/DoD PTSD CPG are noted in Appendix E.

D. Drafting and Finalizing the Guideline

The Work Group wrote, reviewed and edited three drafts of the CPG using an iterative review process to solicit feedback on and make revisions to the CPG. The first and second drafts were posted online for 20 and 14 business days, respectively, for the Work Group to provide feedback. Draft 3 was made available for a 14-day peer review and comment (see External Peer Review). The Work Group reviewed all feedback submitted during each review period and made appropriate revisions to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DoD EBPWG for approval. The Work Group considered the VA/DoD EBPWG's feedback and revised the CPG as appropriate to create the final version. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, pocket card and patient summary. The VA/DoD EBPWG approved the final CPG and toolkit products in June 2023.

Appendix B: Pharmacotherapy

Table B-1: Pharmacotherapy Dosing Table

Therapeutic Category	Initial Dose	Dose Range	Clinical Considerations: Comorbidities and Safety
Antidepressants ***Monotherapy***			• All antidepressants have a Black Box warning for increased risk of suicidality in children and young adults (≤24 years) in short-term studies of MDD and other psychiatric disorders. • Avoid abrupt discontinuation; withdrawal symptoms can occur with sudden discontinuation of SSRIs and SNRIs, paroxetine and venlafaxine in particular. • Paroxetine and sertraline have FDA indications for treating PTSD. • Common adverse effects of the SSRIs and SNRIs include nausea, headache, diarrhea, nervousness, sexual dysfunction, dizziness. • Hyponatremia or SIADH can occur; risk is elevated in patients >65 years. • Venlafaxine can elevate blood pressure; caution is advised with patients with hypertension. • Serotonin syndrome can occur, especially with concomitant medications that affect serotonin.
• Paroxetine	IR: 10–20 mg daily CR: 12.5 mg daily	20–50 mg daily 12.5–50 mg	
• Sertraline	25–50 mg daily	50–200 mg daily	
• Venlafaxine	IR: 25 mg 2 or 3 times a day XR: 37.5 mg daily	75–375 mg in 2–3 divided doses 75–300 mg once daily	
Other Agents			• Prazosin might cause syncope with a sudden loss of consciousness. Syncopal episodes usually occur within 30 to 90 minutes of the initial dose. • Addition of a diuretic, other antihypertensive agents, or a PDE5 inhibitor might cause an additive hypotensive effect.
• Prazosin#	1 mg at bedtime; titrate to clinical response.	3–20 mg at bedtime	

for the treatment of nightmares associated with PTSD

Abbreviations: CR: controlled release; FDA: Food and Drug Administration; IR: immediate release; MDD: major depressive disorder; mg: milligram; PDE5: phosphodiesterase-5; PTSD: posttraumatic stress disorder; SIADH: syndrome of inappropriate antidiuretic hormone; SNRI: serotonin/norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; XR: extended release

Appendix C: Patient Focus Group Methods and Findings

A. Methods

VA and DoD Leadership recruited five participants for the focus group, with support from the Champions and other Work Group members as needed. Although participant recruitment focused on eliciting a range of perspectives likely to be relevant and informative in the CPG development process, patient focus group participants were not intended to be a representative sample of VA and DoD patients. Participants were not incentivized for their participation nor reimbursed for travel expenses. The Work Group, with support from the Lewin Team, identified topics on which patient input was important to consider in developing the CPG. The Lewin Team developed and the Work Group approved a patient focus group guide covering these topics. The focus group facilitator led the discussion, using the guide to elicit the patients' perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all questions were addressed.

B. Patient Focus Group Findings

a. Participants noted the importance of distinguishing that although PTSD is incurable, the condition is manageable over time.

- Participants view their PTSD condition as manageable rather than curable and feel that providers should communicate this fact to their patients accordingly.
- Participants described many PTSD symptoms that impact their lives, including anxiety, fear, aggression, self-isolating, nightmares, edginess, and suicidal ideation.
- Some participants noted that comorbid conditions impact their PTSD, including depression, anxiety, and TBI.
- PTSD impacted participants' relationships in various ways. One participant reported intimacy issues because of sexual trauma, and another indicated family lack of understanding of the condition.

b. Many participants experienced a lag between exposure to trauma and PTSD diagnosis and between PTSD diagnosis and subsequent treatment.

- Many participants attributed this delay to stigma around mental health in the military. Participants explained that Service members do not want to be seen as weak or as a liability and, therefore, they hide their symptoms.
- Participants felt the screening for PTSD within the military was inadequate. They noted that they would welcome more efforts to validate Veterans' experiences and to identify Service members struggling with the assumption that anyone who encounters trauma will need support.

c. *All participants benefited from psychotherapy, and most participants expressed benefits from a combination of psychotherapy and pharmacotherapy.*

- Some participants felt that psychotherapies, including trauma-focused therapies such as cognitive behavioral therapy, cognitive processing therapy, and prolonged exposure therapy, eye movement desensitization and reprocessing therapy, and intensive outpatient programs helped them; others did not.
- Participants expressed appreciation of shared decision making when discussing treatment options with providers. Feeling understood, heard, and validated was central to the success of psychotherapy for participants.
- Participants highlighted the positive impact treatment had on their relationships, reconnecting them with family members and giving them tools to express themselves and their emotions.
- Some participants spoke about the benefits of newer pharmacologic treatments (e.g., ketamine) and were interested in exploring other newer treatments such as psilocybin, cannabis, LSD, and other psychedelics.

d. *Participants expressed varying preferences on care setting. Many participants found benefits from complementary and integrative health treatment approaches and mobile apps and online resources.*

- Most participants prefer in-person care.
- Most participants reported finding benefits from group therapy if the group shared similar experiences and expectations. Participants benefited from hearing others' experiences and perspectives and how others have overcome difficult times.
- Participants emphasized the importance of care coordination among a team of providers and continuity of care.
- Some participants found benefits in using mobile apps or online resources to manage their symptoms; others did not.
- Participants reported benefits from engaging in CIH treatment approaches, such as meditation, mindfulness, yoga, qi gong, tai chi, acupuncture, creative arts therapy, and animal therapy, including equine therapy.

Appendix D: Evidence Table

Table D-1: Evidence Table[a,b,c,d]

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
1.	When screening for PTSD, we suggest using the Primary Care PTSD Screen for DSM-5.	Weak for	**2022 Evidence** (57, 58)	Weak for	Reviewed, New-replaced
2.	For confirmation of the diagnosis of PTSD, we suggest using a validated structured clinician-administered interview, such as the Clinician-Administered PTSD Scale or PTSD Symptom Scale - Interview Version.	Strong for	**2022 Evidence** (59, 60) **Additional References** (61, 62)	Weak for	Reviewed, New-replaced
3.	To detect changes in PTSD symptom severity over time, we suggest the use of a validated instrument, such as the PTSD Checklist for DSM-5, or a structured clinician-administered interview, such as the Clinician-Administered PTSD Scale.	Weak for	**2022 Evidence** (63, 64) **Additional References** (61, 65)	Weak for	Reviewed, New-replaced

[a] 2017 Strength of Recommendation column: The 2017 VA/DoD PTSD CPG was developed using the GRADE approach to determine the strength of each recommendation. Inclusion of more than one 2017 strength of recommendation indicates that more than one 2017 VA/DoD PTSD CPG recommendation is covered by the 2023 recommendation. “Not applicable” indicates that the 2023 VA/DoD PTSD CPG recommendation was a new recommendation, and therefore does not have an associated 2017 strength of recommendation. “Neither for nor against” represents updated language for “N/A” used in the 2017 VA/DoD PTSD CPG.

[b] Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference had to be identified through a systematic evidence review carried out as part of the development of this CPG. The second set of references in the evidence column (called “Additional References”) includes references that provide additional information related to the recommendation but that were not identified through the systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.

[c] 2023 Strength of Recommendation column: The VA/DoD PTSD CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Determining Recommendation Strength and Direction section for more information.

[d] 2023 Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process, the categories, and their definitions.

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
4.	For the prevention of PTSD among individuals who have been exposed to trauma, there is insufficient evidence to recommend for or against psychotherapy or pharmacotherapy in the immediate post-trauma period.	NA	**2017 Evidence** (66-70)	Neither for nor against	Not Reviewed, Amended
5.	For the prevention of PTSD among patients diagnosed with acute stress disorder, we suggest trauma-focused cognitive behavioral psychotherapy.	Strong for	**2022 Evidence** (71) **2017 Evidence** (67, 70, 77)	Weak for	Reviewed, New-replaced
6.	For the prevention of PTSD among patients diagnosed with acute stress reaction/acute stress disorder, there is insufficient evidence to recommend for or against any pharmacotherapy.	NA	**2022 Evidence** (71, 78) **2017 Evidence** (77, 79)	Neither for nor against	Reviewed, New-replaced
7.	We recommend individual psychotherapies, listed in Recommendation 8, over pharmacologic interventions for the treatment of PTSD.	Strong for	**2022 Evidence**: (80) **2017 Evidence** (81-83) **Additional References** (85-87)	Strong for	Reviewed, New-replaced
8.	We recommend the individual, manualized trauma-focused psychotherapies for the treatment of PTSD: Cognitive Processing Therapy, Eye Movement Desensitization and Reprocessing, or Prolonged Exposure.	Strong for	**2022 Evidence** (88-94, 98, 101) **2017 Evidence** (95, 96) **Additional References** (97, 102-104)	Strong for	Reviewed, Amended
9.	We suggest the following individual, manualized psychotherapies for the treatment of PTSD: Ehlers' Cognitive Therapy for PTSD, Present-Centered Therapy, or Written Exposure Therapy.	Weak for	**2022 Evidence** (88, 105) **2017 Evidence** (95, 96)	Weak for	Reviewed, New-replaced

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
10.	There is insufficient evidence to recommend for or against the following individual psychotherapies for the treatment of PTSD: Accelerated Resolution Therapy, Adaptive Disclosure, Acceptance and Commitment Therapy, Brief Eclectic Psychotherapy, Dialectical Behavior Therapy, Emotional Freedom Techniques, Impact on Killing, Interpersonal Psychotherapy, Narrative Exposure Therapy, Prolonged Exposure in Primary Care, psychodynamic therapy, psychoeducation, Reconsolidation of Traumatic Memories, Seeking Safety, Stress Inoculation Training, Skills Training in Affective and Interpersonal Regulation, Skills Training in Affective and Interpersonal Regulation in Primary Care, supportive counseling, Thought Field Therapy, Trauma-Informed Guilt Reduction, or Trauma Management Therapy.	NA	**2022 Evidence** (88, 108-111, 115, 124, 125) **2017 Evidence** (112)	Neither for nor against	Reviewed, New-replaced
11.	There is insufficient evidence to recommend using individual components of manualized psychotherapy protocols over, or in addition to, the full therapy protocol for the treatment of PTSD.	Reviewed, New-added	**2022 Evidence** (124, 126) **2017 Evidence** (72, 75, 96, 127-130) **Additional Reference** (131)	Neither for nor against	Reviewed, Not Changed
12.	There is insufficient evidence to recommend for or against any specific manualized group therapy for the treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (108, 132, 144) **2017 Evidence** (145, 146) **Additional References** (131, 143)	Neither for nor against	Reviewed, New-replaced

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
13.	There is insufficient evidence to recommend using group therapy as an adjunct for the primary treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (108, 132, 144) **2017 Evidence** (145, 146) **Additional References** (131, 143)	Neither for nor against	Reviewed, New-replaced
14.	There is insufficient evidence to recommend for or against the following couples therapies for the treatment of PTSD: Behavioral Family Therapy, Structured Approach Therapy, or Cognitive Behavioral Conjoint Therapy.	Reviewed, Amended	**2022 Evidence** (108, 109, 147, 148) **2017 Evidence** (149, 150) **Additional Reference** (152)	Neither for nor against	Reviewed, Not Changed
15.	We recommend paroxetine, sertraline, or venlafaxine for the treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (153) **2017 Evidence** (81, 154)	Strong for	Reviewed, New-replaced
16.	There is insufficient evidence to recommend for or against amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (153, 155) **2017 Evidence** (81, 154)	Neither for nor against	Reviewed, New-replaced
17.	There is insufficient evidence to recommend for or against psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.	NA	**NA**	Neither for nor against	Reviewed, New-added

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
18.	We suggest against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (153, 155-158) **2017 Evidence** (81, 159)	Weak against	Reviewed, New-replaced
19.	We recommend against benzodiazepines for the treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (153) **2017 Evidence** (160)	Strong against	Reviewed, New-replaced
20.	We recommend against cannabis or cannabis derivatives for the treatment of PTSD.	Reviewed, New-added	**2017 Evidence** (161-164) **Additional Reference** (165)	Strong against	Reviewed, Amended
21.	There is insufficient evidence to recommend for or against the combination or augmentation of psychotherapy (see Recommendation 8 and Recommendation 9) or medications (see Recommendation 15) with any psychotherapy or medication for the treatment of PTSD (see Recommendation 22 for antipsychotic medications and Recommendation 23 for 3,4-methylenedioxymethamphetamine).	Reviewed, New-replaced Reviewed, New-added	**2022 Evidence** (84, 157, 166) **2017 Evidence** (167-169, 172)	Neither for nor against	Reviewed, New-replaced
22.	We suggest against aripiprazole, asenapine, brexpiprazole, cariprazine, iloperidone, lumateperone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone for augmentation of medications for the treatment of PTSD.	Strong against	**2022 Evidence** (157) **2017 Evidence** (170, 173-176) **Additional Reference** (177)	Weak against	Reviewed, New-replaced

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
23.	There is insufficient evidence to recommend for or against 3,4-methylenedioxymethamphetamine assisted psychotherapy for the treatment of PTSD.	NA	**2022 Evidence** (157)	Neither for nor against	Reviewed, New-added
24.	There is insufficient evidence to recommend for or against the following somatic therapies for the treatment of PTSD: capnometry-assisted respiratory therapy, hyperbaric oxygen therapy, neurofeedback, NightWare©, repetitive transcranial magnetic stimulation, stellate ganglion block, or transcranial direct current stimulation.	Reviewed, New-replaced	**2022 Evidence** (179-189) **2017 Evidence** (190, 191)	Neither for nor against	Reviewed, New-replaced
25.	We suggest against electroconvulsive therapy or vagus nerve stimulation for treatment of PTSD.	Reviewed, New-replaced	**2017 Evidence** (190-192)	Weak against	Reviewed, New-replaced
26.	We suggest Mindfulness-Based Stress Reduction® for the treatment of PTSD.	NA	**2022 Evidence** (193) **2017 Evidence** (200) **Additional References** (201, 202)	Weak for	Reviewed, New-replaced
27.	There is insufficient evidence to recommend for or against the following mind-body interventions for the treatment of PTSD: acupuncture, Cognitively Based Compassion Training Veteran version, creative arts therapies (e.g., music, art, dance), guided imagery, hypnosis or self-hypnosis, Loving Kindness Meditation, Mantram Repetition Program, Mindfulness-Based Cognitive Therapy, other mindfulness trainings (e.g., integrative exercise, Mindfulness-Based Exposure Therapy, brief mindfulness training), relaxation training, somatic experiencing, tai chi or qigong, Transcendental Meditation®, and yoga.	Reviewed, New-replaced	**2022 Evidence** (203-217) **2017 Evidence** (200, 218)	Neither for nor against	Reviewed, New-replaced

#	Recommendation	2017 Strength of Recommendation	Evidence	2023 Strength of Recommendation	2023 Recommendation Category
28.	There is insufficient evidence to recommend for or against the following interventions for the treatment of PTSD: recreational therapy, aerobic or non-aerobic exercise, animal-assisted therapy (e.g., canine, equine), and nature experiences (e.g., fishing, sailing).	Reviewed, New-replaced	**Additional Reference** (219)	Neither for nor against	Reviewed, New-replaced
29.	We recommend secure video teleconferencing to deliver treatments in Recommendation 8 and Recommendation 9 when that therapy has been validated for use with video teleconferencing or when other options are unavailable.	Reviewed, New-replaced	**2022 Evidence** (223-225) **2017 Evidence** (220-222)	Strong for	Reviewed, New-replaced
30.	There is insufficient evidence to recommend for or against mobile apps or other self-help-based interventions for the treatment of PTSD.	NA	**2022 Evidence** (226)	Neither for nor against	Reviewed, New-added
31.	There is insufficient evidence to recommend for or against facilitated internet-based cognitive behavioral therapy for the treatment of PTSD.	Reviewed, New-replaced	**2022 Evidence** (229) **2017 Evidence** (233-239)	Neither for nor against	Reviewed, New-replaced
32.	We suggest prazosin for the treatment of nightmares associated with PTSD.	Reviewed, New-replaced	**2022 Evidence** (240-242) **2017 Evidence** (244-248)	Weak for	Reviewed, Amended
33.	There is insufficient evidence to recommend for or against the following treatments for nightmares associated with PTSD: Imagery Rehearsal Therapy, Exposure Relaxation and Rescripting Therapy, Imaging Rescripting and Reprocessing Therapy, or NightWare.	NA	**2022 Evidence** (249, 252)	Neither for nor against	Reviewed, New-added
34.	We suggest that the presence of co-occurring substance use disorder and/or other disorder(s) not preclude treatments in Recommendation 8 and Recommendation 9 for PTSD.	Reviewed, New-replaced Reviewed, Amended	**2022 Evidence** (253, 254, 257-266) **2017 Evidence** (112, 255, 256, 267)	Weak for	Reviewed, New-replaced

Appendix E: 2017 Recommendation Categorization Table

Table E-1. 2017 VA/DoD PTSD CPG Recommendation Categorization Table[a,b,c,d,e,f]

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG Recommendation #
1	We recommend engaging patients in shared decision making (SDM), which includes educating patients about effective treatment options.	Strong For	Not Reviewed, Amended	Not Reviewed, Deleted	-
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	Not Reviewed, Deleted	-
3	We suggest periodic screening for PTSD using validated measures such as the Primary Care PTSD Screen (PC-PTSD) or the PTSD Checklist.	Weak For	Not Reviewed, Amended	Reviewed, New-replaced	1

[a] 2017 CPG Recommendation # column: This indicates the recommendation number of the recommendation in the 2017 VA/DoD PTSD CPG.
[b] 2017 CPG Recommendation Text column: This contains the wording of each recommendation from the 2017 VA/DoD PTSD CPG.
[c] 2017 CPG Strength of Recommendation column: The 2017 VA/DoD PTSD CPG used the GRADE approach to determine the strength of each recommendation.
[d] 2017 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2017 VA/DoD PTSD CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.
[e] 2023 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2023 VA/DoD PTSD CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.
[f] PTSD CPG Recommendation # column: For recommendations carried forward to the 2017 VA/DoD PTSD CPG, this column indicates the new recommendation or recommendations to which they correspond.

