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

Department of Veterans Affairs

Department of Defense

Clinician Summary

QUALIFYING STATEMENTS

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

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

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

These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 3.0 – 2017

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I. Introduction

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

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

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

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

II. How to Use the Clinical Practice Guideline

The VA/DoD PTSD CPG can be used in a variety of ways. It can be used by general clinicians or specialists to study and consider the latest information on management of PTSD and how and whether to incorporate that information or recommendations into their practice. The CPG covers diagnosis and assessment, prevention of PTSD, treatment of ASD, treatment of PTSD, as well as treatment of PTSD in the presence of co-occurring conditions. Patients can examine the guideline to educate themselves and better understand their treatment options and expectations. A healthcare system can use the CPG to assure that its clinicians and patients have the resources available to compassionately and effectively offer treatment in a timely,

culturally sensitive manner. The guideline can also be used to suggest specific education for identified gaps.

The guideline is not intended as a standard of care and should not be used as such. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advances and patterns evolve. Today there is variation among state regulations, and the guideline does not cover the variety of ever-changing state regulations that may be pertinent. The ultimate judgement regarding a particular clinical procedure or treatment course must be made by the individual clinician, in light of the patient's clinical presentation, patient preferences, and the available diagnostic and treatment options. As noted previously, the guideline can assist care providers, but the use of a CPG must always be considered as a recommendation, within the context of a provider's clinical judgment and patient values and preferences, in the care for an individual patient.

III. Recommendations

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

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

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

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

A. Grading Recommendations

The Champions and Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: [2]

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

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

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

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

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

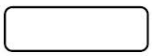
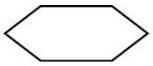
- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence…")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option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

IV. Algorithm

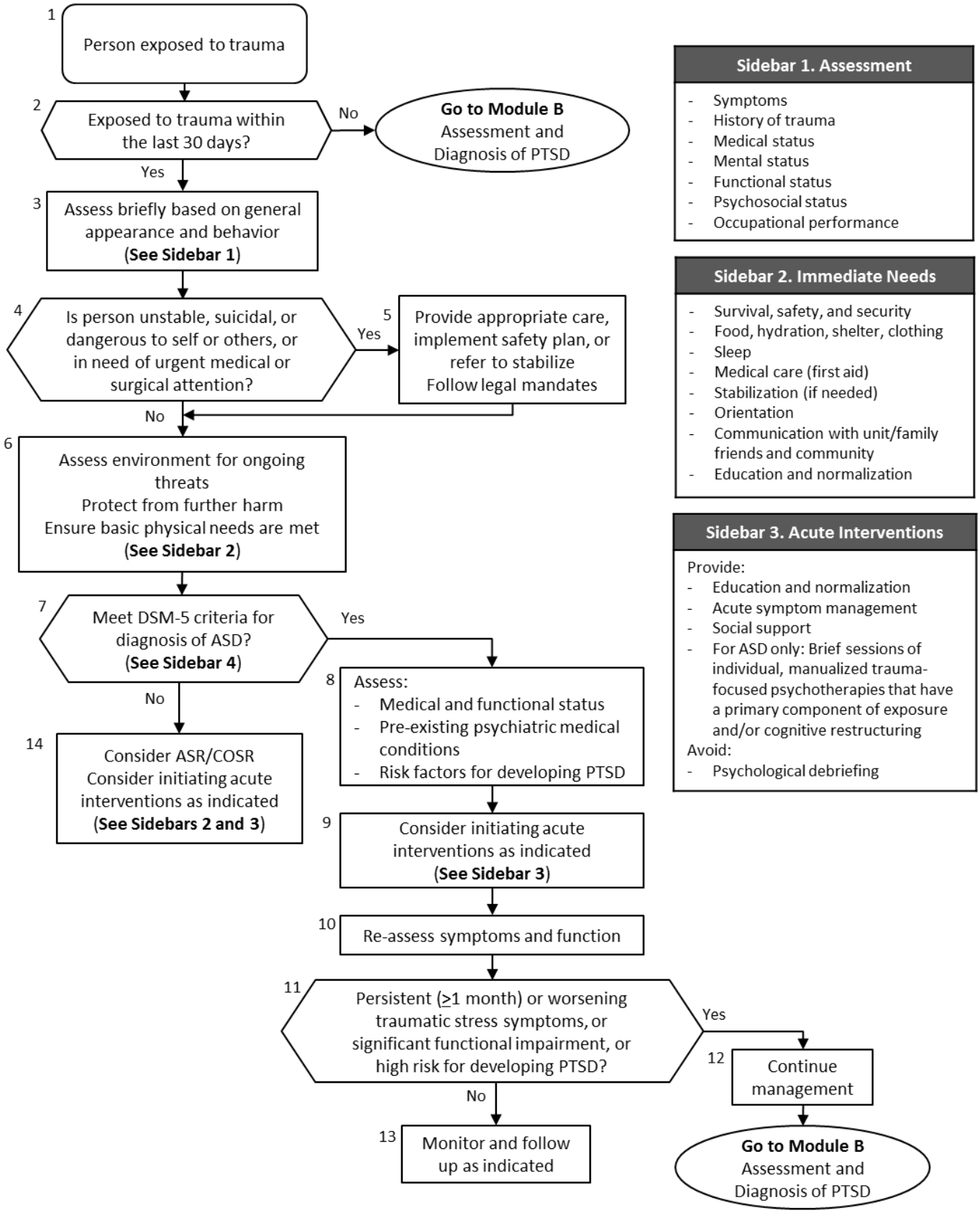
This CPG includes an algorithm that is designed to facilitate understanding of the clinical pathway and decision making process used in management of PTSD. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more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

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

A clinical algorithm diagrams a guideline into a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[3]

