

# Workplace Mental Health - Posttraumatic Stress Disorder

Effective October 1, 2025

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# **SUMMARY OF RECOMMENDATIONS**

The following summary table contains evidence-based recommendations for evaluating and managing posttraumatic stress disorder (PTSD) from the Workplace Mental Health Panel. These recommendations are based on critically appraised higher quality research evidence or, when such evidence was unavailable or inconsistent, on expert consensus as required in ACOEM's Methodology. Recommendations are made under the following categories:

- Strongly Recommended, "A" Level
- Moderately Recommended, "B" Level
- Recommended, "C" Level
- Insufficient Recommended (Consensus-based), "I" Level
- Insufficient No Recommendation (Consensus-based), "I" Level
- Insufficient Not Recommended (Consensus-based), "I" Level
- Not Recommended, "C" Level
- Moderately Not Recommended, "B" Level
- Strongly Not Recommended, "A" Level

Category	Recommendation	Evidence
Diagnostic Interventions	Screening Tools for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Psychological/Psychiatric Evaluation for Acute Stress Disorder (ASD) or Posttraumatic Stress Disorder (PTSD)	Recommended, Insufficient Evidence (I)
	Psychometric Testing for Acute Stress Disorder (ASD) or Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Pharmacogenomic Testing for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Functional MRI for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Insufficient Evidence (I)
Education and Exercise	TARGET Educational Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Educational Training for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Aerobic Exercise for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)

Category	Recommendation	Evidence
	Strengthening and Resistance Exercises for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Yoga for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
Behavioral and Psychological	Group Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
Interventions	Cognitive Behavioral Therapy for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Cognitive Processing Therapy for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Online or Computer-Administered CBT for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Stress Inoculation Training for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Insufficient Evidence (I)
	Imagery Rehearsal Training for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Brief Eclectic Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Narrative Exposure Therapy for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Seeking Safety Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Dialectical Behavioral Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Acceptance and Commitment Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Behavioral Activation for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Insufficient Evidence (I)
	Guided Imagery for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Mindfulness for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)

Category	Recommendation	Evidence
	Meditation for Posttraumatic Stress Disorder (PTSD)	Recommended, Insufficient Evidence (I)
	Well-Being Therapy for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Insufficient Evidence (I)
	Exposure Therapy for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Virtual Reality Exposure Therapy for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Individual Debriefing for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Group Debriefing for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Psychodynamic Psychotherapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Interpersonal Therapy for Posttraumatic Stress Disorder (PTSD)	Recommended, Insufficient Evidence (I
	Present-Centered Therapy for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Skills Training for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Hypnotherapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Combined Eye Movement Desensitization and Reprocessing (EMDR) with Cognitive Behavioral Therapy (CBT) for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Tapping Techniques (Thought Field Therapy, Emotional Freedom Therapy) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Emotional Freedom Techniques (EFT) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Neurofeedback (Brain-Computer Interface) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)

Category	Recommendation	Evidence
	Written Exposure Therapy/Writing Therapy for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Animal-Assisted Therapy for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Self-help Apps for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Sleep Hygiene for Posttraumatic Stress Disorder (PTSD)	Recommended, Insufficient Evidence (I)
Medications	Sertraline (Zoloft) for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Paroxetine (Paxil) for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Fluoxetine (Prozac) for Posttraumatic Stress Disorder (PTSD)	Recommended, Insufficient Evidence (I)
	Fluvoxamine for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Escitalopram (Lexapro) for Posttraumatic Stress Disorder (PTSD)	Moderately Not Recommended, Evidence (B)
	Citalopram (Celexa) for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Vilazodone (Vibryd) for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Vortioxetine for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Venlafaxine for Posttraumatic Stress Disorder (PTSD)	Moderately Recommended, Evidence (B)
	Amitriptyline for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Desipramine for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Imipramine (Tofranil) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)

Category	Recommendation	Evidence
	Nortriptyline (Pamelor) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Mirtazapine (Remeron) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Phenelzine (Nardil) for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Trazodone for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Nefazodone for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)
	Bupropion (Wellbutrin, Zyban) for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Benzodiazepines for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Gabapentin for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Lamotrigine (Lamictal) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Topiramate (Topamax) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Valproic Acid for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Tiagabine (Gabatril) for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Aripiprazole (Abilify) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Quetiapine (Seroquel) for Posttraumation Stress Disorder (PTSD)	Recommended, Insufficient Evidence (I)
	Risperidone (Risperdal) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Olanzapine (Zyprexa) for Posttraumatic Stress Disorder (PTSD)	Recommended, Evidence (C)

Category	Recommendation	Evidence
	Propranolol for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Prazosin (Minipress) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Guanfacine (Intuniv) for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Clonidine for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Doxazosin (Cardura) for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Cannabinoids for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Ketamine for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Insufficient Evidence (I)
	MDMA for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Nutraceuticals for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Omega-3 Fatty Acids for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Oxytocin for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Hydrocortisone for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
Electrical Therapies	Transcranial Magnetic Stimulation (TMS/rTMS) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Transcranial Direct Current Stimulation (TDCS) for Posttraumatic Stress Disorder (PTSD)	No Recommendation, Insufficient Evidence (I)
	Deep Brain Stimulation for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Evidence (C)
	Vagal Nerve Stimulation for Posttraumatic Stress Disorder (PTSD)	Not Recommended, Insufficient Evidence (I)

# **INTRODUCTION**

Responses to physical and psychological trauma range widely <sup>(1, 2)</sup> and can include withdrawal, depressed mood, anxiety, nonspecific somatic complaints, acute stress disorder (ASD), and posttraumatic stress disorder (PTSD).

Acute stress disorder occurs within the first month after a traumatic event. PTSD is not diagnosed until more than 1 month after a traumatic event. PTSD and ASD can be categorized based on mechanism (e.g., war-related trauma, other trauma, death) or severity (e.g., disabled, partially disabled, not disabled).

Approximately 41% of the US adult population has been exposed to at least one potentially traumatic event in their lifetime <sup>(3)</sup>. The same study reported that the prevalence of posttraumatic stress symptoms in the past year was 2.1% and the prevalence of PTSD in the past year was 0.7% among adults in the United States <sup>(3)</sup>. Thus, a small proportion of those exposed to extreme stressors go on to develop PTSD. When patients develop PTSD, one study found that 20%, 27%, 50% and 77% of cases recovered within 3 months, 6 months, 24 months, and 10 years, respectively <sup>(4)</sup>, although others report higher recovery rates <sup>(5, 6)</sup>. However, while this study determined that patients were symptomatic after those periods of time, it did not explore whether or not these patients had any disability secondary to PTSD. A systematic review reported the remission rate for PTSD ranged from 6% to 92%, highlighting a relative lack of quality studies <sup>(1)</sup>. The diagnosis of PTSD has also been associated with the stigma of being a perceived sign of weakness, especially in military or first responders. The presence of perceived stigma and lack of organizational support for PTSD sufferers has been associated with increased risk of PTSD symptoms <sup>(7)</sup>.

In a meta-analysis of 30 studies including 2.1 million patients with PTSD, 47% of patients had an increased risk of subsequent mortality and 32% had an increased time to death in studies reporting time-to-event data <sup>(8)</sup>. Because the substrate populations were largely male and veterans, the degree(s) to which other factors may drive these data are unclear. Regardless of effects of potential confounding factors and/or effect modification, patients with PTSD may have increased risk of death, which indicates that secondary preventive measures may be necessary.

The types of trauma commonly associated with PTSD include experiencing an actual or potential severe injury, life-threatening circumstances, a physical or sexual assault, or other extreme social or natural events. The prevalence rates are difficult to specify, as the risks of industrial accidents, motor vehicle crashes, assault, and sexual trauma vary from one setting to the next.

When considering the prevalence of PTSD, it may be helpful to review the prevalence of traumas that could potentially cause PTSD. The Bureau of Labor Statistics (BLS) notes that in 2023, there were a total of 5,283 fatal work injuries recorded in the United States, with a fatal injury rate of 3.5 per 100,000 full-time equivalent (FTE) workers <sup>(9)</sup>. The BLS does not document how many of these fatalities were witnessed by one or more coworkers, but witnessing a fatal injury is a trauma sufficient to precipitate acute stress disorder or PTSD in the observer. The BLS also notes that workplace violence—including assaults and suicides—accounted for 14 percent of all work-related fatal occupational injuries in 2016 <sup>(9)</sup>.

Nonfatal injuries can also be sufficiently traumatic to precipitate PTSD. In particular, traumatic amputations, impalement, crush injuries, motor vehicle accidents, falls from height, burns, explosions, animal attacks, and assaults could also potentially precipitate PTSD. Interestingly, according to BLS data, in 2016 violent workplace injuries were more common than work-related motor vehicle injuries.

Studies of trauma suggest that the risk of PTSD is associated with both the severity and the type of the trauma. The World Health Organization (WHO) reported the highest proportions of the burden of PTSD worldwide are rape (13.1%), sexual assault (15.1%), being stalked (9.8%), and the unexpected death of a loved one (11.6%) <sup>(10)</sup>. One study of trauma severity found that "the prevalence of PTSD approached 100% when traumatic exposure reached extreme levels" <sup>(11)</sup>. In the occupational medicine setting, the trauma of combat (as opposed to assault or being threatened with a weapon) is generally confined to members of the military with war-related military service. In contrast, the trauma of rape or sexual assault can occur in either the military or civilian workplace. Note, however, that the Bureau of Labor Statistics does not report data on sexual assault.

# **SIGNS AND SYMPTOMS**

There are many symptoms of PTSD and ASD <sup>(12)</sup>. Symptoms must be unrelated to medication, substance use, and other illnesses. PTSD may occur along with other conditions, such as depression or anxiety disorders.

PTSD symptoms include the following (13, 14, 15):

- Re-experiencing or flashbacks of event
- Unwanted or intrusive memories
- Repetitive and distressing images or sensations
- Nightmares or bad dreams
- Frightening thoughts
- Avoidance of settings, people, and/or places that remind of the event(s) or experience(s)
- Avoiding thoughts or feelings of the event(s)
- Interference with daily life (e.g., relationships and/or work)
- Restlessness
- Being easily startled, hyperarousal
- Hypervigilance
- Feeling tense or on edge
- Feeling stressed
- Difficulty with sleeping and sleep disturbance
- Fatigue
- Anger management issues, angry outbursts
- Negative thoughts about oneself or the world
- Distorted feelings (e.g., guilt, blame)
- Trouble remembering key features of the traumatic event
- Loss of interest in enjoyable activities
- Alienation and/or detachment from friends and family

Signs are fewer in number, and frequently none of these will be present. When present, they may include the following:

- Tachycardia
- Tachypnea
- Sweating while re-experiencing the event or telling of it
- Ease of startle

To be diagnosed with PTSD, an adult must meet the first criterion (exposure to a traumatic event involving actual or threatened death, serious injury, or sexual violence; the exposure can occur through direct experience, witnessing the event, learning about it happening to a close relative or friend, or repeated exposure to aversive details of the trauma) and have all of the following for at least 1 month that are definitively linked to the index incident:

- At least one re-experiencing symptom (flashbacks, recurring memories and/or dreams, distressing thoughts, physical signs of stress)
- At least one avoidance symptom (staying away from places, events, or objects that are reminders of the experience; avoiding thoughts or feelings related to the traumatic event)
- At least two arousal and reactivity symptoms (being easily startled; feeling tense, on guard, or on edge; having difficulty concentrating; having difficulty falling asleep or staying asleep; feeling irritable and having angry or aggressive outbursts; engaging in risky, reckless or destructive behavior)
- At least two cognition and mood symptoms (trouble remembering key features of the traumatic event; negative thoughts about oneself or the world; exaggerated feelings of blame directed toward oneself or others; ongoing negative emotions, such as fear, anger, guilt, or shame; loss of interest in previous activities; feelings of social isolation; difficulty feeling positive emotions such as happiness or satisfaction).

# **INITIAL ASSESSMENT**

The initial assessment requires a comprehensive patient history. The initial step is to define the trauma exposure, ascertain its severity, and real or perceived immediacy to the patient. For PTSD or ASD, the severity should involve either actual or potential threat of death, serious injury or sexual violence <sup>(12)</sup>. Evaluation of topics such as current living situation, employment, education, social interaction levels, substance use, having to work in the same location and or at the same job task where the trauma occurred, and childhood experience should all be considered. While returning to work at the same job site or performing the same job tasks where the trauma occurred may trigger flashbacks, returning to work at a different job task or site may serve as a therapeutic distraction. Assessment of and testing for secondary gain factors and potential factitious disorder and feigning is often required in occupational settings (see also Psychometric Testing). A thorough examination of both physical and mental symptoms is also required in order to differentiate between PTSD and ASD (which differ by duration of >30 days or <30 days duration) from another psychological disorder.

# **ASSESSMENT MEASURES**

There are at least three types of psychological measures: screening tools, outcome measures, and psychological inventories. In most cases, a screening tool attempts to determine if there are any signs that a particular diagnosis might be present and should be further investigated (e.g., an assessment that indicates a referral to a mental/behavioral health professional to determine if PTSD is present). In other cases, screening methods may be used to identify patients that might be a candidate for a certain type of treatment (e. g. an assessment that indicates a referral to a surgeon to assess whether a patient's lumbar condition might respond to a surgical intervention). In either case, a screening assessment is not definitive, but rather serves as an indication that further clinical consideration is indicated prior to making a definitive judgment.

A screening measure is different than an outcome measure. For example, a clinical screen for PTSD would probably include items regarding whether or not the patient was exposed to a traumatic event. Such an item would not be on an outcome measure. That is because an outcome measure only tracks changeable features, and treatment cannot change the historical fact that the patient was exposed to a traumatic event. Thus, a screening measure typically focuses on a few symptoms that may signal a disorder or provide baseline data for monitoring, whereas an outcome measure assesses changeable aspects of a condition which could potentially respond to treatment.

After screening, patients who are thought to potentially have PTSD requiring treatment may be evaluated with a comprehensive evaluation and treated based on that evaluation. Some may undergo psychometric testing with psychological inventories.

Psychological inventories are multidimensional measures that are generally not directly tied to a particular DSM diagnosis and are often not used to assess outcome either. Similar to a clinical interview or taking a medical history, these are intended to provide a broad description of the patient, by measuring a constellation of traits deemed to be relevant to the psychological examination. For a history and psychological examination, a mental/behavioral health professional may use an interview and one or more psychological inventories to assess personality traits, general signs of psychiatric syndromes, psychological coping styles, or other psychiatric constructs. For a biopsychosocial inventory, these would include the assessment of physical symptoms, physical and psychological coping styles, personality traits and an assessment of social support and conflicts.

# **PSYCHOLOGICAL EXAMINATION**

An event is psychologically traumatic to the extent that it is cognitively disorienting and emotionally profound. Psychological trauma has been defined as involving "the loss of the assumptive world." The "assumptive world" is the belief system reflecting all that a person assumes to be true about life, the world, the self and others. These assumptions are grounded on previous experience and are the basis for what a person believes to be true or real, and provide a sense of values, direction and purpose in life (16, 17, 18, 19). A traumatic event is one that in an instant can invalidate all of these cognitive assumptions, leaving the patient feeling profound disorientation (e.g., "I never imagined that this could happen to me."). A traumatic event is also one that elicits profound emotions, including overwhelming

feelings of loss, terror, horror, rage, or guilt. However, learning something deeply upsetting, such as that a lifelong employer is about to lay off them (and only them), would not meet the criteria.

The natural history of PTSD usually begins with acute stress disorder (which is definitionally within 3-30 days of the event). However, following a psychological trauma, a denial of reality, profound dissociation/detachment or amnesia sometimes delays the onset of severe autonomic arousal and the loss of the assumptive world, as the patient may be too cognitively disoriented to conceptualize the events, or to recognize emotions. This may delay the onset of PTSD as well.

The psychological assessment of PTSD begins with diagnosis but goes far beyond the mere determination that the diagnosis exists. PTSD can be associated with multiple other psychological conditions and can evolve over the course of time. In order to develop a treatment plan for PTSD, it is necessary to provide a psychological and perhaps biopsychosocial description of patient's condition, and from that, to develop a treatment plan. The process could be described using the Vortex Paradigm model seen in the Workplace Mental Health Introduction (Figure 1).

The assessment of PTSD must include consideration of the patient's psychiatric history. For example, prior to the trauma, was the patient a resilient person, or insecure, prone to anxiety, and suffering from depression and negative thinking? Prior to the trauma, was the patient stoic, or prone to catastrophizing? Was this the first trauma, or is the patient a survivor of prior psychologically traumatic events, either in adulthood or childhood? Did the patient deal with past traumatic events by substance use? Is the patient prone to feelings of entitlement? Pre-existing risk factors could predispose the patient to exhibit a more intense reaction to the traumatic event.