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG 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	Reviewed, New-replaced	2
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	Reviewed, New-replaced	3
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.	NA	Reviewed, New-replaced	Not Reviewed, Amended	4
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	Reviewed, New-replaced	5
8	For the indicated prevention of PTSD in patients with ASD, there is insufficient evidence to recommend the use of pharmacotherapy.	NA	Reviewed, New-replaced	Reviewed, New-replaced	6
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	Reviewed, New-replaced	7
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	Reviewed, Deleted	-

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG 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	Reviewed, New-replaced	8, 9, 10
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	Reviewed, New-replaced	9, 10
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	Reviewed, New-replaced	10
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	Reviewed, Not Changed	11
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	Reviewed, New-replaced	12,13
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	Reviewed, Not Changed	14

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG 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	Reviewed, New-replaced	15, 16
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	Reviewed, New-replaced	16
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	Reviewed, New-replaced	16, 18
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	Reviewed, New-replaced	18, 19
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	Reviewed, Amended	20

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG 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	Reviewed, New-replaced	16, 21
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	Reviewed, New-replaced	21, 22
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	Reviewed, New-replaced	21
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	Reviewed, New-replaced	22
26	There is insufficient evidence to recommend the combination of exposure therapy with hydrocortisone outside of the research setting.	N/A	Reviewed, New-added	Reviewed, New-replaced	21
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	Reviewed, New-replaced	21
28a	For global symptoms of PTSD, we suggest against the use of prazosin as mono- or augmentation therapy.	Weak Against	Reviewed, New-replaced	Reviewed, New-replaced	18
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	Reviewed, Amended	32

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG Recommendation #
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	Reviewed, New-replaced	21
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	Reviewed, New-replaced	21
31	There is insufficient evidence to recommend for or against starting patients with PTSD on combination pharmacotherapy and psychotherapy.	N/A	Reviewed, New-added	Reviewed, New-replaced	21
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	Reviewed, New-replaced	24, 25
33	There is insufficient evidence to recommend acupuncture as a primary treatment for PTSD.	N/A	Reviewed, New-replaced	Reviewed, New-replaced	27
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	Reviewed, New-replaced	26, 27, 28
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	Reviewed, New-replaced	31
36	We recommend using trauma-focused psychotherapies that have demonstrated efficacy using secure video teleconferencing (VTC) modality when PTSD treatment is delivered via VTC.	Strong For	Reviewed, Amended	Reviewed, New-replaced	29

2017 CPG Recommendation #	2017 CPG Recommendation Text	2017 CPG Strength of Recommendation	2017 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG 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	Reviewed, Amended	32
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	Reviewed, New-replaced	34
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	Reviewed, Deleted	-
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	Reviewed, Deleted	-

Appendix F: Participant List

Rachael Coller, PharmD
Clinical Pharmacist - Pain & Psychiatry,
Naval Medical Center
San Diego, California

Claire Collie, PhD
National Director, Local Evidence Based Psychotherapy Coordinator Program
National Mental Health Director for Quality Assurance and Improvement
Department of Veterans Affairs
Durham, North Carolina

Matthew A. Fuller, PharmD, FASHP, BCPP
National PBM Clinical Pharmacy Program Manager, Psychiatry and Geriatrics
VHA Pharmacy Benefits Management Services Department of Veterans Affairs
Clinical Professor of Psychiatry and Psychology
Case Western Reserve University
Cleveland, Ohio

Jessica L. Hamblen, PhD
Deputy Director for Education, National Center for PTSD
Associate Professor of Psychiatry, Geisel School of Medicine at Dartmouth
White River Junction, Vermont

Paul E. Holtzheimer, MD, MS
Deputy Director for Research, National Center for PTSD
Professor of Psychiatry, Geisel School of Medicine at Dartmouth
White River Junction, Vermont

Marija Kelber, PhD
Section Chief, Evidence Synthesis, Research Translation and Integration, Defense Health Agency, Psychological Health Center of Excellence
Columbia, Maryland

Ursula Kelly, PhD, APRN, ANP-BC, PMHNP-BC, FAANP, FAAN
Nurse Scientist, Atlanta VA Health Care System
Associate Professor,
Emory University Nell Hodgson Woodruff School of Nursing
Atlanta, Georgia

Ariel Lang, PhD, MPH
Director, VA Center of Excellence for Stress and Mental Health
Professor In Residence, Department of Psychiatry, University of California, San Diego
San Diego, California

Kate McGraw, PhD
Chief, Psychological Health Center of Excellence
Research and Engineering Directorate, Defense Health Agency
Silver Spring, Maryland

CAPT Joshua Morganstein, MD
Associate Professor, Department of Military and Emergency Medicine, USUHS
Deputy Director, Center for the Study of Traumatic Stress
Bethesda, Maryland

Sonya B. Norman, PhD
Director, PTSD Consultation Program, VA National Center for PTSD
Professor, Department of Psychiatry, University of California, San Diego
San Diego, California

Katie Papke, LMSW, CAADC, CCTP, CHTVSP
National Social Work Program Office, Care Management and Social Work
Grand Rapids, MI

Ismene Petrakis, MD
Chief of Psychiatry, VA Connecticut Healthcare System, West Haven, CT
Acting Medical Director, VA National Center for PTSD, Clinical Neuroscience Division
Deputy Chair for Veterans Affairs, Yale University
New Haven, Connecticut

David Riggs, PhD
Professor and Chair, Department of Medical and Clinical Psychology, Uniformed Services University of the Health Sciences
Executive Director, Center for Deployment Psychology
Bethesda, Maryland

Paula P. Schnurr, PhD
Executive Director, National Center for PTSD
Professor of Psychiatry, Geisel School of Medicine at Dartmouth
White River Junction, Vermont

Brian Shiner, MD, MPH
Associate Professor, Department of Psychiatry and The Dartmouth Institute
Geisel School of Medicine at Dartmouth
Director, VA Patient Safety Center of Inquiry for Prevention of Suicide
White River Junction, Vermont

Ilse Wiechers, MD, MPP, MHS
National Director for Psychopharmacology & Somatic Treatments
Office of Mental Health and Suicide Prevention, Department of Veterans Affairs
Associate Professor of Clinical Psychiatry University of California, San Francisco
San Francisco, California

Jonathan Wolf, MD
Psychiatrist and Subject Matter Expert for Substance Abuse, Defense Health Agency
Appointed Member, Prince George's County Medical Advisory Board
Potomac, Maryland

Appendix G: Literature Review Search Terms and Strategy

Table G-1. EMBASE and MEDLINE in EMBASE.com Syntax

Question	Set #	Concept	Strategy
KQ 1, KQ 5, KQ 6, KQ 9, KQ 11	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti
	2	Pharmacotherapy (Broad Concepts)	'acute stress disorder'/dm_dr,dm_dt OR 'posttraumatic stress disorder'/exp/dm_dr,dm_dt OR 'drug therapy'/exp OR ((drug* OR medicat* OR medicine* OR pharma*) NEAR/3 (intervention* OR manag* OR therap* OR treat*)) OR pharmaco*:ti,ab
	3	Antidepressants (Broad Concepts)	'antidepressant agent'/exp OR 'anti-depressant*' OR antidepressant*
	4	Selective serotonin reuptake inhibitors (SSRIs)	'serotonin uptake inhibitor'/exp OR citalopram* OR escitalopram* OR fluoxetine* OR fluvoxamine OR paroxetine* OR 'selective serotonin reuptake inhibitor*' OR sertraline* OR ssri*
	5	Serotonin-norepinephrine reuptake inhibitors (SNRIs)	'serotonin noradrenalin reuptake inhibitor'/exp OR desvenlafaxine* OR duloxetine* OR levomilnacipran* OR reboxetine* OR 'serotonin noradrenalin reuptake inhibitor*' OR 'serotonin norepinephrine reuptake inhibitor*' OR snri* OR venlafaxine*
	6	Tricyclic antidepressants (TCA)	'tricyclic antidepressant agent'/exp OR amitriptyline* OR desipramine* OR doxepin* OR imipramine* OR nortriptyline* OR (tricyclic* NEAR/2 ('anti depressant*' OR antidepressant*))
	7	Monoamine oxidase inhibitors (MAOIs)	'monoamine oxidase inhibitor'/exp OR ((mao* OR 'monoamine oxidase') NEAR/2 inhibit*) OR brofaromine* OR phenelzine* OR moclobemide*
	8	Other Antidepressants	'alpha-2 receptor antagonist*' OR bupropion* OR mirtazapine* OR nefazodone* OR 'norepinephrine dopamine reuptake inhibitor*' OR 'serotonin-2 antagonist-reuptake inhibitor*' OR tianeptine* OR trazodone* OR vortioxetine* OR ('μ-opioid receptor' NEAR/3 agonist*)
	9	Antiadrenergics	'alpha adrenergic receptor blocking agent'/exp OR 'anti adrenergic*' OR antiadrenergic* OR clonidine* OR doxazosin* OR guanfacine* OR prazosin* OR propranolol* OR sympatholytic*

Question	Set #	Concept	Strategy
KQ 1, KQ 5, KQ 6, KQ 9, KQ 11 (cont.)	10	Antipsychotics	'neuroleptic agent'/exp OR 'anti psychotic*' OR antipsychotic* OR aripiprazole* OR olanzapine* OR quetiapine* OR risperidone* OR ziprasidone*
	11	Antianxiety (General)	'anxiolytic agent'/exp OR 'anti anxiety' OR antianxiety OR sedative*
	12	Benzodiazepines	'benzodiazepine derivative'/mj OR alprazolam* OR benzodiazepine* OR midazolam*
	13	Nonbenzodiazepines	buspirone* OR cyproheptadine* OR diphenhydramine* OR eszopiclone* OR hydroxyzine* OR 'non benzodiazepine*' OR nonbenzodiazepine* OR zaleplon* OR zolpidem*
	14	Cannabinoids	'cannabinoid'/exp OR 'cannabis'/de OR 'medical cannabis'/de OR cannabi* OR cannabinol* OR (cbd* NEAR/2 oil*) OR dronabinol* OR (medical NEAR/2 marijuana) OR nabilone* OR phytocannabinoid* OR tetrahydrocannabinol* OR thc*
	15	Mood Stabilizers	'anticonvulsive agent'/exp OR 'mood stabilizer'/exp OR anticonvuls* OR 'anti convuls*' OR divalproex* OR gabapentin* OR lamotrigine* OR lithium* OR 'mood stablis*' OR 'mood stabliz*' OR pregabalin* OR tiagabine* OR topiramate* OR valproate OR 'valproic acid'
	16	Psychostimulants	'psychedelic agent'/exp OR 'psychostimulant agent'/exp OR amphetamine* OR LSD OR ‘lysergic acid diethylamide’ OR mdma* OR methylphenidate* OR midomafetamine OR modafinil* OR psilocybin* OR psychedel* OR psychostimul*
	17	Steroids	'steroid'/exp OR dehydroepiandrosterone* OR ganaxolone* OR hydrocortisone* OR mifepristone* OR steroid*
	18	Supplements	inositol* OR 'saiko-keishi-kankyo-to' OR 'saiko-keishi-kankyoto' OR saikokeoshikankyoto OR yohimbine
	19	Other	baclofen* OR 'd-cycloserine' OR 'd-serine' OR dexamethasone* OR esketamine* OR glucocorticoid* OR gr205171 OR gsk561679 OR immunosuppress* OR ketamine* OR 'methylene blue' OR 'methylthioninium chloride' OR minaserin* OR NAC OR ‘N-acetyl cysteine’ OR naltrexone* OR oxytocin* OR pregabalin* OR rivastigmine* OR sirolimus* OR varenicline* OR vilazodone* OR (('gaba-b' OR nicotinic OR nmda) NEAR/2 agonist*) OR ((crf1 OR 'neurokinin-1' OR nmda OR opioid*) NEAR/2 antagonist*) OR (acetylcholinesterase NEAR/2 inhibitor*)
	20	Atypical Antipsychotics	'atypical antipsychotic agent'/exp OR (atypical NEAR/3 ('anti psychotic*' OR antipsychotic*))
	21	Combine Pharmacotherapies	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
	22	Combine PTSD & Pharmacotherapies	#1 AND #21

Question	Set #	Concept	Strategy
KQ 1, KQ 5, KQ 6, KQ 9, KQ 11 (cont.)	23	Systematic Reviews & Meta Analyses	#22 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	24	RCTs	#22 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	25	SRs & RCTs	#23 OR #24
	26	Remove Out of Scope Publication Types	#25 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
	27	Remove Out of Scope Age Ranges	#26 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
	28	Date Limit	#27 AND [2016-2022]/py AND [1-1-1900]/sd NOT [01-05-2022]/sd
KQ 2, KQ 9, KQ 11	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti

Question	Set #	Concept	Strategy
KQ 2, KQ 9, KQ 11 (con.t)	2	Psychotherapy – Trauma Focused	'behavior therapy'/exp OR 'cognitive therapy'/exp OR 'exposure therapy'/exp OR 'eye movement desensitization and reprocessing'/exp OR 'narrative therapy'/exp OR 'trauma-focused cognitive behavioral therapy'/exp OR 'virtual reality exposure therapy'/exp OR 'accelerated resolution therap*':ab,kw,ti OR art:ab,kw,ti OR 'attention bias modification*':ab,kw,ti OR 'attention control train*':ab,kw,ti OR 'behavior therap*':ab,kw,ti OR 'behaviour therap*':ab,kw,ti OR 'behavioral therap*':ab,kw,ti OR 'behavioural therap*':ab,kw,ti OR 'bep tg':ab,kw,ti OR 'brief eclectic psychotherap*':ab,kw,ti OR bep:ab,kw,ti OR cbct:ab,kw,ti OR cbt:ab,kw,ti OR 'cognitive behavioral therap*':ab,kw,ti OR 'cognitive behavioural therap*':ab,kw,ti OR 'cognitive behavioral conjoint therap*':ab,kw,ti OR 'cognitive processing therap*':ab,kw,ti OR 'cognitive therap*':ab,kw,ti OR 'concurrent treatment*':ab,kw,ti OR cope:ab,kw,ti OR cpt:ab,kw,ti OR 'ct-ptsd':ab,kw,ti OR eclectic:ab,kw,ti OR edmr:ab,kw,ti OR eft:ab,kw,ti OR ehlers:ab,kw,ti OR emdr:ab,kw,ti OR 'emotional freedom':ab,kw,ti OR 'exposure therap*':ab,kw,ti OR 'expressive writing':ab,kw,ti OR (('eye movement*' NEAR/3 desensit*):ab,kw,ti) OR 'imagery rehearsal therap*':ab,kw,ti OR 'implosive therap*':ab,kw,ti OR 'letter writing':ab,kw,ti OR mindful*:ab,kw,ti OR 'narrative exposure therap*':ab,kw,ti OR 'narrative therap*':ab,kw,ti OR net:ab,kw,ti OR 'prolonged exposure':ab,kw,ti OR 'reconsolidation of traumatic memories':ab,kw,ti OR rtm:ab,kw,ti OR 'thought field therap*':ab,kw,ti OR 'trauma focused':ab,kw,ti OR 'tf-cbt':ab,kw,ti OR 'virtual reality':ab,kw,ti OR vret:ab,kw,ti OR 'written exposure therap*':ab,kw,ti OR wet:ab,kw,ti OR 'written narrative exposure':ab,kw,ti

Question	Set #	Concept	Strategy
KQ 2, KQ 9, KQ 11 (con.t)	3	Psychotherapy – Non Trauma Focused	'acceptance and commitment therapy'/exp OR 'cognitive behavioral therapy'/exp OR 'couple therapy'/exp OR 'family focused therapy'/de OR 'family therapy'/exp OR 'marital therapy'/exp OR 'mindfulness'/exp OR 'motivational interviewing'/exp OR 'neurolinguistic programming'/exp OR 'psychoanalysis'/exp OR 'psychodynamic psychotherapy'/exp OR 'psychoeducation'/exp OR 'psychotherapy'/exp OR 'acceptance and commitment therap*':ab,kw,ti OR act:ab,kw,ti OR 'behavioral activation':ab,kw,ti OR 'behavioural activation':ab,kw,ti OR 'cognitive behavioral therapy for insomnia':ab,kw,ti OR 'cbt-i':ab,kw,ti OR 'couples counsel*':ab,kw,ti OR 'couples therap*':ab,kw,ti OR 'emotion focused couples therap*':ab,kw,ti OR 'family counsel*':ab,kw,ti OR 'family therap*':ab,kw,ti OR 'imagery rehearsal training':ab,kw,ti OR 'integrated cbt':ab,kw,ti OR icbt:ab,kw,ti OR irt:ab,kw,ti OR 'interpersonal therap*':ab,kw,ti OR ipt:ab,kw,ti OR 'marital therap*':ab,kw,ti OR 'marriage counsel*':ab,kw,ti OR 'marriage therap*':ab,kw,ti OR mbsr:ab,kw,ti OR 'metacognitive therap*':ab,kw,ti OR mindful*:ab,kw,ti OR 'motivational enhancement therap*':ab,kw,ti OR 'motivational interview*':ab,kw,ti OR 'neurolinguistic programming':ab,kw,ti OR pct:ab,kw,ti OR 'present centered therap*':ab,kw,ti OR 'problem solving':ab,kw,ti OR psychoanalysis:ab,kw,ti OR psychodynamic*:ab,kw,ti OR psychoeducation:ab,kw,ti OR psychotherap*:ab,kw,ti OR 'relapse prevention':ab,kw,ti OR relaxation:ab,kw,ti OR 'seeking safety':ab,kw,ti OR sit:ab,kw,ti OR 'skills training in affect and interpersonal regulation':ab,kw,ti OR 'socioenvironmental therap*':ab,kw,ti OR stair:ab,kw,ti OR 'stress inoculation therap*':ab,kw,ti OR 'supportive counsel*':ab,kw,ti OR (((brief OR 'short term' OR 'time limited') NEAR/2 (cbt OR counsel* OR intervention* OR therap* OR treatment*)):ab,kw,ti)
	4	Combine Psychotherapies	#2 or #3
	5	PTSD & Psychotherapies	#1 AND #4
	6	SRs & Meta Analyses	#5 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	7	RCTs	#5 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	8	SRs & RCTs	#7 OR #6

Question	Set #	Concept	Strategy
KQ 2, KQ 9, KQ 11 (con.t)	9	Remove Out of Scope Publication Types	#8 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
	10	Remove Out of Scope Age Ranges	#9 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
	11	Date Limit	#10 AND [2016-2022]/py AND [1-1-1900]/sd NOT [01-05-2022]/sd
KQ 3, KQ 9, KQ 11	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti

Question	Set #	Concept	Strategy
KQ 3, KQ 9, KQ 11 (cont.)	2	Interventions	'brain depth stimulation'/exp OR 'deep brain stimulator'/exp OR 'electroconvulsive therapy'/de OR 'hyperbaric oxygen'/de OR 'neurofeedback'/de OR 'stellate ganglion block'/de OR 'transcranial electrical stimulation'/exp OR 'transcranial magnetic stimulation'/exp OR 'vagus nerve stimulation'/de OR 'convulsive therap*':ab,kw,ti OR 'cranial electrotherap*':ab,kw,ti OR 'deep brain':ab,kw,ti OR ecs:ab,kw,ti OR ect:ab,kw,ti OR 'electric shock therap*':ab,kw,ti OR 'electroconvulsive therap*':ab,kw,ti OR 'electroconvulsant therap*':ab,kw,ti OR 'electroconvulsive shock therap*':ab,kw,ti OR 'electroconvulsive treat*':ab,kw,ti OR 'electroshock therap*':ab,kw,ti OR 'electroshock treat*':ab,kw,ti OR hbot:ab,kw,ti OR 'high pressure o':ab,kw,ti OR 'high pressure oxygen':ab,kw,ti OR 'hyperbaric medicine':ab,kw,ti OR 'hyperbaric o2':ab,kw,ti OR 'hyperbaric oxygen*':ab,kw,ti OR mert:ab,kw,ti OR neurofeedback:ab,kw,ti OR (biologic* AND (intervention* OR therap* OR treat*)):ab,kw,ti OR ((('rapid eye movement*' OR rem) NEAR/3 desensit*):ab,kw,ti) OR 'rem-d':ab,kw,ti OR remd:ab,kw,ti OR sgb:ab,kw,ti OR 'shock therap*':ab,kw,ti OR 'stellate block*':ab,kw,ti OR 'stellate ganglion block*':ab,kw,ti OR rtms:ab,kw,ti OR tdcs:ab,kw,ti OR 'theta burst stimulat*':ab,kw,ti OR tms:ab,kw,ti OR 'transcranial direct current stimulat*':ab,kw,ti OR 'transcranial magnetic stimulat*':ab,kw,ti OR 'transcutaneous electric* acupoint stimulat*':ab,kw,ti OR vagal:ab,kw,ti OR vagus:ab,kw,ti OR vns:ab,kw,ti
	3	Combine	#1 AND #2
	4	SRs & Meta Analyses	#3 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	5	RCTs	#3 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	6	SRs & RCTs	#4 OR #5
	7	Remove Out of Scope Publication Types	#6 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