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

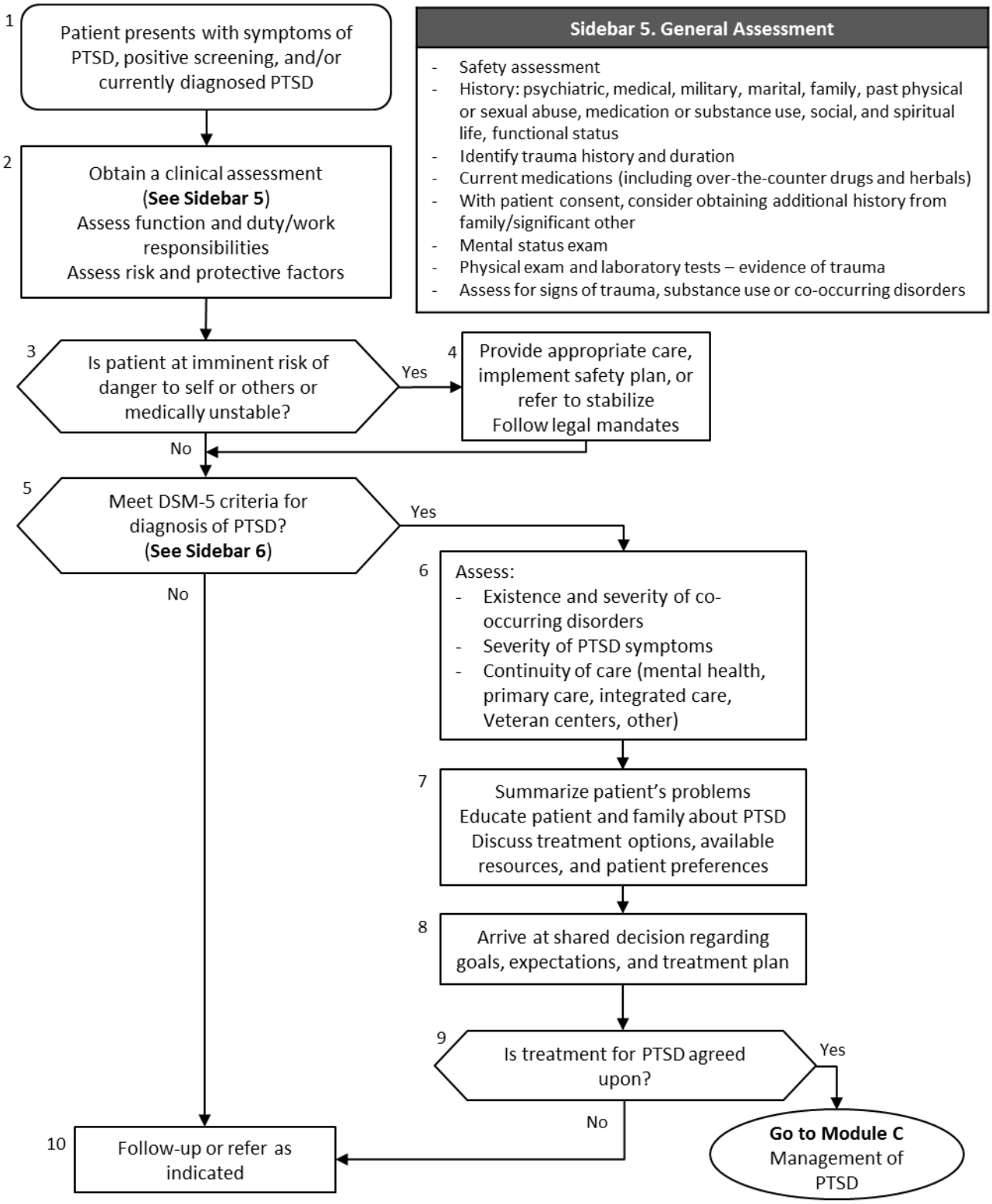
Module A: Acute Stress Reaction/Disorder



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

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

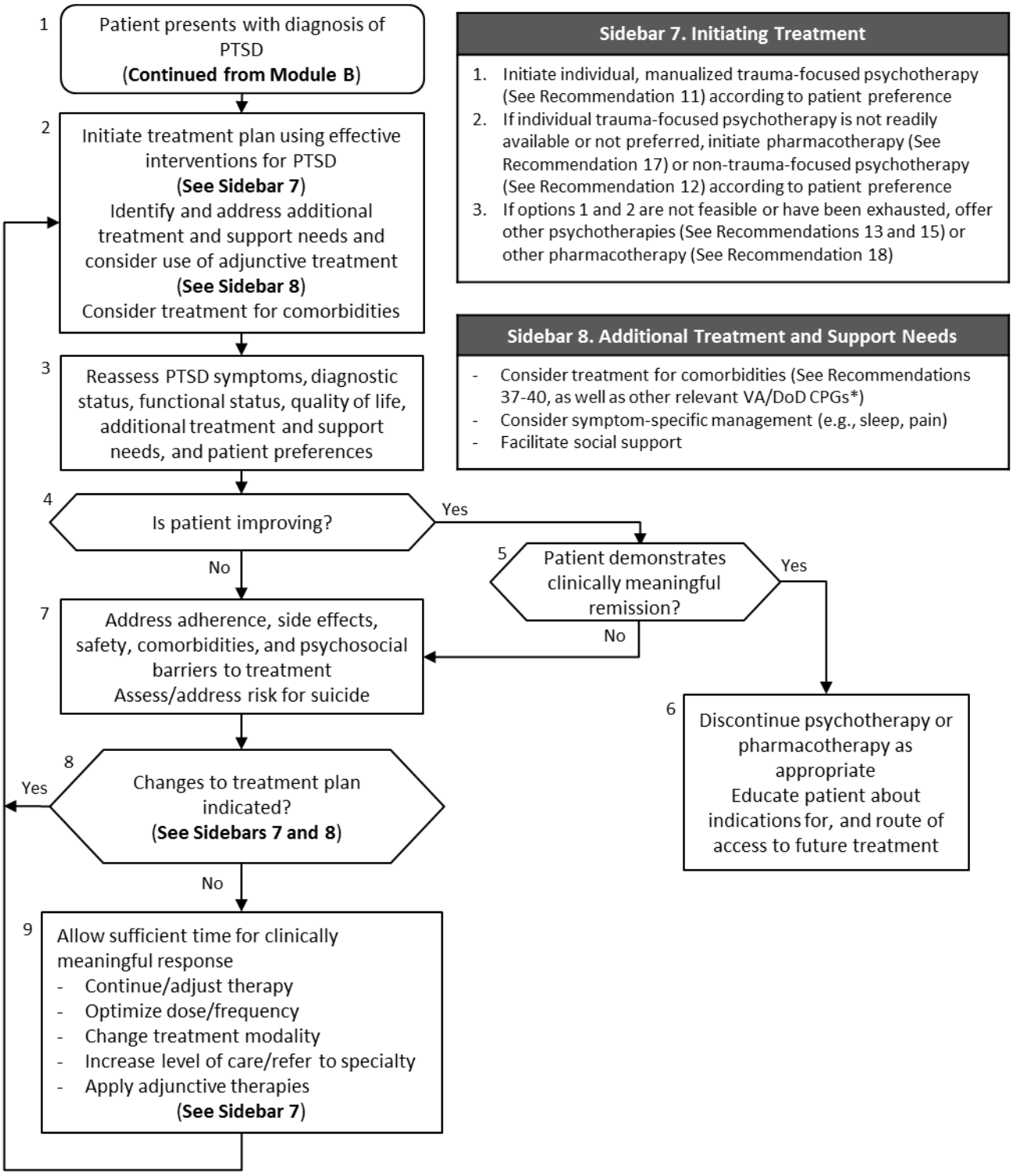
Module B: Assessment and Diagnosis of Posttraumatic Stress Disorder



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

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

Module C: Management of Posttraumatic Stress Disorder



Sidebar 7. Initiating Treatment

1. Initiate individual, manualized trauma-focused psychotherapy (See Recommendation 11) according to patient preference
2. If individual trauma-focused psychotherapy is not readily available or not preferred, initiate pharmacotherapy (See Recommendation 17) or non-trauma-focused psychotherapy (See Recommendation 12) according to patient preference
3. If options 1 and 2 are not feasible or have been exhausted, offer other psychotherapies (See Recommendations 13 and 15) or other pharmacotherapy (See Recommendation 18)

Sidebar 8. Additional Treatment and Support Needs

- Consider treatment for comorbidities (See Recommendations 37-40, as well as other relevant VA/DoD CPGs*)
- Consider symptom-specific management (e.g., sleep, pain)
- Facilitate social support

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

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

V. Scope of the Clinical Practice Guideline

The VA/DoD PTSD CPG is designed to assist providers in managing or co-managing patients with PTSD and related conditions (e.g., ASD). Moreover, the patient population of interest for the CPG is adults who are eligible for care in the VA and DoD healthcare delivery systems. It includes Veterans as well as deployed and non-deployed active duty Service Members, Guard, and Reserve. The CPG does not provide recommendations for the management of PTSD in children or adolescents. Regardless of setting, any patient in the healthcare system should ideally have access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances.