There is also a social aspect to PTSD assessment. Patients with PTSD are trying to regain a sense of personal security, and often must redefine relationships. Consequently, the patient's support system is especially important. Thus, important aspects of PTSD assessment include assessing the patient's degree of perceived support from family, workplace, and clinicians. How does the patient's role change at work and at home? Does the patient feel supported in those environments, or are those environments rife with conflict? Does the patient have a clear pathway for return to work and functioning, or was this a disabling injury? Instead of disabling injury since the focus of the guidelines is on functional impairment, this can be re-written to say "was this an injury resulting in functional impairment"

There are other social aspects to PTSD. Was the injury the result of random events, or does the patient feel victimized by the irresponsible behavior of another? Is the patient being asked to return to work at the job tasks where the trauma occurred? Is there a sense of moral injury as a result of military, other trauma, or forced exposure (e.g., COVID)? Is the patient litigating for financial compensation, and will the patient's report of symptoms alter disability settlements? These factors can shape the course of recovery.

Lastly, there may be a biological aspect to the evaluation of PTSD. In the case we have been considering, PTSD is associated with a severe physical injury to the self. In other cases, though, PTSD is a purely psychic trauma. For example, suppose in this scenario, the patient did not sustain any physical injury at all, but rather by accident caused a friend's hand to be amputated. This is a purely psychic injury and is traumatic in a different way.

When physical injury co-occurs with PTSD, then PTSD and its related conditions may be superimposed on a chronic pain disorder. This requires a biopsychosocial assessment model, rather than psychological assessment (see ACOEM Chronic Pain Guideline). In conjunction with the physical injury, intense emotional distress associated with PTSD may contribute to central sensitization, heightened pain perception, somatic preoccupation, stress-related psychophysiological disorders, and the perception of disability. Social avoidance or phobias may interfere with adherence to treatment, as can distorted cognitions such as catastrophizing or fear-avoidance/kinesiophobia. The overall pain the patient experiences may be a combination of nociceptive pain, neuropathic pain including phantom pain, and vivid recollections of the pain experienced during amputation, which may activate the brain's pain center, blurring the distinction between nociceptive and psychic pain.

For the mental/behavioral health professional, the assessment of the patient goes well beyond simply determining whether or not PTSD exists. Rather, by describing the patient's condition from a biopsychosocial perspective, a treatment plan can be devised. To accomplish this, the mental/behavioral health professional should select both interview questions and psychological measures that allow the comprehensive assessment and description of the patient's condition. Further, this assessment should include measures of validity in order to assess any tendency on the part of the patient to bias the information that is presented. Finally, consideration should be given to the possibility that the measures and methods of assessment used have taken steps to ensure fairness to the individual patient and are not prone to bias against patients based on age, race, ethnicity, language, education, gender, medical status, or other relevant dimensions. Based on this information, the biopsychosocial assessment of the patient attempts to diagnose the patient, describe the biopsychosocial features of a patient's condition, and to develop a plan to facilitate the patient's return to function.

# **COMORBIDITIES**

Individuals with PTSD are 80% more likely than those without PTSD to have at least one other mental disorder, including depression, anxiety, or substance use (20).

In the National comorbidity survey, men with PTSD had 6. 9 times higher odds of having a major depressive episode, while women with PTSD had a 4. 1 times higher odds of major depressive episode. The National comorbidity survey also found that men with PTSD had a 5. 9 times higher odds of having generalized anxiety disorder, while women had 2. 8 times higher odds of generalized anxiety disorder <sup>(21)</sup>. Stress disorders have also been implicated in the etiology of various somatic conditions. Overall, there is evidence that suggested PTSD is associated with gastrointestinal disorders and cardiovascular disease <sup>(22)</sup>.

# **DIAGNOSTIC CRITERIA**

ASD and PTSD have comparable diagnostic criteria, differing by duration of symptoms with ASD lasting 3-30 days and PTSD lasting over 30 days <sup>(12)</sup>. After ruling out factitious disorder, malingering or other primary or secondary gain issues, the diagnosis of PTSD is based primarily on symptoms <sup>(12)</sup>, although signs (e.g., tachycardia on re-experiences or intrusive thoughts) may be helpful. Psychometric testing is also often helpful. While significant

trauma exposure (death, serious injury, sexual violence <sup>(12)</sup> is the *essential condition* for PTSD to develop, the stressor alone may not be sufficient to generate PTSD <sup>(23)</sup>. Increasingly, a comprehensive understanding of PTSD is believed possible only by looking beyond the historical conceptualization of PTSD as a pathological but essentially universal response to encountering a traumatic stressor <sup>(23, 24)</sup>. While this was the most prevalent view of the diagnosis since it was first specified in the DSM-III in 1980 <sup>(25)</sup>, this diagnostic conceptualization illustrates that the predominant recent diagnostic systems, including the DSM-IV-TR and ICD-10, approach the classification of fear circuitry and stress-based disorders through "neither mode-of-acquisition-based nor brain-evolution-based" approaches <sup>(26)</sup>.

Concerns about overdiagnosis of PTSD have been expressed, in part due to increasing rates of diagnosis, while others have expressed concerns about underdiagnosis (27, 28, 29, 30). Whether underdiagnosis or overdiagnosis, it is critical to assure PTSD diagnoses meet diagnostic criteria while excluding confounding diagnoses and situations (e.g., normative and temporary responses to stress, a more accurate diagnosis such as Adjustment Disorder; feigning, especially in compensation settings that are susceptible to secondary gains).

Diagnostic criteria for PTSD differ somewhat depending on the criteria used, with DSM-5-TR and ICD-11 being the two common systems.

#### **DSM-5-TR CRITERIA**

"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.
- 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). Note: In children older than 6 years, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed.
  - 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s). Note: In children, there may be frightening dreams without recognizable content.
  - 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.) Note: In children, trauma-specific reenactment may occur in play.
- 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).
- 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 of 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).
- 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 remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).
  - 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," 'The world is completely dangerous," "My whole nervous system is permanently ruined").
  - 3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.
  - 4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).
  - 5. Markedly diminished interest or participation in significant activities.
  - 6. Feelings of detachment or estrangement from others.
  - 7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
- 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).

- F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.
- G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- 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 the following:

- 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).
- 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)"
(12)

# ICD-10-CM CRITERIA (F43. 1)

#### ICD-11 criteria include:

- Exposure to an extremely threatening or horrific event or series of events.
- Symptoms include re-experiencing, avoidance, and persistent perceptions of heightened current threat
- Symptoms last for at least several weeks.
- There is significant impairment in personal, family, social, educational, occupational, or other important areas of functioning.

# **DIAGNOSTIC DIVERGENCE**

There are multiple diagnostic definitions of PTSD, which are similar yet distinct. The DSM-5-TR and ICD-11 definitions of PTSD are listed above, and a summary of the divergence of PTSD definitions are listed below. Although they all adopt the same core set of symptoms and thus have considerable overlap, there are noteworthy differences between them. It should be noted that although the DSM-5-TR definition of PTSD is probably the most accepted one in the United States (see above) and ICD-11 is the standard elsewhere, the vast majority of moderate- and high-quality PTSD research reviewed in this guideline is based on older diagnostic criteria. Knowledge of the differences between these definitions

may be helpful in interpreting some research findings. It is also necessary to distinguish between related issues such as burnout, compassion fatigue, and PTSD.

#### **DIAGNOSTIC RECOMMENDATIONS**

# **SCREENING TOOLS**

There are various posttraumatic stress disorder screening tools. The PCL-5 is a screening tool commonly used to detect PTSD <sup>(31)</sup>. A PTSD checklist has also been developed <sup>(32)</sup>. Other screening tools (e.g., anxiety, depression, substance use, suicidality) are reviewed in relevant guidelines. Importantly, screening tools are not diagnostic, rather screening tools should beget further structured interview, clinical examination inquiries, and/or diagnostic testing.

# **SCREENING TOOLS FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### Recommended

Screening tools are recommended for the evaluation of patients who are at risk of posttraumatic stress disorder (PTSD).

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

#### **Indications**

Patients at risk of PTSD (e.g., those have sustained an at-risk event). Evaluation should include focus on ASD, PTSD, anxiety disorders, depressive disorders, substance use disorders, and risk of suicide.

#### **Benefits**

Earlier identification of potential PTSD, assisting directing the patient to appropriate mental health services that include diagnostic confirmation.

# Harms

Medicalization of cases that would have resolved without treatment. Inappropriate labeling, especially in the absence of confirmatory analyses.

# Frequency/Dose/Duration

Generally only one administration.

# Rationale

There are several quality studies for most of the PTSD screening tools, and screening tools include: PTSD Checklist, Injured Trauma Survivor Screen, Primary Care PTSD Screen,

Posttraumatic Distress Inventory, International Trauma Questionnaire, and the Posttraumatic Adjustment scale, which mostly assessed nonoccupational populations (Hawn et al., 2022, Levitt et al., 2021, Dupont et al., 2024, Kleiman et al., 2020, Moshier et al., 2018, Schroeder et al., 2024, Danböck et al., 2023, Litvin et al., 2024, Garabiles et al., 2023, Georgescu, 2024, Blackwell, 2023, Blanchard et al., 2023, Hoeboer et al., 2024, Stockton et al., 2024). The Injured Trauma Survivor Screen, Posttraumatic Distress Inventory, Clinician-Administered PTSD Scale, Primary Care PTSD, screen and PTSD Checklist have been suggested as being successful in post-injury, veterans, and first responder patients (Ennis et al., 2021, Robertson, 2019, Guest et al., 2018, Jenkins-Guarnieri et al., 2023, Roberts et al., 2021, Raines et al., 2024, Weathers et al., 2018, Morrison et al., 2021, Lee et al., 2024, Bressington et al., 2024, Bovin et al., 2021). Reviews have suggested screening tests have sufficient accuracy to be used for screening at-risk populations (Meneses et al., 2021, Shields et al., 2021). PTSD screening tools are efficient, low cost, and are recommended.

# **Evidence**

A comprehensive literature search was conducted using PubMed, CINAHL, Cochrane Library, and Google Scholar with date limits of 2018 to the present using the following terms: Screening tools; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, and efficiency. We found and reviewed 287 articles in PubMed using Most Recent tab, and we did a secondary search in PubMed using Best Match tab to find and review 287 articles, 219 in CINAHL, 195 in Cochrane Library, 17, 100 in Google Scholar, and 0 from other sources†. We considered for inclusion 7 from PubMed, 7 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 14 articles considered for inclusion, 13 diagnostic studies and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **PSYCHOLOGICAL / PSYCHIATRIC EVALUATION**

There are numerous screening and psychometric testing batteries. Screening tools generally include fewer items, emphasize high sensitivity, and require less education to administer. Psychometric tests generally have secure item pools, specific administration protocols that must be followed, greater specificity, and require professionally trained health professionals to administer. Although these instruments may suggest a diagnosis, neither screening nor psychometric tests are capable of making a diagnosis. The diagnosis should only be concluded after careful analysis of all available data, including from a thorough history and/or clinical interview.

# PSYCHOLOGICAL/PSYCHIATRIC EVALUATION FOR ACUTE STRESS DISORDER (ASD) OR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Psychological/psychiatric evaluation is recommended for patients with potential acute stress disorder (ASD) or posttraumatic stress disorder (PTSD).

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** High

#### **Indications**

Evaluation of patients with potential ASD or PTSD. Evaluation is recommended to especially include focus on ASD, PTSD, anxiety disorders, depressive disorders, substance use disorders, and risk of suicide.

#### **Benefits**

Make and/or confirm diagnosis after analyses of screening, test results and interview.

# Frequency/Dose/Duration

Initial evaluation to diagnose. Subsequent appointments for treatment. Includes performance and interpretation of screening and diagnostic testing.

#### Rationale

There are no quality studies comparing mental health evaluations to assessments without them, which is typical of older and traditional evaluation processes; thus, the evidence is insufficient. Yet, mental health evaluations are essential to make, secure, and/or confirm a diagnosis, so there is high confidence that they are needed. They also set the stage for subsequent treatment plans. Therefore, psychological/psychiatric evaluation is recommended for patients with ASD or PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, CINAHL, Cochrane Library, and Google Scholar with date limits of 2018 to the present using the following terms: Interview, Psychological OR psychiatric evaluation; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, and efficiency. We found and reviewed 1780 articles in PubMed using Most Recent tab, and we did a secondary search in PubMed using Best Match tab to find and review 1, 780 articles, 101 in CINAHL, 437 in Cochrane Library, 20, 300 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from

other sources. Of the 4 articles considered for inclusion, 3 diagnostic studies and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### **PSYCHOMETRIC TESTING**

There are many psychometric tests that have been used for evaluation of mental health including for ASD and PTSD patients. Examples include Acute Stress Disorder Scale, Clinically Administered PTSD Scale (33, 34, 35, 36, 37, 38, 39, 40, 41). Tests for feigning are also commonly viewed as necessary in testing patients with PTSD; feigning behavior can occur for multiple reasons. Further, when feigning behavior is suspected or identified, a more in-depth evaluation should occur and this evaluation must include the assessment of multiple information sources (e.g., medical records, employment records, surveillance tapes, if available, etc.).

A cautionary note is that although symptom validity testing is a crucial aspect of PTSD diagnosis, symptom overreporting can occur for many reasons, including factors directly related to genuine PTSD symptoms (e.g., inattentive responding, which can be due to concentration difficulties in PTSD). Symptom overreporting can also be caused by dissociation and alexithymia, both of which can be related to genuine PTSD (42). As such, symptom overreporting does *not* necessarily preclude a diagnosis of PTSD. A patient could be simultaneously engaging in symptom overreporting while also having a genuine diagnosis of PTSD. For this reason, it is important that diagnostic assessment of PTSD occur in a multimodal, multi-method fashion, and be done by a professional who is trained to properly interpret symptom validity measures in a biopsychosocial context.

# PSYCHOMETRIC TESTING FOR ACUTE STRESS DISORDER (ASD) OR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Psychometric testing is recommended for individuals presenting with signs and symptoms consistent with acute stress disorder (ASD) or posttraumatic stress disorder (PTSD).

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** High

#### **Indications**

For individuals presenting with signs and symptoms consistent with ASD or PTSD, and/or among those having screed positive for PTSD/ASD. Evaluation should especially include focus on ASD, PTSD, anxiety disorders, depressive disorders, substance use disorders, and

risk of suicide. Tests to detect feigning are often required, especially in the context of those seeking compensation.

#### **Benefits**

Provide psychometric evidence regarding potential for ASD or PTSD or other mental health disorder.

#### **Harms**

Medicalization of cases that would have resolved without treatment. Inappropriate labeling if there is overreliance on a test in the absence of careful analyses of the entirety of the clinical evidence.

# Frequency/Dose/Duration

One-time test battery administration unless otherwise indicated. Requires administration by a professionally trained mental health professional (Hovens et al., 1994, Hyer, 1996, Griffin MG, 2004).

#### Rationale

There are moderate-quality studies that suggest utility of psychometric tests for ASD (Bryant et al., 2000, Edmondson et al., 2010) and PTSD (Hunt et al., 2017, Hovens et al., 1994, Hyer, 1996, Griffin MG, 2004, Foa et al., 2016, Foa et al., 2000, Pupo et al., 2011, Vaishnavi et al., 2006)(Byllesby et al., 2022, Garabiles et al., 2023, Georgescu, 2024, Guest et al., 2018, Hoeboer et al., 2024, Ito et al., 2019, Kleiman et al., 2020). Psychometric testing has negligible adverse effects, is moderately costly, and is recommended for assisting in the diagnosis of ASD and PTSD. Psychometric testing for other conditions (e.g., anxiety, depression) is reviewed in other guidelines.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, CINAHL, Cochrane Library, and Google Scholar with date limits of 2018 to the present using the following terms: Psychometrics OR psychometric tests; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, and efficiency. We found and reviewed 381 articles in PubMed using Most Recent tab, and we did a secondary search in PubMed using Best Match tab to find and review 381 articles, 7 in CINAHL, 235 in Cochrane Library, 17, 100 in Google Scholar, and 0 from other sources†. We considered for inclusion 38 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 45 articles considered for inclusion, 45 diagnostic studies and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **PHARMACOGENOMICS TESTING**

Pharmacogenomic testing has been used to attempt to customize treatment for patients with PTSD (43, 44, 45).

# PHARMACOGENOMIC TESTING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of pharmacogenomic testing in the evaluation of posttraumatic stress disorder (PTSD).

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

Quality studies have not shown that pharmacogenomic testing alters the clinical management of patients with PTSD (Kitzmiller et al., 2011). Therefore, there is no recommendation.