Question	Set #	Concept	Strategy
KQ 3, KQ 9, KQ 11 (cont.)	8	Remove Out of Scope Age Ranges	#7 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
	9	Date Limit	#8 AND [2016-2022]/py AND [1-1-1900]/sd NOT [01-05-2022]/sd
KQ 4, KQ 9, KQ 11	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti

Question	Set #	Concept	Strategy
KQ 4, KQ 9, KQ 11 (cont.)	2	CAM Interventions	'acupuncture'/exp OR 'alternative medicine'/exp OR 'animal assisted therapy'/exp OR 'art therapy'/de OR 'biofeedback'/exp OR 'dance therapy'/de OR 'diet supplementation'/de OR 'dietary supplement'/de OR 'drama therapy'/exp OR 'exercise'/exp OR 'guided imagery'/exp OR 'herbal medicine'/de OR 'homeopathic agent'/de OR 'hypnosis'/de OR 'integrative medicine'/de OR 'meditation'/exp OR 'mindfulness'/exp OR 'music therapy'/exp OR 'phytotherapy'/de OR 'psychodrama'/de OR 'qigong'/de OR 'recreation'/exp OR 'recreational therapy'/de OR 'relaxation training'/exp OR 'self help'/exp OR 'tai chi'/de OR 'yoga'/exp OR acupuncture:ab,kw,ti OR ((('animal assisted' OR art* OR canine* OR creativ* OR dance OR dog* OR drama* OR equine OR horse* OR movement OR music OR recreation*) NEAR/3 (intervention* OR therap*)):ab,kw,ti) OR (((alternative OR complementary OR integrative) NEAR/3 (intervention* OR medicine OR treatment*)):ab,kw,ti) OR autohypnosis:ab,kw,ti OR biofeedback:ab,kw,ti OR ((diet* NEAR/3 supplement*):ab,kw,ti) OR exercise:ab,kw,ti OR fishing:ab,kw,ti OR 'guided imagery':ab,kw,ti OR herbs:ab,kw,ti OR herbal:ab,kw,ti OR homeopath*:ab,kw,ti OR hypno*:ab,kw,ti OR mantram:ab,kw,ti OR meditation:ab,kw,ti OR meditate*:ab,kw,ti OR mindbody:ab,kw,ti OR 'mind body':ab,kw,ti OR mindful*:ab,kw,ti OR phytotherapy:ab,kw,ti OR 'progressive muscle relaxation':ab,kw,ti OR psychodrama:ab,kw,ti OR qigong:ab,kw,ti OR relaxation:ab,kw,ti OR 'self help':ab,kw,ti OR 'self-hypno*':ab,kw,ti OR 'somatic experiencing':ab,kw,ti OR 'tai chi':ab,kw,ti OR 'tai ji':ab,kw,ti OR yoga:ab,kw,ti
	3	Combine Interventions	#1 AND #2
	4	SRs & Meta Analyses	#3 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	5	RCTs	#3 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	6	SRs & RCTs	#4 OR #5

Question	Set #	Concept	Strategy
KQ 4, KQ 9, KQ 11 (cont.)	7	Remove Out of Scope Publication Types	#6 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
	8	Remove Out of Scope Age Ranges	#7 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
	9	Date Limit	#8 AND [2016-2022]/py AND [1-1-1900]/sd NOT [01-05-2022]/sd
KQ 7	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti
	2	Group/Peer Interventions	'encounter group'/de OR 'group therapy'/de OR 'peer group'/exp OR 'social support'/exp OR 'support group'/exp OR 'community therap*':ab,kw,ti OR 'community treatment*':ab,kw,ti OR 'encounter group*':ab,kw,ti OR 'group psychotherap*':ab,kw,ti OR 'group setting':ab,kw,ti OR 'group therap*':ab,kw,ti OR 'group treatment*':ab,kw,ti OR 'peer group*':ab,kw,ti OR 'peer support':ab,kw,ti OR 'self-help':ab,kw,ti OR 'support group*':ab,kw,ti OR 'supportive psychotherap*':ab,kw,ti OR 'supportive therap*':ab,kw,ti
	3	Combine PTSD & Interventions	#1 AND #2

Question	Set #	Concept	Strategy
KQ 7 (cont.)	4	SRs & Meta Analyses	#3 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	5	RCTs	#3 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	6	SRs & RCTs	#4 OR #5
	7	Remove Out of Scope Publication Types	#6 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
	8	Remove Out of Scope Age Ranges	#7 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
KQ 10	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti
	2	Co-morbidities	'comorbidity'/exp OR ((comorbid* OR 'co occur*' OR general OR multimorbid* OR physical) NEAR/2 (health OR condition* OR disease*)) OR comorbid*:ti OR 'co occur*':ti OR multimorbid*:ti
	3	Combine PTSD & Co-morbidities	#1 AND #2

Question	Set #	Concept	Strategy
KQ 10 (cont.)	4	SRs & Meta Analyses	#3 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	5	RCTs	#3 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	6	Observational studies	#3 AND ('case control study'/exp OR 'cohort analysis'/de OR 'cross-sectional study'/de OR 'longitudinal study'/exp OR 'observational study'/de OR 'prospective study'/de OR 'retrospective study'/de OR 'case control':ti,ab OR cohort*:ti,ab OR 'cross sectional':ti,ab OR epidemiologic*:ti,ab OR longitudinal*:ti,ab OR observational*:ti,ab OR prospective*:ti,ab OR registr*:ti,ab OR retrospective*:ti,ab)
	7	Combine Study Types	#4 OR #5 OR #6
	8	Remove Out of Scope Publication Types	#7 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
	9	Remove Out of Scope Age Ranges	#8 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
	10	Date Limit	#9 AND [2016-2022]/py AND [1-1-1900]/sd NOT [01-05-2022]/sd

Question	Set #	Concept	Strategy
KQ 12	1	PTSD	'acute stress disorder'/exp OR 'posttraumatic stress disorder'/exp OR 'acute stress disorder*':ab,kw,ti OR 'acute stress reaction*':ab,kw,ti OR 'battle fatigue':ab,kw,ti OR 'combat disorder*':ab,kw,ti OR 'combat fatigue':ab,kw,ti OR 'combat stress*':ab,kw,ti OR 'post-traumatic neuros?s':ab,kw,ti OR 'post-traumatic psychos?s':ab,kw,ti OR 'post-traumatic stress*':ab,kw,ti OR 'post-traumatic syndrome*':ab,kw,ti OR 'posttraumatic neuros?s':ab,kw,ti OR 'posttraumatic psychos?s':ab,kw,ti OR 'posttraumatic stress*':ab,kw,ti OR 'posttraumatic syndrome*':ab,kw,ti OR ptsd:ab,kw,ti OR 'stress disorder*':ab,kw,ti OR 'stress reaction*':ab,kw,ti OR 'trauma syndrome*':ab,kw,ti OR 'traumatic stress*':ab,kw,ti OR 'war neuros?s':ab,kw,ti
	2	Interview & Questionnarie Tools	'mass screening'/exp OR 'psychological rating scale'/de OR 'questionnaire'/de OR 'screening test'/exp OR ((assess* OR confirm* OR detect* OR diag* OR rating OR suspect* OR screen*) NEAR/2 (index OR indices OR instrument* OR interview* OR questionnaire* OR scale OR scales OR survey* OR tool*)) OR 'clinician-administered ptsd scale' OR 'caps-5' OR 'primary care ptsd screen' OR 'pc-ptsd-5' OR 'ptsd symptom scale' OR 'pss-i-5' OR 'structured clinical interview' OR 'scid ptsd module' OR 'posttraumatic diagnostic scale' OR 'pds-5' OR 'ptsd checklist' OR 'pcl-5'
	3	Combine PTSD & Tools	#1 AND #2
	4	SRs & Meta Analyses	#3 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science')) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol' OR 'scoping review'):ti)
	5	RCTs	#3 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	6	Diagnostic Studies	#3 AND ('accuracy':de OR (area NEXT/1 under NEXT/3 curve) OR auc OR 'diagnosis'/exp/mj OR diagnos*:ti OR 'diagnostic accuracy' OR 'diagnostic error*' OR 'diagnostic error'/exp OR 'diagnostic test accuracy':de OR 'differential diagnosis'/exp OR ((false OR true) NEAR/1 (positive OR negative)) OR likelihood OR 'maximum likelihood method':de OR ppv OR precision OR 'precision'/exp OR 'prediction and forecasting' OR 'prediction and forecasting'/exp OR 'predictive value'/exp OR 'predictive value' OR 'receiver operating characteristic' OR 'receiver operating characteristic':de OR 'roc curve' OR 'roc curve'/exp OR 'sensitivity and specificity':de OR ('sensitivity' AND 'specficity'))
	7	Combine Study Types	#4 OR #5 OR #6

Question	Set #	Concept	Strategy
KQ 12 (cont.)	8	Remove Out of Scope Publication Types	#7 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
	9	Remove Out of Scope Age Ranges	#8 NOT ((adolescen*:ti OR babies:ti OR baby:ti OR boy*:ti OR child*:ti OR girl*:ti OR infancy:ti OR infant*:ti OR juvenile*:ti OR neonat*:ti OR newborn*:ti OR nurser*:ti OR paediatric*:ti OR pediatric*:ti OR preschool*:ti OR 'school age*':ti OR schoolchildren*:ti OR teen*:ti OR toddler*:ti OR youth*:ti) NOT (adult*:ti,ab OR father*:ti OR matern*:ti,ab OR men:ti,ab OR mother*:ti OR parent*:ti OR patern*:ti,ab OR women:ti,ab))
	10	Date Limit	#9 AND [2016-2022]/py AND [1-1-1900]/sd NOT [01-05-2022]/sd

Appendix H: Alternative Text Descriptions of Algorithm

The following outline narratively describes the Management of PTSD Algorithm. An explanation of the purpose of the algorithm and description of the various shapes used within the algorithm can be found in the Algorithm section. The sidebars referenced within this outline can also be found in the Algorithm section.

Module A: Acute Stress Reaction/Disorder

1. The algorithm begins with Box 1, in the shape of a rounded rectangle: "Person has been exposed to trauma."
2. Box 1 connects to Box 2, in the shape of a hexagon, which asks, "Exposed to trauma within the last 30 days?"
    a. If the answer is "No" to Box 2, then Box 3, in the shape of a hexagon, asks, "Persistent or worsening traumatic stress symptoms or at risk for PTSD?"
        i. If the answer is "Yes" to Box 3, then Box 4, in the shape of an oval: "**Go to Module B.** Assessment and Diagnosis of PTSD"
        ii. If the answer is "No" to Box 3, then Box 6, in the shape of an oval: "Assess for other needs and refer as appropriate."
    b. If the answer is "Yes" to Box 2, then Box 5, in the shape of a rectangle: "Assess environments for ongoing threats. Protect from further harm. Ensure basic physical needs are met (**see Sidebar 1**)."
3. Box 5 connects to Box 7, in the shape of a hexagon, which asks, "Is person unstable, suicidal, or dangerous to self or others or in need of urgent medical or surgical attention (**see Sidebar 2** and **VA/DoD Suicide CPG**)?"
    a. If the answer is "Yes" to Box 7, then Box 8, in the shape of a rectangle: "Provide appropriate care, conduct lethal means assessment, implement safety plan, or refer to stabilize. Follow reporting mandates as appropriate. (**refer to VA/DoD Suicide CPG**)"
        i. Box 8 connects to Box 9.
    b. If the answer is "No" to Box 7, then Box 9, in the shape of a rectangle: "Assess history, symptoms, and signs, particularly for ASR/ASD (**see Sidebar 3**)."
4. Box 9 connects to Box 10, in the shape of a hexagon, which asks, "Meet DSM-5 criteria for a diagnosis of ASD (**see Sidebar 3**)?"
    a. If the answer is "No" to Box 10, then Box 11, in the shape of a rectangle: "Consider ASR/COSR and other mental health diagnoses. Consider initiating acute interventions as indicated (**see Sidebar 5**)."

   b. If the answer is “Yes” to Box 10, then Box 12, in the shape of a rectangle: "Initiate individual, trauma-focused, brief cognitive behavioral therapy (**see Sidebar 4**).”

5. Box 12 connects to Box 13, in the shape of a rectangle: “Re-assess symptoms and function.”
6. Box 13 connects to Box 14, in the shape of a hexagon, which asks, “Persistent (≥1 month) or worsening traumatic stress symptoms or high risk for developing PTSD?”
   a. If the answer is “Yes” to Box 14, then Box 16: “**Go to Module B.** Assessment and Diagnosis of PTSD”
   b. If the answer is “No” to Box 14, then Box 15, in the shape of a rectangle: “Monitor and follow up as indicated.”

Module B: Assessment and Diagnosis of Posttraumatic Stress Disorder

1. The module begins with Box 17, in the shape of a rounded rectangle: “Patient presents with symptoms of PTSD or positive screening or is currently diagnosed with PTSD.”
2. Box 17 connects to Box 18, in the shape of a rectangle: “Obtain a clinical assessment (**see Sidebar 6**). Assess function and duty/work responsibilities. Assess risk and protective factors.”
3. Box 18 connects to Box 19, in the shape of a hexagon, which asks, “Is patient at imminent risk of danger to self or others or medically unstable?”
   a. If the answer is “Yes” to Box 19, then Box 20, in the shape of a rectangle: “Provide appropriate care and lethal means assessment, implement safety plan, or refer to stabilize. Follow reporting mandates as appropriate (**see VA/DoD Suicide CPG**).”
      i. Box 20 connects to Box 21.
   b. If the answer is “No” to Box 19, then Box 21, in the shape of a hexagon, asks, “Meet criteria for the diagnosis of PTSD (**see Sidebar 7**)?”
      i. If the answer is “No” to Box 21, proceed to Box 27, in the shape of an oval: “Follow-up or refer as indicated.”
      ii. If the answer is “Yes” to Box 21, then Box 22, in the shape of a rectangle: “Assess: Severity of PTSD symptoms (**see Sidebar 8**); Existence and severity of co-occurring disorders; Individual’s current and past mental health treatment, particularly of PTSD or PTSD symptoms; and Availability of care options (mental health, primary care, integrated care, Readjustment Counseling Centers, other).”

4. Box 22 connects to Box 23, in the shape of a rectangle: “Summarize patient’s problems. Educate patient and family about PTSD. Discuss treatment options, available resources, and patient preferences.”
5. Box 23 connects to Box 24, in the shape of a rectangle: “Arrive at shared decision regarding goals, expectations, and treatment plan.”
6. Box 24 connects to Box 27, in the shape of a hexagon, which asks, “Is treatment for PTSD agreed upon?”
    a. If the answer is “Yes” to Box 25, proceed to Box 26: “**Go to Module C.** Management of PTSD”
    b. If the answer is “No” to Box 25, proceed to Box 27: “**Follow-up or refer as indicated.**”

Module C: Management of Posttraumatic Stress Disorder

1. The module begins with Box 28, in the shape of a rounded rectangle: “Patient presents with diagnosis of PTSD and agrees to treatment (**continued from Module B**).”
2. Box 28 connects to Box 29, in the shape of a rectangle: “Initiate treatment plan using effective interventions for PTSD (**see Sidebar 9**). Identify and address additional treatment and support needs (**see Sidebar 10**). Consider treatment for comorbidities. Assess/address risk for suicide (**see VA/DoD Suicide CPG**).”
3. Box 29 connects to Box 30, in the shape of a rectangle: “After sufficient time has passed for a clinically meaningful response (**see Sidebar 11**), reassess PTSD symptoms (**see Sidebar 8**), diagnostic status, functional status, quality of life, additional treatment and support needs, and patient preferences. Assess/address risk for suicide (**see VA/DoD Suicide CPG**).”
4. Box 30 connects to Box 31, in the shape of a hexagon, which asks, “Is patient improving?”
    a. If the answer is “Yes” to Box 31, then Box 33, in the shape of a hexagon, asks, “Has the patient demonstrated clinically meaningful remission?”
        i. If the answer is “Yes” to Box 33, then Box 34, in the shape of an oval: “Develop maintenance plan through shared decision making (**see Sidebar 12**).”
        ii. If the answer is “No” to Box 33, then Box 32, in the shape of a rectangle: “Address adherence, dosage, side effects, safety, comorbidities, and psychosocial barriers to treatment. Assess/address risk for suicide.”
    b. If the answer is “No” to Box 31, proceed to Box 32 in the shape of a rectangle: “Address adherence, dosage, side effects, safety,

comorbidities, and psychosocial barriers to treatment. Assess/address risk for suicide."

5. Box 32 connects to Box 35, in the shape of a hexagon, which asks, "Changes to treatment plan indicated (**see Sidebars 9 and 10**)?"
    a. If the answer is "Yes" to Box 35, return to Box 29.
    b. If the answer is "No" to Box 35, proceed to Box 36, in the shape of a rectangle: "Continue to adjust therapy, optimize dose/frequency, and consider treatment of comorbidities."
6. Box 36 connects to Box 29.