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

VI. Guideline Work Group

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VII. Recommendation Discussion

A. General Clinical Management

a. Patient-centered Care

VA/DoD CPGs encourage clinicians to use a patient-centered care approach that is individualized based on patient needs, treatment goals, prior treatment experience, and preferences. Whenever possible, all patients in the healthcare system should be offered access to evidence-based interventions. When properly executed, patient-centered care may decrease patient anxiety, increase trust in clinicians, and improve knowledge and treatment adherence.[4,5] As part of the patient-centered care approach, clinicians should review the outcomes of previous self-change efforts, past treatment experiences, and discuss these outcomes (including reasons for treatment dropout) with the patient. Clinicians should explain treatment options to patients including the benefits of accepting a referral to a mental health specialist, an expert in evidence-based PTSD treatments. The clinician should discuss any concerns the patient has and explore any identified treatment barriers. Often, clinicians have concerns that a patient may not be able to tolerate a trauma-focused treatment. It is important to note that there is no data to suggest that comorbidities or other factors indicate that a patient will not benefit from these treatments. Nor is there data to suggest that clinicians can accurately predict which patients will or will not benefit from one of these treatments. It is therefore important that clinicians inform all patients with PTSD about the availability of trauma-focused psychotherapy.

b. Shared Decision Making

The shared decision making (SDM) process has the goal of considering patient preference in treatment decisions to improve patient-centered care, decision quality, and treatment outcomes. In SDM, the patient and provider together review treatment options and compare the benefits, harms, and risks of each with the goal of selecting the option that best meets the patient's needs.

Much of the SDM research has focused on evaluating decision aids, tools that educate patients about treatment options as a way to facilitate SDM. There were two randomized controlled trials (RCTs) examining decision aids for PTSD treatment reviewed for this guideline.[6,7] Consistent with the larger literature on decision aids, both trials suggested that relative to usual care, patients who received a

decision aid were more likely to select and receive evidence-based treatment. One trial also found that receipt of the decision aid was linked to improved clinical outcomes, PTSD knowledge, and decisional conflict.[6] The Work Group based its strong recommendation on the substantial literature supporting SDM in other conditions. The process of SDM maximizes the likelihood that patient preference is taken into account and the benefits outweigh any potential harms.

c. Collaborative Care

The collaborative care model is an evidence-based approach to integrating physical and behavioral health services that is usually provided within the primary care setting.[8] Many collaborative care models generally involve a stepped-care approach to symptom management, using a predetermined treatment sequence that starts with simple, low-intensity interventions first. The use of collaborative care interventions that employ or facilitate active engagement in evidence-based PTSD treatments in the primary care setting appears to increase patient compliance with treatment, improve patient satisfaction, and potentially reduce premature termination of treatment when delivered in the primary care setting.[9-15]

Among the RCTs reviewed, statistically significant findings included increased patient satisfaction using technology-enhanced stepped collaborative care compared to usual care,[10,11] reduction in PTSD symptoms,[9] PTSD remission across all models of collaborative care studied,[9] and improvements in PTSD and depression when telehealth was used to deliver Cognitive Processing Therapy (CPT) in collaborative care.[11] Care management alone did not appear to be effective for PTSD, whereas the stepped care aspects of the models evaluated did appear to improve outcomes.[9,10,16] Given the increased patient compliance with PTSD treatment and improvement in patient satisfaction correlated with the use of the collaborative care model studies reviewed, the potential benefits outweigh risk of harm.

B. Diagnosis and Assessment of Posttraumatic Stress Disorder

Identification of individuals with PTSD is essential to ensure that they receive appropriate treatment. Moreover, screening is often considered a key step in the diagnostic process. Screening for PTSD can be performed in primary and specialty care settings, and both VA and DoD mandate screening either in context with combat deployments or in primary care settings. One-time screening is not recommended because PTSD is a disorder with a fluctuating course for many people. VA recommends annual screening for the first five years following separation and then every five years thereafter. DoD recommends routine screening throughout deployment cycles. Both VA and DoD have relied most heavily on the Primary Care PTSD Screen (PC-PTSD) and PTSD Checklist (PCL) for various screening purposes.[17] No screening measure or cutpoint should be the sole basis for diagnosis.

A comprehensive diagnostic evaluation of PTSD should include determination of DSM criteria, acute risk of harm to self or others, functional status, medical history, past treatment history, and relevant family history.[18] Diagnosis can be made on the basis of a clinical interview or a structured diagnostic interview such as the Clinician-Administered PTSD Scale (CAPS),[19] Posttraumatic Stress Disorder Symptom Scale Interview for DSM-5 (PSSI-I),[20] or Structured Clinical Interview for DSM-5 (SCID-5).[21] If diagnosis is

based on clinical interview in any setting, it can be helpful to administer a self-report questionnaire such as the PTSD Checklist for DSM-5 (PCL-5)[22] along with other routine self-report screening tools, such as the Patient Health Questionnaire-9 (PHQ-9) and Alcohol Use Disorders Identification Test—Consumption (AUDIT-C).[23-25] In addition to their utility in screening and diagnosis, brief questionnaires such as the PCL-5 can be used to assess symptom severity and monitor treatment response.