# **Evidence**

A comprehensive literature search was conducted using PubMed, CINAHL, Cochrane Library, and Google Scholar with date limits of 2018 to the present using the following terms: pharmacogenomic testing, pharmacogenomic testing; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, and efficiency. We found and reviewed 4 articles in PubMed using Most Recent tab, and we did a secondary search in PubMed using Best Match tab to find and review 4 articles, 0 in CINAHL, 1 in Cochrane Library, 3710 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **FUNCTIONAL MRI**

Functional MRI is purportedly sensitive to changes in neural activity after a traumatic brain injury, and thus some project it has a theoretical basis in the evaluation of PTSD (46, 47, 48, 49, 50, 51, 52)

# **FUNCTIONAL MRI FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### Not Recommended

Functional MRI is not recommended for the diagnosis of posttraumatic stress disorder (PTSD).

**Strength of evidence** Not Recommended, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There are a few quality studies assessing the use of functional MRI for the diagnosis of PTSD, however while these studies show some changes attributed to PTSD, they do not clearly define a distinct use that results in altered management (see also ACOEM TBI Guideline) (Ke et al., 2017, Jung et al., 2016, Fu et al., 2019, Fonzo et al., 2017, Etkin et al., 2019, Nkrumah et al., 2024)(Jantzen, 2010). While these studies suggest potentially promising research avenues to potentially assist in identifying therapeutic targets, at this time, they do not clearly define altered treatment paths. Thus, fMRI is not recommended for the diagnosis of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, CINAHL, Cochrane Library, and Google Scholar with date limits of 2018 to the present using the following terms: Functional MRI, Magnetic Resonance Imaging; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, and efficiency. We found and reviewed 899 articles in PubMed using Most Recent tab, and we did a secondary search in PubMed using Best Match tab to find and review 899 articles, 23 in CINAHL, 33 in Cochrane Library, 17600 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 diagnostic studies and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of

100 articles that contain no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### TREATMENT RECOMMENDATIONS

# **OVERVIEW**

Treatment recommendations are based on the available quality evidence as described in the <u>ACOEM Methodology</u>. Algorithms were also developed to assist clinicians. Consistent with other guidelines, *acute* denotes up to 1 month, *subacute* is from 1 to 3 months, and *chronic* is 3+ months. Accordingly, for simplification purposes, acute stress disorder falls only within the acute timeframe.

There are many trials of various interventions in nonoccupational populations, including refugees from various countries residing in European countries, non-Western victims of sexual abuse, and childhood abuse victims. These trials were generally excluded from the evidence base and decision-making process for specific guidance due to potential inapplicability of findings.

The primary initial intervention is cognitive behavioral therapy (CBT), which may include any or multiple of several methods or techniques. Exposure therapy (e.g., prolonged/exposure therapy, virtual reality training) is often incorporated as part of CBT and also has evidence of efficacy, although it is less frequently prescribed.

The primary non-psychological interventions are medications, and the strongest evidence is for SSRI and SNRI anti-depressants. The strongest and most consistent evidence is in support of sertraline. Other potential medications include paroxetine, mirtazapine, citalopram and venlafaxine. Aerobic and strengthening exercises are supported by quality data but may be less frequently prescribed and specific benchmarks of exercises have not been well defined.

There are few medications with FDA indications for PTSD. These recommendations are based upon the available quality data <sup>(53)</sup>. Additional important considerations are tolerability and compliance. Ambien and other sleeping aid medications, such as melatonin, diphenhydramine, or valerian, may be utilized but there is no quality literature to support usage.

Beyond the guidance and highest quality evidence, there also are known social determinants of outcome such as low education/illiteracy, poverty or cultural differences which can negatively affect outcomes. These issues are part of the biopsychosocial model. These are not psychological disorders per se, but supportive therapy and individualized problem-solving are often used to address these social factors that could otherwise interfere with care.

A guideline from the American Psychological Association <sup>(54)</sup> may be a helpful tool, especially for psychological interventions.

# **EDUCATION AND EXERCISE**

# **TARGET EDUCATIONAL THERAPY**

Education about a disorder is routine and customary in healthcare. Trauma Affect Regulation, also known as TARGET, is a type of educational therapy that has been used in the treatment of PTSD <sup>(55, 56)</sup>. Affect regulation teaches a specific set of skills called "FREEDOM" to help patients deal with emotional and physical reactivity to specific traumatic stimuli <sup>(55, 56)</sup>. FREEDOM stands for focusing, recognizing triggers, emotion awareness, evaluating thoughts, defining goals, choosing options, and making a positive contribution to the world by regulating emotions <sup>(55, 56)</sup>.

# TARGET EDUCATIONAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of TARGET educational therapy as an adjunct treatment for patients with posttraumatic stress disorder (PTSD).

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### **Indications**

Individuals with PTSD as an adjunct treatment.

#### **Benefits**

Resolution or improvement in PTSD symptoms.

#### **Harms**

14% of women reported worsening of symptoms (Ford et al., 2013).

# Frequency/Dose/Duration

Twelve 75-minute sessions for as long as necessary (Ford et al., 2013, Ford JD, 2006). Consists of three core TARGET components: education, teaching and guided practice of FREEDOM skill sequence, and experiential exercise (Ford et al., 2013, Ford JD, 2006).

# Indications for discontinuation

Resolution of symptoms, noncompliance, lack of efficacy, or adverse effects.

#### Rationale

There is sparse quality evidence for the use of TARGET for PTSD. The largest trial suggested efficacy, but participants (mothers with victimization-related PTSD) had low compliance and

high dropout problems, raising some issues about both robustness of the conclusion and applicability to an occupational population (Ford et al., 2011). One study compared TARGET to supportive group therapy, with both groups showing decreased PTSD symptom severity and the TARGET group showing improvement in forgiveness (Ford et al., 2013). TARGET has low adverse effects, is low to moderate cost depending upon treatment duration, and has some evidence to support efficacy. However, the study population is not clearly generalizable to a population of workers; thus, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TARGET; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2 articles in PubMed, 2 in CINAHL, 3 in Cochrane Library, 1 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **EDUCATIONAL TRAINING**

Education about a disorder is routine and customary in healthcare. However, educational training goes beyond mere education and may involve teaching skills to help patients deal with PTSD symptoms. Educational programs use various methods, including online training to conduct motivational interviewing, teaching goal setting, and behavioral task assignments (57, 58, 59)

# **EDUCATIONAL TRAINING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

# No Recommendation

There is no recommendation for the use of educational training for patients with posttraumatic stress disorder (PTSD).

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

Evidence regarding efficacy of education for a preventive and/or treatment strategy substantially conflicts. Some studies have shown an overall lack of efficacy (Sijbrandij et al., 2006), and one study reported efficacy (Ruzek et al., 2014). A comparative trial with a mindfulness app suggested comparable (in)efficacy (Cox et al., 2019). A trial of patients with both PTSD and LBP suggested efficacy, although it was not possible to distinguish effects regarding PTSD (Benedict et al., 2024). Clearly, education about a particular condition remains warranted; however, education as a stand-alone treatment strategy has inconclusive efficacy. Thus, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Education, Education training, Educational training; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 147 articles in PubMed, 2 in CINAHL, 97 in Cochrane Library, 136000 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 4 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### **EXERCISE**

Exercise has been used to treat PTSD symptoms <sup>(12, 60-62)</sup>. Those with PTSD are reportedly more likely to participate in unhealthy behaviors such as smoking, alcohol consumption, lack of exercise, or have comorbid conditions such as diabetes or obesity <sup>(63-69)</sup>.

Yoga has been used as an adjunctive therapy to address the cognitive, emotional, and physiological symptoms associated with PTSD (70-83).

# AEROBIC EXERCISE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Aerobic exercise is recommended for treatment of PTSD.

# **Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

#### **Indications**

PTSD symptoms sufficient to warrant treatment. Other first-line treatments include CBT, prolonged/exposure therapy, strengthening exercise and SSRIs. However, those with significant cardiac disease or significant potential for cardiovascular disease should be evaluated prior to instituting vigorous exercises with regard to health screening and risk stratification (ACSM, 2025).

#### **Benefits**

Reduction in PTSD symptoms, improved sleep, and improvements in overall well-being.

# **Harms**

Negligible.

# Frequency/Dose/Duration

Aerobic exercise (treadmill, walking, biking, etc.) for at least 3 times per week (LeBouthillier et al., 2017). Dose is not well defined in quality studies, however, exercise targets based on age-related heart rate targets may be helpful (e.g., American College of Sports Medicine).

### Indications for discontinuation

Resolution, non-compliance, unanticipated adverse event.

#### Rationale

Exercise has been used for treatment of PTSD (Brinsley et al., 2021, Ramos-Sanchez et al., 2021, Purnell et al., 2021, Björkman et al., 2022, Tan et al., 2023, Wang et al., 2023, Yuan et al., 2025). Several moderate-quality studies consistently suggest efficacy for both aerobic exercise (Bryant et al., 2023, Hall et al., 2020, Browne et al., 2021) and aerobic exercise combined with resistance training (Pieper et al., 2024, Jäger et al., 2024, Goldstein et al., 2018, Neylan et al., 2025, Greene et al., 2024, McGranahan et al., 2025, Fetzner et al., 2015, Powers et al., 2015, LeBouthillier et al., 2017). In another study (Fetzner et al., 2015), all three groups improved regardless of "attentional focus," which was hypothesized to influence the outcome yet appears to have not, as all groups had the same exercise regimen. Two studies had the limitation of waitlist and/or usual care biases (LeBouthillier et al., 2017). Systematic reviews have concluded there is efficacy of aerobic exercise (Björkman et al., 2022, Martinez-Calderon et al., 2024, Ramos-Sanchez et al., 2021, Wang et al., 2023, Yuan et al., 2025, Oppizzi et al., 2018, Jadhakhan et al., 2022). Aerobic exercise has low adverse effects, is of low to moderate cost depending upon whether achieved in group sessions or via a personal trainer or therapist, consistently shows efficacy, and thus is recommended for PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: aerobic exercise; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 776 articles in PubMed, 19 in CINAHL, 0 in Cochrane Library, 18200 in Google Scholar, and 0 from other sources†. We considered for inclusion 24 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 24 articles considered for inclusion, 15 randomized trials and 9 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### STRENGTHENING AND RESISTANCE EXERCISES FOR PTSD

#### Recommended

Strengthening and resistance exercises are recommended for treatment of PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

#### **Indications**

PTSD symptoms sufficient to warrant treatment. However, those with significant cardiac disease or significant potential for cardiovascular disease should be evaluated prior to instituting vigorous exercises, with regard to health screening and risk stratification (ACSM, 2021).

# **Benefits**

Reduction in PTSD symptoms, improved sleep, and improvements in overall well-being.

#### **Harms**

Negligible.

# Frequency/Dose/Duration

Strengthening and resistance exercises (e.g., weights) at least 2 times per week (LeBouthillier et al., 2017) for at least 30 minutes/session is recommended, which based on the published literature, and should nearly always be combined with aerobic exercises.

#### Rationale

Exercise has been used for treatment of PTSD (Brinsley et al., 2021, Ramos-Sanchez et al., 2021, Purnell et al., 2021, Björkman et al., 2022, Tan et al., 2023, Wang et al., 2023, Yuan et al., 2025). Nearly all of the quality evidence combined aerobic exercise with strengthening/resistance training (LeBouthillier et al., 2017, Powers et al., 2015, Fetzner et al., 2015, Pieper et al., 2024, Jäger, 2024, Goldstein et al., 2018, Neylan et al., 2025, Voorendonk et al., 2023, Greene et al., 2024, McGranahan et al., 2025). Small pilot studies solely assessed resistance training (Whitworth et al., 2019, Whitworth et al., 2019, Pebole et al., 2024). In another study (Fetzner et al., 2015), all three groups improved regardless of "attentional focus," which was hypothesized to influence the outcome yet appears to have not, as all groups had the same exercise regimen. Two studies had the limitation of waitlist and/or usual care biases (LeBouthillier et al., 2017). One trial included exercise in both arms to assess trauma-focused CBT vs. supportive care (Andersen et al., 2021). Systematic reviews have concluded there is efficacy of exercise (Björkman et al., 2022, Martinez-Calderon et al., 2024, Ramos-Sanchez et al., 2021, Wang et al., 2023, Yuan et al., 2025, Oppizzi et al., 2018, Jadhakhan et al., 2022). Strengthening exercise has low adverse effects, is of low to moderate cost depending upon whether achieved in group sessions or via a personal trainer or therapist. The evidence is nearly entirely combined with aerobic exercise. Thus, although there is consistently evidence of efficacy of combined exercises (LeBouthillier et al., 2017, Powers et al., 2015, Fetzner et al., 2015, Pieper et al., 2024, Jäger, 2024, Goldstein et al., 2018, Neylan et al., 2025, Voorendonk et al., 2023, Greene et al., 2024, McGranahan et al., 2025), strengthening/resistance exercises are recommended and should generally be prescribed in combinations of aerobic plus strengthening/resistance exercises for PTSD.

# **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: strengthening exercise; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 776 articles in PubMed, 19 in CINAHL, 0 in Cochrane Library, 18200 in Google Scholar, and 0 from other sources†. We considered for inclusion 24 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 24 articles considered for inclusion, 15 randomized trials and 9 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we

review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# YOGA FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Yoga is recommended for the treatment of patients with posttraumatic stress disorder (PTSD).

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

#### **Indications**

PTSD sufficient to require alternate therapies for symptom improvement. PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Various elements of CBT (including prolonged/exposure therapy) should generally be tried first; aerobic and strengthening exercise also should generally be tried ahead of yoga, although yoga may be appropriate for an earlier treatment strategy among patients with personal preference desiring this treatment. Often yoga is used in combination as an adjunct with other therapies such as CBT and/or medication.

#### **Benefits**

Improvements in PTSD symptoms. Increased flexibility, aerobic fitness, and overall well-being.

# Harms

Negligible, muscle soreness.

# Frequency/Dose/Duration

One of the higher-quality studies used weekly sessions consisting of 60 minutes per session for 10 weeks (van der Kolk et al., 2014), although other studies have reported efficacy with more intense intervention of 22 hours for 5 days, then weekly 2 hour group sessions for 4 weeks, then monthly for 5 months (Carter et al., 2013).

#### Indications for discontinuation

Lack of PTSD symptom improvement or sufficient improvement to not warrant further sessions; noncompliance; intolerance.

#### Rationale

Yoga has been used for treatment of PTSD (Taylor et al., 2020, Cramer et al., 2018, Kelly et al., 2018, Kysar-Moon et al., 2021, Yi et al., 2021, Nejadghaderi et al., 2024). Several moderate-quality studies nearly all suggest yoga improves PTSD symptoms (van der Kolk et al., 2014, Carter et al., 2013, Quiñones et al., 2015, Reddy et al., 2014)(Davis et al., 2020, Davis et al., 2023, Kelly et al., 2021, Yi et al., 2022). One trial suggested a lack of efficacy (Martin et al., 2015) and another suggested that CBT is superior (Haller et al., 2023). Another trial suggested equivalency with cognitive processing therapy (Zaccari et al., 2023). Some studies show sustained improvements for up to 6 months (Carter et al., 2013) and one study suggests symptom improvement up to 18 months (Rhodes et al., 2016). Systematic reviews have generally suggested weak evidence of efficacy (Cramer et al., 2018, Kelly et al., 2018, Kysar-Moon et al., 2021, Laplaud et al., 2023, Nejadghaderi et al., 2024, Taylor et al., 2020). Yoga has negligible adverse effects, is low to moderate cost (depending on whether self-directed or supervised), and has some evidence of efficacy. Therefore, yoga is recommended for adjunctive use in patients with PTSD, although the overall evidence suggests aerobic, with or without strengthening/resistance exercise should generally be trialed first.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Yoga; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 77 articles in PubMed, 60 in CINAHL, 55 in Cochrane Library, 16, 700 in Google Scholar, and 0 from other sources†. We considered for inclusion 18 from PubMed, 4 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 23 articles considered for inclusion, 16 randomized trials and 7 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# PSYCHOLOGICAL INTERVENTIONS AND COPING STRATEGIES GROUP THERAPY

Psychoeducational group therapy has three treatment phases:

- sharing personal traumatic event's effects on sense of self with group,
- exploring effects of events on an individual's interpersonal relationships and discussing coping skills,

and lastly exploring counseling and dealing with the trauma for the future (84, 85).

Group therapy has been suggested to be effective in helping patients with PTSD address interpersonal relationship problems and improve self-esteem <sup>(84, 85, 86)</sup>. A few studies have examined using couple's therapy as a form of group therapy to help patients manage PTSD symptoms <sup>(86, 87)</sup>.