Appendix I: Abbreviations

Abbreviation	Definition
ACT	Acceptance and Commitment Therapy
AHRQ	Agency for Healthcare Research and Quality
ART	Accelerated Resolution Therapy
ASD	Acute Stress Disorder
ASR	Acute Stress Response
BF	Behavioral Family Therapy
CAPS-5	Clinician-Administered Posttraumatic Stress Disorder Scale for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision
CBCT	Cognitive Behavioral Conjoint Therapy
CBT	Cognitive Behavioral Therapy
CIH	Complementary and integrative health
CISD	Critical Incident Stress Debriefing
COSR	Combat and operational stress reaction
CPG	Clinical Practice Guideline
CPT	Cognitive Processing Therapy
CT	Cognitive Therapy
DMT	Dimethyltryptamine
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DSM-5-TR	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision
EBPWG	Evidence-Based Practice Work Group
ECT	Electroconvulsive therapy
EMDR	Eye Movement Desensitization and Reprocessing
FDA	Food and Drug Administration
FTF	Face-to-face
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HBOT	Hyperbaric oxygen therapy
I-CBT	Internet-based cognitive behavioral therapy
IPT	Interpersonal Psychotherapy
IRT	Imagery Rehearsal Therapy
KQ	Key question
LGB	Lesbian, gay, or bisexual
LSD	Lysergic acid diethylamide
MBSR	Mindfulness-Based Stress Reduction
MDD	Major Depressive Disorder
MDMA	3,4-methylenedioxymethamphetamine
MHS	Military Health System
MRP	Mantram Repetition Program
MST	Military Sexual Trauma

Abbreviation	Definition
MVA	Motor vehicle accident
NAM	National Academy of Medicine
NESARC-III	Wave 3 National Epidemiologic Survey on Alcohol and Related Conditions
NET	Narrative Exposure Therapy
NHRVS	National Health and Resilience in Veterans Study
NICE	National Institute for Health and Care Excellence
NNT	Number needed to treat
NVVLS	National Vietnam Veterans Longitudinal Study
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
PCGT	Present-Centered Group Therapy
PCL-5	PTSD Checklist for DSM-5
PC-PTSD-5	Primary Care PTSD Screen for DSM-5
PCT	Present-Centered Therapy
PE	Prolonged Exposure
PE-PC	Prolonged Exposure in Primary Care
PICOTS	Population, intervention, comparison, outcome, timing, and setting
PSS-I	PTSD Symptom Scale-I
PSSI-5	PTSD Symptom Scale - Interview Version
PTSD	Posttraumatic stress disorder
QoL	Quality of life
RCT	Randomized controlled trial
RTM	Reconsolidation of Traumatic Memories
rTMS	Repetitive transcranial magnetic stimulation
SAT	Structured Approach Therapy
SGB	Stellate ganglion block
SIT	Stress Inoculation Training
SNRI	Serotonin-norepinephrine reuptake inhibitor
SR	Systematic review
SSRI	Selective serotonin reuptake inhibitor
STAIR	Skills Training in Affect and Interpersonal Regulation
STAIR-PC	Skills Training in Affective and Interpersonal Regulation in Primary Care
SUD	Substance use disorder
TAU	Treatment as usual
TBI	Traumatic brain injury
TMT	Trauma Management Therapy
TrIGR	Trauma-Informed Guilt Reduction
USPSTF	U.S. Preventive Services Task Force
VA	Veteran Affairs

Abbreviation	Definition
VHA	Veterans Health Administration
VNS	Vagus nerve stimulation
VRET	Virtual Reality Exposure Therapy
VTC	Video teleconferencing
WET	Written Exposure Therapy

References

1. U.S. Department of Veterans Affairs/Department of Defense Health Executive Committee (HEC). Evidence Based Practice Work Group Charter [updated January 9, 2017]. Available from: www.healthquality.va.gov/documents/EvidenceBasedPracticeWGCharter123020161.pdf.
2. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. Journal of clinical epidemiology. 2011;64(4):395-400. Epub 2011/01/05. doi: 10.1016/j.jclinepi.2010.09.012. PubMed PMID: 21194891.
3. Isserlin L, Zerach G, Solomon Z. Acute stress responses: A review and synthesis of ASD, ASR, and CSR. American Journal of Orthopsychiatry. 2008;78:423-9. doi: 10.1037/a0014304.
4. Adler AB, Gutierrez IA. Acute Stress Reaction in Combat: Emerging Evidence and Peer-Based Interventions. Curr Psychiatry Rep. 2022;24(4):277-84. Epub 2022/03/31. doi: 10.1007/s11920-022-01335-2. PubMed PMID: 35353322; PubMed Central PMCID: PMCPMC8965216.
5. West JW, CH. Combat and Operational Stress Control. Borden Institue. 2019;37:573-84.
6. Association AP. Diagnostic and statistical manual of mental disorders, Text Revision (DSM-5-TR®). Fifth, Text Revision ed. Arlington, VA: American Psychiatric Association; 2022.
7. Goldstein RB, Smith SM, Chou SP, Saha TD, Jung J, Zhang H, et al. The epidemiology of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Soc Psychiatry Psychiatr Epidemiol. 2016;51(8):1137-48. Epub 2016/04/24. doi: 10.1007/s00127-016-1208-5. PubMed PMID: 27106853; PubMed Central PMCID: PMCPMC4980174.
8. Lehavot K, Goldberg SB, Chen JA, Katon JG, Glass JE, Fortney JC, et al. Do trauma type, stressful life events, and social support explain women veterans' high prevalence of PTSD? Soc Psychiatry Psychiatr Epidemiol. 2018;53(9):943-53. Epub 20180623. doi: 10.1007/s00127-018-1550-x. PubMed PMID: 29936598; PubMed Central PMCID: PMCPMC6521967.
9. Goldberg S, TL S, K L, JG K, JA C, JE G, et al. Mental Health Treatment Delay: A Comparison Among Civilians and Veterans of Different Service Eras. Psychiatric Services. 2019;70(5):358-66. doi: 10.1176/appi.ps.201800444. PubMed PMID: 30841842.
10. Gates MA, Holowka DW, Vasterling JJ, Keane TM, Marx BP, Rosen RC. Posttraumatic stress disorder in Veterans and military personnel: epidemiology, screening, and case recognition. Psychol Serv. 2012;9(4):361-82. Epub 2012/11/15. doi: 10.1037/a0027649. PubMed PMID: 23148803.
11. Kok BC, Herrell RK, Thomas JL, Hoge CW. Posttraumatic stress disorder associated with combat service in Iraq or Afghanistan: reconciling prevalence differences between studies. J Nerv Ment Dis. 2012;200(5):444-50. Epub 2012/05/04. doi: 10.1097/NMD.0b013e3182532312. PubMed PMID: 22551799.

12. Ramchand R, Schell TL, Karney BR, Osilla KC, Burns RM, Caldarone LB. Disparate prevalence estimates of PTSD among service members who served in Iraq and Afghanistan: possible explanations. J Trauma Stress. 2010;23(1):59-68. Epub 2010/02/06. doi: 10.1002/jts.20486. PubMed PMID: 20135699.
13. Richardson LK, Frueh BC, Acierno R. Prevalence estimates of combat-related post-traumatic stress disorder: critical review. The Australian and New Zealand journal of psychiatry. 2010;44(1):4-19. Epub 2010/01/16. doi: 10.3109/00048670903393597. PubMed PMID: 20073563; PubMed Central PMCID: PMCPMC2891773.
14. Meadows SO, Engel CC, Collins RL, Beckman RL, Breslau J, Bloom EL, et al. 2018 Department of Defense Health Related Behaviors Survey (HRBS): Results for the Reserve Component. Santa Monica, CA: RAND Corporation; 2021a.
15. Meadows SO, Engel CC, Collins RL, Beckman RL, Breslau J, Bloom EL, et al. 2018 Department of Defense Health Related Behaviors Survey (HRBS): Results for the Active Component. Santa Monica, CA: RAND Corporation; 2021b.
16. Ramchand R, Rudavsky R, Grant S, Tanielian T, Jaycox L. Prevalence of, risk factors for, and consequences of posttraumatic stress disorder and other mental health problems in military populations deployed to Iraq and Afghanistan. Curr Psychiatry Rep. 2015;17 (5):37. Epub 2015/04/16. doi: 10.1007/s11920-015-0575-z. PubMed PMID: 25876141.
17. Pieter C, Henk FvdM. What work-related exposures are associated with post-traumatic stress disorder? A systematic review with meta-analysis. BMJ Open. 2021;11(8):e049651. doi: 10.1136/bmjopen-2021-049651.
18. Obuobi-Donkor G, Oluwasina F, Nkire N, Agyapong VIO. A Scoping Review on the Prevalence and Determinants of Post-Traumatic Stress Disorder among Military Personnel and Firefighters: Implications for Public Policy and Practice. Int J Environ Res Public Health. 2022;19(3). Epub 2022/02/16. doi: 10.3390/ijerph19031565. PubMed PMID: 35162587; PubMed Central PMCID: PMCPMC8834704.
19. Lofgreen AM, Carroll KK, Dugan SA, Karnik NS. An Overview of Sexual Trauma in the U.S. Military. Focus (Am Psychiatr Publ). 2017;15(4):411-9. doi: 10.1176/appi.focus. 20170024. PubMed PMID: 31975872.
20. Wilson LC. The Prevalence of Military Sexual Trauma: A Meta-Analysis. Trauma Violence Abuse. 2018;19(5):584-97. Epub 2018/11/13. doi: 10.1177/1524838016683459. PubMed PMID: 30415636.
21. Morris EE, Smith JC, Farooqui SY, Surís AM. Unseen battles: the recognition, assessment, and treatment issues of men with military sexual trauma (MST). Trauma Violence Abuse. 2014;15(2):94-101. Epub 2013/11/16. doi: 10.1177/1524838013511540. PubMed PMID: 24231941.
22. Bell M, Dardis C, Vento S, Street A. Victims of Sexual Harassment and Assault in the Military: Understanding Risks and Promoting Recovery. Military Psychology. 2017;30. doi: 10.1037/mil0000144.
23. Defense USDo. Query of unpublished administrative health data. 2022.
24. Campbell MSP, O'Gallagher KBA, Smolenski DJP, Stewart LBA, Otto J, Belsher BEP, et al. Longitudinal Relationship of Combat Exposure With Mental Health Diagnoses in the

Military Health System. Military Medicine. 2021;186(Supplement_1):160-6. doi: 10.1093/milmed/usaa301.

25. Kelber MS, Liu X, O'Gallagher K, Stewart LT, Belsher BE, Morgan MA, et al. Women in combat: The effects of combat exposure and gender on the incidence and persistence of posttraumatic stress disorder diagnosis. J Psychiatr Res. 2021;133:16-22. Epub 20201203. doi: 10.1016/j.jpsychires.2020.12.010. PubMed PMID: 33302161.
26. Otto JL, Peters ZJ, O'Gallagher KG, Stewart LT, Campbell MS, Bush N, et al. Evaluating measures of combat deployment for U.S. Army personnel using various sources of administrative data. Ann Epidemiol. 2019;35:66-72. Epub 20190411. doi: 10.1016/j.annepidem.2019.04.001. PubMed PMID: 31078385.
27. Cameron KL, Sturdivant RX, Baker SP. Trends in the incidence of physician-diagnosed posttraumatic stress disorder among active-duty U.S. military personnel between 1999 and 2008. Military Medical Research. 2019;6(1):8. doi: 10.1186/s40779-019-0198-5.
28. Judkins JL, Moore BA, Collette TL, Hale WJ, Peterson AL, Morissette SB. Incidence Rates of Posttraumatic Stress Disorder Over a 17-Year Period in Active Duty Military Service Members. Journal of Traumatic Stress. 2020;33(6):994-1006. doi: https://doi.org/10.1002/jts.22558.
29. Division AFHS. Update: Mental health disorders and mental health problems, active component, U.S. Armed Forces, 2016-2020. Msmr. 2021;28(8):2-9. Epub 20210801. PubMed PMID: 34622649.
30. Wisco BE, Nomamiukor FO, Marx BP, Krystal JH, Southwick SM, Pietrzak RH. Posttraumatic Stress Disorder in US Military Veterans: Results From the 2019-2020 National Health and Resilience in Veterans Study. J Clin Psychiatry. 2022;83(2). Epub 20220222. doi: 10.4088/JCP.20m14029. PubMed PMID: 35192748.
31. Merians AN, Gross G, Spoont MR, Bellamy CD, Harpaz-Rotem I, Pietrzak RH. Racial and ethnic mental health disparities in U.S. Military Veterans: Results from the National Health and Resilience in Veterans Study. J Psychiatr Res. 2023;161:71-6. Epub 2023/03/12. doi: 10.1016/j.jpsychires.2023.03.005. PubMed PMID: 36905842.
32. Na PJ, Schnurr PP, Pietrzak RH. Mental health of U.S. combat veterans by war era: Results from the National health and Resilience in veterans study. Journal of Psychiatric Research. 2022. doi: https://doi.org/10.1016/j.jpsychires.2022.12.019.
33. Kulka R, Schlenger WE, Fairbank JA, Hough RL, Jordan BK, Marmar CR, et al. National Vietnam Veterans Readjustment Study (NVVRS): Description, current status, and initial PTSD prevalence estimates. Washington, DC: Veterans Administration. 1988.
34. Marmar CR, Schlenger W, Henn-Haase C, Qian M, Purchia E, Li M, et al. Course of Posttraumatic Stress Disorder 40 Years After the Vietnam War: Findings From the National Vietnam Veterans Longitudinal Study. JAMA psychiatry. 2015;72(9):875-81. Epub 2015/07/23. doi: 10.1001/jamapsychiatry.2015.0803. PubMed PMID: 26201054.
35. Cypel Y, Schnurr PP, Schneiderman AI, Culpepper WJ, Akhtar FZ, Morley SW, et al. The mental health of Vietnam theater veterans-the lasting effects of the war: 2016-2017 Vietnam Era Health Retrospective Observational Study. J Trauma Stress. 2022;35(2):605-18. Epub 20220315. doi: 10.1002/jts.22775. PubMed PMID: 35290689; PubMed Central PMCID: PMCPMC9310606.

36. Magruder K, Serpi T, Kimerling R, Kilbourne AM, Collins JF, Cypel Y, et al. Prevalence of Posttraumatic Stress Disorder in Vietnam-Era Women Veterans: The Health of Vietnam-Era Women's Study (HealthVIEWS). JAMA psychiatry. 2015;72(11):1127-34. Epub 2015/10/08. doi: 10.1001/jamapsychiatry.2015.1786. PubMed PMID: 26445103.

37. Greenberg G, Hoff R. 2020 Veterans with PTSD Data Sheet: National, VISN, and VAMC Tables. In: Center NPE, editor. West Haven, CT: Northeast Program Evaluation Center; 2020.

38. Harpaz-Rotem I, Hoff R. FY2020 Overview of PTSD Patient Population Data Sheet. In: Operations VOoMH, editor. West Haven, CT: Northeast Program Evaluation Center; 2020.

39. Livingston NA, Lynch KE, Hinds Z, Gatsby E, DuVall SL, Shipherd JC. Identifying Posttraumatic Stress Disorder and Disparity Among Transgender Veterans Using Nationwide Veterans Health Administration Electronic Health Record Data. LGBT Health. 2022;9(2):94-102. Epub 2022/01/05. doi: 10.1089/lgbt.2021.0246. PubMed PMID: 34981963.

40. Schnurr PP, Wachen JS, Green BL, Kaltman S. Trauma exposure, PTSD, and physical health. PTSD: Science and practice—A comprehensive handbook, 3rd edition. New York, NY, US: The Guilford Press; 2021. p. 462-79.

41. Forehand JA, Peltzman T, Westgate CL, Riblet NB, Watts BV, Shiner B. Causes of Excess Mortality in Veterans Treated for Posttraumatic Stress Disorder. American Journal of Preventive Medicine. 2019;57(2):145-52. doi: 10.1016/j.amepre.2019.03.014.

42. Ransohoff DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. Jama. 2013;309(2):139-40. Epub 2013/01/10. doi: 10.1001/jama.2012.156703. PubMed PMID: 23299601.

43. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. Journal of clinical epidemiology. 2013;66(7):719-25. Epub 2013/01/15. doi: 10.1016/j.jclinepi.2012.03.013. PubMed PMID: 23312392.

44. Schunemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. Health research policy and systems / BioMed Central. 2006;4:22. Epub 2006/12/07. doi: 10.1186/1478-4505-4-22. PubMed PMID: 17147811; PubMed Central PMCID: PMCPmc1697808.

45. Newberry SJ, Ahmadzai N, Motala A, Tsertsvadze A, Maglione M, Ansari MT, et al. AHRQ Methods for Effective Health Care. Surveillance and identification of signals for updating systematic reviews: Implementation and early experience. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013.

46. U.S. Preventive Services Task Force. Procedure Manual Appendix VI. Criteria for Assessing Internal Validity of Individual Studies 2017. Available from: https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual/procedure-manual-appendix-vi-criteria-assessing-internal-validity-individual-studies.

47. National Institute for Health and Care Excellence. The guidelines manual. London: National Institute for Health and Care Excellence, 2012.

48. Martinez Garcia L, McFarlane E, Barnes S, Sanabria AJ, Alonso-Coello P, Alderson P. Updated recommendations: an assessment of NICE clinical guidelines. Implementation science : IS. 2014;9:72. Epub 2014/06/13. doi: 10.1186/1748-5908-9-72. PubMed PMID: 24919856; PubMed Central PMCID: PMCPmc4067507.

49. U.S. Department of Veteran Affairs, Department of Defense. Guideline for Guidelines: Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup; [updated January 29, 2019]. Available from: http://www.healthquality.va.gov/policy/index.asp.

50. Financial Relationships Between VHA Health Care Professionals and Industry: U.S. Department of Veterans Affairs, Veterans Health Administration; [updated November 24, 2014]. Available from: https://www.ethics.va.gov/docs/policy/VHA_Handbook_1004_07_Financial_Relationships.pdf.

51. Clinical Practice Guidelines We Can Trust. Washington, DC: National Academies Press, 2011.

52. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: Definitions and applications to improve outcomes. Journal of the American Academy of Nurse Practitioners. 2008;20(12):600-7. Epub 2009/01/06. doi: 10.1111/j.1745-7599.2008.00360.x. PubMed PMID: 19120591.

53. Stewart M, Brown JB, Donner A, McWhinney IR, Oates J, Weston WW, et al. The impact of patient-centered care on outcomes. J Fam Pract. 2000;49(9):796-804. Epub 2000/10/14. PubMed PMID: 11032203.

54. National Learning Consortium. Shared Decision Making 2013. Available from: https://www.healthit.gov/sites/default/files/nlc_shared_decision_making_fact_sheet.pdf.

55. Institute of Medicine. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington DC: National Academies Press, 2001.

56. Society for Medical Decision Making Committee on Standardization of Clinical Algorithms. Proposal for clinical algorithm standards. Med Decis Making. 1992;12(2):149-54. Epub 1992/04/01. PubMed PMID: 1573982.

57. Bovin MJ, Kimerling R, Weathers FW, Prins A, Marx BP, Post EP, et al. Diagnostic Accuracy and Acceptability of the Primary Care Posttraumatic Stress Disorder Screen for the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) Among US Veterans. JAMA Netw Open. 2021;4(2):e2036733. Epub 20210201. doi: 10.1001/jamanetworkopen.2020.36733. PubMed PMID: 33538826; PubMed Central PMCID: PMCPMC7862990.

58. Prins A, Bovin MJ, Smolenski DJ, Marx BP, Kimerling R, Jenkins-Guarnieri MA, et al. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): Development and Evaluation Within a Veteran Primary Care Sample. J Gen Intern Med. 2016;31(10):1206-11. Epub 20160511. doi: 10.1007/s11606-016-3703-5. PubMed PMID: 27170304; PubMed Central PMCID: PMCPMC5023594.

59. Jackson CE, Currao A, Fonda JR, Kenna A, Milberg WP, McGlinchey RE, et al. Research utility of a CAPS-IV and CAPS-5 hybrid interview: Posttraumatic stress symptom and diagnostic concordance in recent-era U.S. veterans. J Trauma Stress. 2022;35(2):570-80. Epub 20211231. doi: 10.1002/jts.22771. PubMed PMID: 34973042; PubMed Central PMCID: PMCPMC9035140.