C. Prevention of Posttraumatic Stress Disorder

Prevention of PTSD is described using a hierarchy based on the risk of the population evaluated. *Universal prevention* strategies target the general population and are not directed at a specific at-risk group. There are currently no recommended strategies for universal prevention of PTSD. *Selective prevention* targets individuals who are at higher than average risk for developing PTSD and includes strategies delivered to trauma-exposed individuals who have not yet developed symptoms or meet criteria for ASD or PTSD. *Indicated prevention* includes strategies to prevent PTSD in individuals with symptoms of ASD or meet criteria for ASD.

a. Selective Prevention of Posttraumatic Stress Disorder

Interventions among individuals exposed to trauma (e.g., trauma-focused psychotherapy, Critical Incident Stress Debriefing (CISD), the Battlemind debriefing intervention, and a variety of medications) have not been consistently effective in preventing PTSD. While trauma-focused psychotherapy shows promise, evidence is limited to a single-site study.[26] Neither CISD nor Battlemind debriefing were found to reduce PTSD at six months, and CISD was associated with increased incidence and severity of PTSD at 13 months follow-up.[27,28] Likewise, medications tested to prevent PTSD (e.g., beta-blockers, benzodiazepines, selective serotonin reuptake inhibitors [SSRIs], antiepileptic drugs) were not found to be consistently effective in reducing incidence of PTSD. While hydrocortisone administration during life-threatening medical illnesses was associated with significantly less PTSD and depression symptoms at three months,[29-32] it is unclear if these findings can be generalized to non-medical traumatic events and there is concern about the safety of the high doses administered. In light of these findings there is insufficient evidence to recommend trauma-focused psychotherapy or pharmacotherapy in the immediate post-trauma period.

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

Among the interventions for treatment of ASD, brief trauma-focused psychotherapy has been found to be effective in reducing incidence of PTSD at six and 12 months without significant reported adverse effects.[27,33] However, treatment with escitalopram was not effective in preventing PTSD in individuals who met criteria for ASD.[34,35] In light of this evidence, brief trauma-focused psychotherapy is recommended for individuals with ASD.

D. Treatment of Posttraumatic Stress Disorder

a. Treatment Selection

The Work Group's recommendation to use individual trauma-focused psychotherapy over pharmacotherapy reflects the current state of the research into PTSD treatment. Although there are few

data that reflect direct head-to-head comparisons of trauma-focused psychotherapy and a first-line medication for treating PTSD, two recent meta-analyses compared the treatment effects of psychotherapies and pharmacotherapies.[36,37] The results of these meta-analyses strongly indicate that trauma-focused psychotherapies impart greater change with regard to core PTSD symptoms than pharmacotherapies, and that these improvements persist for longer time periods. This appears true even when restricting the meta-analyses to studies that utilized "active" treatments such as Present-Centered Therapy (PCT) (as opposed to waitlist or treatment as usual) as control groups for psychotherapy studies.

The recommendation to prioritize individual trauma-focused psychotherapy over pharmacotherapy was made in consideration of several factors in addition to the apparent differences in the magnitude of change associated with the two treatment modalities. First, the risks for negative side effects or negative reactions to the treatment are generally greater with pharmacologic treatments than with psychotherapies. Second, the positive effects of medication treatment diminish over time and are lost when medications are stopped. Third, comments from participants in the focus group and a growing body of literature indicate a patient preference for psychotherapy over pharmacotherapy.[6,38,39]

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

b. Psychotherapy

For this CPG, trauma-focused psychotherapy is defined as therapy that uses cognitive, emotional, or behavioral techniques to facilitate processing a traumatic experience and in which the trauma focus is a central component of the therapeutic process.[40] The trauma-focused psychotherapies with the strongest evidence from clinical trials are Prolonged Exposure (PE),[41] CPT,[42] and Eye Movement Desensitization and Reprocessing (EMDR).[43,44] These treatments have been tested in numerous clinical trials, in patients with complex presentations and comorbidities, compared to active control conditions, have long-term follow-up, and have been validated by research teams other than the developers. Other manualized protocols that have sufficient evidence to recommend use are: specific cognitive behavioral therapies for PTSD,[45-53] Brief Eclectic Psychotherapy (BEP),[54-56] Narrative Exposure Therapy (NET),[57,58] and written narrative exposure.[59,60] There are other psychotherapies that meet the definition of trauma-focused treatment for which there is currently insufficient evidence to recommend for or against their use.

If trauma-focused psychotherapy is not available or if a patient prefers a treatment that does not require focusing on trauma, the Work Group suggests individual, manualized psychotherapy that is not trauma-focused. SIT, PCT, and IPT are the non-trauma-focused therapies with the most evidence derived from clinical trials that have involved direct comparisons with first-line trauma-focused therapies.

A wide variety of manualized protocols, including Dialectical Behavior Therapy,[61] Skills Training In Affect and Interpersonal Regulation, [62] Acceptance and Commitment Therapy,[63] Seeking Safety,[64] hypnosis,[65] brief psychodynamic therapy,[66] and supportive counseling,[48,67,68] have all been used in the treatment of PTSD. However, at this time there are insufficient data to argue for or against the use of these protocols in treating PTSD. Further research is needed in order to make a recommendation for or against their routine use in patients with PTSD.

The Work Group does not recommend adding or removing components from evidence based psychotherapy protocols. If modifications to an established protocol (e.g., PE, CPT, EMDR) are clinically necessary, the modifications should be empirically and theoretically guided, and with understanding of the core components of trauma-focused psychotherapies considered most therapeutically active.

The limited data on the efficacy of group therapy for PTSD indicates that it is not as effective as individual therapy. However, some patients with PTSD may prefer manualized group psychotherapy over other treatment formats. The research has not shown any particular model of manualized trauma-focused or non-trauma-focused group psychotherapy for PTSD to be superior to other active interventions, such as PCT, psychoeducation, or treatment as usual. However, group psychotherapy is better than no treatment in reducing PTSD symptoms.[69]

In some cases, Veterans may prefer PTSD treatment that includes attention focused on their intimate relationships. It is not yet known if a couples-based approach is as effective as individual trauma-focused therapy for PTSD. Overall, there is promising but limited evidence in support of trauma-focused couples therapy for PTSD.

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

c. Pharmacotherapy

For those patients who choose not to engage in or are unable to access trauma-focused psychotherapy, the use of sertraline, paroxetine, fluoxetine, or venlafaxine as monotherapy is recommended based on the results of three systematic reviews.[36,37,70] The benefits of these medications outweigh the potential harms. The most frequent adverse effects of SSRIs include sexual dysfunction, increased sweating, gastrointestinal upset, and drowsiness/fatigue.

Additionally, although recent research is lacking, older research has demonstrated modest therapeutic effects from nefazodone, imipramine, and phenelzine. Clinicians are reminded that both nefazodone and phenelzine have potentially serious toxicities and should be managed carefully.

The Work Group suggests against the use of quetiapine, olanzapine, and other atypical antipsychotics (and recommends against risperidone) due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks. Antipsychotics can produce metabolic adverse effects (harms) that may exacerbate a patient's comorbidities or result in new medical problems. These and other adverse effects and drug-drug interactions limit the acceptability of atypical antipsychotics by patients and healthcare providers.

Additionally, 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. We recommend against the use of risperidone as monotherapy for the primary treatment of PTSD due to very low quality of evidence and because the potential harms outweigh the benefits.

Preliminary evidence that natural and synthetic cannabinoids could improve PTSD symptoms, particularly nightmares, is offset by the significant side effects including tolerance, dependence, withdrawal syndrome, psychosis, cognitive deficits, and respiratory symptoms if smoked. A lack of well-designed RCTs evaluating the efficacy of cannabinoids in large samples of patients with PTSD, together with its serious side effects, does not support the use of natural or synthetic cannabinoids as a treatment for PTSD.