# **GROUP THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### No Recommendation

There is no recommendation for the use of group therapy in the treatment of posttraumatic stress disorder (PTSD). However, cognitive processing therapy (CPT) can be administered in a group setting (see separate recommendation).

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

Group therapy approaches have been used for treatment of PTSD (Mahoney et al., 2019, Schwartze et al., 2019, Schleyer et al., 2022)(Classen et al., 2011, Resick et al., 2017, Wachen et al., 2022, Sloan et al., 2018, Beck et al., 2021, Neylan et al., 2025, Ready et al., 2018, Davis et al., 2019, Sautter et al., 2015, Harris et al., 2018, Sundquist et al., 2015). There is limited evidence assessing the use of group therapy compared with individualized treatment for PTSD. One study showed that couples-based group therapy was effective in in improving PTSD symptoms versus education (Sautter et al., 2015). However, despite having a usual care bias, there were no differences between groups which compared mindfulness theory to usual care (Sundquist et al., 2015). Group compared with individual cognitive processing therapy has also reportedly found better treatment gains in the individual sessions (Resick et al., 2017, Wachen et al., 2022). Multiple trials compared various group-based treatments, including one showing trauma-focused group psychotherapy vs. present-focused psychotherapy were superior to wait-listed controls (Classen et al., 2011), one showing group exposure therapy was superior to present-centered group therapy (Ready et al., 2018), another showed mindfulness-based stress reduction was superior to presentcentered group therapy) and one showed building spiritual strength was superior to group PCT (Harris et al., 2018). Systematic reviews also found limited and heterogeneity of the evidence (Mahoney et al., 2019, Schleyer et al., 2022, Schwartze et al., 2019).

Group therapy has low adverse effects, is moderate cost depending upon treatment duration, and has conflicting evidence of efficacy with some evidence suggesting individualized treatment is superior and other evidence suggesting the specific group-therapy content may be quite important. Thus, there is no recommendation for PTSD. However, the threshold for using group therapy should be low, especially for those with quite limited potentially suggestive evidence, including group exposure therapy, mindfulness-based stress reduction and building spiritual strength.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Group therapy; Psychotherapy, group; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 136 articles in PubMed, 73 in CINAHL, 169 in Cochrane Library, 17000 in Google Scholar, and 0 from other sources†. We considered for inclusion 8 from PubMed, 3 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 13 articles considered for inclusion, 10 randomized trials and 3 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **COGNITIVE BEHAVIORAL THERAPY (CBT)**

Cognitive behavioral therapy (CBT) has been used to treat PTSD <sup>(88, 89, 90, 91)</sup>. It involves helping patients to change unhelpful behaviors and thought patterns. A variety of component therapies that are related include cognitive therapy, cognitive processing therapy, relaxation therapy, and various types of exposure therapy. Mind-body interventions are reviewed separately, although they are often used with CBT; mind-body interventions attempt to achieve stress relief encompass a variety of techniques designed to use the mind to impact physical functioning and improve health <sup>(92)</sup>, including yoga, meditation, deep breathing, emotional freedom techniques, hypnotherapeutic techniques, art therapy, music therapy, spiritual-based interventions, guided imagery, neurofeedback techniques, and mindfulness.

# COGNITIVE BEHAVIORAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Cognitive behavioral therapy (CBT) is recommended for the treatment of PTSD. (See additional recommendations for specific components of CBT).

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

#### **Indications**

PTSD sufficient to require first-line therapy. CBT may be used as the stand-alone treatment for PTSD. CBT often includes prolonged/exposure therapy (Bryant et al., 2013, Bryant et al., 2008) and relaxation therapies, which are reviewed separately in this guideline.

#### **Benefits**

Improvement in PTSD symptoms.

#### **Harms**

Infrequent and negligible.

# Frequency/Dose/Duration

Weekly to twice-weekly sessions of 60-100 minutes, generally for a minimum of 6 weeks and up to 3 months (Monson et al., 2012, Talbot et al., 2014, Bryant et al., 2008, Ehlers et al., 2014, Resick et al., 2015).

# Indications for discontinuation

Resolution of PTSD symptoms, noncompliance, lack of efficacy, or adverse effects.

#### Rationale

Many moderate-quality studies are largely consistent in suggesting efficacy of CBT for PTSD (Bryant et al., 2013, Bryant et al., 2008, Monson et al., 2012, Bryant et al., 2008, Ehlers et al., 2014, Resick et al., 2015, Bryant, 1999, Bryant et al., 1998, Cottraux et al., 2008, Mills et al., 2012, Back et al., 2016, Blanchard et al., 2003, Difede et al., 2007)(Bryant, 2018, O'Donnell et al., 2012, Sloan et al., 2018, Pigeon et al., 2022). Many studies reported improved sleep, fewer nightmares, less depression, and less anxiety with CBT (Talbot et al., 2014, Engel et al., 2015)(Bryant et al., 2008, O'Donnell et al., 2012). Some studies suggest that combination therapy, such as cognitive restructuring and exposure therapy, is superior to CBT alone (Bryant et al., 2008). A three-arm trial of brief exposure CBT, prolonged expoosure CBT, and wait list found both CBT arms efficacious (Bryant, 2018). One study found earlier intervention resulted in superior mental health outcomes at 1 year (O'Donnell et al., 2012), while another suggested early intervention was preventive (Shalev et al., 2012). Limited evidence suggests treatment gains have been reportedly maintained up to 1 year (Ivarsson et al., 2014). Systematic reviews and meta-analyses have found similar results (Alshahrani et al., 2022, Ennis et al., 2020, Haerizadeh et al., 2020, Semerci et al., 2023), although the 1year durability of the effects is uncertain (Macedo et al., 2018), as is its role in prevention (Pham et al., 2019).

There is limited evidence for trauma-focused CBT. One trial suggested superiority to a wait-listed control (Zemestani et al., 2022). Another trial suggested efficacy, but the sample size was small resulting in a low-quality trial (Hinsberger et al., 2017). A third trial suggested no differences between trauma-focused CBT vs. individual supportive therapy (Andersen et al., 2021).

CBT has low adverse effects, is moderate cost depending upon treatment duration, and has broad and consistent evidence of efficacy for the treatment of PTSD. Thus, CBT is recommended for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cognitive Behavioral Therapy, Cognitive Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 766 articles in PubMed, 302 in CINAHL, 40 in Cochrane Library, 21300 in Google Scholar, and 0 from other sources. We considered for inclusion 33 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 37 articles considered for inclusion, 13 randomized trials and 24 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **COGNITIVE PROCESSING THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### Recommended

The use of cognitive processing therapy as a component of cognitive behavioral therapy is recommended for the treatment of PTSD.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Moderate

# **Indications**

PTSD sufficient to require first-line therapy. CPT may be used as the stand-alone treatment for PTSD.

#### **Benefits**

Improvement in PTSD symptoms, sleep and suicidality.

#### Harms

Negligible.

# Frequency/Dose/Duration

Weekly to twice-weekly sessions of 60-100 minutes, generally a minimum of 6 weeks and up to 3 months (Monson et al., 2012, Talbot et al., 2014, Bryant et al., 2008, Ehlers et al., 2014, Resick et al., 2015).

#### Indications for discontinuation

Resolution of PTSD symptoms, noncompliance, lack of efficacy, or adverse effects.

#### **Rationale**

There are many moderate quality trials suggesting efficacy of cognitive processing therapy (CPT) (Resick, 2008, Resick et al., 2017, Wachen et al., 2022, Walter et al., 2023, Simpson et al., 2022, Jak et al., 2019, Jaffe et al., 2021, Fitzpatrick et al., 2023, Graziano et al., 2024). Some trials used CPT as an active treatment in all trial arms (Bryan, 2024). One trial found modest statistical superiority of prolonged exposure compared with CPT (Schnurr et al., 2022, Moshier et al., 2024). Superiority of dialectical behavior therapy vs. CPT including at 9 months after treatment has been reported (Vonderlin et al., 2024). Noninferiority of written exposure therapy (Sloan et al., 2018, Alpert et al., 2020, Lee et al., 2021) and breathingbased meditation (Bayley et al., 2022). Low-quality trials also suggest efficacy (Holder et al., 2018, Holliday et al., 2018, Holliday et al., 2018, Gobin et al., 2018, Morland LA, 2015, Wells et al., 2019, Peterson et al., 2022, Litz et al., 2021). Systematic reviews and meta-analyses conclude there is evidence of efficacy of CPT for treatment of PTSD (Asmundson et al., 2019, Ackland et al., 2023, Sciarrino et al., 2020, Mikolić et al., 2019, Yunitri et al., 2023). CPT has low adverse effects, is moderate cost depending upon treatment duration, and has fairly consistent evidence of efficacy for the treatment of PTSD, and is thus recommended for PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TREATMENT TOPIC; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 211 articles in PubMed, 187 in CINAHL, 86 in Cochrane Library, 17100 in Google Scholar, and 0 from other sources†. We considered for inclusion 16 from PubMed, 4 from CINAHL, 28 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the articles considered for inclusion, 44 randomized trials and 7 systematic reviews met the inclusion criteria.

<sup>†</sup> The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are

reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

ONLINE OR COMPUTER-ADMINISTERED CBT FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Online or computer-administered CBT is recommended for the treatment of PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

#### **Indications**

PTSD sufficient to require first-line therapy. CBT may be used as the stand-alone treatment for PTSD. CBT often includes prolonged/exposure therapy (Bryant et al., 2013, Bryant et al., 2008) and relaxation therapies, which are reviewed separately in this guideline.

#### **Benefits**

Improvement in PTSD symptoms.

## Harms

Infrequent and negligible.

# Frequency/Dose/Duration

Weekly to twice-weekly sessions of 60-100 minutes, generally for a minimum of 6 weeks and up to 3 months (Monson et al., 2012, Talbot et al., 2014, Bryant et al., 2008, Ehlers et al., 2014, Resick et al., 2015).

#### Indications for discontinuation

Resolution of PTSD symptoms, non-compliance, lack of efficacy, or adverse effects.

#### Rationale

Several moderate-quality trials have suggested efficacy of internet-administered CBT compared with wait-list control, treatment as usual, and delayed treatment attention (Ivarsson et al., 2014, Spence J, 2011, Hobfoll, 2016, Lewis et al., 2017, Knaevelsrud, 2007, Knaevelsrud, 2010, Knaevelsrud et al., 2017). There are a few other trials of internet-based treatments, such as therapist-assisted online psychological therapies; however, they are insufficient in numbers for evidence-based guidance (Ehlers et al., 2023). Systematic reviews

suggest efficacy and acceptability of computer-administered CBT (Paiva et al., 2024, Simon et al., 2019). Internet/computer-administered CBT has low adverse effects, is low cost, and has consistent evidence of efficacy for the treatment of PTSD, and thus is recommended.

### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: computer-assisted cognitive therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 10 articles in PubMed, 26 in CINAHL, 1 in Cochrane Library, 17, 500 in Google Scholar, and 1 from other sources†. We considered for inclusion 2 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 5 articles considered for inclusion, 3 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

STRESS INOCULATION TRAINING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

# **Not Recommended**

Stress inoculation training is not recommended for treatment of PTSD.

**Strength of evidence** Not Recommended, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

One trial showed narrative exposure therapy was superior to stress inoculation training (Hensel-Dittmann D, 2011). The second quality trial suggested EMDR was superior to stress inoculation training with prolonged exposure therapy (Lee et al., 2002). Stress inoculation training has low adverse effects, is moderate cost depending upon treatment duration, has no quality evidence of efficacy (with trials suggesting inferiority to other treatments), and thus is not recommended.

### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: stress inoculation

training; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 3 in CINAHL, 2 in Cochrane Library, 5120 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **IMAGERY REHEARSAL TRAINING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Not Recommended**

The use of imagery rehearsal training is not recommended for the treatment of PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

#### Rationale

One trial of imagery rehearsal training (IRT) was unable to show superiority of IRT added to CBT (Harb et al., 2019), while another trial found mostly comparable results of additive treatment (Belleville et al., 2023). Another trial found IRT was not superior to sleep and nightmare management (Cook, 2010). A lack of benefit was shown for additive therapy with mianserin (Sandahl et al., 2021, Nielsen et al., 2024). One trial found superiority to usual care, but was likely affected by a usual care bias (Ulmer, 2011), while another trial with wait-list control bias suggested efficacy (Krakow, 2001). IRT has low adverse effects and is moderate cost, depending upon treatment duration. However, all of the highest quality trials showed a lack of efficacy. Thus, it is not recommended for treatment of PTSD.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Imagery Rehearsal Training, Imagery Rehearsal Therapy, Imagery Psychotherapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found

and reviewed 44 articles in PubMed, 4 in CINAHL, 4 in Cochrane Library, in 17400 Google Scholar, and 0 from other sources.† We considered for inclusion 2 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 3 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# BRIEF ECLECTIC THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of brief eclectic therapy as a component of cognitive behavioral therapy in the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There are few trials of brief eclectic therapy. One trial and several follow-up studies of that trial suggested efficacy (Nijdam et al., 2012, Nijdam, 2013, Nijdam, 2015, Nijdam et al., 2018). The other study was possibly affected by a randomization failure and wait-control bias (Lindauer, 2005). A systematic review found little evidence to support the use of brief eclectic therapy (Yunitri et al., 2023). Thus, the evidence base is insufficient to sustain a recommendation in favor of brief eclectic therapy for treatment of PTSD.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TREATMENT TOPIC; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2 articles in PubMed, 4 in CINAHL, 0 in Cochrane Library, 17, 200 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## NARRATIVE EXPOSURE THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

The use of narrative exposure therapy as a component of cognitive behavioral therapy is recommended for the treatment of PTSD.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

#### **Indications**

PTSD sufficient to require first-line therapy. CBT may be used as the stand-alone treatment for PTSD. CBT often includes prolonged/exposure therapy (Bryant et al., 2013, Bryant et al., 2008) and relaxation therapies, which are reviewed separately in this guideline.

#### **Benefits**

Improvement in PTSD symptoms.

# Harms

Infrequent and negligible.

# Frequency/Dose/Duration

Weekly to twice-weekly sessions of 60-100 minutes, generally for a minimum of 6 weeks and up to 3 months (Monson et al., 2012, Talbot et al., 2014, Bryant et al., 2008, Ehlers et al., 2014, Resick et al., 2015).

## Indications for discontinuation

Resolution of PTSD symptoms, noncompliance, lack of efficacy, or adverse effects.

## Rationale

Several moderate quality trials suggest efficacy of narrative exposure therapy (Steuwe et al., 2021, Wigard et al., 2024, Alghamdi, 2015, Hensel-Dittmann D, 2011, Hijazi et al., 2014, Stenmark et al., 2013). One of those trials suggested a higher rate of remission than dialectical behavior therapy (Steuwe et al., 2021). Another trial showed narrative exposure

therapy was superior to stress inoculation training (Hensel-Dittmann D, 2011). Systematic reviews and metanalyses concluded narrative exposure therapy had evidence of efficacy (Lely et al., 2019, Raghuraman et al., 2021, Thompson et al., 2018, Siehl et al., 2021, Haktanir et al., 2024, Jericho et al., 2022), including one study suggesting superiority to non-trauma-focused treatment (Grech et al., 2020). One review suggested the literature suggested efficacy, but the results could be accounted for by publication biases (Wei et al., 2021).

Narrative exposure therapy has low adverse effects, is moderate cost depending upon treatment duration, has some relatively consistent evidence of modest efficacy for the treatment of PTSD, and thus is recommended for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Narrative Exposure Therapy, Narrative Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 109 articles in PubMed, 26 in CINAHL, 91 in Cochrane Library, 17500 in Google Scholar, and 1 from other sources.† We considered for inclusion 10 from PubMed, 3 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 1 from other sources. Of the 19 articles considered for inclusion, 10 randomized trials and 9 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### SEEKING SAFETY THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of Seeking Safety therapy for the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

### Rationale

There are few trials that may be applicable to workers. One trial found benefit of seeking safety therapy among those with combined PTSD and substance use disorder (Schäfer et al.,

2019). Another trial found that Creating Change was superior to Seeking Safety (Najavits et al., 2018). An interactive Seeking Safety app was reportedly more successful than a noninteractive app for combined PTSD and substance use disorder (Najavits et al., 2024). One systematic review and meta-analysis reported some evidence of efficacy among those with both PTSD and substance use disorders (Sherman et al., 2023). Because evidence is sparse, there is no recommendation regarding Seeking Safety therapy for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Seeking safety therapy, Seeking safety; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 32 articles in PubMed, 23 in CINAHL, 32 in Cochrane Library, 2390 in Google Scholar, and 0 from other sources†. We considered for inclusion 15 from PubMed, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 17 articles considered for inclusion, 16 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# DIALECTICAL BEHAVIORAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of dialectical behavioral therapy as a component of cognitive behavioral therapy in the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There are no quality studies involving typical worker populations. One RCT reported efficacy among female survivors of childhood abuse (Bohus et al., 2020). One systematic review with meta-analysis reported moderate effects in reducing PTSD symptoms with dialectical behavioral therapy (Prillinger et al., 2024). Because the evidence for treatment of workers is sparse, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Dialectical behavioral therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 21 articles in PubMed, 11 in CINAHL, 9 in Cochrane Library, 17, 300 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

ACCEPTANCE AND COMMITMENT THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

# No Recommendation

There is no recommendation regarding acceptance and commitment therapy for treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There is one moderate quality RCT among veterans with anxiety disorders including PTSD that reported equal (in)efficacy of acceptance and commitment therapy vs. present-centered therapy (Lang et al., 2017). A systematic review concluded there is evidence of efficacy, although the studies included were largely non-randomized (Rowe-Johnson et al., 2024). Because evidence is sparse, there is no recommendation.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: acceptance and commitment therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial,

controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 101 articles in PubMed, 46 in CINAHL, 3 in Cochrane Library, 17, 600 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 46 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 3 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# BEHAVIORAL ACTIVATION FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Behavioral activation is not recommended for treatment of PTSD.