60. Weathers FW, Bovin MJ, Lee DJ, Sloan DM, Schnurr PP, Kaloupek DG, et al. The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5): Development and initial psychometric evaluation in military veterans. Psychol Assess. 2018;30(3):383-95. Epub 20170511. doi: 10.1037/pas0000486. PubMed PMID: 28493729; PubMed Central PMCID: PMCPMC5805662.

61. Foa EB, McLean CP, Zang Y, Zhong J, Rauch S, Porter K, et al. Psychometric properties of the Posttraumatic Stress Disorder Symptom Scale Interview for DSM-5 (PSSI-5). Psychol Assess. 2016;28(10):1159-65. Epub 20151221. doi: 10.1037/pas0000259. PubMed PMID: 26691507.

62. Foa EB, Tolin DF. Comparison of the PTSD Symptom Scale-Interview Version and the Clinician-Administered PTSD scale. J Trauma Stress. 2000;13(2):181-91. doi: 10.1023/a:1007781909213. PubMed PMID: 10838669.

63. Lee DJ, Weathers FW, Thompson-Hollands J, Sloan DM, Marx BP. Concordance in PTSD symptom change between DSM-5 versions of the Clinician-Administered PTSD Scale (CAPS-5) and PTSD Checklist (PCL-5). Psychol Assess. 2022;34(6):604-9. Epub 20220407. doi: 10.1037/pas0001130. PubMed PMID: 35389681; PubMed Central PMCID: PMCPMC9437843.

64. Marx BP, Lee DJ, Norman SB, Bovin MJ, Sloan DM, Weathers FW, et al. Reliable and clinically significant change in the clinician-administered PTSD Scale for DSM-5 and PTSD Checklist for DSM-5 among male veterans. Psychol Assess. 2022;34(2):197-203. Epub 20211223. doi: 10.1037/pas0001098. PubMed PMID: 34941354; PubMed Central PMCID: PMCPMC9022599.

65. Monson CM, Gradus JL, Young-Xu Y, Schnurr PP, Price JL, Schumm JA. Change in posttraumatic stress disorder symptoms: do clinicians and patients agree? Psychol Assess. 2008;20(2):131-8. doi: 10.1037/1040-3590.20.2.131. PubMed PMID: 18557690.

66. Rothbaum BO, Kearns MC, Price M, Malcoun E, Davis M, Ressler KJ, et al. Early intervention may prevent the development of posttraumatic stress disorder: a randomized pilot civilian study with modified prolonged exposure. Biol Psychiatry. 2012;72(11):957-63. Epub 2012/07/07. doi: 10.1016/j.biopsych.2012.06.002. PubMed PMID: 22766415; PubMed Central PMCID: PMCPMC3467345.

67. Forneris CA, Gartlehner G, Brownley KA, Gaynes BN, Sonis J, Coker-Schwimmer E, et al. Interventions to prevent post-traumatic stress disorder: a systematic review. Am J Prev Med. 2013;44(6):635-50. Epub 2013/05/21. doi: 10.1016/j.amepre.2013.02.013. PubMed PMID: 23683982.

68. Hoge EA, Worthington JJ, Nagurney JT, Chang Y, Kay EB, Feterowski CM, et al. Effect of acute posttrauma propranolol on PTSD outcome and physiological responses during script-driven imagery. CNS Neurosci Ther. 2012;18(1):21-7. Epub 20110110.

doi: 10.1111/j.1755-5949.2010.00227.x. PubMed PMID: 22070357; PubMed Central PMCID: PMCPMC6493400.

69. Amos T, Stein DJ, Ipser JC. Pharmacological interventions for preventing post-traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2014(7):Cd006239. Epub 20140708. doi: 10.1002/14651858.CD006239.pub2. PubMed PMID: 25001071.

70. Kliem S, Kröger C. Prevention of chronic PTSD with early cognitive behavioral therapy. A meta-analysis using mixed-effects modeling. Behav Res Ther. 2013;51(11):753-61. Epub 2013/10/01. doi: 10.1016/j.brat.2013.08.005. PubMed PMID: 24077120.

71. Bisson JI, Wright LA, Jones KA, Lewis C, Phelps AJ, Sijbrandij M, et al. Preventing the onset of post traumatic stress disorder. Clin Psychol Rev. 2021;86:102004. Epub 2021/04/16. doi: 10.1016/j.cpr.2021.102004. PubMed PMID: 33857763.

72. Bryant RA, Moulds ML, Guthrie RM, Dang ST, Mastrodomenico J, Nixon RD, et al. A randomized controlled trial of exposure therapy and cognitive restructuring for posttraumatic stress disorder. J Consult Clin Psychol. 2008;76(4):695-703. doi: 10.1037/a0012616. PubMed PMID: 18665697.

73. Bryant RA, Sackville T, Dang ST, Moulds M, Guthrie R. Treating acute stress disorder: an evaluation of cognitive behavior therapy and supportive counseling techniques. Am J Psychiatry. 1999;156(11):1780-6. Epub 1999/11/30. doi: 10.1176/ajp.156.11.1780. PubMed PMID: 10553743.

74. Bryant RA, Moulds ML, Guthrie RM, Nixon RDV. The additive benefit of hypnosis and cognitive-behavioral therapy in treating acute stress disorder. J Consult Clin Psychol. 2005;73(2):334-40. Epub 2005/03/31. doi: 10.1037/0022-006x.73.2.334. PubMed PMID: 15796641.

75. Bryant RA, Moulds ML, Guthrie RM, Dang ST, Nixon RD. Imaginal exposure alone and imaginal exposure with cognitive restructuring in treatment of posttraumatic stress disorder. J Consult Clin Psychol. 2003;71(4):706-12. Epub 2003/08/20. doi: 10.1037/0022-006x.71.4.706. PubMed PMID: 12924676.

76. Bryant RA, Harvey AG, Dang ST, Sackville T, Basten C. Treatment of acute stress disorder: a comparison of cognitive-behavioral therapy and supportive counseling. J Consult Clin Psychol. 1998;66(5):862-6. doi: 10.1037//0022-006x.66.5.862. PubMed PMID: 9803707.

77. Shalev AY, Ankri Y, Israeli-Shalev Y, Peleg T, Adessky R, Freedman S. Prevention of posttraumatic stress disorder by early treatment: results from the Jerusalem Trauma Outreach And Prevention study. Arch Gen Psychiatry. 2012;69(2):166-76. Epub 2011/10/05. doi: 10.1001/archgenpsychiatry.2011.127. PubMed PMID: 21969418.

78. Borrelli J, Jr., Starr A, Downs DL, North CS. Prospective Study of the Effectiveness of Paroxetine on the Onset of Posttraumatic Stress Disorder, Depression, and Health and Functional Outcomes After Trauma. J Orthop Trauma. 2019;33(2):e58-e63. Epub 2018/10/03. doi: 10.1097/bot.0000000000001342. PubMed PMID: 30277987.

79. Suliman S, Seedat S, Pingo J, Sutherland T, Zohar J, Stein DJ. Escitalopram in the prevention of posttraumatic stress disorder: a pilot randomized controlled trial. BMC Psychiatry. 2015;15:24. Epub 2015/04/18. doi: 10.1186/s12888-015-0391-3. PubMed PMID: 25885650; PubMed Central PMCID: PMCPMC4337322.

80. Merz J, Schwarzer G, Gerger H. Comparative Efficacy and Acceptability of Pharmacological, Psychotherapeutic, and Combination Treatments in Adults With Posttraumatic Stress Disorder: A Network Meta-analysis. JAMA psychiatry. 2019;76(9):904-13. doi: 10.1001/jamapsychiatry.2019.0951. PubMed PMID: 31188399; PubMed Central PMCID: PMCPMC6563588.

81. Lee DJ, Schnitzlein CW, Wolf JP, Vythilingam M, Rasmusson AM, Hoge CW. Psychotherapy versus Pharmacotherapy for Posttraumatic stress Disorder: Systemic Review and Meta-Analyses to Determine First-Line Treatments. Depress Anxiety. 2016;33(9):792-806. Epub 20160429. doi: 10.1002/da.22511. PubMed PMID: 27126398.

82. Watts BV, Schnurr PP, Mayo L, Young-Xu Y, Weeks WB, Friedman MJ. Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. J Clin Psychiatry. 2013;74(6):e541-50. doi: 10.4088/jcp.12r08225. PubMed PMID: 23842024.

83. Watts BV, Schnurr PP, Zayed M, Young-Xu Y, Stender P, Llewellyn-Thomas H. A randomized controlled clinical trial of a patient decision aid for posttraumatic stress disorder. Psychiatr Serv. 2015;66(2):149-54. Epub 20141015. doi: 10.1176/appi.ps.201400062. PubMed PMID: 25322473.

84. Rauch SAM, Kim HM, Powell C, Tuerk PW, Simon NM, Acierno R, et al. Efficacy of Prolonged Exposure Therapy, Sertraline Hydrochloride, and Their Combination Among Combat Veterans With Posttraumatic Stress Disorder: A Randomized Clinical Trial. JAMA psychiatry. 2019;76(2):117-26. Epub 2018/12/06. doi: 10.1001/jamapsychiatry.2018.3412. PubMed PMID: 30516797; PubMed Central PMCID: PMCPMC6439753

85. Swift JK, Greenberg RP, Tompkins KA, Parkin SR. Treatment refusal and premature termination in psychotherapy, pharmacotherapy, and their combination: A meta-analysis of head-to-head comparisons. Psychotherapy (Chic). 2017;54(1):47-57. doi: 10.1037/pst0000104. PubMed PMID: 28263651.

86. Simiola V, Neilson EC, Thompson R, Cook JM. Preferences for trauma treatment: A systematic review of the empirical literature. Psychological Trauma: Theory, Research, Practice, and Policy. 2015;7:516-24. doi: 10.1037/tra0000038.

87. Zoellner LA, Roy-Byrne PP, Mavissakalian M, Feeny NC. Doubly Randomized Preference Trial of Prolonged Exposure Versus Sertraline for Treatment of PTSD. Am J Psychiatry. 2019;176(4):287-96. Epub 2018/10/20. doi: 10.1176/appi.ajp.2018.17090995. PubMed PMID: 30336702.

88. Jericho B, Luo A, Berle D. Trauma-focused psychotherapies for post-traumatic stress disorder: A systematic review and network meta-analysis. Acta Psychiatr Scand. 2022;145(2):132-55. Epub 20210917. doi: 10.1111/acps.13366. PubMed PMID: 34473342.

89. Sloan DM, Marx BP, Resick PA, Young-McCaughan S, Dondanville KA, Straud CL, et al. Effect of Written Exposure Therapy vs Cognitive Processing Therapy on Increasing Treatment Efficiency Among Military Service Members With Posttraumatic Stress Disorder: A Randomized Noninferiority Trial. JAMA Netw Open. 2022;5(1):e2140911. Epub 20220104. doi: 10.1001/jamanetworkopen.2021.40911. PubMed PMID: 35015065; PubMed Central PMCID: PMCPMC8753496.

90. Thompson-Hollands J, Marx BP, Lee DJ, Resick PA, Sloan DM. Long-term treatment gains of a brief exposure-based treatment for PTSD. Depress Anxiety. 2018;35(10):985-91. Epub 20180824. doi: 10.1002/da.22825. PubMed PMID: 30144228; PubMed Central PMCID: PMCPMC6168424.

91. Sloan DM, Marx BP, Lee DJ, Resick PA. A Brief Exposure-Based Treatment vs Cognitive Processing Therapy for Posttraumatic Stress Disorder: A Randomized Noninferiority Clinical Trial. JAMA psychiatry. 2018;75(3):233-9. doi: 10.1001/jamapsychiatry.2017.4249. PubMed PMID: 29344631; PubMed Central PMCID: PMCPMC5843538.

92. McLean CP, Levy HC, Miller ML, Tolin DF. Exposure therapy for PTSD in military populations: A systematic review and meta-analysis of randomized clinical trials. J Anxiety Disord. 2022;90:102607. Epub 20220728. doi: 10.1016/j.janxdis.2022.102607. PubMed PMID: 35926254.

93. McLean CP, Levy HC, Miller ML, Tolin DF. Exposure therapy for PTSD: A meta-analysis. Clin Psychol Rev. 2022;91:102115. Epub 20211221. doi: 10.1016/j.cpr.2021.102115. PubMed PMID: 34954460.

94. Morina N, Hoppen TH, Kip A. Study quality and efficacy of psychological interventions for posttraumatic stress disorder: a meta-analysis of randomized controlled trials. Psychol Med. 2021;51(8):1-11. Epub 20210512. doi: 10.1017/s0033291721001641. PubMed PMID: 33975654; PubMed Central PMCID: PMCPMC8223238.

95. Jonas DE, Cusack K, Forneris CA, Wilkins TM, Sonis J, Middleton JC, et al. AHRQ Comparative Effectiveness Reviews. Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder (PTSD). Rockville (MD): Agency for Healthcare Research and Quality (US); 2013.

96. Cusack K, Jonas DE, Forneris CA, Wines C, Sonis J, Middleton JC, et al. Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. Clin Psychol Rev. 2016;43:128-41. Epub 20151102. doi: 10.1016/j.cpr.2015.10.003. PubMed PMID: 26574151.

97. Schnurr PP, Chard KM, Ruzek JI, Chow BK, Resick PA, Foa EB, et al. Comparison of Prolonged Exposure vs Cognitive Processing Therapy for Treatment of Posttraumatic Stress Disorder Among US Veterans: A Randomized Clinical Trial. JAMA Network Open. 2022;5(1):e2136921-e. doi: 10.1001/jamanetworkopen.2021.36921.

98. Foa EB, McLean CP, Zang Y, Rosenfield D, Yadin E, Yarvis JS, et al. Effect of Prolonged Exposure Therapy Delivered Over 2 Weeks vs 8 Weeks vs Present-Centered Therapy on PTSD Symptom Severity in Military Personnel: A Randomized Clinical Trial. Jama. 2018;319(4):354-64. doi: 10.1001/jama.2017.21242. PubMed PMID: 29362795; PubMed Central PMCID: PMCPMC5833566.

99. Forbes D, Lloyd D, Nixon RD, Elliott P, Varker T, Perry D, et al. A multisite randomized controlled effectiveness trial of cognitive processing therapy for military-related posttraumatic stress disorder. J Anxiety Disord. 2012;26(3):442-52. Epub 20120124. doi: 10.1016/j.janxdis.2012.01.006. PubMed PMID: 22366446.

100. Monson CM, Schnurr PP, Resick PA, Friedman MJ, Young-Xu Y, Stevens SP. Cognitive processing therapy for veterans with military-related posttraumatic stress disorder.

J Consult Clin Psychol. 2006;74(5):898-907. doi: 10.1037/0022-006x.74.5.898. PubMed PMID: 17032094.

101. Edwards-Stewart A, Smolenski DJ, Bush NE, Cyr BA, Beech EH, Skopp NA, et al. Posttraumatic Stress Disorder Treatment Dropout Among Military and Veteran Populations: A Systematic Review and Meta-Analysis. J Trauma Stress. 2021;34(4):808-18. Epub 20210201. doi: 10.1002/jts.22653. PubMed PMID: 33524199.
102. Harik JM, Grubbs KM, Hamblen JL. Retracted: The Impact of Treatment Description Format on Patient Preferences for Posttraumatic Stress Disorder Treatment. Journal of Traumatic Stress. 2020;33(4):455-64. doi: https://doi.org/10.1002/jts.22528.
103. Shifrin A, Sharma S, Zeifman RJ, Roth ML, Gifford S, Monson CM. Posttraumatic stress disorder treatment preference: Prolonged exposure therapy, cognitive processing therapy, or medication therapy? Psychol Serv. 2022. Epub 20220711. doi: 10.1037/ser0000688. PubMed PMID: 35816575.
104. Wachen JS, Dondanville KA, Evans WR, Morris K, Cole A. Adjusting the Timeframe of Evidence-Based Therapies for PTSD-Massed Treatments. Current Treatment Options in Psychiatry. 2019;6(2):107-18. doi: 10.1007/s40501-019-00169-9.
105. Belsher BE, Beech E, Evatt D, Smolenski DJ, Shea MT, Otto JL, et al. Present-centered therapy (PCT) for post-traumatic stress disorder (PTSD) in adults. Cochrane Database Syst Rev. 2019;2019(11). Epub 20191118. doi: 10.1002/14651858.CD012898.pub2. PubMed PMID: 31742672; PubMed Central PMCID: PMCPMC6863089.
106. Ehlers A, Hackmann A, Grey N, Wild J, Liness S, Albert I, et al. A randomized controlled trial of 7-day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. Am J Psychiatry. 2014;171(3):294-304. doi: 10.1176/appi.ajp.2013.13040552. PubMed PMID: 24480899; PubMed Central PMCID: PMCPMC4082238.
107. Ehlers A, Clark DM, Hackmann A, McManus F, Fennell M, Herbert C, et al. A randomized controlled trial of cognitive therapy, a self-help booklet, and repeated assessments as early interventions for posttraumatic stress disorder. Arch Gen Psychiatry. 2003;60(10):1024-32. doi: 10.1001/archpsyc.60.10.1024. PubMed PMID: 14557148.
108. Lewis C, Roberts NP, Gibson S, Bisson JI. Dropout from psychological therapies for post-traumatic stress disorder (PTSD) in adults: systematic review and meta-analysis. Eur J Psychotraumatol. 2020;11(1):1709709. Epub 20200309. doi: 10.1080/20008198.2019.1709709. PubMed PMID: 32284816; PubMed Central PMCID: PMCPMC7144189.
109. Mavranezouli I, Megnin-Viggars O, Daly C, Dias S, Welton NJ, Stockton S, et al. Psychological treatments for post-traumatic stress disorder in adults: a network meta-analysis. Psychol Med. 2020;50(4):542-55. Epub 20200217. doi: 10.1017/s0033291720000070. PubMed PMID: 32063234.
110. Litz BT, Rusowicz-Orazem L, Doros G, Grunthal B, Gray M, Nash W, et al. Adaptive disclosure, a combat-specific PTSD treatment, versus cognitive-processing therapy, in deployed marines and sailors: A randomized controlled non-inferiority trial. Psychiatry Res. 2021;297:113761. Epub 20210124. doi: 10.1016/j.psychres.2021.113761. PubMed PMID: 33540206.

111. Norman SB, Capone C, Panza KE, Haller M, Davis BC, Schnurr PP, et al. A clinical trial comparing trauma-informed guilt reduction therapy (TrIGR), a brief intervention for trauma-related guilt, to supportive care therapy. Depress Anxiety. 2022;39(4):262-73. Epub 20220125. doi: 10.1002/da.23244. PubMed PMID: 35075738.

112. Roberts NP, Roberts PA, Jones N, Bisson JI. Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: A systematic review and meta-analysis. Clin Psychol Rev. 2015;38:25-38. Epub 20150303. doi: 10.1016/j.cpr.2015.02.007. PubMed PMID: 25792193.

113. Lindauer RJ, Booij J, Habraken JB, van Meijel EP, Uylings HB, Olff M, et al. Effects of psychotherapy on regional cerebral blood flow during trauma imagery in patients with post-traumatic stress disorder: a randomized clinical trial. Psychol Med. 2008;38(4):543-54. Epub 20070906. doi: 10.1017/s0033291707001432. PubMed PMID: 17803835.

114. Hensel-Dittmann D, Schauer M, Ruf M, Catani C, Odenwald M, Elbert T, et al. Treatment of traumatized victims of war and torture: a randomized controlled comparison of narrative exposure therapy and stress inoculation training. Psychother Psychosom. 2011;80(6):345-52. Epub 20110806. doi: 10.1159/000327253. PubMed PMID: 21829046.