Currently, there is insufficient evidence to recommend for or against monotherapy or augmentation therapy for eszopiclone, escitalopram, bupropion, desipramine, doxepin, D-serine, duloxetine, desvenlafaxine, fluvoxamine, levomilnacipran, mirtazapine, nortriptyline, trazodone, vilazodone, vortioxetine, buspirone, hydroxyzine, cyproheptadine, zaleplon, and zolpidem.

See Table 1 below and Appendix A: Pharmacotherapy Dosing Table for dosing information.

Table 1. Medication Monotherapy for the Treatment of PTSD by Recommendation and Strength of Evidence

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

*The Work Group determined there was no high quality evidence regarding medication monotherapy

^FDA approved for PTSD

±Serious potential toxicity, should be managed carefully

†No data were captured in the evidence review for the CPG and were not considered in development of this table

‡ Studies of these drugs did not meet the inclusion criteria for the systematic evidence review due to poor quality

d. Augmentation Therapy

There are currently insufficient data and/or known adverse effect profiles for topiramate, baclofen, and pregabalin to recommend use as augmentation therapy. The Work Group also recommends against the use of atypical antipsychotics, benzodiazepines, and divalproex as augmentation therapy due to low quality evidence and potential adverse effects. Currently, there is insufficient evidence also for the use of mirtazapine in combination with sertraline. Additionally, there has either been inconsistent evidence or insufficient evidence for the use of D-cycloserine or hydrocortisone in combination with exposure therapy.

Table 2. Medication Augmentation and Combination* Pharmacotherapy for the Treatment of PTSD by Recommendation and Strength of Evidence

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

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

e. Prazosin

Global Posttraumatic Stress Disorder Symptoms

We suggest against prazosin as monotherapy or augmentation therapy for global symptoms of PTSD based on lack of demonstrated efficacy. Although some small studies had demonstrated significant improvement with prazosin compared to placebo in global PTSD symptoms, the recent VA Cooperative Study, which had almost twice as many subjects as the other four studies combined, showed no difference in the total CAPS and Clinical Global Impression of Change Scale (CGIC) scores in the prazosin and placebo arms; it also demonstrated a placebo effect that appeared larger than that seen in the other four trials.[71]

Nightmares and Sleep Quality

Despite the fact that prazosin has been used for managing PTSD-associated nightmares in recent years, we found insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy for nightmares or sleep disturbance associated with PTSD. Specifically, positive results in nearly all of the smaller studies reviewed [72-75] were contradicted by negative results in the much larger and stronger VA Cooperative Study.[71]

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

f. Combination Therapy

Although many patients show clinical improvement in response to recommended evidence-based psychotherapies and/or pharmacotherapies, a sizable proportion of patients are partial- or non-responders. Determining what to do for these patients is a clinically important question, yet the limited evidence available is insufficient to guide clinical decision making. Only a few studies have examined the benefits of administering medication and psychotherapy to either augment a single initial modality following inadequate response, or as a combination at the outset of therapy. In the absence of evidence to guide decision making, clinicians treating partial- or non-responders should rely on their clinical judgment, use an SDM approach, and take patient preferences into consideration.

g. Non-pharmacologic Biological Treatments

There is considerable interest in alternatives to either psychotherapy or pharmacology for the primary treatment of PTSD. However, there is currently insufficient evidence to recommend the majority of somatic therapies, including repetitive transcranial magnetic stimulation (rTMS), electroconvulsive therapy (ECT), hyperbaric oxygen therapy (HBOT), stellate ganglion block (SGB), or vagal nerve stimulation (VNS). Based upon a lack of high quality RCTs supporting the efficacy of rTMS, ECT, HBOT, SGB, or VNS, the Work Group is unable to recommend their use for the primary treatment of PTSD.

h. Complementary and Integrative Treatments

The Work Group acknowledges the widespread use of complementary and integrative health (CIH) practices as part of the treatment of individuals with PTSD in the DoD and VA healthcare systems. It is important to clarify that we are not recommending against the treatments but rather we are saying that, at this time, the research does not support the use of any CIH practice for the primary treatment of PTSD. These practices hold promise as interventions to improve wellness and promote recovery.

Even though the evidence is trending positively for the use of acupuncture, based on the lack of sham control and other study limitations, the Work Group's assessment was that the current available evidence was still insufficient to recommend acupuncture as a primary treatment modality for PTSD. Practitioners should consider factors such as patient preference and treatment availability when determining CIH treatment options.

There were more clinical trials available for meditation than for any other CIH modality. Grading the body of evidence for meditation overall was complicated by the heterogeneity of the types of meditation that had been assessed. Meditation is promising and may provide a safe, self-administered, and inexpensive intervention for PTSD. Unfortunately, the current research clearly does not establish its efficacy. Additional

high quality trials with adequate power, active control conditions, and longer follow-up periods are needed.

Evidence suggests that yoga may be effective for PTSD. No major adverse events have been reported in the yoga interventions. However, the Work Group judged the evidence to be insufficient due to study limitations.

A number of other CIH modalities were reviewed, but none were found to have sufficient evidence to support any recommendations regarding their use.[76] Although there is much interest in the area of animal-assisted therapy, no studies evaluating the use of interventions with animals, such as equine therapy or canine therapy, met the threshold for inclusion in the review. At this time, there is no evidence to support their use for the primary treatment of PTSD.

i. Technology-based Treatment Modalities

We suggest internet-based cognitive behavioral therapy (iCBT) with feedback provided by a qualified facilitator (e.g., care manager, trained peer, therapist) as an alternative to no treatment for improvement in PTSD symptoms. Although it is not as well supported as other primary treatments for PTSD, iCBT may be suggested for patients who refuse other treatment interventions. iCBT may be useful to increase access to services and reduce stigma in seeking services. Before recommending iCBT to patients, clinicians should review the content to ensure its accuracy and ethical application.

We recommend using trauma-focused psychotherapies that have demonstrated efficacy using secure video teleconferencing (VTC) modality when PTSD treatment is delivered via VTC. Although there are fewer studies examining the delivery of evidence-based treatments through VTC than those delivered in-person, there appears to be similar efficacy. VTC interventions are encouraged when in-person interventions are not feasible, the patient would benefit from more frequent contact than is feasible with face-to-face sessions, or the patient declines in-person treatment. There are some concerns associated with treatment delivery through VTC such as technical support, computer literacy, and human factors in using technology. Potential advantages include increased access and decreased stigma.

Providers using technology-assisted interventions should regularly encourage patients to complete the interventions and endeavor to maintain and strengthen the therapeutic relationship (e.g., through telephone contact), build patient rapport, stress practice, and ensure adequacy of safety protocols. Providers should ensure that their work complies with the regulations and procedures of the organization in which they are employed, legal standards, and the ethical standards of their professions. Patient confidentiality and safety should be monitored closely.