**Strength of evidence** Not Recommended, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There is one moderate quality RCT suggesting comparable (in)efficacy comparing behavioral activation-CPT vs. CPT, which suggests lack of efficacy (Walter et al., 2023). Because evidence is sparse, and available evidence suggests lack of efficacy, behavioral activation is not recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Behavioral Activation; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 788 articles in PubMed, 180 in CINAHL, 59 in Cochrane Library, 20, 600 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are

reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## MIND-BODY INTERVENTIONS

Mind-body interventions have been used for PTSD patients to attempt to relieve stress and encompass a variety of techniques designed to use the mind to impact physical functioning and improve health <sup>(93, 94)</sup>. These include relaxation, meditation, deep breathing, emotional freedom techniques, hypnotherapeutic techniques, art therapy, music therapy, spiritual-based interventions, guided imagery, neurofeedback techniques, and mindfulness <sup>(94, 95, 96, 97, 98, 99, 100)</sup>

## **GUIDED IMAGERY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### Recommended

Guided imagery is recommended for the treatment of patients with PTSD after treatment trials with greater evidence of efficacy (e.g., CBT, CPT, exposure therapy, aerobic and strengthening exercises) are tried first, with acceptability being an important factor.

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** Low

## **Indications**

Individuals with PTSD. However, because evidence is limited, other treatments with greater evidence of efficacy (e.g., CBT, CPT, exposure therapy, aerobic and strengthening exercises) should be tried first.

#### **Benefits**

Improvement in PTSD symptoms.

#### **Harms**

Negligible.

## Frequency/Dose/Duration

Weekly 2. 5-hour sessions of mindfulness therapy.

# **Indications for discontinuation**

Symptom resolution or lack of efficacy.

#### Rationale

Trials have suggested efficacy of guided imagery, including that it has equivalent efficacy to EMDR and linguistic processing (Boterhoven de Haan et al., 2020, Assmann et al., 2024, Kuck et al., 2023, Brown et al., 2018). It has also been reportedly effective in combination with other treatments (Kip, 2013, Jain, 2012). Guided imagery has also been used in trials in both arms (Isserles, 2021, Guzick et al., 2024). A systematic review and meta-analysis has reported some evidence of efficacy (Kroener et al., 2023).

Guided imagery has low adverse effects, is moderately costly depending upon treatment duration, has some evidence of efficacy, and thus is recommended for PTSD. However, because evidence is limited, other treatments with greater evidence of efficacy (e.g., CBT, exercises, CPT, exposure therapy) should be trialed first.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TREATMENT TOPIC; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 64 articles in PubMed, 11 in CINAHL, 28 in Cochrane Library, 17, 500 in Google Scholar, and 0 from other sources†. We considered for inclusion 14 from PubMed, 1 from CINAHL, 2 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 16 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# MINDFULNESS FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### **Sometimes Recommended**

Mindfulness is selectively recommended for the treatment of patients with PTSD after treatments with greater evidence of efficacy (e.g., CBT, CPT, exposure therapy, aerobic and strengthening exercises) are tried first, while also based on patient acceptability of the treatment approach.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

#### **Indications**

Individuals with PTSD, generally after CBT, CPT, exposure therapy, aerobic and strengthening exercises have been utilized.

## **Benefits**

Improvement in PTSD symptoms.

#### Harms

Negligible.

# Frequency/Dose/Duration

Weekly 2. 5-hour sessions of mindfulness therapy.

## Indications for discontinuation

Symptom resolution or lack of efficacy.

#### **Rationale**

Mindfulness has been assessed and found better than wait-listed control (Kelly, 2016, Dumarkaite et al., 2022). However, two studies comparing mindfulness with treatment as usual found a lack of efficacy, despite having treatment-as-usual bias (Kearney et al., 2013, Nordbrandt et al., 2020). One trial found mindfulness-based stress reduction to be superior to present-centered group therapy (Davis et al., 2019), while another found efficacy of mindfulness-based CBT (Jasbi et al., 2018).

A systematic review and meta-analysis of mindfulness-based interventions for veterans noted some efficacy, although there were problems with acceptability (Goldberg et al., 2020). Another review of mindfulness-based stress reduction concluded there was evidence of efficacy in the few studies available (Liu et al., 2022). The overall lack of rigorous trials and few trials available was elsewhere noted in reviews (Marchand et al., 2021, Ramachandran et al., 2023).

Mindfulness interventions have low adverse effects, are moderately costly depending upon treatment duration, have some evidence of efficacy, and thus are recommended for PTSD. However, because evidence is limited, mindfulness is selectively recommended for the treatment of patients with PTSD after treatment with CBT, exercises, CPT and exposure therapy, while also based on patient acceptability of the treatment approach.

# **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Mindfulness;

post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 115 articles in PubMed, 84 in CINAHL, 3 in Cochrane Library, 17700 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 2 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 8 articles considered for inclusion, 4 randomized trials and 4 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# MEDITATION FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

# **Sometimes Recommended**

The use of meditation is recommended for the treatment of select patients with PTSD after treatments with greater evidence of efficacy (e.g., CBT, CPT, exposure therapy, aerobic and strengthening exercises) are tried first, with acceptability being an important factor.

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** Low

## **Indications**

For patients with PTSD as an adjunct to other first-line therapies (e.g., CBT, prolonged/exposure, aerobic exercise, strengthening exercise or SSRI/SRNIs).

## **Benefits**

Improvement in PTSD symptoms.

## **Harms**

Negligible.

## Frequency/Dose/Duration

Improvement in PTSD symptoms.

# **Indications for discontinuation**

Resolution of symptoms or lack of efficacy.

#### Rationale

There is limited evidence for the use of meditation to treat PTSD. The evidence base is highly heterogenous, often with widely varying co-interventions (e.g., deep breathing, various types of meditation, diving, multi-sport activities, and yoga) (Seppälä et al., 2014, Bonamer, 2023, Kelsven et al., 2024, Oman, 2015, Bayley et al., 2022). One trial suggested equivalency between meditation and CPT (Bayley et al., 2022). Another reported superiority of meditation to PCT (Kelsven et al., 2024).

Meditation has negligible adverse effects, is of minimal cost (if any), has some limited evidence of efficacy, and is therefore recommended for selective use in the treatment of patients with PTSD as adjunctive therapy, after treatment trials with CBT, CPT, exercises, and exposure therapy, with acceptability of meditation as treatment being an important factor.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: meditation; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 39 articles in PubMed, 29 in CINAHL, 14 in Cochrane Library, 18, 300 in Google Scholar, and 0 from other sources\*. We considered for inclusion 10 from PubMed, 1 from CINAHL, 1 from Cochrane Library, 6 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 10 randomized trials and 8 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## WELL-BEING THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Well-being therapy (e.g., therapy to enhance purpose in life, environmental mastery, personal growth, autonomy, self-acceptance and positive relationships (Ryff CD, 1989) is not recommended for treatment of PTSD.

Strength of evidence Not Recommended, Insufficient Evidence (I)

#### Level of confidence Low

#### Rationale

There are few quality studies assessing well-being therapy, with one reporting mostly negative results when compared with treatment-as-usual despite having a tau bias and thus suggesting lack of efficacy (Radstaak et al., 2020). Because evidence is sparse, and available evidence suggests lack of efficacy, well-being therapy is not recommended.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: well being therpay; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2876 articles in PubMed, 95 in CINAHL, 179 in Cochrane Library, 21, 800 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **EXPOSURE THERAPY**

Exposure therapy involves the use of a variety of exercises which make a patient confront a traumatic memory and reorganize it <sup>(101)</sup>. Exposure therapies are often combined with CBT. This may be done through imaginal exposure, narrative exposure, in vivo exposure to a traumatic event <sup>(102, 103)</sup>, and/or virtual reality exposure. Prolonged exposure therapy (PE) is a treatment that involves forced visual confrontation of trauma-related stimuli <sup>(104-110)</sup>.

Virtual reality exposure therapy (VRET) has been used to treat phobias and change behavior (111-113). VRET also has been suggested as an effective treatment for PTSD (102, 103, 114, 115).

# **EXPOSURE THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### Recommended

The use of exposure therapy and prolonged exposure therapy is recommended for the treatment of patients with PTSD.

# **Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** High

#### **Indications**

PTSD sufficient to require first-line therapy. Other first-line treatments include CBT (often done in conjunction), aerobic exercise, strengthening exercise, and SSRIs. Combination therapy (exposure therapy plus cognitive restructuring) is reportedly superior (Bryant et al., 2008).

## **Benefits**

Improvement in PTSD symptoms and reduction in emotional response to traumatic stimuli, helping to emotionally process a traumatic experience (Cusack et al., 2016, McLean et al., 2013). Low-quality cohort data from a large population-based sample of 847, 217 suggest there may be a lowered risk of suicide among veterans who are treated with cognitive processing therapy or prolonged exposure (Saulnier KG, 2024).

## **Harms**

Increased symptoms, intolerance.

# Frequency/Dose/Duration

Weekly 90-minute sessions for 10 weeks (Schnurr et al., 2007). This often includes introducing the visual confrontation of the trauma and repeatedly visiting the trauma memory (McLean et al., 2013, Cooper et al., 2017).

## **Indications for discontinuation**

Resolution of symptoms, noncompliance, lack of efficacy, or adverse events.

# Rationale

There are many moderate-quality studies showing efficacy of exposure therapy/prolonged exposure in the treatment of PTSD (Schnurr et al., 2007, Markowitz et al., 2015, Bryant et al., 2008, Bryant, 2018, Asukai et al., 2010, Saulnier KG, 2024, Foa et al., 2018, Foa et al., 2022, Taylor et al., 2003, McLean et al., 2019, Brown et al., 2019, Litz, 2012, Dell et al., 2023, Coffey et al., 2016, Norman et al., 2019, Lyons et al., 2023, Lyons et al., 2021, Tripp et al., 2020, Tripp et al., 2021, Capone et al., 2020, Peterson et al., 2023, Ready et al., 2018, Beidel et al., 2017, Osuch, 2009, Olden, 2017, Rauch, 2015, de Bont et al., 2013, Zoellner, 2017, Simon et al., 2008, Jun et al., 2013, Nacasch, 2011, Nacasch, 2015, Shalev et al., 2012, Difede et al., 2022, Powers et al., 2015, Thrasher, 2010, Ruglass, 2017, Acierno, 2017, Lee et al., 2002, Duran et al., 2021, Castillo, 2016, Horesh, 2017, Arntz, 2007, Moshier et al., 2024, Schneier et al., 2012, Sloan, 2012, Wisco, 2016, Mills et al., 2012, Beidel, 2011, Davis, 2011, Schnurr et al., 2019, Schnurr et al., 2022, Thompson-Hollands et al., 2023, Stirman et al.,

2021, Tarrier et al., 2000, McLay et al., 2017, Wells, 2015, Marks, 1998, Yehuda et al., 2015)(Schnurr et al., 2007).

One study compared prolonged exposure therapy to present-centered therapy in female veterans with PTSD showing significant improvement in PTSD symptoms (Schnurr et al., 2007). Other studies compared exposure therapy or prolonged exposure therapy to interpersonal psychotherapy and found comparable efficacy between both interventions (Markowitz et al., 2015, Bryant et al., 2008), suggesting that combination therapy (exposure therapy plus cognitive restructuring) is best. Another study found female civilian trauma survivors with PTSD and depressive symptoms had improved PTSD with prolonged exposure therapy over waitlisted controls (Asukai et al., 2010). Low-quality cohort data from a large population-based sample of 847, 217 suggest there may be a lowered risk of mortality from suicide among veterans treated with cognitive processing therapy or prolonged exposure therapy (Saulnier KG, 2024).

A trial comparing sertraline with prolonged exposure therapy found both effective, but advantages for prolonged exposure therapy and patient preference was felt to be an important factor to drive compliance (Zoellner et al., 2019, Graham et al., 2020, Burton et al., 2021); in a post-hoc analysis, they reported comparable early response rates but early responders in the sertraline group were more likely to achieve good end-state functioning after treatment (Graham et al., 2018). One three-arm RCT with secondary reports found comparable results over 24 weeks comparing 1) sertraline plus enhanced medical management, 2) prolonged exposure plus placebo and 3) prolonged exposure plus sertraline, although there was a trend towards less efficacy in the prolonged exposure plus placebo group (Rauch et al., 2019, Allard et al., 2021, Tripp et al., 2021, Porter et al., 2024, Luciano et al., 2023, Rauch et al., 2022).

A systematic review with meta-analysis concluded there were medium to large effects compared with waitlist and treatment as usual controls (McLean et al., 2022). A systematic review concluded that there was evidence of VR-administered exposure therapy (Deng et al., 2019).

Exposure therapy/prolonged exposure has low adverse effects, is moderate cost depending upon treatment duration, has many studies suggesting efficacy, and thus is recommended as a first-line treatment for PTSD.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Exposure Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 952 articles in PubMed, 187 in CINAHL, 35 in Cochrane Library, 20, 500 in Google Scholar, and 0 from other sources\*. We considered for inclusion 4 from PubMed, 3 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar,

and 0 from other sources. Of the 7 articles considered for inclusion, 4 randomized trials and 3 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## NARRATIVE EXPOSURE THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

The use of narrative exposure therapy as a component of cognitive behavioral therapy is recommended for the treatment of PTSD.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

#### **Indications**

PTSD sufficient to require first-line therapy. CBT may be used as the stand-alone treatment for PTSD. CBT often includes prolonged/exposure therapy (Bryant et al., 2013, Bryant et al., 2008) and relaxation therapies, which are reviewed separately in this guideline.

#### **Benefits**

Improvement in PTSD symptoms.

#### **Harms**

Infrequent and negligible.

## Frequency/Dose/Duration

Weekly to twice-weekly sessions of 60-100 minutes, generally for a minimum of 6 weeks and up to 3 months (Monson et al., 2012, Talbot et al., 2014, Bryant et al., 2008, Ehlers et al., 2014, Resick et al., 2015).

## Indications for discontinuation

Resolution of PTSD symptoms, noncompliance, lack of efficacy, or adverse effects.

#### Rationale

Several moderate quality trials suggest efficacy of narrative exposure therapy (Steuwe et al., 2021, Wigard et al., 2024, Alghamdi, 2015, Hensel-Dittmann D, 2011, Hijazi et al., 2014, Stenmark et al., 2013). One of those trials suggested a higher rate of remission than dialectical behavior therapy (Steuwe et al., 2021). Another trial showed narrative exposure therapy was superior to stress inoculation training (Hensel-Dittmann D, 2011). Systematic reviews and metanalyses concluded narrative exposure therapy had evidence of efficacy (Lely et al., 2019, Raghuraman et al., 2021, Thompson et al., 2018, Siehl et al., 2021, Haktanir et al., 2024, Jericho et al., 2022), including one study suggesting superiority to non-trauma-focused treatment (Grech et al., 2020). One review suggested the literature suggested efficacy, but the results could be accounted for by publication biases (Wei et al., 2021).

Narrative exposure therapy has low adverse effects, is moderate cost depending upon treatment duration, has some relatively consistent evidence of modest efficacy for the treatment of PTSD, and thus is recommended for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Narrative Exposure Therapy, Narrative Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 109 articles in PubMed, 26 in CINAHL, 91 in Cochrane Library, 17500 in Google Scholar, and 1 from other sources.† We considered for inclusion 10 from PubMed, 3 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 1 from other sources. Of the 19 articles considered for inclusion, 10 randomized trials and 9 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

VIRTUAL REALITY EXPOSURE THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Virtual reality exposure therapy is recommended for the treatment of patients with PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs.