115. Eshuis LV, van Gelderen MJ, van Zuiden M, Nijdam MJ, Vermetten E, Olff M, et al. Efficacy of immersive PTSD treatments: A systematic review of virtual and augmented reality exposure therapy and a meta-analysis of virtual reality exposure therapy. J Psychiatr Res. 2021;143:516-27. Epub 20201117. doi: 10.1016/j.jpsychires.2020.11.030. PubMed PMID: 33248674.

116. McLay RN, Baird A, Webb-Murphy J, Deal W, Tran L, Anson H, et al. A Randomized, Head-to-Head Study of Virtual Reality Exposure Therapy for Posttraumatic Stress Disorder. Cyberpsychol Behav Soc Netw. 2017;20(4):218-24. Epub 20170227. doi: 10.1089/cyber.2016.0554. PubMed PMID: 28394217.

117. Reger GM, Koenen-Woods P, Zetocha K, Smolenski DJ, Holloway KM, Rothbaum BO, et al. Randomized controlled trial of prolonged exposure using imaginal exposure vs. virtual reality exposure in active duty soldiers with deployment-related posttraumatic stress disorder (PTSD). J Consult Clin Psychol. 2016;84(11):946-59. Epub 20160908. doi: 10.1037/ccp0000134. PubMed PMID: 27606699.

118. van Gelderen MJ, Nijdam MJ, Haagen JFG, Vermetten E. Interactive Motion-Assisted Exposure Therapy for Veterans with Treatment-Resistant Posttraumatic Stress Disorder: A Randomized Controlled Trial. Psychotherapy and Psychosomatics. 2020;89(4):215-27. doi: 10.1159/000505977.

119. Botella C, García-Palacios A, Guillen V, Baños RM, Quero S, Alcaniz M. An adaptive display for the treatment of diverse trauma PTSD victims. Cyberpsychol Behav Soc Netw. 2010;13(1):67-71. Epub 2010/06/10. doi: 10.1089/cyber.2009.0353. PubMed PMID: 20528295.

120. Gamito P, Oliveira J, Rosa P, Morais D, Duarte N, Oliveira S, et al. PTSD elderly war veterans: a clinical controlled pilot study. Cyberpsychol Behav Soc Netw. 2010;13(1):43-8. Epub 2010/06/10. doi: 10.1089/cyber.2009.0237. PubMed PMID: 20528292.

121. McLay RN, Wood DP, Webb-Murphy JA, Spira JL, Wiederhold MD, Pyne JM, et al. A randomized, controlled trial of virtual reality-graded exposure therapy for post-traumatic

stress disorder in active duty service members with combat-related post-traumatic stress disorder. Cyberpsychol Behav Soc Netw. 2011;14(4):223-9. Epub 2011/02/22. doi: 10.1089/cyber.2011.0003. PubMed PMID: 21332375.

122. Ready DJ, Gerardi RJ, Backscheider AG, Mascaro N, Rothbaum BO. Comparing virtual reality exposure therapy to present-centered therapy with 11 U.S. Vietnam veterans with PTSD. Cyberpsychol Behav Soc Netw. 2010;13(1):49-54. Epub 2010/06/10. doi: 10.1089/cyber.2009.0239. PubMed PMID: 20528293.
123. Maguen S, Burkman K, Madden E, Dinh J, Bosch J, Keyser J, et al. Impact of Killing in War: A Randomized, Controlled Pilot Trial. J Clin Psychol. 2017;73(9):997-1012. Epub 2017/03/16. doi: 10.1002/jclp.22471. PubMed PMID: 28294318.
124. Melton H, Meader N, Dale H, Wright K, Jones-Diette J, Temple M, et al. Interventions for adults with a history of complex traumatic events: the INCiTE mixed-methods systematic review. Health Technol Assess. 2020;24(43):1-312. doi: 10.3310/hta24430. PubMed PMID: 32924926; PubMed Central PMCID: PMCPMC7520719.
125. Cigrang JA, Rauch SA, Mintz J, Brundige AR, Mitchell JA, Najera E, et al. Moving effective treatment for posttraumatic stress disorder to primary care: A randomized controlled trial with active duty military. Fam Syst Health. 2017;35(4):450-62. doi: 10.1037/fsh0000315. PubMed PMID: 29283612.
126. Coventry PA, Meader N, Melton H, Temple M, Dale H, Wright K, et al. Psychological and pharmacological interventions for posttraumatic stress disorder and comorbid mental health problems following complex traumatic events: Systematic review and component network meta-analysis. PLoS Med. 2020;17(8):e1003262. Epub 20200819. doi: 10.1371/journal.pmed.1003262. PubMed PMID: 32813696; PubMed Central PMCID: PMCPMC7446790.
127. Foa EB, Hembree EA, Cahill SP, Rauch SA, Riggs DS, Feeny NC, et al. Randomized trial of prolonged exposure for posttraumatic stress disorder with and without cognitive restructuring: outcome at academic and community clinics. J Consult Clin Psychol. 2005;73(5):953-64. doi: 10.1037/0022-006x.73.5.953. PubMed PMID: 16287395.
128. Marks I, Lovell K, Noshirvani H, Livanou M, Thrasher S. Treatment of posttraumatic stress disorder by exposure and/or cognitive restructuring: a controlled study. Arch Gen Psychiatry. 1998;55(4):317-25. doi: 10.1001/archpsyc.55.4.317. PubMed PMID: 9554427.
129. Foa EB, Dancu CV, Hembree EA, Jaycox LH, Meadows EA, Street GP. A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. J Consult Clin Psychol. 1999;67(2):194-200. doi: 10.1037//0022-006x.67.2.194. PubMed PMID: 10224729.
130. Resick PA, Galovski TE, Uhlmansiek MO, Scher CD, Clum GA, Young-Xu Y. A randomized clinical trial to dismantle components of cognitive processing therapy for posttraumatic stress disorder in female victims of interpersonal violence. J Consult Clin Psychol. 2008;76(2):243-58. doi: 10.1037/0022-006x.76.2.243. PubMed PMID: 18377121; PubMed Central PMCID: PMCPMC2967760.
131. Resick PA, Monson CM, Chard KM. Cognitive processing therapy for PTSD: A comprehensive manual. New York, NY, US: The Guilford Press; 2017. xv, 312-xv, p.

132. Schwartze D, Barkowski S, Strauss B, Knaevelsrud C, Rosendahl J. Efficacy of group psychotherapy for posttraumatic stress disorder: Systematic review and meta-analysis of randomized controlled trials. Psychother Res. 2019;29(4):415-31. Epub 20171127. doi: 10.1080/10503307.2017.1405168. PubMed PMID: 29179647.

133. Beck JG, Coffey SF, Foy DW, Keane TM, Blanchard EB. Group cognitive behavior therapy for chronic posttraumatic stress disorder: an initial randomized pilot study. Behav Ther. 2009;40(1):82-92. Epub 20080709. doi: 10.1016/j.beth.2008.01.003. PubMed PMID: 19187819.

134. Castillo DT, Chee CL, Nason E, Keller J, C'De Baca J, Qualls C, et al. Group-delivered cognitive/exposure therapy for PTSD in women veterans: A randomized controlled trial. Psychological Trauma: Theory, Research, Practice, and Policy. 2016;8:404-12. doi: 10.1037/tra0000111.

135. Falsetti SA, Resnick HS, Davis JL. Multiple channel exposure therapy for women with PTSD and comorbid panic attacks. Cogn Behav Ther. 2008;37(2):117-30. doi: 10.1080/16506070801969088. PubMed PMID: 18470742.

136. Zlotnick C, Shea TM, Rosen K, Simpson E, Mulrenin K, Begin A, et al. An affect-management group for women with posttraumatic stress disorder and histories of childhood sexual abuse. J Trauma Stress. 1997;10(3):425-36. doi: 10.1023/a:1024841321156. PubMed PMID: 9246650.

137. Zlotnick C, Johnson J, Najavits LM. Randomized controlled pilot study of cognitive-behavioral therapy in a sample of incarcerated women with substance use disorder and PTSD. Behav Ther. 2009;40(4):325-36. Epub 20081031. doi: 10.1016/j.beth.2008.09.004. PubMed PMID: 19892078; PubMed Central PMCID: PMCPMC3031094.

138. Krupnick JL, Green BL, Stockton P, Miranda J, Krause E, Mete M. Group interpersonal psychotherapy for low-income women with posttraumatic stress disorder. Psychother Res. 2008;18(5):497-507. doi: 10.1080/10503300802183678. PubMed PMID: 18816001.

139. Resick PA, Wachen JS, Dondanville KA, Pruiksma KE, Yarvis JS, Peterson AL, et al. Effect of Group vs Individual Cognitive Processing Therapy in Active-Duty Military Seeking Treatment for Posttraumatic Stress Disorder: A Randomized Clinical Trial. JAMA psychiatry. 2017;74(1):28-36. doi: 10.1001/jamapsychiatry.2016.2729. PubMed PMID: 27893032.

140. Resick PA, Wachen JS, Mintz J, Young-McCaughan S, Roache JD, Borah AM, et al. A randomized clinical trial of group cognitive processing therapy compared with group present-centered therapy for PTSD among active duty military personnel. J Consult Clin Psychol. 2015;83(6):1058-68. Epub 20150504. doi: 10.1037/ccp0000016. PubMed PMID: 25939018.

141. Schnurr PP, Friedman MJ, Foy DW, Shea MT, Hsieh FY, Lavori PW, et al. Randomized trial of trauma-focused group therapy for posttraumatic stress disorder: results from a department of veterans affairs cooperative study. Arch Gen Psychiatry. 2003;60(5):481-9. doi: 10.1001/archpsyc.60.5.481. PubMed PMID: 12742869.

142. Classen C, Koopman C, Nevill-Manning K, Spiegel D. A preliminary report comparing trauma-focused and present-focused group therapy against a wait-listed condition among childhood sexual abuse survivors with PTSD. Haworth Press; 2001. p. 265-88.

143. Sloan DM, Unger W, Lee DJ, Beck JG. A Randomized Controlled Trial of Group Cognitive Behavioral Treatment for Veterans Diagnosed With Chronic Posttraumatic Stress Disorder. J Trauma Stress. 2018;31(6):886-98. Epub 20181129. doi: 10.1002/jts.22338. PubMed PMID: 30499227; PubMed Central PMCID: PMCPMC6295345.

144. Mahoney A, Karatzias T, Hutton P. A systematic review and meta-analysis of group treatments for adults with symptoms associated with complex post-traumatic stress disorder. J Affect Disord. 2019;243:305-21. Epub 20180917. doi: 10.1016/j.jad.2018.09.059. PubMed PMID: 30261446.

145. Bisson JI, Roberts NP, Andrew M, Cooper R, Lewis C. Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. Cochrane Database Syst Rev. 2013;2013(12):Cd003388. Epub 20131213. doi: 10.1002/14651858.CD003388.pub4. PubMed PMID: 24338345; PubMed Central PMCID: PMCPMC6991463.

146. Sloan, Feinstein B, Gallagher M, Beck JG, Keane T. Efficacy of Group Treatment for Posttraumatic Stress Disorder Symptoms: A Meta-Analysis. Psychological Trauma Theory Research Practice and Policy. 2013;5:176-83. doi: 10.1037/a0026291.

147. Suomi A, Evans L, Rodgers B, Taplin S, Cowlishaw S. Couple and family therapies for post-traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2019;12(12):Cd011257. Epub 20191204. doi: 10.1002/14651858.CD011257.pub2. PubMed PMID: 31797352; PubMed Central PMCID: PMCPMC6890534.

148. Morland LA, Knopp KC, Khalifian CE, Macdonald A, Grubbs KM, Mackintosh MA, et al. A randomized trial of brief couple therapy for PTSD and relationship satisfaction. J Consult Clin Psychol. 2022;90(5):392-404. doi: 10.1037/ccp0000731. PubMed PMID: 35604746.

149. Monson CM, Fredman SJ, Macdonald A, Pukay-Martin ND, Resick PA, Schnurr PP. Effect of cognitive-behavioral couple therapy for PTSD: a randomized controlled trial. Jama. 2012;308(7):700-9. doi: 10.1001/jama.2012.9307. PubMed PMID: 22893167; PubMed Central PMCID: PMCPMC4404628.

150. Sautter FJ, Glynn SM, Cretu JB, Senturk D, Vaught AS. Efficacy of structured approach therapy in reducing PTSD in returning veterans: A randomized clinical trial. Psychol Serv. 2015;12(3):199-212. doi: 10.1037/ser0000032. PubMed PMID: 26213789.

151. Glynn SM, Eth S, Randolph ET, Foy DW, Urbaitis M, Boxer L, et al. A test of behavioral family therapy to augment exposure for combat-related posttraumatic stress disorder. J Consult Clin Psychol. 1999;67(2):243-51. doi: 10.1037//0022-006x.67.2.243. PubMed PMID: 10224735.

152. Pukay-Martin ND, Fredman SJ, Martin CE, Le Y, Haney A, Sullivan C, et al. Effectiveness of cognitive behavioral conjoint therapy for posttraumatic stress disorder (PTSD) in a U.S. Veterans Affairs PTSD clinic. Journal of Traumatic Stress. 2022;35(2):644-58. doi: https://doi.org/10.1002/jts.22781.

153. Williams T, Phillips NJ, Stein DJ, Ipser JC. Pharmacotherapy for post traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2022;3(3):Cd002795. Epub 20220302. doi: 10.1002/14651858.CD002795.pub3. PubMed PMID: 35234292; PubMed Central PMCID: PMCPMC8889888.

154. Hoskins M, Pearce J, Bethell A, Dankova L, Barbui C, Tol WA, et al. Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. Br J Psychiatry. 2015;206(2):93-100. doi: 10.1192/bjp.bp.114.148551. PubMed PMID: 25644881.

155. Yan JZ, Liu JL, Li XZ, Zhang ZX, Liu RB, Zhang C, et al. Effectiveness, Acceptability and Safety of Pharmaceutical Management for Combat-Related PTSD in Adults Based on Systematic Review of Twenty-Two Randomized Controlled Trials. Front Pharmacol. 2021;12:805354. Epub 2022/02/05. doi: 10.3389/fphar.2021.805354. PubMed PMID: 35115944; PubMed Central PMCID: PMCPMC8804358.

156. Dunlop BW, Rakofsky JJ, Newport DJ, Mletzko-Crowe T, Barone K, Nemeroff CB, et al. Efficacy of Vortioxetine Monotherapy for Posttraumatic Stress Disorder: A Randomized, Placebo-Controlled Trial. J Clin Psychopharmacol. 2021;41(2):172-9. Epub 2021/02/16. doi: 10.1097/jcp.0000000000001363. PubMed PMID: 33587394.

157. Hoskins MD, Bridges J, Sinnerton R, Nakamura A, Underwood JFG, Slater A, et al. Pharmacological therapy for post-traumatic stress disorder: a systematic review and meta-analysis of monotherapy, augmentation and head-to-head approaches. European Journal of Psychotraumatology. 2021b;12(1):1802920. doi: 10.1080/20008198.2020.1802920.

158. Abdallah CG, Roache JD, Gueorguieva R, Averill LA, Young-McCaughan S, Shiroma PR, et al. Dose-related effects of ketamine for antidepressant-resistant symptoms of posttraumatic stress disorder in veterans and active duty military: a double-blind, randomized, placebo-controlled multi-center clinical trial. Neuropsychopharmacology. 2022;47(8):1574-81. Epub 2022/01/21. doi: 10.1038/s41386-022-01266-9. PubMed PMID: 35046508; PubMed Central PMCID: PMCPMC8767037

159. Feder A, Parides MK, Murrough JW, Perez AM, Morgan JE, Saxena S, et al. Efficacy of intravenous ketamine for treatment of chronic posttraumatic stress disorder: a randomized clinical trial. JAMA psychiatry. 2014;71(6):681-8. doi: 10.1001/jamapsychiatry.2014.62. PubMed PMID: 24740528.

160. Guina J, Rossetter SR, De RB, Nahhas RW, Welton RS. Benzodiazepines for PTSD: A Systematic Review and Meta-Analysis. J Psychiatr Pract. 2015;21(4):281-303. Epub 2015/07/15. doi: 10.1097/pra.0000000000000091. PubMed PMID: 26164054.

161. Steenkamp MM, Blessing EM, Galatzer-Levy IR, Hollahan LC, Anderson WT. Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder: A literature review. Depress Anxiety. 2017;34(3):207-16. Epub 2017/03/01. doi: 10.1002/da.22596. PubMed PMID: 28245077.

162. Kansagara D, O'Neil M, Nugent S, Freeman M, Low A, Kondo K, et al. VA Evidence-based Synthesis Program Reports. Benefits and Harms of Cannabis in Chronic Pain or Post-traumatic Stress Disorder: A Systematic Review. Washington (DC): Department of Veterans Affairs (US); 2017.

163. Wilkinson ST, Radhakrishnan R, D'Souza DC. A Systematic Review of the Evidence for Medical Marijuana in Psychiatric Indications. J Clin Psychiatry. 2016;77(8):1050-64. Epub 2016/08/26. doi: 10.4088/JCP.15r10036. PubMed PMID: 27561138.

164. Belendiuk KA, Baldini LL, Bonn-Miller MO. Narrative review of the safety and efficacy of marijuana for the treatment of commonly state-approved medical and psychiatric

disorders. Addict Sci Clin Pract. 2015;10:10. Epub 2015/04/22. doi: 10.1186/s13722-015-0032-7. PubMed PMID: 25896576; PubMed Central PMCID: PMCPMC4636852.

165. Bonn-Miller MO, Sisley S, Riggs P, Yazar-Klosinski B, Wang JB, Loflin MJE, et al. The short-term impact of 3 smoked cannabis preparations versus placebo on PTSD symptoms: A randomized cross-over clinical trial. PLoS One. 2021;16(3):e0246990. Epub 2021/03/18. doi: 10.1371/journal.pone.0246990. PubMed PMID: 33730032; PubMed Central PMCID: PMCPMC7968689

166. Hoskins MD, Sinnerton R, Nakamura A, Underwood JFG, Slater A, Lewis C, et al. Pharmacological-assisted Psychotherapy for Post-Traumatic Stress Disorder: a systematic review and meta-analysis. Eur J Psychotraumatol. 2021a;12(1):1853379. Epub 2021/03/09. doi: 10.1080/20008198.2020.1853379. PubMed PMID: 33680344; PubMed Central PMCID: PMCPMC7874936.

167. Schneier FR, Neria Y, Pavlicova M, Hembree E, Suh EJ, Amsel L, et al. Combined prolonged exposure therapy and paroxetine for PTSD related to the World Trade Center attack: a randomized controlled trial. Am J Psychiatry. 2012;169(1):80-8. Epub 2011/09/13. doi: 10.1176/appi.ajp.2011.11020321. PubMed PMID: 21908494; PubMed Central PMCID: PMCPMC3606709.

168. Popiel A, Zawadzki B, Pragłowska E, Teichman Y. Prolonged exposure, paroxetine and the combination in the treatment of PTSD following a motor vehicle accident. A randomized clinical trial - The "TRAKT" study. J Behav Ther Exp Psychiatry. 2015;48:17-26. Epub 20150128. doi: 10.1016/j.jbtep.2015.01.002. PubMed PMID: 25677254.