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

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

The vast majority of patients with PTSD will have one or more co-occurring conditions. Two of the most common are sleep disturbance (present in 90-100% of Veterans with PTSD [77,78]) and substance use disorder (SUD) (present in 12% to 48% of Veterans with PTSD [79]). This CPG presents strategies for

treating PTSD in the presence of these and other co-morbid conditions. However, discussion of primary treatments for the co-occurring conditions themselves is beyond the scope of this guideline.

Because of the high prevalence of comorbid conditions in the PTSD population, screening for other psychiatric and medical disorders is warranted (see also the VA/DoD CPGs for the Management of Major Depressive Disorder [MDD][1], Assessment and Management of Patients at Risk for Suicide[2], and Management of Bipolar Disorder[3]). Associated high-risk behaviors (e.g., substance use, unsafe weapon storage, dangerous driving, unprotected sex, needle sharing) should also be assessed in patients with PTSD and addressed in the treatment plan. It is generally best to employ a collaborative care treatment strategy involving other medical and mental health specialists to address these health concerns simultaneously with PTSD. (See Recommendation 2 in full CPG regarding collaborative care).

RCTs have found good tolerance and efficacy for various trauma-focused PTSD treatments in patients with comorbid psychotic disorders,[80] personality disorders,[81] severe mental illness,[82] dissociation,[83,84] anger,[85] suicidal ideation,[86] and depression.[85] One RCT reviewed by the Work Group also found no evidence of adverse outcomes when using exposure-based psychotherapy in patients with PTSD and cardiovascular disease.[87] The Work Group did not find any studies meeting the threshold for review that examined the common comorbidities of traumatic brain injury (TBI) or pain, but readers are encouraged to reference the VA/DoD CPG for the Management of Concussion/mTBI[4] and the VA/DoD CPG for the Management of Chronic Multisymptom Illness[5] [CMI] for the primary assessment and management of these conditions. Recommendations regarding other common co-occurring conditions are as follows:

- Suicidality (see Recommendation 4 in the full CPG and the VA/DoD CPG for Assessment and Management of Patients at Risk for Suicide[2])
    - Suicidality should be assessed early on and carefully monitored at each visit.
- SUD (see Recommendation 38 in the full CPG and the VA/DoD CPG for Management of SUD[6])
    - Patients with PTSD and SUD (including nicotine use disorder) can both tolerate and benefit from concurrent treatment for both conditions.
    - The presence of an SUD should not prevent concurrent treatment with evidence-based, trauma-focused therapy for PTSD.

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

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

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

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

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

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

  - Non-trauma-focused therapies, such as Seeking Safety, are not recommended for the treatment of PTSD in the presence of an SUD due to lack of evidence for improvement in core PTSD symptoms and mixed evidence regarding improvement in SUD symptoms.
  - Topiramate and prazosin may reduce alcohol consumption, but have not demonstrated efficacy in improving the primary symptoms of PTSD. However, desipramine and paroxetine may reduce both alcohol consumption and core PTSD symptoms.
  - Combining medications and psychotherapy may be another effective strategy for treating PTSD and co-occurring SUDs.
- Sleep Disturbance (see Recommendations 28a, 28b, 39, and 40 in the full CPG)
  - Providers should examine potential causes of sleep disturbance independently of PTSD, particularly with respect to underlying medical, dietary, and environmental etiologies.
  - For patients with PTSD and Sleep Disturbance, Cognitive Behavioral Therapy for Insomnia should be considered first-line treatment, with medication considered a second-line intervention following a SDM discussion about potential harms and benefits.
  - The data are inconclusive regarding the best choice of intervention for nightmares. We found insufficient evidence to recommend for or against the use of prazosin, and the data are inconclusive regarding the best choice of psychotherapy.

Appendix A: Pharmacotherapy Dosing Table

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

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

*Strong For recommendation

±Weak For recommendation

References

1. U.S. Department of Veteran Affairs, Department of Defense. Guideline for guidelines. Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup; Revised April 10, 2013.
2. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: The significance and presentation of recommendations. *J Clin Epidemiol.* Jul 2013;66(7):719-725.
3. Society for Medical Decision Making Committee on Standardization of Clinical Algorithms. Proposal for clinical algorithm standards. *Med Decis Making.* Apr-Jun 1992;12(2):149-154.
4. Bertakis KD, Azari R. Patient-centered care is associated with decreased health care utilization. *J Am Board Fam Med.* May-Jun 2011;24(3):229-239.
5. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: Definitions and applications to improve outcomes. *J Am Acad Nurse Pract.* Dec 2008;20(12):600-607.
6. 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.* Feb 1 2015;66(2):149-154.
7. Mott JM, Stanley MA, Street RL, Jr., Grady RH, Teng EJ. Increasing engagement in evidence-based PTSD treatment through shared decision-making: A pilot study. *Mil Med.* Feb 2014;179(2):143-149.
8. Unützer J, Harbin H, Schoenbaum M, Druss B. The collaborative care model: An approach for integrating physical and mental health care in medicaid health homes (pp. 1–13). *Health Home, Information Resource Center. Retreived from https://www.medicaid.gov/state-resource-center/medicaid-state-technical-assistance/health-homes-technical-assistance/health-home-information-resource-center.html.* 2013.
9. Zatzick D, Jurkovich G, Rivara FP, et al. A randomized stepped care intervention trial targeting posttraumatic stress disorder for surgically hospitalized injury survivors. *Ann Surg.* Mar 2013;257(3):390-399.
10. Zatzick D, O'Connor SS, Russo J, et al. Technology-enhanced stepped collaborative care targeting posttraumatic stress disorder and comorbidity after injury: A randomized controlled trial. *J Trauma Stress.* Oct 2015;28(5):391-400.
11. Fortney JC, Pyne JM, Kimbrell TA, et al. Telemedicine-based collaborative care for posttraumatic stress disorder: A randomized clinical trial. *JAMA Psychiatry.* Jan 2015;72(1):58-67.
12. Schnurr PP, Friedman MJ, Oxman TE, et al. RESPECT-PTSD: Re-engineering systems for the primary care treatment of PTSD, a randomized controlled trial. *J Gen Intern Med.* Jan 2013;28(1):32-40.
13. Meredith LS, Eisenman DP, Han B, et al. Impact of collaborative care for underserved patients with PTSD in primary care: A randomized controlled trial. *J Gen Intern Med.* May 2016;31(5):509-517.
14. Craske MG, Stein MB, Sullivan G, et al. Disorder-specific impact of coordinated anxiety learning and management treatment for anxiety disorders in primary care. *Arch Gen Psychiatry.* Apr 2011;68(4):378-388.
15. Peek C. Lexicon for behavioral health and primary care integration: Concepts and definitions developed by expert concensus. *Rockville, MD: Agency for Healthcare Research and Quality Retrieved from http://integrationacademy.ahrq.gov/sites/default/files/Lexicon.pdf.* 2013.
16. Engel CC, Jaycox LH, Freed MC, et al. Centrally assisted collaborative telecare for posttraumatic stress disorder and depression among military personnel attending primary care: A randomized clinical trial. *JAMA internal medicine.* 2016;176(7):948-956.
17. Spoont MR, Williams JW, Jr., Kehle-Forbes S, Nieuwsma JA, Mann-Wrobel MC, Gross R. Does this patient have posttraumatic stress disorder?: Rational clinical examination systematic review. *JAMA.* Aug 04 2015;314(5):501-510.