## **Benefits**

Improvement in PTSD symptoms.

#### Harms

Increased symptoms, intolerance.

# Frequency/Dose/Duration

Once to twice weekly 90 minutes sessions for 5 weeks (McLay et al., 2017, Rothbaum BO, 1997).

#### Indications for discontinuation

Resolution of symptoms, noncompliance, adverse effects, or lack of efficacy for PTSD.

#### Rationale

There are multiple moderate-quality studies showing evidence of efficacy for virtual reality, including trials comparing with exposure therapy (showing equivalency), prolonged exposure (showing equivalency) and treatment as usual (showing superiority) (McLay et al., 2017, Tarrier et al., 2000, Reger et al., 2016, Smith et al., 2015, Rothbaum et al., 2014, Difede et al., 2014, Beidel et al., 2017, McLay et al., 2011). VRE was used in both treatment groups in multiple studies (Rothbaum et al., 2014, Difede et al., 2014, Beidel et al., 2017). A systematic review with metanalysis concluded there were medium to large effects compared with waitlist and treatment as usual controls (McLean et al., 2022). A systematic review concluded that there was evidence of VR-administered exposure therapy (Deng et al., 2019). Virtual reality has low adverse effects, is moderate to high cost depending upon duration of treatment, has evidence of efficacy, and is therefore recommended for treatment of PTSD.

# **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Virtual reality exposure therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 32 articles in PubMed, 69 in CINAHL, 17 in Cochrane Library, 17, 500 in Google Scholar, and 0 from other sources†. We

considered for inclusion 7 from PubMed, 1 from CINAHL, 2 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 5 randomized trials and 6 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

WRITTEN EXPOSURE THERAPY/WRITING THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## Recommended

Written exposure therapy/writing therapy is selectively recommended for treatment of PTSD after treatment with CBT, exercises, CPT and prolonged/exposure therapy for which there is considerably more evidence.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

#### **Indications**

PTSD patients after treatment with CBT, exercises, CPT and prolonged/exposure therapy are prescribed, as those treatments have considerably more evidence.

## **Benefits**

Reduction in PTSD symptoms.

## **Harms**

Negligible.

# Frequency/Dose/Duration

Five to seven 45- to 60-minute sessions (Sloan et al., 2022).

## Indications for discontinuation

Completion of a course, noncompliance, lack of efficacy.

#### Rationale

One trial with six reports found writing therapy to be equally effective as CPT (Sloan et al., 2018, Shayani et al., 2024, Alpert et al., 2020, Alpert et al., 2023, Lee et al., 2021). Another trial found written exposure therapy to be noninferior to prolonged exposure (Sloan et al., 2023). Other trials found CPT to be superior to written accounts (Resick, 2008, Jaffe et al., 2021, Fitzpatrick et al., 2023) or equally effective as written exposure therpay (Sloan et al., 2022). Systematic reviews and meta-analyses have reported evidence of efficacy in comparison with wait-list controls and sham writing (Dawson et al., 2021, DeJesus et al., 2024, Qian et al., 2020).

Because written exposure therapy/writing therapy has negligible adverse effects and some evidence of efficacy, it is selectively recommended for treatment of PTSD after treatment with CBT, exercises, CPT, and prolonged/exposure therapy, for which there is considerably more evidence.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: ("written"[All Fields] AND ("implosive therapy" [MeSH Terms] OR ("implosive" [All Fields] AND "therapy" [All Fields]) OR "implosive therapy"[All Fields] OR ("exposure"[All Fields] AND "therapy"[All Fields]) OR "exposure therapy"[All Fields])) OR ("written"[All Fields] AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy" [MeSH Subheading] OR "therapy" [All Fields] OR "therapy s" [All Fields] OR "therapys"[All Fields])) OR written exposure therapy OR writing therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, posttraumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 150 articles in PubMed, 90 in CINAHL, 405 in Cochrane Library, 17, 500 in Google Scholar, and 0 from other sources<sup>†</sup>. We considered for inclusion 21 from PubMed, 3 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 27 articles considered for inclusion, 21 randomized trials and 4 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### **DEBRIEFING**

Individual debriefing is psychological treatment intended to reduce the psychological morbidity that arises after exposure to trauma and has been used for PTSD <sup>(36, 116)</sup>. Group debriefing is a type of psychological debriefing involving crisis intervention models with the

aim of mitigating trauma related to PTSD (117, 118). Critical incident stress debriefing has been used to treat PTSD (116-123).

# INDIVIDUAL DEBRIEFING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of individual debriefing in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

Quality studies conflict regarding efficacy of individual debriefing for treatment of PTSD. Two studies show lack of efficacy (Sijbrandij et al., 2006), and one shows efficacy (Bisson et al., 2004). Individual debriefing has low adverse effects, is low to moderate cost depending upon duration of treatment, has conflicting evidence of efficacy, and thus there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Individual debriefing; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 106 articles in PubMed, 0 in CINAHL, 41 in Cochrane Library, 17500 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **GROUP DEBRIEFING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### **Not Recommended**

Group debriefing and critical incident stress debriefing are not recommended for the treatment of patients with or at risk of PTSD.

# **Strength of evidence** Moderately Not Recommended, Evidence (B) **Level of confidence** Moderate

#### Rationale

Three moderate-quality trials show lack of efficacy of group debriefing/critical incident stress debriefing (Devilly et al., 2008, Tarquinio et al., 2016, Marchand, 2006). Group debriefing has moderate adverse effects, is low to moderate cost depending upon treatment duration, has evidence of lack of efficacy, and thus is not recommended for the treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Group Debriefing, Group Psychological Debriefing, Debriefing; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 42 articles in PubMed, 14 in CINAHL, 35 in Cochrane Library, 15600 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### **PSYCHODYNAMIC PSYCHOTHERAPY**

Psychodynamic psychotherapy involves therapists encouraging patients with PTSD to address and process through thoughts and emotions that have been suppressed surrounding the traumatic event in their life (124, 125, 126, 127, 128).

# PSYCHODYNAMIC PSYCHOTHERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

# No Recommendation

There is no recommendation for or against the use of psychodynamic psychotherapy in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There is no quality evidence for using psychodynamic psychotherapy in the treatment of PTSD. Psychodynamic psychotherapy has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, has no quality evidence for efficacy, and thus there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Psychodynamic Psychotherapy, Psychotherapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1696 articles in PubMed, 226 in CINAHL, 79 in Cochrane Library, 16800 in Google Scholar, and 0 from other sources.† We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **INTERPERSONAL THERAPY**

Interpersonal therapy has been used to treat PTSD (129).

# INTERPERSONAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

The use of interpersonal therapy is recommended for the treatment of patients with PTSD.

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** Low

#### **Indications**

Chronic PTSD sufficiently symptomatic to require treatment (Markowitz et al., 2015).

#### **Benefits**

Improved PTSD symptoms.

#### **Harms**

Negligible.

# Frequency/Dose/Duration

Weekly interpersonal psychotherapy for 14 weeks; 50 minutes per weekly session was used in the highest quality study (Markowitz et al., 2015).

## Indications for discontinuation

Completion of a course of treatment, sufficient resolution of symptoms and/or noncompliance.

#### Rationale

The highest-quality study suggested comparable efficacy to exposure therapy (Markowitz et al., 2015); thus, interpersonal therapy is recommended.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Interpersonal Therapy, Socioenvironmental Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed articles in 266 PubMed, in 15 CINAHL, 0 in Cochrane Library, 18800 in Google Scholar, and 1 from other sources.† We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# PRESENT-CENTERED THERAPY

# PRESENT-CENTERED THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Present-centered therapy is recommended for treatment of PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

#### **Indications**

Present-centered therapy is recommended for treatment of PTSD, treatment of PTSD, although generally after or with CBT and prolonged exposure therapy.

## **Benefits**

Improved PTSD symptoms severity.

#### Harms

Negligible.

# Frequency/Dose/Duration

Typically, 10-14 treatment sessions occur over 2-8 weeks (Belsher et al., 2019), although one trial used approximately 30 sessions (Ready et al., 2018, Schnurr et al., 2019).

# **Indications for discontinuation**

Completion of a course, non-compliance.

# **Rationale**

Many trials have assessed present-centered therapy and found it effective in comparison with controls, including wait-list control and trauma-focused CBT (Resick et al., 2015, Resick et al., 2017, Dondanville et al., 2019, Sloan et al., 2018, Beck et al., 2021, Graziano et al., 2024, Johnson et al., 2020, Classen et al., 2011, Najavits et al., 2018, Holliday et al., 2018, Holliday et al., 2018, Lang et al., 2017). It was also found to be comparable/non-inferior to CBT which has proven efficacy (Foa et al., 2018, Taylor et al., 2020, McLean et al., 2019, Brown et al., 2019). Mindfulness-based stress reduction was reportedly superior to CPT (Davis et al., 2019). One trial found Building Spiritual Strength to be superior to CPT (Harris et al., 2018). PCT is reportedly inferior to prolonged exposure therapy (Schnurr et al., 2007, Thompson-Hollands et al., 2023, Stirman et al., 2021, Schnurr et al., 2019). A Cochrane review concluded there is moderate evidence of efficacy (Belsher et al., 2019).

Present-centered therapy has low adverse effects, is moderate cost depending upon treatment duration, and has consistent evidence of efficacy for the treatment of PTSD. Thus, it is recommended for treatment of PTSD, but generally after or with CBT, exercises, and prolonged exposure therapy.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Present-centered therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 46 articles in PubMed, 28 in CINAHL, 227 in Cochrane Library, 3 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 1 from CINAHL, 5 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 8 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **SKILLS TRAINING**

Skills training for PTSD is a type of therapy, such as Stress Inoculation Training (SIT) or Skills for Psychological Recovery (SPR), that teaches individuals concrete strategies to manage PTSD symptoms. These skills may inc. lude problem-solving, relaxation techniques, improving thinking patterns, and building social support to help survivors cope with trauma and improve their overall ability to function in daily life

## SKILLS TRAINING FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

# Recommended

Skills training is recommended for treatment of patients with PTSD.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

# **Indications**

Skills training is recommended for treatment of PTSD.

#### **Benefits**

Improved PTSD symptoms, social support, emotion regulation, depression and negative cognitions.

#### Harms

Negligible.

# Frequency/Dose/Duration

12-weekly sessions were used in the highest quality trial (Cloitre et al., 2024).

## Indications for discontinuation

Completion of a course, noncompliance.

#### Rationale

There are a few trials of skills training, and all suggest modest efficacy (Cloitre et al., 2024, Karatzias et al., 2024, Wigard et al., 2024), including reported superiority to PCT (Cloitre et al., 2024). Skills training has low adverse effects, some quality evidence of efficacy and is thus recommended for treatment of PTSD.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cognitive Behavioral Therapy, Cognitive Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 343 articles in PubMed, 31 in CINAHL, 148 in Cochrane Library, 19000 in Google Scholar, and 0 from other sources.† We considered for inclusion 5 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 5 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **HYPNOTHERAPY**

Hypnosis has been used to treat PTSD (130, 131, 132).

# HYPNOTHERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against the use of hypnotherapy in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There are no sham-controlled studies and no studies compared with treatments with known levels of efficacy. One trial suggested CBT has greater influence compared with supportive counseling, while adding hypnotherapy to CBT had minimal additive benefit (Bryant et al., 2005, Bryant et al., 2006). Another study compared hypnotherapy to Zolpidem and found comparable (in)efficacy (Abramowitz et al., 2008). In another study (Galovski et al., 2016), there was improved sleep and depressive symptoms but this study had a high dropout rate and did not improve core PTSD symptoms. Hypnotherapy has low adverse effects, is moderate cost depending upon treatment duration, and has no quality evidence of efficacy; thus, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hypnotherapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 51 articles in PubMed, 9 in CINAHL, 47 in Cochrane Library, 7, 840 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# EYE MOVEMENT DESENSITIZATION AND REPROCESSING (EMDR)

Eye movement desensitization and reprocessing (EMDR) is an eight-phase psychotherapy that consists of multiple cointerventions including exposing clients to selected traumatic images and cognitions, while inducing saccadic eye movements (133, 134, 135, 136, 137, 138, 139, 140).

COMBINED EYE MOVEMENT DESENSITIZATION AND REPROCESSING (EMDR) WITH COGNITIVE BEHAVIORAL THERAPY (CBT) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### Recommended

Eye movement desensitization and reprocessing (EMDR) combined with cognitive behavioral therapy (CBT) is recommended for the treatment of PTSD. Treatment with eye movements alone is not recommended.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Moderate

#### **Indications**

Patients with PTSD.

#### **Benefits**

Reduced PTSD symptoms and severity of symptoms.

#### **Harms**

Negligible. If the eye movement component is taught without including CBT, the treatment may be ineffective.

#### Indications for discontinuation

Resolution, completion of a course, noncompliance.

# Rationale

EMDR includes multiple therapies, or co-interventions, including those known to be effective (e.g., cognitive behavioral therapy, exposure therapy). Thus, the literature base is mostly confounded by those co-interventions.

There are many moderate-quality studies of EMDR (van der Kolk et al., 2016, Taylor et al., 2003, Sack et al., 2016, Högberg et al., 2007, Nijdam et al., 2012, Karatzias et al., 2011, de Bont et al., 2013, Lee et al., 2002)(Nijdam, 2018, Susanty et al., 2022, Boterhoven de Haan et al., 2020, Assmann et al., 2024, Kuck et al., 2023, Voorendonk et al., 2023, Jarero et al., 2019, Covers et al., 2021). The highest-quality study, which is also the only sham-controlled trial, found a lack of efficacy (Sack et al., 2016) regarding the eye movement component.

Another trial of the eye movements compared with retrieval-only found no differences (Susanty et al., 2022). Thus, no trials were able to document efficacy of the eye movement components alone with these heterogeneous EMDR treatments, which raises major concerns about prescriptions of only eye movements without CBT.

EMDR has been reported to be equivalent to prolonged/exposure (van den Berg et al., 2015, Power, 2002, Voorendonk et al., 2023)(van den Berg et al., 2015, Power, 2002), worse than exposure (Taylor et al., 2003), equivalent to emotional freedom training (Karatzias et al., 2011), superior to biofeedback, equivalent to imagery rescripting (Boterhoven de Haan et al., 2020, Assmann et al., 2024, Kuck et al., 2023), and equivalent to brief eclectic therapy (Nijdam et al., 2012). One trial of additive therapy of EMDR vs. Narrative Therapy with both groups getting Skills Training in Affective and Interpersonal Regulation (STAIR) found no differences (Wigard et al., 2024). These results raise questions of response biases. A study to test the concept of earlier intervention to reduce PTSD severity in rape victims failed to find differences (Covers et al., 2021). One study also suggested a potential to reduce symptoms in first responders with ongoing exposures (Jarero et al., 2019). There are many low-quality studies, including those with small sample sizes (van Heemstra et al., 2024, Stanbury et al., 2020, Every-Palmer et al., 2024, Matthijssen et al., 2024, Ironson et al., 2021, Ahmadi, 2015, Wilson et al., 1995).

One systematic review and metanalysis found a lack of efficacy of EMDR for reduction in PTSD symptoms (Hudays et al., 2022), while another noted short-term reduction in PTSD symptoms that were not maintained at 3 months (Khan et al., 2018). Another study found that the effect sizes to reduce symptoms were small (Rasines-Laudes et al., 2023). One systematic review and meta-analysis found there were no differences compared with other psychological treatments in reducing PTSD severity, achieving response, or attaining remission (Wright et al., 2024).

EMDR has low adverse effects, is moderate cost depending upon duration of treatment, and has evidence of efficacy if combined with CBT. Yet, the eye movements component alone has quality evidence of inefficacy compared with sham. Thus, the eye component part of this therapy is not recommended. EMDR that is combined with CBT is recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TREATMENT TOPIC; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 6 articles in PubMed, 369 in CINAHL, 31 in Cochrane Library, 7, 620 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 3 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 3 randomized trials and 6 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **TAPPING TECHNIQUES**

Tapping techniques, such as Emotional Freedom Therapy and Thought field therapy (TFT; also known as the Callahan technique), are therapeutic tools used to attempt to relieve anxiety and other symptoms (141, 142). TFT is an approach developed from a mix of three modalities and theories: acupuncture, chiropractic, and psychotherapy (143). A typical TFT session will involve tapping on the face, hand, and body while the patient produces feelings, thoughts, or memories that are the target for treatment (e.g., anxiety, sadness, and restlessness) (141, 142). Each TFT session will include a set of protocol or algorithm, which designates the specific acupoint to be tapped, as well as the order in which they are to be tapped. Symptoms of PTSD, such as hyperarousal, dissociation, and defensive avoidance, are targeted using a trauma treatment protocol (141, 142, 143).