169. Simon NM, Connor KM, Lang AJ, Rauch S, Krulewicz S, LeBeau RT, et al. Paroxetine CR augmentation for posttraumatic stress disorder refractory to prolonged exposure therapy. J Clin Psychiatry. 2008;69(3):400-5. Epub 2008/03/20. doi: 10.4088/jcp.v69n0309. PubMed PMID: 18348595.

170. Rothbaum BO, Killeen TK, Davidson JR, Brady KT, Connor KM, Heekin MH. Placebo-controlled trial of risperidone augmentation for selective serotonin reuptake inhibitor-resistant civilian posttraumatic stress disorder. J Clin Psychiatry. 2008;69(4):520-5. Epub 2008/02/19. doi: 10.4088/jcp.v69n0402. PubMed PMID: 18278987.

171. Brunet A, Saumier D, Liu A, Streiner DL, Tremblay J, Pitman RK. Reduction of PTSD Symptoms With Pre-Reactivation Propranolol Therapy: A Randomized Controlled Trial. Am J Psychiatry. 2018;175(5):427-33. Epub 2018/01/13. doi: 10.1176/appi.ajp.2017.17050481. PubMed PMID: 29325446.

172. Rothbaum BO, Cahill SP, Foa EB, Davidson JR, Compton J, Connor KM, et al. Augmentation of sertraline with prolonged exposure in the treatment of posttraumatic stress disorder. J Trauma Stress. 2006;19(5):625-38. Epub 2006/11/01. doi: 10.1002/jts.20170. PubMed PMID: 17075912.

173. Krystal JH, Pietrzak RH, Rosenheck RA, Cramer JA, Vessicchio J, Jones KM, et al. Sleep disturbance in chronic military-related PTSD: clinical impact and response to adjunctive risperidone in the Veterans Affairs cooperative study #504. J Clin Psychiatry. 2016;77(4):483-91. Epub 2016/02/19. doi: 10.4088/JCP.14m09585. PubMed PMID: 26890894.

174. Bartzokis G, Lu PH, Turner J, Mintz J, Saunders CS. Adjunctive risperidone in the treatment of chronic combat-related posttraumatic stress disorder. Biol Psychiatry. 2005;57(5):474-9. Epub 2005/03/02. doi: 10.1016/j.biopsych.2004.11.039. PubMed PMID: 15737661.

175. Naylor JC, Kilts JD, Bradford DW, Strauss JL, Capehart BP, Szabo ST, et al. A pilot randomized placebo-controlled trial of adjunctive aripiprazole for chronic PTSD in US military Veterans resistant to antidepressant treatment. Int Clin Psychopharmacol. 2015;30(3):167-74. Epub 2015/02/04. doi: 10.1097/yic.0000000000000061. PubMed PMID: 25647451.

176. Stein MB, Kline NA, Matloff JL. Adjunctive olanzapine for SSRI-resistant combat-related PTSD: a double-blind, placebo-controlled study. Am J Psychiatry. 2002;159(10):1777-9. Epub 2002/10/03. doi: 10.1176/appi.ajp.159.10.1777. PubMed PMID: 12359687.

177. Pillinger T, McCutcheon RA, Vano L, Mizuno Y, Arumuham A, Hindley G, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. The Lancet Psychiatry. 2020;7(1):64-77. doi: 10.1016/S2215-0366(19)30416-X.

178. McNamee S, Devenot N, Buisson M. Studying Harms Is Key to Improving Psychedelic-Assisted Therapy-Participants Call for Changes to Research Landscape. JAMA psychiatry. 2023;80(5):411-2. Epub 2023/03/30. doi: 10.1001/jamapsychiatry.2023.0099. PubMed PMID: 36988924.

179. Kan RLD, Zhang BBB, Zhang JJQ, Kranz GS. Non-invasive brain stimulation for posttraumatic stress disorder: a systematic review and meta-analysis. Transl Psychiatry. 2020;10(1):168. Epub 20200528. doi: 10.1038/s41398-020-0851-5. PubMed PMID: 32467579; PubMed Central PMCID: PMCPMC7256039.

180. Belsher BE, Beech EH, Reddy MK, Smolenski DJ, Rauch SAM, Kelber M, et al. Advances in repetitive transcranial magnetic stimulation for posttraumatic stress disorder: A systematic review. J Psychiatr Res. 2021;138:598-606. Epub 20210508. doi: 10.1016/j.jpsychires.2021.05.011. PubMed PMID: 33992983.

181. Nicholson AA, Ros T, Densmore M, Frewen PA, Neufeld RWJ, Théberge J, et al. A randomized, controlled trial of alpha-rhythm EEG neurofeedback in posttraumatic stress disorder: A preliminary investigation showing evidence of decreased PTSD symptoms and restored default mode and salience network connectivity using fMRI. Neuroimage Clin. 2020;28:102490. Epub 20201105. doi: 10.1016/j.nicl.2020.102490. PubMed PMID: 33395981; PubMed Central PMCID: PMCPMC7708928.

182. Steingrimsson S, Bilonic G, Ekelund AC, Larson T, Stadig I, Svensson M, et al. Electroencephalography-based neurofeedback as treatment for post-traumatic stress disorder: A systematic review and meta-analysis. Eur Psychiatry. 2020;63(1):e7. Epub 20200131. doi: 10.1192/j.eurpsy.2019.7. PubMed PMID: 32093790; PubMed Central PMCID: PMCPMC8057448.

183. Fruchtman-Steinbok T, Keynan JN, Cohen A, Jaljuli I, Mermelstein S, Drori G, et al. Amygdala electrical-finger-print (AmygEFP) NeuroFeedback guided by individually-tailored Trauma script for post-traumatic stress disorder: Proof-of-concept. Neuroimage

Clin. 2021;32:102859. Epub 20211015. doi: 10.1016/j.nicl.2021.102859. PubMed PMID: 34689055; PubMed Central PMCID: PMCPMC8551212.

184. Hanling SR, Hickey A, Lesnik I, Hackworth RJ, Stedje-Larsen E, Drastal CA, et al. Stellate Ganglion Block for the Treatment of Posttraumatic Stress Disorder: A Randomized, Double-Blind, Controlled Trial. Reg Anesth Pain Med. 2016;41(4):494-500. Epub 2016/05/18. doi: 10.1097/aap.0000000000000402. PubMed PMID: 27187898.
185. Rae Olmsted KL, Bartoszek M, Mulvaney S, McLean B, Turabi A, Young R, et al. Effect of Stellate Ganglion Block Treatment on Posttraumatic Stress Disorder Symptoms: A Randomized Clinical Trial. JAMA psychiatry. 2020;77(2):130-8. Epub 2019/11/07. doi: 10.1001/jamapsychiatry.2019.3474. PubMed PMID: 31693083; PubMed Central PMCID: PMCPMC6865253
186. Doenyas-Barak K, Catalogna M, Kutz I, Levi G, Hadanny A, Tal S, et al. Hyperbaric oxygen therapy improves symptoms, brain's microstructure and functionality in veterans with treatment resistant post-traumatic stress disorder: A prospective, randomized, controlled trial. PLoS One. 2022;17(2):e0264161. Epub 2022/02/23. doi: 10.1371/journal.pone.0264161. PubMed PMID: 35192645; PubMed Central PMCID: PMCPMC8863239.
187. Jamison AL, Slightam C, Bertram F, Kim S, Roth WT. Randomized clinical trial of capnometry-assisted respiratory training in veterans with posttraumatic stress disorder hyperarousal. Psychol Trauma. 2022;14(5):883-93. Epub 2019/12/06. doi: 10.1037/tra0000525. PubMed PMID: 31804108; PubMed Central PMCID: PMCPMC7272253.
188. Smits FM, Geuze E, Schutter D, van Honk J, Gladwin TE. Effects of tDCS during inhibitory control training on performance and PTSD, aggression and anxiety symptoms: a randomized-controlled trial in a military sample. Psychol Med. 2021:1-11. Epub 2021/03/25. doi: 10.1017/s0033291721000817. PubMed PMID: 33757606.
189. Ahmadizadeh MJ, Rezaei M, Fitzgerald PB. Transcranial direct current stimulation (tDCS) for post-traumatic stress disorder (PTSD): A randomized, double-blinded, controlled trial. Brain Res Bull. 2019;153:273-8. Epub 2019/09/29. doi: 10.1016/j.brainresbull.2019.09.011. PubMed PMID: 31560945.
190. Berlim MT, Van Den Eynde F. Repetitive transcranial magnetic stimulation over the dorsolateral prefrontal cortex for treating posttraumatic stress disorder: an exploratory meta-analysis of randomized, double-blind and sham-controlled trials. Can J Psychiatry. 2014;59(9):487-96. Epub 2015/01/08. doi: 10.1177/070674371405900905. PubMed PMID: 25565694; PubMed Central PMCID: PMCPMC4168811.
191. Boggio PS, Rocha M, Oliveira MO, Fecteau S, Cohen RB, Campanhã C, et al. Noninvasive brain stimulation with high-frequency and low-intensity repetitive transcranial magnetic stimulation treatment for posttraumatic stress disorder. J Clin Psychiatry. 2010;71(8):992-9. Epub 2010/01/07. doi: 10.4088/JCP.08m04638blu. PubMed PMID: 20051219; PubMed Central PMCID: PMCPMC3260527.
192. Cohen H, Kaplan Z, Kotler M, Kouperman I, Moisa R, Grisaru N. Repetitive transcranial magnetic stimulation of the right dorsolateral prefrontal cortex in posttraumatic stress disorder: a double-blind, placebo-controlled study. Am J Psychiatry. 2004;161(3):515-24. Epub 2004/03/03. doi: 10.1176/appi.ajp.161.3.515. PubMed PMID: 14992978.

193. Liu C, Beauchemin J, Wang X, Lee MY. Integrative Body-Mind-Spirit (I-BMS) Interventions for Posttraumatic Stress Disorder (PTSD): A Review of the Outcome Literature. Journal of Social Service Research. 2018;44(4):482-93. doi: 10.1080/01488376.2018.1476299.

194. Polusny MA, Erbes CR, Thuras P, Moran A, Lamberty GJ, Collins RC, et al. Mindfulness-Based Stress Reduction for Posttraumatic Stress Disorder Among Veterans: A Randomized Clinical Trial. Jama. 2015;314(5):456-65. doi: 10.1001/jama.2015.8361. PubMed PMID: 26241597.

195. Bremner JD, Mishra S, Campanella C, Shah M, Kasher N, Evans S, et al. A Pilot Study of the Effects of Mindfulness-Based Stress Reduction on Post-traumatic Stress Disorder Symptoms and Brain Response to Traumatic Reminders of Combat in Operation Enduring Freedom/Operation Iraqi Freedom Combat Veterans with Post-traumatic Stress Disorder. Front Psychiatry. 2017;8:157. Epub 2017/09/12. doi: 10.3389/fpsyt.2017.00157. PubMed PMID: 28890702; PubMed Central PMCID: PMCPMC5574875.

196. Kearney DJ, Simpson TL, Malte CA, Felleman B, Martinez ME, Hunt SC. Mindfulness-based Stress Reduction in Addition to Usual Care Is Associated with Improvements in Pain, Fatigue, and Cognitive Failures Among Veterans with Gulf War Illness. Am J Med. 2016;129(2):204-14. Epub 2015/11/01. doi: 10.1016/j.amjmed.2015.09.015. PubMed PMID: 26519614.

197. Liu Q, Zhu J, Zhang W. The efficacy of mindfulness-based stress reduction intervention 3 for post-traumatic stress disorder (PTSD) symptoms in patients with PTSD: A meta-analysis of four randomized controlled trials. Stress Health. 2022;38(4):626-36. Epub 2022/03/08. doi: 10.1002/smi.3138. PubMed PMID: 35253353.

198. Davis LL, Whetsell C, Hamner MB, Carmody J, Rothbaum BO, Allen RS, et al. A Multisite Randomized Controlled Trial of Mindfulness-Based Stress Reduction in the Treatment of Posttraumatic Stress Disorder. Psychiatr Res Clin Pract. 2019;1(2):39-48. Epub 20180913. doi: 10.1176/appi.prcp.20180002. PubMed PMID: 34113802; PubMed Central PMCID: PMCPMC8189576.

199. Possemato K, Bergen-Cico D, Treatman S, Allen C, Wade M, Pigeon W. A Randomized Clinical Trial of Primary Care Brief Mindfulness Training for Veterans with PTSD. J Clin Psychol. 2016;72(3):179-93. Epub 20151127. doi: 10.1002/jclp.22241. PubMed PMID: 26613203.

200. Wahbeh H, Goodrich E, Goy E, Oken BS. Mechanistic Pathways of Mindfulness Meditation in Combat Veterans With Posttraumatic Stress Disorder. J Clin Psychol. 2016;72(4):365-83. Epub 20160121. doi: 10.1002/jclp.22255. PubMed PMID: 26797725; PubMed Central PMCID: PMCPMC4803530.

201. Hoge EA, Bui E, Mete M, Dutton MA, Baker AW, Simon NM. Mindfulness-Based Stress Reduction vs Escitalopram for the Treatment of Adults With Anxiety Disorders: A Randomized Clinical Trial. JAMA psychiatry. 2023;80(1):13-21. Epub 2022/11/10. doi: 10.1001/jamapsychiatry.2022.3679. PubMed PMID: 36350591; PubMed Central PMCID: PMCPMC9647561.

202. de Vibe M, Bjorndal A, Fattah S, Dyrdal GM, Halland E, Tanner-Smith EE. Mindfulness-based stress reduction (MBSR) for improving health, quality of life and social functioning

in adults: a systematic review and meta-analysis. Campbell Systematic Reviews. 2017;13(1).

203. Grant S, Colaiaco B, Motala A, Shanman R, Sorbero M, Hempel S. Acupuncture for the Treatment of Adults with Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis. J Trauma Dissociation. 2018;19(1):39-58. Epub 20170309. doi: 10.1080/15299732.2017.1289493. PubMed PMID: 28151093.
204. Nidich S, Mills PJ, Rainforth M, Heppner P, Schneider RH, Rosenthal NE, et al. Non-trauma-focused meditation versus exposure therapy in veterans with post-traumatic stress disorder: a randomised controlled trial. Lancet Psychiatry. 2018;5(12):975-86. Epub 20181115. doi: 10.1016/s2215-0366(18)30384-5. PubMed PMID: 30449712.
205. Heffner KL, Crean HF, Kemp JE. Meditation programs for veterans with posttraumatic stress disorder: Aggregate findings from a multi-site evaluation. Psychol Trauma. 2016;8(3):365-74. Epub 20160111. doi: 10.1037/tra0000106. PubMed PMID: 26752098.
206. Bellehsen M, Stoycheva V, Cohen BH, Nidich S. A Pilot Randomized Controlled Trial of Transcendental Meditation as Treatment for Posttraumatic Stress Disorder in Veterans. J Trauma Stress. 2022;35(1):22-31. Epub 20210318. doi: 10.1002/jts.22665. PubMed PMID: 33734493.
207. Bormann JE, Thorp SR, Smith E, Glickman M, Beck D, Plumb D, et al. Individual Treatment of Posttraumatic Stress Disorder Using Mantram Repetition: A Randomized Clinical Trial. Am J Psychiatry. 2018;175(10):979-88. Epub 2018/06/21. doi: 10.1176/appi.ajp.2018.17060611. PubMed PMID: 29921143.
208. Álvarez-Pérez Y, Rivero-Santana A, Perestelo-Pérez L, Duarte-Díaz A, Ramos-García V, Toledo-Chávarri A, et al. Effectiveness of Mantra-Based Meditation on Mental Health: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2022;19(6). Epub 20220313. doi: 10.3390/ijerph19063380. PubMed PMID: 35329068; PubMed Central PMCID: PMCPMC8949812.
209. Kearney DJ, Malte CA, Storms M, Simpson TL. Loving-Kindness Meditation vs Cognitive Processing Therapy for Posttraumatic Stress Disorder Among Veterans: A Randomized Clinical Trial. JAMA Netw Open. 2021;4(4):e216604. Epub 20210401. doi: 10.1001/jamanetworkopen.2021.6604. PubMed PMID: 33861329; PubMed Central PMCID: PMCPMC8052593.
210. Davis LW, Schmid AA, Daggy JK, Yang Z, O'Connor CE, Schalk N, et al. Symptoms improve after a yoga program designed for PTSD in a randomized controlled trial with veterans and civilians. Psychol Trauma. 2020;12(8):904-12. Epub 20200420. doi: 10.1037/tra0000564. PubMed PMID: 32309986.
211. Cramer H, Anheyer D, Saha FJ, Dobos G. Yoga for posttraumatic stress disorder - a systematic review and meta-analysis. BMC Psychiatry. 2018;18(1):72. Epub 20180322. doi: 10.1186/s12888-018-1650-x. PubMed PMID: 29566652; PubMed Central PMCID: PMCPMC5863799.
212. Zhu L, Li L, Li XZ, Wang L. Mind-Body Exercises for PTSD Symptoms, Depression, and Anxiety in Patients With PTSD: A Systematic Review and Meta-Analysis. Front Psychol. 2021;12:738211. Epub 20220118. doi: 10.3389/fpsyg.2021.738211. PubMed PMID: 35153889; PubMed Central PMCID: PMCPMC8833099.

213. Lang AJ, Malaktaris AL, Casmar P, Baca SA, Golshan S, Harrison T, et al. Compassion Meditation for Posttraumatic Stress Disorder in Veterans: A Randomized Proof of Concept Study. J Trauma Stress. 2019;32(2):299-309. Epub 20190331. doi: 10.1002/jts.22397. PubMed PMID: 30929283.

214. Goldstein LA, Mehling WE, Metzler TJ, Cohen BE, Barnes DE, Choucroun GJ, et al. Veterans Group Exercise: A randomized pilot trial of an Integrative Exercise program for veterans with posttraumatic stress. J Affect Disord. 2018;227:345-52. Epub 2017/11/18. doi: 10.1016/j.jad.2017.11.002. PubMed PMID: 29145076.

215. Thorp SR, Glassman LH, Wells SY, Walter KH, Gebhardt H, Twamley E, et al. A randomized controlled trial of prolonged exposure therapy versus relaxation training for older veterans with military-related PTSD. J Anxiety Disord. 2019;64:45-54. Epub 20190221. doi: 10.1016/j.janxdis.2019.02.003. PubMed PMID: 30978622.

216. Brom D, Stokar Y, Lawi C, Nuriel-Porat V, Ziv Y, Lerner K, et al. Somatic Experiencing for Posttraumatic Stress Disorder: A Randomized Controlled Outcome Study. J Trauma Stress. 2017;30(3):304-12. Epub 20170606. doi: 10.1002/jts.22189. PubMed PMID: 28585761; PubMed Central PMCID: PMCPMC5518443.

217. Wu C-J, Lee S-Y, editors. After the interventionafter the intervention an evaluation and analysis of visual art therapy in the treatment of PTSD2020.

218. Engel CC, Cordova EH, Benedek DM, Liu X, Gore KL, Goertz C, et al. Randomized effectiveness trial of a brief course of acupuncture for posttraumatic stress disorder. Med Care. 2014;52(12 Suppl 5):S57-64. doi: 10.1097/mlr.0000000000000237. PubMed PMID: 25397825.