18. Reardon A, Brief D, Miller M, Keane T. Assessment of PTSD and its comorbidities in adults. *Handbook of PTSD: science and practice. 2nd ed. New York: Guilford.* 2014:369-390.
19. Weathers F, Blake D, Schnurr P, Kaloupek D, Marx B, Keane T. The clinician-administered PTSD scale for DSM-5 (CAPS-5). *Interview available from the National Center for PTSD at www.ptsd.va.gov.* 2013.
20. Foa EB, McLean CP, Zang Y, et al. Psychometric properties of the posttraumatic stress disorder symptom scale interview for DSM-5 (PSSI-5). *Psychol Assess.* Oct 2016;28(10):1159-1165.
21. First M, Williams J, Karg R, Spitzer R. Structured clinical interview for DSM-5 disorders, clinician version (SCID-5-CV). *Arlington, VA: American Psychiatric Association.* 2015.
22. Bovin MJ, Marx BP, Weathers FW, et al. Psychometric properties of the PTSD checklist for diagnostic and statistical manual of mental disorders-fifth edition (PCL-5) in veterans. *Psychol Assess.* Nov 2016;28(11):1379-1391.
23. Kroenke K, Spitzer RL, Williams JB. The patient health questionnaire-2: Validity of a two-item depression screener. *Med Care.* Nov 2003;41(11):1284-1292.
24. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med.* Sep 2001;16(9):606-613.
25. Bradley KA, Kivlahan DR, Zhou XH, et al. Using alcohol screening results and treatment history to assess the severity of at-risk drinking in Veterans Affairs primary care patients. *Alcohol Clin Exp Res.* Mar 2004;28(3):448-455.
26. Rothbaum BO, Kearns MC, Price M, et al. Early intervention may prevent the development of posttraumatic stress disorder: A randomized pilot civilian study with modified prolonged exposure. *Biol Psychiatry.* Dec 01 2012;72(11):957-963.
27. Forneris CA, Gartlehner G, Brownley KA, et al. Interventions to prevent post-traumatic stress disorder: A systematic review. *Am J Prev Med.* Jun 2013;44(6):635-650.
28. Mulligan K, Fear NT, Jones N, et al. Postdeployment battlemind training for the U.K. Armed forces: A cluster randomized controlled trial. *J Consult Clin Psychol.* Jun 2012;80(3):331-341.
29. Schelling G, Briegel J, Roozendaal B, Stoll C, Rothenhausler HB, Kapfhammer HP. The effect of stress doses of hydrocortisone during septic shock on posttraumatic stress disorder in survivors. *Biol Psychiatry.* Dec 15 2001;50(12):978-985.
30. Delahanty DL, Gabert-Quillen C, Ostrowski SA, et al. The efficacy of initial hydrocortisone administration at preventing posttraumatic distress in adult trauma patients: A randomized trial. *CNS Spectr.* Apr 2013;18(2):103-111.
31. Zohar J, Yahalom H, Kozlovsky N, et al. High dose hydrocortisone immediately after trauma may alter the trajectory of PTSD: Interplay between clinical and animal studies. *Eur Neuropsychopharmacol.* Nov 2011;21(11):796-809.
32. Weis F, Kilger E, Roozendaal B, et al. Stress doses of hydrocortisone reduce chronic stress symptoms and improve health-related quality of life in high-risk patients after cardiac surgery: A randomized study. *J Thorac Cardiovasc Surg.* Feb 2006;131(2):277-282.
33. Kliem S, Kroger C. Prevention of chronic PTSD with early cognitive behavioral therapy. A meta-analysis using mixed-effects modeling. *Behav Res Ther.* Nov 2013;51(11):753-761.
34. 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.* Feb 2012;69(2):166-176.
35. 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.
36. 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.* Sep 2016;33(9):792-806.

37. 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.* Jun 2013;74(6):e541-550.
38. Simiola V, Neilson EC, Thompson R, Cook JM. Preferences for trauma treatment: A systematic review of the empirical literature. *Psychol Trauma.* Nov 2015;7(6):516-524.
39. 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.* 2017;54(1):47-57.
40. Schnurr PP. Focusing on trauma-focused psychotherapy for posttraumatic stress disorder. *Current Opinion in Psychology.* 2017;14:56-60.
41. Foa EB, Hembree EA, Cahill SP, 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.* Oct 2005;73(5):953-964.
42. Resick PA, Nishith P, Weaver TL, Astin MC, Feuer CA. A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. *J Consult Clin Psychol.* Aug 2002;70(4):867-879.
43. Shapiro F. Eye movement desensitization: A new treatment for post-traumatic stress disorder. *J Behav Ther Exp Psychiatry.* Sep 1989;20(3):211-217.
44. Rothbaum BO, Astin MC, Marsteller F. Prolonged exposure versus eye movement desensitization and reprocessing (EMDR) for PTSD rape victims. *J Trauma Stress.* Dec 2005;18(6):607-616.
45. Ehlers A, Clark DM, Hackmann A, 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.* Oct 2003;60(10):1024-1032.
46. Ehlers A, Grey N, Wild J, et al. Implementation of cognitive therapy for PTSD in routine clinical care: Effectiveness and moderators of outcome in a consecutive sample. *Behav Res Ther.* Nov 2013;51(11):742-752.
47. Ehlers A, Hackmann A, Grey N, 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.* Mar 2014;171(3):294-304.
48. Blanchard EB, Hickling EJ, Devineni T, et al. A controlled evaluation of cognitive behavioural therapy for posttraumatic stress in motor vehicle accident survivors. *Behav Res Ther.* Jan 2003;41(1):79-96.
49. Bryant RA, Mastrodomenico J, Felmingham KL, et al. Treatment of acute stress disorder: A randomized controlled trial. *Arch Gen Psychiatry.* Jun 2008;65(6):659-667.
50. Bryant RA, Moulds ML, Guthrie RM, et al. A randomized controlled trial of exposure therapy and cognitive restructuring for posttraumatic stress disorder. *J Consult Clin Psychol.* Aug 2008;76(4):695-703.
51. Kubany ES, Hill EE, Owens JA, et al. Cognitive trauma therapy for battered women with PTSD (CTT-BW). *J Consult Clin Psychol.* Feb 2004;72(1):3-18.
52. 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.* Apr 1998;55(4):317-325.
53. Power K, McGoldrick T, Brown K, et al. A controlled comparison of eye movement desensitization and reprocessing versus exposure plus cognitive restructuring versus waiting list in the treatment of post-traumatic stress disorder. *Clinical Psychology & Psychotherapy.* 2002;9(5):299-318.
54. Gersons BP, Carlier IV, Lamberts RD, van der Kolk BA. Randomized clinical trial of brief eclectic psychotherapy for police officers with posttraumatic stress disorder. *J Trauma Stress.* Apr 2000;13(2):333-347.
55. Lindauer RJ, Gersons BP, van Meijel EP, et al. Effects of brief eclectic psychotherapy in patients with posttraumatic stress disorder: Randomized clinical trial. *J Trauma Stress.* Jun 2005;18(3):205-212.