Although they are similarly named, Emotional Freedom Techniques are not a tapping technique, but instead a form of counseling that incorporates the physical tapping of the body on acupuncture points while simultaneously having the patient focus on traumatic events as a form of self-acceptance therapy (144, 145). It is similar to Thought Field Therapy and is typically used as adjunct therapy. With EFT, the client verbalizes the problem with a statement such as, "Even though I have this phobia, I totally and utterly love and accept myself," which purportedly allows patients to manage symptoms of PTSD (146).

TAPPING TECHNIQUES (THOUGHT FIELD THERAPY, EMOTIONAL FREEDOM THERAPY) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against the use of tapping techniques (thought field therapy and emotional freedom therapy) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There are sparse trials, none of which are compared with sham or an intervention with known level of efficacy. The sole moderate-quality trial was additionally subject to waitlist control bias (Irgens et al., 2012). In the absence of quality evidence of efficacy, there is no recommendation.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Tapping Technique, Thought Field Therapy, Emotional Freedom Therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 35 articles in PubMed, 5 in CINAHL, 133 in Cochrane Library, 14200 in Google Scholar, and 0 from other sources.† We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

EMOTIONAL FREEDOM TECHNIQUES (EFT) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against the use of emotional freedom techniques (EFT) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There are sparse trials, none of which are compared with sham or an intervention with known level of efficacy. The sole moderate-quality trials are additionally subject to waitlist control biases (Church et al., 2016). In the absence of quality evidence of efficacy, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Emotional Freedom Techniques, EFT, Tapping; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic

review, retrospective, and prospective studies. We found and reviewed 18 articles in PubMed, 7 in CINAHL, 3 in Cochrane Library, 10900 in Google Scholar, and 0 from other sources<sup>†</sup>. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **NEUROFEEDBACK**

Neurofeedback (also called EEG biofeedback or neurotherapy) has been used to treat anxiety, affective disorders, and PTSD (98, 147, 148, 149, 150, 151, 152).

# NEUROFEEDBACK (BRAIN-COMPUTER INTERFACE) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against the use of neurofeedback (brain-computer device and interface) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There is sparse quality evidence for the use of neurofeedback for PTSD. One moderate-quality study suggests improved PTSD symptoms in chronic PTSD, but the intervention was against a wait-listed control (van der Kolk et al., 2016). Systematic reviews report favorable results, although these also have considerable methodological issues (Askovic et al., 2023, Panisch et al., 2020, Steingrimsson et al., 2020). Thus, the overall evidence base is of low quality. Neurofeedback has low to moderate adverse effects and is moderate cost, depending upon treatment duration; however, in the absence of quality evidence of efficacy, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Neurofeedback, Electroencephalography, Brain-Computer Device and Interface; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial,

randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 64 articles in PubMed, 17 in CINAHL, 316 in Cochrane Library, 4620 in Google Scholar, and 2 from other sources†. We considered for inclusion 7 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 9 articles considered for inclusion, 5 randomized trials and 4 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **ANIMAL-ASSISTED THERAPY**

Animal-assisted therapy is the inclusion of animals in psychiatric treatment, such as dogs and horses (153, 154, 155) and has been used in treatment of PTSD (156, 157, 158).

# ANIMAL-ASSISTED THERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for or against the use of animal-assisted therapy in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

A moderate-quality trial showed minimal differences between groups with a service dog versus an emotional support dog for veterans with PTSD (Richerson et al., 2023). A crossover RCT that used self-described PTSD as the case definition showed that among those with high PTSD symptoms, walking with a person resulted in decreases in alphaamylase while walking with a dog did not; and that walking with either reduced cortisol among those with low PTSD symptom severity (Krause-Parello et al., 2020). An experimental model with subjects exposed to a traumatic video suggested that there were comparable results whether the subject was accompanied during viewing by a friendly dog or a friendly person (Lass-Hennemann et al., 2014). There are many low-quality studies suggesting improvements in symptoms with animals, especially the use of service dogs for veterans (Kloep et al., 2017). Nearly all evidence is concerning dogs, although they are naturally not the only animal possible. Systematic reviews also reported no significant quality evidence while also reporting the lower quality studies appeared to show some benefits (Chirico et al., 2022, Leighton et al., 2022). As there is no quality evidence clearly showing benefit of

animal-assisted therapy, there is no recommendation for this therapy for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Animal assisted therapy, Animal-assisted therapy, Animal-facilitated therapy, Pet-assisted therapy, Pet-facilitated therapy, AAT, ; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 30 articles in PubMed, 11 in CINAHL, 25 in Cochrane Library, 2900 in Google Scholar, and 0 from other sources†. We considered for inclusion 6 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 5 randomized trials and 4 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **SELF-HELP APPS**

# SELF-HELP APPS FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

# No Recommendation

There is no recommendation for or against self-help CBT-based apps for treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

Currently, there is some quality evidence for a few self-help apps (Bisson et al., 2022, Bisson et al., 2023, Belleville et al., 2023). There is one trial showing lack of efficacy (Riello et al., 2021). Yet, there are many hundreds of apps commercially available, there are concerns about the quality of those apps, and nearly all have no quality evidence of efficacy (Sander et al., 2020). Thus, there is no recommendation for or against self-help apps.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Self-help, Self-

care; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 119 articles in PubMed, 51 in CINAHL, 323 in Cochrane Library, 17500 in Google Scholar, and 0 from other sources†. We considered for inclusion 13 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 15 articles considered for inclusion, 13 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **SLEEP HYGIENE**

# **SLEEP HYGIENE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Sometimes Recommended**

Education in sleep hygiene is selectively recommended for those with PTSD who have sleep disruptions that are not addressed generally after trialing CBT, CPT, aerobic and/or strengthening exercises.

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** Low

## **Indications**

PTSD patients with sleep disturbance whose symptoms are not adequately addressed after trialing CBT, CPT, and aerobic exercises.

## **Benefits**

Improved quality and quantity of sleep.

## **Harms**

Negligible.

# Frequency/Dose/Duration

One or two sessions of training.

Education in sleep hygiene has been widely used; however, there is no quality evidence base for its application to PTSD. Training in sleep hygiene has no significant adverse effects, is low cost and is selectively recommended for those patients with PTSD who are having sleep disturbances, particularly after institution of CBT, CPT, and exercises.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Sleep hygiene; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 24 articles in PubMed, 27 in CINAHL, 4 in Cochrane Library, 5310 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 6 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 1 randomized trial and 6 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **MEDICATIONS**

There are few medications with FDA indications for PTSD, which may be related to the costs of RCTs for medications that are already approved for other indications. These recommendations are based upon the available quality data <sup>(53)</sup>. Additional important considerations are tolerability and compliance. In general, behavioral/nonmedication approaches are advised as first-line treatments; when medication is needed, sertraline is often used.

# **SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**

SERTRALINE (ZOLOFT) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## Recommended

Sertraline (Zoloft) is moderately recommended for the treatment of patients with PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

## **Indications**

PTSD sufficient to require medication and/or other first-line therapy(ies) such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise. Sertraline is also used to treat anxiety, depression, panic disorder and obsessive-compulsive disorder (OCD); thus, patients with those other concomitant disorders may be good candidates for sertraline.

#### **Benefits**

Improvements in PTSD symptoms.

## Harms

Worsening depression, serotonin syndrome, pregnancy risk category C, allergic reactions, irregular heartbeat, hyponatremia, bleeding, suicidal ideation, and suicide attempts in pediatric and young adult populations. Mania in bipolar patients. Avoid using with MAO inhibitors, as increases risks of serotonin syndrome. Common minor adverse effects include: sleepiness, nervousness, insomnia, dizziness, nausea, tremor, skin rash, constipation, upset stomach, loss of appetite, headache, dry mouth, diaphoresis and weight loss. Abrupt termination of Sertraline may cause adverse gastrointestinal effects including cramping, nausea, vomiting, diarrhea as well as flu-like symptoms, loss of appetite, lightheadedness, fatigue, headache, dizziness, insomnia and memory loss.

Restlessness and sleep disturbances, vivid dreams, diarrhea, headache, dizziness, fatigue, sexual dysfunction, weight gain, hyponatremia, possible increased risk of nonvertebral fractures, bleeding. Symptoms of abrupt discontinuation include: nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C (sertraline, fluoxetine, escitalopram, and citalopram), pregnancy risk class D (paroxetine) (Therapeutics, 2016).

# Frequency/Dose/Duration

Most moderate-quality RCTs treating PTSD patients prescribed 25-50 mg daily and the dose was typically increased in weekly intervals of flexible doses until the desired response is observed; maximum doses of 50-200 mg/day were used in the quality studies (Li et al., 2017, Rauch et al., 2019, Zoellner et al., 2019) (Brady et al., 2005, Davidson JR, 2001, Panahi et al., 2011, Zohar et al., 2002). Fast escalations in dose are often not tolerated.

#### Indications for discontinuation

Lack of efficacy, adverse effects, resolution of PTSD sufficiently to not require medication.

Multiple moderate-quality studies suggest efficacy of sertraline compared with placebo for treatment of PTSD (Li et al., 2017, Davidson JR, 2001, Panahi et al., 2011, Zohar et al., 2002, Rapaport et al., 2002, Brady et al., 2000) and only one lower-quality study showed lack of efficacy (Friedman et al., 2007). One study reported (Rapaport et al., 2002) sustained results with patients reporting improved quality of life and less relapse. A trial comparing sertraline with prolonged exposure therapy found both effective, but advantages for prolonged exposure therapy and patient preference was felt to be an important factor to drive compliance (Zoellner et al., 2019, Graham et al., 2020, Burton et al., 2021); in a post-hoc analysis, they reported comparable early response rates but early responders in the sertraline group were more likely to achieve good end-state functioning after treatment (Graham et al., 2018).

One three-arm RCT with secondary reports found comparable results over 24 weeks comparing 1) sertraline plus enhanced medical management, 2) prolonged exposure plus placebo and 3) prolonged exposure plus sertraline, although there was a trend towards less efficacy in the prolonged exposure plus placebo group (Rauch et al., 2019, Allard et al., 2021, Tripp et al., 2020, Porter et al., 2024, Luciano et al., 2023, Rauch et al., 2022). A Cochrane review found evidence of efficacy of SSRIs, however, it aggregated all types into one analysis and did not analyze for differences in efficacy (Williams et al., 2022). Sertraline has low adverse effects, is low to moderate cost depending on duration of treatment, has quality evidence of efficacy for treatment of PTSD, and thus is recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TREATMENT TOPIC; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 48 articles in PubMed, 13 in CINAHL, 28 in Cochrane Library, 719 in Google Scholar, and 0 from other sources†. We considered for inclusion 19 from PubMed, 1 from CINAHL, 4 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 25 articles considered for inclusion, 20 randomized trials and 5 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# PAROXETINE (PAXIL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## Recommended

Paroxetine (Paxil) is moderately recommended for the treatment of patients with PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Paroxetine is sometimes not used until sertraline has been tried, due to its increased problems with sedation and withdrawal symptoms. Paroxetine is also used to treat anxiety, depression, panic disorder and OCD, thus patients with those other concomitant disorders may be good candidates for Paroxetine especially if treatment with PE or CBT has not proven effective.

## **Benefits**

Improvements in PTSD symptoms.

#### **Harms**

Worsening depression, serotonin syndrome, pregnancy risk category D, allergic reactions, irregular heartbeat, hyponatremia, bleeding, suicidal ideation, and suicide attempts in pediatric and young adult populations. Mania in bipolar patients. Avoid using with MAO inhibitors, as increases risks of serotonin syndrome. Common minor adverse effects include: sleepiness, nervousness, insomnia, dizziness, tremor, constipation, loss of appetite, headache, dry mouth, and weight gain. Compared to other SSRIs, paroxetine has a higher incidence of severe withdrawal syndrome compared to other SSRIs. Symptoms of abrupt discontinuation include: nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C (sertraline, fluoxetine, escitalopram, and citalopram), pregnancy risk class D (paroxetine) (Therapeutics, 2016).

# Frequency/Dose/Duration

Most quality studies treating PTSD patients prescribed 20-40 mg daily and the dose was typically increased on weekly intervals of flexible doses until the desired response is observed, to a maximum dose of 50-60 mg/day.

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

All sufficiently-sized placebo-controlled quality studies suggest efficacy (Schneier et al., 2012, Tucker et al., 2001, Marshall et al., 2001, Fani et al., 2009). Some reporting greater efficacy with prolonged exposure or lack of additive benefit of paroxetine to prolonged exposure (Simon et al., 2008, Popiel et al., 2015). One study compared paroxetine to mirtazapine and found paroxetine non-superior to mirtazapine (Seo et al., 2010). Paroxetine has also been trials for prevention of the onset of PTSD after trauma in a low quality trial and found a trend towards efficacy (Borrelli et al., 2019). Paroxetine has low adverse effects, is low to moderate cost depending on duration of treatment, has evidence of efficacy for treatment of PTSD, and is recommended for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Paroxetine; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 311 articles in PubMed, 67 in CINAHL, 91 in Cochrane Library, 14800 in Google Scholar, and 0 from other sources.† We considered for inclusion 3 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 4 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## FLUOXETINE (PROZAC) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## Recommended

Fluoxetine (Prozac) is recommended for the treatment of patients with PTSD.

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** Low

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. PTSD sufficiently severe to require medication, although main efficacy may be relapse prevention. CBT and Prolonged Exposure

have better evidence of efficacy and thus are used first-line to treat PTSD and there is also better evidence of efficacy for Sertraline and Paroxetine. Fluoxetine is also used to treat anxiety, depression, panic disorder and OCD, thus patients with those other concomitant disorders may be reasonable candidates for fluoxetine.

## **Benefits**

Improvements in PTSD symptoms.

#### Harms

Worsening depression, serotonin syndrome, pregnancy risk category D, allergic reactions, irregular heartbeat, hyponatremia, bleeding, suicidal ideation, and suicide attempts in pediatric and young adult populations. Mania in bipolar patients. Avoid using with MAO inhibitors, as increases risks of serotonin syndrome. Common minor adverse effects include: sleepiness, nervousness, insomnia, dizziness, nausea, tremor, skin rash, constipation, upset stomach, loss of appetite, headache, dry mouth, diaphoresis and weight loss. Abrupt termination of paroxetine may cause adverse gastrointestinal effects including cramping, nausea, vomiting, diarrhea as well as flu-like symptoms, loss of appetite, lightheadedness, fatigue, headache, dizziness, insomnia, sexual dysfunction and weight gain. Compared to other SSRIs, paroxetine has a higher incidence of severe withdrawal syndrome compared to other SSRIs.

Restlessness and sleep disturbances, vivid dreams, diarrhea, headache, dizziness, fatigue, sexual dysfunction, weight gain, hyponatremia, possible increased risk of nonvertebral fractures, bleeding. Symptoms of abrupt discontinuation include: nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C (sertraline, fluoxetine, escitalopram, and citalopram), pregnancy risk class D (paroxetine) (Therapeutics, 2016).

Prozac has a long half-life; thus, adverse effects are slow to resolve after discontinuation.

## Frequency/Dose/Duration

Fluoxetine 20 mg/day with increased doses not more frequently than weekly intervals of flexible doses increased to a maximum of 60 mg/day until desired response is observed. Should allow sufficient time to reach steady state before escalating dose.

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

There are multiple moderate-quality studies that substantially conflict regarding efficacy of fluoxetine (Connor et al., 1999, Barnett et al., 2002, Martenyi et al., 2007, van der Kolk et al., 2007). The largest study is statistically negative (Martenyi et al., 2007). However, there are two studies suggesting that fluoxetine may have some efficacy in PTSD symptom maintenance preventing relapse (Martenyi et al., 2002, Barnett et al., 2002). Fluoxetine has low adverse effects, is low to moderate cost depending on duration of treatment, has limited evidence of efficacy, and is an SSRI where other SSRIs appear effective, and is therefore recommended for select treatment of PTSD. The other SSRIs have better evidence of efficacy and should generally be preferred.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Fluoxetine; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 3 in CINAHL, 3 in Cochrane Library, 11300 in Google Scholar, and 1 from other sources†. We considered for inclusion 0 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 9 from Google Scholar, and 1 from other sources. Of the 11 articles considered for inclusion, 0 randomized trials and 11 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## FLUVOXAMINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for or against the use of fluvoxamine in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There is little quality evidence regarding fluvoxamine for PTSD and no quality placebocontrolled trials. One moderate-quality RCT showed comparable efficacy between fluvoxamine and reboxetine in MVA PTSD survivors (Spivak et al., 2006). However, the evidence supporting reboxetine for PTSD symptoms is also limited and conflicting as well as its efficacy for depression as evidenced by the combined systematic review and meta-analysis of all RCTs using reboxetine (Krishnadas R, 2010). Fluvoxamine also requires twice-daily dosing, which may be less convenient. Fluvoxamine has low adverse effects, is low to moderate cost depending on duration of treatment, and has no clear documented efficacy; therefore, there is no recommendation for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Fluvoxamine, Fluvoxamine maleate, Luvox, Selective serotonin reuptake inhibitors, Serotonin reuptake inhibitors; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 48 articles in PubMed, 17 in CINAHL, 35 in Cochrane Library, 11600 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **ESCITALOPRAM (LEXAPRO) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## Recommended

Escitalopram (Lexapro) is recommended for the treatment of patients with PTSD.