219. Affairs DoV. A Randomized Trial of Differential Effectiveness of Service Dog Pairing Versus Emotional Support Dog Pairing to Improve Quality of Life for Veterans with PTSD. 2020.

220. Maieritsch KP, Smith TL, Hessinger JD, Ahearn EP, Eickhoff JC, Zhao Q. Randomized controlled equivalence trial comparing videoconference and in person delivery of cognitive processing therapy for PTSD. J Telemed Telecare. 2016;22(4):238-43. Epub 20150730. doi: 10.1177/1357633x15596109. PubMed PMID: 26231819.

221. Yuen EK, Gros DF, Price M, Zeigler S, Tuerk PW, Foa EB, et al. Randomized Controlled Trial of Home-Based Telehealth Versus In-Person Prolonged Exposure for Combat-Related PTSD in Veterans: Preliminary Results. J Clin Psychol. 2015;71(6):500-12. Epub 20150325. doi: 10.1002/jclp.22168. PubMed PMID: 25809565.

222. Morland LA, Mackintosh MA, Rosen CS, Willis E, Resick P, Chard K, et al. Telemedicine versus In-Person Delivery of Cognitive Processing Therapy for Women with Posttraumatic Stress Disorder: A Randomized Noninferiority Trial. . Depress Anxiety. 2015;32(11):811-20. Epub 20150803. doi: 10.1002/da.22397. PubMed PMID: 26243685.

223. McClellan MJ, Osbaldiston R, Wu R, Yeager R, Monroe AD, McQueen T, et al. The effectiveness of telepsychology with veterans: A meta-analysis of services delivered by videoconference and phone. Psychol Serv. 2022;19(2):294-304. Epub 20210204. doi: 10.1037/ser0000522. PubMed PMID: 33539135.

224. Morland LA, Mackintosh MA, Glassman LH, Wells SY, Thorp SR, Rauch SAM, et al. Home-based delivery of variable length prolonged exposure therapy: A comparison of

clinical efficacy between service modalities. Depress Anxiety. 2020;37(4):346-55. Epub 20191224. doi: 10.1002/da.22979. PubMed PMID: 31872563.

225. Liu L, Thorp SR, Moreno L, Wells SY, Glassman LH, Busch AC, et al. Videoconferencing psychotherapy for veterans with PTSD: Results from a randomized controlled non-inferiority trial. J Telemed Telecare. 2020;26(9):507-19. Epub 2019/06/20. doi: 10.1177/1357633x19853947. PubMed PMID: 31216210.
226. Goreis A, Felnhofer A, Kafka JX, Probst T, Kothgassner OD. Efficacy of Self-Management Smartphone-Based Apps for Post-traumatic Stress Disorder Symptoms: A Systematic Review and Meta-Analysis. Front Neurosci. 2020;14:3. Epub 20200124. doi: 10.3389/fnins.2020.00003. PubMed PMID: 32038153; PubMed Central PMCID: PMCPMC6992648.
227. Kuhn E, Kanuri N, Hoffman JE, Garvert DW, Ruzek JI, Taylor CB. A randomized controlled trial of a smartphone app for posttraumatic stress disorder symptoms. J Consult Clin Psychol. 2017;85(3):267-73. Epub 2017/02/22. doi: 10.1037/ccp0000163. PubMed PMID: 28221061.
228. Miner A, Kuhn E, Hoffman JE, Owen JE, Ruzek JI, Taylor CB. Feasibility, acceptability, and potential efficacy of the PTSD Coach app: A pilot randomized controlled trial with community trauma survivors. Psychol Trauma. 2016;8(3):384-92. Epub 2016/04/06. doi: 10.1037/tra0000092. PubMed PMID: 27046668.
229. Simon N, Robertson L, Lewis C, Roberts NP, Bethell A, Dawson S, et al. Internet-based cognitive and behavioural therapies for post-traumatic stress disorder (PTSD) in adults. Cochrane Database Syst Rev. 2021;5(5):Cd011710. Epub 20210520. doi: 10.1002/14651858.CD011710.pub3. PubMed PMID: 34015141; PubMed Central PMCID: PMCPMC8136365.
230. Lewis C, Roberts NP, Andrew M, Starling E, Bisson JI. Psychological therapies for post-traumatic stress disorder in adults: systematic review and meta-analysis. Eur J Psychotraumatol. 2020;11(1):1729633. Epub 2020/04/15. doi: 10.1080/20008198.2020.1729633. PubMed PMID: 32284821; PubMed Central PMCID: PMCPMC7144187.
231. Littleton H, Grills AE, Kline KD, Schoemann AM, Dodd JC. The From Survivor to Thriver program: RCT of an online therapist-facilitated program for rape-related PTSD. J Anxiety Disord. 2016;43:41-51. Epub 2016/08/12. doi: 10.1016/j.janxdis.2016.07.010. PubMed PMID: 27513363; PubMed Central PMCID: PMCPMC5056149.
232. McLean CP, Foa EB, Dondanville KA, Haddock CK, Miller ML, Rauch SAM, et al. The effects of web-prolonged exposure among military personnel and veterans with posttraumatic stress disorder. Psychol Trauma. 2021;13(6):621-31. Epub 2020/11/20. doi: 10.1037/tra0000978. PubMed PMID: 33211517.
233. Spence J, Titov N, Johnston L, Jones MP, Dear BF, Solley K. Internet-based trauma-focused cognitive behavioural therapy for PTSD with and without exposure components: a randomised controlled trial. J Affect Disord. 2014;162:73-80. Epub 20140325. doi: 10.1016/j.jad.2014.03.009. PubMed PMID: 24767009.
234. Spence J, Titov N, Dear BF, Johnston L, Solley K, Lorian C, et al. Randomized controlled trial of Internet-delivered cognitive behavioral therapy for posttraumatic stress disorder. Depress Anxiety. 2011;28(7):541-50. doi: 10.1002/da.20835. PubMed PMID: 21721073.

235. Ivarsson D, Blom M, Hesser H, Carlbring P, Enderby P, Nordberg R, et al. Guided internet-delivered cognitive behavior therapy for post-traumatic stress disorder: A randomized controlled trial. Internet Interventions. 2014;1(1):33-40. doi: https://doi.org/10.1016/j.invent.2014.03.002.

236. Hobfoll SE, Blais RK, Stevens NR, Walt L, Gengler R. Vets prevail online intervention reduces PTSD and depression in veterans with mild-to-moderate symptoms. J Consult Clin Psychol. 2016;84(1):31-42. Epub 20150831. doi: 10.1037/ccp0000041. PubMed PMID: 26322788.

237. Knaevelsrud C, Brand J, Lange A, Ruwaard J, Wagner B. Web-based psychotherapy for posttraumatic stress disorder in war-traumatized Arab patients: randomized controlled trial. J Med Internet Res. 2015;17(3):e71. Epub 20150320. doi: 10.2196/jmir.3582. PubMed PMID: 25799024; PubMed Central PMCID: PMCPMC4385175.

238. Possemato K, Kuhn E, Johnson E, Hoffman JE, Owen JE, Kanuri N, et al. Using PTSD Coach in primary care with and without clinician support: a pilot randomized controlled trial. Gen Hosp Psychiatry. 2016;38:94-8. Epub 20150925. doi: 10.1016/j.genhosppsych.2015.09.005. PubMed PMID: 26589765.

239. Engel CC, Litz B, Magruder KM, Harper E, Gore K, Stein N, et al. Delivery of self training and education for stressful situations (DESTRESS-PC): a randomized trial of nurse assisted online self-management for PTSD in primary care. Gen Hosp Psychiatry. 2015;37(4):323-8. Epub 20150413. doi: 10.1016/j.genhosppsych.2015.04.007. PubMed PMID: 25929985; PubMed Central PMCID: PMCPMC4762212.

240. Reist C, Streja E, Tang CC, Shapiro B, Mintz J, Hollifield M. Prazosin for treatment of post-traumatic stress disorder: a systematic review and meta-analysis. CNS Spectr. 2021;26(4):338-44. Epub 2020/05/05. doi: 10.1017/s1092852920001121. PubMed PMID: 32362287.

241. Zhang Y, Ren R, Sanford LD, Yang L, Ni Y, Zhou J, et al. The effects of prazosin on sleep disturbances in post-traumatic stress disorder: a systematic review and meta-analysis. Sleep Med. 2020;67:225-31. Epub 2020/01/24. doi: 10.1016/j.sleep.2019.06.010. PubMed PMID: 31972510; PubMed Central PMCID: PMCPMC6986268.

242. McCall WV, Pillai A, Case D, McCloud L, Nolla T, Branch F, et al. A Pilot, Randomized Clinical Trial of Bedtime Doses of Prazosin Versus Placebo in Suicidal Posttraumatic Stress Disorder Patients With Nightmares. J Clin Psychopharmacol. 2018;38(6):618-21. Epub 2018/10/20. doi: 10.1097/jcp.0000000000000968. PubMed PMID: 30335633.

243. Raskind MA, Peskind ER, Chow B, Harris C, Davis-Karim A, Holmes HA, et al. Trial of Prazosin for Post-Traumatic Stress Disorder in Military Veterans. N Engl J Med. 2018;378(6):507-17. Epub 2018/02/08. doi: 10.1056/NEJMoa1507598. PubMed PMID: 29414272.

244. Raskind MA, Peskind ER, Kanter ED, Petrie EC, Radant A, Thompson CE, et al. Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. Am J Psychiatry. 2003;160(2):371-3. Epub 2003/02/04. doi: 10.1176/appi.ajp.160.2.371. PubMed PMID: 12562588.

245. Raskind MA, Peskind ER, Hoff DJ, Hart KL, Holmes HA, Warren D, et al. A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in

combat veterans with post-traumatic stress disorder. Biol Psychiatry. 2007;61(8):928-34. Epub 2006/10/31. doi: 10.1016/j.biopsych.2006.06.032. PubMed PMID: 17069768.

246. Raskind MA, Peterson K, Williams T, Hoff DJ, Hart K, Holmes H, et al. A trial of prazosin for combat trauma PTSD with nightmares in active-duty soldiers returned from Iraq and Afghanistan. Am J Psychiatry. 2013;170(9):1003-10. Epub 2013/07/13. doi: 10.1176/appi.ajp.2013.12081133. PubMed PMID: 23846759.

247. Germain A, Richardson R, Moul DE, Mammen O, Haas G, Forman SD, et al. Placebo-controlled comparison of prazosin and cognitive-behavioral treatments for sleep disturbances in US Military Veterans. J Psychosom Res. 2012;72(2):89-96. Epub 2012/01/28. doi: 10.1016/j.jpsychores.2011.11.010. PubMed PMID: 22281448; PubMed Central PMCID: PMCPMC3267960.

248. Khachatryan D, Groll D, Booij L, Sepehry AA, Schütz CG. Prazosin for treating sleep disturbances in adults with posttraumatic stress disorder: a systematic review and meta-analysis of randomized controlled trials. Gen Hosp Psychiatry. 2016;39:46-52. Epub 2015/12/09. doi: 10.1016/j.genhosppsych.2015.10.007. PubMed PMID: 26644317.

249. Yücel DE, van Emmerik AAP, Souama C, Lancee J. Comparative efficacy of imagery rehearsal therapy and prazosin in the treatment of trauma-related nightmares in adults: A meta-analysis of randomized controlled trials. Sleep Med Rev. 2020;50:101248. Epub 20191128. doi: 10.1016/j.smrv.2019.101248. PubMed PMID: 31855732.

250. Krakow B, Hollifield M, Johnston L, Koss M, Schrader R, Warner TD, et al. Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: a randomized controlled trial. Jama. 2001;286(5):537-45. doi: 10.1001/jama.286.5.537. PubMed PMID: 11476655.

251. Cook JM, Harb GC, Gehrman PR, Cary MS, Gamble GM, Forbes D, et al. Imagery rehearsal for posttraumatic nightmares: a randomized controlled trial. J Trauma Stress. 2010;23(5):553-63. doi: 10.1002/jts.20569. PubMed PMID: 20839311.

252. Harb GC, Cook JM, Phelps AJ, Gehrman PR, Forbes D, Localio R, et al. Randomized Controlled Trial of Imagery Rehearsal for Posttraumatic Nightmares in Combat Veterans. J Clin Sleep Med. 2019;15(5):757-67. Epub 20190515. doi: 10.5664/jcsm.7770. PubMed PMID: 31053215; PubMed Central PMCID: PMCPMC6510682.

253. Slotema CW, Wilhelmus B, Arends LR, Franken IHA. Psychotherapy for posttraumatic stress disorder in patients with borderline personality disorder: a systematic review and meta-analysis of its efficacy and safety. Eur J Psychotraumatol. 2020;11(1):1796188. Epub 20200916. doi: 10.1080/20008198.2020.1796188. PubMed PMID: 33062206; PubMed Central PMCID: PMCPMC7534189.

254. Sin J, Spain D, Furuta M, Murrells T, Norman I. Psychological interventions for post-traumatic stress disorder (PTSD) in people with severe mental illness. Cochrane Database Syst Rev. 2017;1(1):Cd011464. Epub 20170124. doi: 10.1002/14651858.CD011464.pub2. PubMed PMID: 28116752; PubMed Central PMCID: PMCPMC6464771.

255. Wolf EJ, Lunney CA, Schnurr PP. The influence of the dissociative subtype of posttraumatic stress disorder on treatment efficacy in female veterans and active duty service members. J Consult Clin Psychol. 2016;84(1):95-100. Epub 20150713.

doi: 10.1037/ccp0000036. PubMed PMID: 26167946; PubMed Central PMCID: PMCPMC4830387.

256. Rizvi SL, Vogt DS, Resick PA. Cognitive and affective predictors of treatment outcome in Cognitive Processing Therapy and Prolonged Exposure for posttraumatic stress disorder. Behav Res Ther. 2009;47(9):737-43. Epub 20090617. doi: 10.1016/j.brat.2009.06.003. PubMed PMID: 19595295; PubMed Central PMCID: PMCPMC3467002.
257. Jak AJ, Jurick S, Crocker LD, Sanderson-Cimino M, Aupperle R, Rodgers CS, et al. SMART-CPT for veterans with comorbid post-traumatic stress disorder and history of traumatic brain injury: a randomised controlled trial. J Neurol Neurosurg Psychiatry. 2019;90(3):333-41. Epub 20181215. doi: 10.1136/jnnp-2018-319315. PubMed PMID: 30554135.
258. Simpson TL, Goldberg SB, Louden DKN, Blakey SM, Hawn SE, Lott A, et al. Efficacy and acceptability of interventions for co-occurring PTSD and SUD: A meta-analysis. J Anxiety Disord. 2021;84:102490. Epub 20211026. doi: 10.1016/j.janxdis.2021.102490. PubMed PMID: 34763220; PubMed Central PMCID: PMCPMC8819868.
259. Norman SB, Trim R, Haller M, Davis BC, Myers US, Colvonen PJ, et al. Efficacy of Integrated Exposure Therapy vs Integrated Coping Skills Therapy for Comorbid Posttraumatic Stress Disorder and Alcohol Use Disorder: A Randomized Clinical Trial. JAMA psychiatry. 2019;76(8):791-9. doi: 10.1001/jamapsychiatry.2019.0638. PubMed PMID: 31017639; PubMed Central PMCID: PMCPMC6487906.
260. Back SE, Killeen T, Badour CL, Flanagan JC, Allan NP, Ana ES, et al. Concurrent treatment of substance use disorders and PTSD using prolonged exposure: A randomized clinical trial in military veterans. Addict Behav. 2019;90:369-77. Epub 20181127. doi: 10.1016/j.addbeh.2018.11.032. PubMed PMID: 30529244; PubMed Central PMCID: PMCPMC6488423.
261. Kline AC, Cooper AA, Rytwinski NK, Feeny NC. The Effect of Concurrent Depression on PTSD Outcomes in Trauma-Focused Psychotherapy: A Meta-Analysis of Randomized Controlled Trials. Behav Ther. 2021;52(1):250-66. Epub 20200506. doi: 10.1016/j.beth.2020.04.015. PubMed PMID: 33483121; PubMed Central PMCID: PMCPMC7826446.
262. Norr AM, Smolenski DJ, Reger GM. Effects of prolonged exposure and virtual reality exposure on suicidal ideation in active duty soldiers: An examination of potential mechanisms. J Psychiatr Res. 2018;103:69-74. Epub 20180512. doi: 10.1016/j.jpsychires.2018.05.009. PubMed PMID: 29783077.
263. Peck KR, Schumacher JA, Stasiewicz PR, Coffey SF. Adults with Comorbid Posttraumatic Stress Disorder, Alcohol Use Disorder, and Opioid Use Disorder: The Effectiveness of Modified Prolonged Exposure. J Trauma Stress. 2018;31(3):373-82. Epub 20180522. doi: 10.1002/jts.22291. PubMed PMID: 29786898; PubMed Central PMCID: PMCPMC6097633.
264. Resick PA, LoSavio ST, Wachen JS, Dillon KH, Nason EE, Dondanville KA, et al. Predictors of Treatment Outcome in Group or Individual Cognitive Processing Therapy for Posttraumatic Stress Disorder Among Active Duty Military. Cognit Ther Res. 2020;44(3):611-20. doi: 10.1007/s10608-020-10085-5. PubMed PMID: 35431370; PubMed Central PMCID: PMCPMC9009298.

265. Straud CL, Dondanville KA, Hale WJ, Wachen JS, Mintz J, Litz BT, et al. The Impact of Hazardous Drinking Among Active Duty Military With Posttraumatic Stress Disorder: Does Cognitive Processing Therapy Format Matter? J Trauma Stress. 2021;34(1):210-20. Epub 20201019. doi: 10.1002/jts.22609. PubMed PMID: 33078467.

266. Verplaetse TL, Ralevski E, Roberts W, Gueorguieva R, McKee SA, Petrakis IL. Alcohol Abstainer Status and Prazosin Treatment in Association with Changes in Posttraumatic Stress Disorder Symptoms in Veterans with Comorbid Alcohol Use Disorder and Posttraumatic Stress Disorder. Alcohol Clin Exp Res. 2019;43(4):741-6. Epub 20190219. doi: 10.1111/acer.13969. PubMed PMID: 30698839; PubMed Central PMCID: PMCPMC6443463.

267. Haller M, Norman SB, Cummins K, Trim RS, Xu X, Cui R, et al. Integrated Cognitive Behavioral Therapy Versus Cognitive Processing Therapy for Adults With Depression, Substance Use Disorder, and Trauma. J Subst Abuse Treat. 2016;62:38-48. Epub 20151126. doi: 10.1016/j.jsat.2015.11.005. PubMed PMID: 26718130.

268. Taylor DJ, Pruiksma KE, Hale W, McLean CP, Zandberg LJ, Brown L, et al. Sleep problems in active duty military personnel seeking treatment for posttraumatic stress disorder: presence, change, and impact on outcomes. Sleep. 2020;43(10). Epub 2020/04/05. doi: 10.1093/sleep/zsaa065. PubMed PMID: 32246153.

269. Agency for Health Research and Quality. The Effective Health Care Program stakeholder guide Appendix D: Research questions & PICO(TS) 2011. Available from: https://www.ahrq.gov/research/findings/evidence-based-reports/stakeholderguide/appendixc.html.

270. Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. Journal of clinical epidemiology. 2013;66(7):726-35. Epub 2013/04/11. doi: 10.1016/j.jclinepi.2013.02.003. PubMed PMID: 23570745.