56. Nijdam MJ, Gersons BP, Reitsma JB, de Jongh A, Olff M. Brief eclectic psychotherapy v. Eye movement desensitisation and reprocessing therapy for post-traumatic stress disorder: Randomised controlled trial. *Br J Psychiatry.* Mar 2012;200(3):224-231.
57. Ertl V, Pfeiffer A, Schauer E, Elbert T, Neuner F. Community-implemented trauma therapy for former child soldiers in northern uganda: A randomized controlled trial. *JAMA.* Aug 3 2011;306(5):503-512.
58. Stenmark H, Catani C, Neuner F, Elbert T, Holen A. Treating PTSD in refugees and asylum seekers within the general health care system. A randomized controlled multicenter study. *Behav Res Ther.* Oct 2013;51(10):641-647.
59. Sloan DM, Marx BP, Bovin MJ, Feinstein BA, Gallagher MW. Written exposure as an intervention for PTSD: A randomized clinical trial with motor vehicle accident survivors. *Behav Res Ther.* Oct 2012;50(10):627-635.
60. Resick PA, Galovski TE, O'Brien Uhlmansiek M, 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.* Apr 2008;76(2):243-258.
61. Linehan M. *Cognitive-behavioral treatment of borderline personality disorder.* New York: Guilford Press; 1993.
62. Cloitre M, Stovall-McClough KC, Nooner K, et al. Treatment for PTSD related to childhood abuse: A randomized controlled trial. *American Journal of Psychiatry.* 2010;167(8):915-924.
63. Walser RD, Westrup D. *Acceptance and commitment therapy for the treatment of post-traumatic stress disorder and trauma-related problems: A practitioner's guide to using mindfulness and acceptance strategies.* New Harbinger Publications; 2007.
64. 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.* Jun 2015;38:25-38.
65. Spiegel H, Spiegel D. *Trance and treatment: Clinical uses of hypnosis.* American Psychiatric Pub; 2008.
66. Brom D, Kleber RJ, Defares PB. Brief psychotherapy for posttraumatic stress disorders. *J Consult Clin Psychol.* Oct 1989;57(5):607-612.
67. 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.* Aug 2003;71(4):706-712.
68. Foa EB, Rothbaum BO, Riggs DS, Murdock TB. Treatment of posttraumatic stress disorder in rape victims: A comparison between cognitive-behavioral procedures and counseling. *J Consult Clin Psychol.* Oct 1991;59(5):715-723.
69. Sloan DM, Feinstein BA, Gallagher MW, Beck JG, Keane TM. Efficacy of group treatment for posttraumatic stress disorder symptoms: A meta-analysis. *Psychological Trauma: Theory, Research, Practice, and Policy.* 2013;5(2):176.
70. Hoskins M, Pearce J, Bethell A, et al. Pharmacotherapy for post-traumatic stress disorder: Systematic review and meta-analysis. *Br J Psychiatry.* Feb 2015;206(2):93-100.
71. VA Cooperative Study #563. Prazosin and combat trauma PTSD (PACT). *ClinicalTrials.gov, NCT00532493.* Accessed February 16, 2016.
72. Raskind MA, Peskind ER, Kanter ED, et al. Reduction of nightmares and other PTSD symptoms in combat Veterans by prazosin: A placebo-controlled study. *Am J Psychiatry.* Feb 2003;160(2):371-373.
73. Raskind MA, Peskind ER, Hoff DJ, 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.* Apr 15 2007;61(8):928-934.

74. Raskind MA, Peterson K, Williams T, et al. A trial of prazosin for combat trauma PTSD with nightmares in active-duty soldiers returned from Iraq and Afghanistan. *Am J Psychiatry.* Sep 2013;170(9):1003-1010.
75. Germain A, Richardson R, Moul DE, et al. Placebo-controlled comparison of prazosin and cognitive-behavioral treatments for sleep disturbances in US military Veterans. *J Psychosom Res.* Feb 2012;72(2):89-96.
76. Wahbeh H, Senders A, Neuendorf R, Cayton J. Complementary and alternative medicine for posttraumatic stress disorder symptoms: A systematic review. *J Evid Based Complementary Altern Med.* Mar 27 2014;19(3):161-175.
77. Neylan TC, Marmar CR, Metzler TJ, et al. Sleep disturbances in the Vietnam generation: Findings from a nationally representative sample of male Vietnam veterans. *Am J Psychiatry.* Jul 1998;155(7):929-933.
78. Lewis V, Creamer M, Failla S. Is poor sleep in Veterans a function of post-traumatic stress disorder? *Mil Med.* Sep 2009;174(9):948-951.
79. Jacobson IG, Ryan MA, Hooper TI, et al. Alcohol use and alcohol-related problems before and after military combat deployment. *JAMA.* Aug 13 2008;300(6):663-675.
80. van den Berg DP, de Bont PA, van der Vleugel BM, et al. Prolonged exposure vs eye movement desensitization and reprocessing vs waiting list for posttraumatic stress disorder in patients with a psychotic disorder: A randomized clinical trial. *JAMA Psychiatry.* Mar 2015;72(3):259-267.
81. Markowitz JC, Petkova E, Biyanova T, Ding K, Suh EJ, Neria Y. Exploring personality diagnosis stability following acute psychotherapy for chronic posttraumatic stress disorder. *Depress Anxiety.* Dec 2015;32(12):919-926.
82. Mueser KT, Gottlieb JD, Xie H, et al. Evaluation of cognitive restructuring for post-traumatic stress disorder in people with severe mental illness. *The British Journal of Psychiatry.* 2015;206(6):501-508.
83. 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.* Jan 2016;84(1):95-100.
84. Halvorsen JO, Stenmark H, Neuner F, Nordahl HM. Does dissociation moderate treatment outcomes of narrative exposure therapy for PTSD? A secondary analysis from a randomized controlled clinical trial. *Behav Res Ther.* Jun 2014;57:21-28.
85. 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.* Sep 2009;47(9):737-743.
86. Gallegos AM, Streltzov NA, Stecker T. Improving treatment engagement for returning Operation Enduring Freedom and Operation Iraqi Freedom Veterans with posttraumatic stress disorder, depression, and suicidal ideation. *J Nerv Ment Dis.* May 2016;204(5):339-343.
87. Shemesh E, Annunziato RA, Rubinstein D, et al. Screening for depression and suicidality in patients with cardiovascular illnesses. *Am J Cardiol.* 2009;104(9):1194-1197.