**Strength of evidence** Recommended, Insufficient Evidence (I) **Level of confidence** Low

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Should have generally not responded to sertraline, which appears to be superior (Tucker et al., 2003).

#### **Benefits**

Improvements in PTSD symptoms.

#### **Harms**

Restlessness and sleep disturbances, vivid dreams, diarrhea, headache, dizziness, fatigue, sexual dysfunction, weight gain, hyponatremia, possible increased risk of nonvertebral fractures, bleeding. Symptoms of abrupt discontinuation include: nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C (sertraline, fluoxetine, escitalopram, and citalopram), pregnancy risk class D (paroxetine) (Therapeutics, 2016).

# Frequency/Dose/Duration

Escitalopram 10-20 mg/day with flexible daily doses increased at varying intervals per responses (Suliman et al., 2015).

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

## Rationale

There are two moderate-quality studies suggesting lack of efficacy for escitalopram for PTSD when compared to CBT or PE or placebo (Shalev et al., 2012, Suliman et al., 2015). Yet, the enantiomer citalopram has a moderate-quality study suggesting superiority to placebo but inferiority to sertraline (see separate recommendation). Further that escitalopram should theoretically be more effective than citalopram due to the L-isomer. One moderate quality study trialing escitalopram for prevention of PTSD failed to find efficacy for that purpose (Zohar et al., 2018). Escitalopram has low adverse effects, is moderate cost, but has evidence of lacking efficacy, although its enantiomer has evidence suggesting efficacy. Thus, escitalopram is recommended with insufficient evidence.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Escitalopram, Lexapro, Cipralex, Selective serotonin reuptake inhibitors, Serotonin uptake inhibitors; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 52 articles in PubMed, 17 in CINAHL, 34 in Cochrane Library, 13400 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# CITALOPRAM (CELEXA) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## Recommended

Citalopram (Celexa) is recommended for the treatment of patients with PTSD.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Moderate

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Should have generally not responded to sertraline, which appears to be superior (Tucker et al., 2003).

## **Benefits**

Improvements in PTSD symptoms.

#### **Harms**

Restlessness and sleep disturbances, vivid dreams, diarrhea, headache, dizziness, fatigue, sexual dysfunction, weight gain, hyponatremia, possible increased risk of nonvertebral fractures, bleeding. Symptoms of abrupt discontinuation include: nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C (sertraline, fluoxetine, escitalopram, and citalopram), pregnancy risk class D (paroxetine) (Therapeutics, 2016).

# Frequency/Dose/Duration

Citalopram 20-50 mg/day with flexible daily doses increased at varying intervals per responses (Tucker et al., 2003).

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

One moderate-quality study comparing citalopram to sertraline and placebo found sertraline to be superior to citalopram, but both medications were superior to placebo (Tucker et al., 2003). One study added baclofen but had a significant dropout rate (Manteghi et al., 2014). One 4-arm trial of bereaved adults who had complicated grief compared 1) citalopram, 2) placebo, 3) citalopram plus complicated grief treatment, and 4) placebo plus complicated grief treatment and reported complicated grief treatment to be superior, with citalopram assisting among those with depressive symptoms (Shear, 2016, Na et al., 2021). Citalopram has low adverse effects, is low to moderate cost depending upon the duration of treatment, has some evidence showing efficacy, and is thus selectively recommended for those who have generally not responded to sertraline, which has evidence of stronger efficacy.

#### Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Citalopram, celexa, seropram; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 15 articles in PubMed, 1 in CINAHL, 4 in Cochrane Library, 5, 000 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## VILAZODONE (VIBRYD) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Vilazodone (Vibryd) is not recommended for the treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

There is little quality evidence assessing vilazodone for PTSD. One study has shown an apparent lack of efficacy compared to placebo (Ramaswamy et al., 2017). Vilazodone has low to moderate adverse effects, is of low-moderate cost depending upon duration of treatment, and has no proven efficacy for PTSD. Therefore, vilazodone is not recommended.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Vilazodone; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 297 articles in PubMed, 62 in CINAHL, 93 in Cochrane Library, 13500 in Google Scholar, and 0 from other sources.† We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **VORTIOXETINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Not Recommended**

Vortioxetine is not recommended for treatment of PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

One trial reported lack of efficacy of vortioxetine for treatment of PTSD (Dunlop et al., 2021); thus, it is not recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Vortioxetine; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials,

randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 0 in CINAHL, 4 in Cochrane Library, 0 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1, 060 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS)**

**VENLAFAXINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)** 

#### Recommended

Venlafaxine is moderately recommended for the treatment of patients with PTSD.

**Strength of evidence** Moderately Recommended, Evidence (B) **Level of confidence** Moderate

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Venlafaxine may be used after CBT and PE or is also recommended as first line PTSD therapy.

## **Benefits**

Improvements in PTSD symptoms.

## **Harms**

Increased sweating, tachycardia, and urinary retention, nausea, vomiting, increased blood pressure. Symptoms of abrupt discontinuation include: increase in blood pressure, False-positive urine immunoassay screening tests for phencyclidine (PCP) and amphetamine, prolonged QT interval, pregnancy risk category C (Therapeutics, 2016).

# Frequency/Dose/Duration

Venlafaxine XR 37. 5 mg/day for 1 week, increasing by approx. 75 mg/week up to approx. 225 mg/day; or 75-300 mg/day flexible dosing per manufacturer's recommendations.

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

## Rationale

There are several moderate-quality studies evaluating venlafaxine for PTSD (Davidson, 2006, Davidson et al., 2006, Davidson et al., 2012, Rothbaum et al., 2008, Stein et al., 2009, Stein et al., 2013), and venlafaxine has evidence of efficacy. Venlafaxine has low to moderate adverse effects, is low to moderate cost depending upon duration of treatment, has been shown to be effective, and is thus recommended for treatment of PTSD.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Venlafaxine hydrochloride, venlafaxine; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 273 articles in PubMed, 54 in CINAHL, 89 in Cochrane Library, 11700 in Google Scholar, and 0 from other sources.† We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **TRICYCLIC ANTIDEPRESSANTS (TCAS)**

## AMITRIPTYLINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of amitriptyline in the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There are no quality studies assessing the use of amitriptyline for PTSD. There is one low-quality study showing a trend towards efficacy over placebo, but this study had a high

dropout rate (Davidson et al., 1990). Other studies of TCAs conflict (see recommendations for desipramine and imipramine). Amitriptyline has low to moderate adverse effects, is low to moderate cost depending upon duration of treatment, has no quality evidence of efficacy for PTSD, and thus there is no recommendation for amitriptyline.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: amitriptyline; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 272 articles in PubMed, 52 in CINAHL, 89 in Cochrane Library, 3910 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **DESIPRAMINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## No Recommendation

There is no recommendation for the use of designamine in the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There is one moderate-quality study that shows a lack of efficacy for desipramine for PTSD versus placebo (Reist et al., 1989). Yet, there is evidence suggestive of efficacy for another TCA, imipramine. Desipramine has low to moderate adverse effects, is low to moderate cost depending upon duration of treatment, and there is conflicting evidence of efficacy among the TCAs; thus, there is no recommendation for PTSD. However, there are other indications for use of desipramine and TCAs.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: desipramine; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 11 articles in PubMed, 2 in CINAHL, 0 in Cochrane Library, 6, 660 in Google Scholar, and 0 from other sources<sup>†</sup>. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

**IMIPRAMINE (TOFRANIL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)** 

## No Recommendation

There is no recommendation for the use of imipramine (Tofranil) in the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There are few quality studies of imipramine for the treatment of PTSD. The highest-quality RCT compared imipramine to phenelzine to placebo, showing that both drugs were better than placebo but phenelzine was better than imipramine (Frank et al., 1988). In another study, there were exposure differences, which likely biased the study outcomes and high dropout rates (Kosten et al., 1991). It has been suggested that imipramine is effective in combination with psychotherapy for improving sleep and reducing flashbacks, but this was a non-RCT sample of 10 patients (Burstein A, 1984). However, there is evidence suggesting lack of efficacy for desipramine. Imipramine has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, and has some limited evidence of efficacy, but other evidence for TCAs is negative; thus, there is no recommendation for treatment of PTSD. There are other indications for use of TCAs.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Imipramine; post-

traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 270 articles in PubMed, 42 in CINAHL, 88 in Cochrane Library, 15700 in Google Scholar, and 0 from other sources\*. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# NORTRIPTYLINE (PAMELOR) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of nortriptyline (Pamelor) in the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There are no quality studies assessing nortriptyline for PTSD and thus there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Nortriptyline, pamelor, tricyclic antidepressants; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 6 articles in PubMed, 1 in CINAHL, 2 in Cochrane Library, 7110 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

<sup>†</sup> The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we

review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## MIRTAZAPINE (REMERON) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation regarding mirtazapine (Remeron) for the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There are a few moderate-quality studies using mirtazapine for PTSD. However, one shows greater efficacy for paroxetine (Seo et al., 2010). There is evidence of conflicting efficacy versus placebo with two moderate-quality trials suggesting efficacy (Davidson et al., 2003, Schneier et al., 2015), while another larger trial was negative (Davis et al., 2020). Mirtazapine has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, and has conflicting evidence of efficacy; thus, there is no recommendation.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Mirtazapine; Remeron; antidepressive agents, tricyclic; tricyclic antidepressants; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 17 articles in PubMed, 2 in CINAHL, 12 in Cochrane Library, 7110 in Google Scholar, and 0 from other sources\*. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **MONOAMINE OXIDASE INHIBITORS (MAOIS)**

# PHENELZINE (NARDIL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Sometimes Recommended**

Phenelzine (Nardil) is selectively recommended as a treatment for patients with PTSD, as it has limited evidence of effectiveness while also having major interactions with many other medications.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Moderate

## **Indications**

PTSD sufficient to require first-line therapy such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Phenelzine may be used after first-line PTSD therapies, and would generally be recommended after medications with greater evidence of efficacy, such as sertraline.

#### **Benefits**

Improvements in PTSD symptoms.

## **Harms**

Severe adverse effects of phenelzine are typically related to use of serotonergic medications and/or consumption of food high in tyramine or dopamine and include: severe allergic reaction, hypertensive crisis, sudden and severe headache, chest pain, rapid or slow heart rate. Stop medication 10 days before elective surgery to avoid hypertensive crisis. Adverse effects also include: neck stiffness, nausea and vomiting, cold sweats, profuse sweating, vision problems, photophobia, chest pain, insomnia, swelling, rapid weight gain; agitation, unusual thoughts or behavior, rash. serotonin syndrome, hypertensive crisis, sleep disturbances, orthostatic hypotension, sexual dysfunction, and weight gain.

# Frequency/Dose/Duration

Phenelzine 15 mg/d flexible dosing up to 75 mg/d to achieve at least 90% MAO inhibition (Frank et al., 1988).

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

There are few quality studies of phenazine for the treatment of PTSD. The highest quality RCT compared phenelzine to imipramine to placebo, showing that both drugs were better than placebo but phenelzine was better than imipramine (Frank et al., 1988). In another study, there were exposure differences that likely biased the study outcomes and high dropout rates (Kosten et al., 1991). It has been suggested that phenelzine is effective in combination with psychotherapy for improving sleep and for reducing flashbacks (a non-RCT sample of ten patients (Burstein, 1984)). Phenelzine has low to high adverse effects depending on multiple factors (e.g., adherence to dietary requirements, prescriber's awareness of prescribing requirements and contraindications), is low to moderate cost depending upon treatment duration, and has some evidence of efficacy; thus, phenelzine is recommended for the treatment of PTSD although generally after trials of multiple other medications.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Phenelzine, Nardil, Monoamine oxidase inhibitors; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 4 articles in PubMed, 0 in CINAHL, 0 in Cochrane Library, 2780 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## ATYPICAL ANTIDEPRESSANTS

# TRAZODONE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of trazodone in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

There is no quality evidence of efficacy of trazodone for PTSD. Trazodone has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, has no proven efficacy for PTSD symptoms, and therefore there is no recommendation. There are other indications for trazodone.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Trazodone; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 0 in CINAHL, 7 in Cochrane Library, 2, 330 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **NEFAZODONE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Sometimes Recommended**

Nefazodone is selectively recommended for the treatment of patients with PTSD.

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

## **Indications**

PTSD sufficient to require multiple first-line therapies such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, and SSRIs. Other medications should generally also be tried first because adverse effects limit the utility of nefazodone.

## **Benefits**

Improvements in PTSD symptoms.

## Harms

Severe adverse effects limit use of nefazodone include: severe allergic reaction, irregular heartbeat, fever muscle tremors, unusual bleeding, fainting, weakness, rash, nausea,

headache, somnolence. Rare but serious effects reported include liver failure and liver necrosis. Common adverse effects include: constipation, stomach pains, dry mouth, cough, nausea, difficulty concentrating, memory problems, sexual dysfunction, ringing in ears, sleep problems.

Structurally similar to trazodone; has been withdrawn from the market in some countries because of rare severe hepatotoxicity (Therapeutics, 2016).

# Frequency/Dose/Duration

Nefazodone 100 mg/twice a day titrated up to 300-600 mg/twice a day as per manufacturer's recommendations.

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

## Rationale

One moderate-quality, placebo-controlled trial found efficacy of nefazodone, although the dropout rate was high (Davis et al., 2004). Another trial showed nefazodone had comparable efficacy to sertraline (McRae et al., 2004), which has known efficacy for PTSD. Nefazodone has considerable adverse effects that limit its utility (and resulted in downgrading of this recommendation), is moderate cost depending upon duration of treatment, and has quality evidence of efficacy; thus, it is selectively recommended for treatment of PTSD.

# **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Nefazodone; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 25 articles in PubMed, 0 in CINAHL, 31 in Cochrane Library, 784 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of

100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **BUPROPION (WELLBUTRIN, ZYBAN) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Not Recommended**

Bupropion (Wellbutrin, Zyban) is not recommended as a treatment for patients with PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

#### Rationale

The sole quality, placebo-controlled trial suggests lack of efficacy of bupropion for treatment of PTSD (Becker et al., 2007). There is evidence for smoking cessation. Bupropion has low adverse effects, is low to moderate cost depending upon treatment duration, but appears ineffective for PTSD symptoms. Therefore, bupropion is not recommended for PTSD. There are other indications for bupropion.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Bupropion OR Wellbutrin OR Zyban; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 22 articles in PubMed, 2 in CINAHL, 18 in Cochrane Library, 3, 630 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **BENZODIAZEPINES**

Anxiety, irritability, and insomnia associated with PTSD have been treated with benzodiazepines, although the risks (especially addiction and tolerance, harms when taken with alcohol) associated with benzodiazepines have been generally thought to outweigh any short-term benefits (159, 160).

# BENZODIAZEPINES FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Benzodiazepines are not recommended for the treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

Trials of benzodiazepines for treatment of PTSD have found a lack of efficacy, with one trial of clonazepam suggesting a lack of efficacy (Cates et al., 2004), and another of temazepam (Mellman, 2002) showing a lack of efficacy. One trial of alprazolam as a co-intervention found no clear evidence of the utility of alprazolam (Rothbaum et al., 2014). A Cochrane review reported a lack of evidence of efficacy (Williams et al., 2022). Benzodiazepines have low to moderate adverse effects that include addiction potential, are low to moderate cost depending upon duration of treatment, have no quality evidence of efficacy for treatment of specific PTSD symptoms, and therefore are not recommended. There are other indications for benzodiazepines.

#### Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Benzodiazepines; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 104 articles in PubMed, 7 in CINAHL, 78 in Cochrane Library, 15, 800 in Google Scholar, and 0 from other sources†. We considered for inclusion 7 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 5 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **ANTICONVULSANTS**

# GABAPENTIN FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### **Not Recommended**

Gabapentin is not recommended for the treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

There is one moderate-quality RCT showing lack of efficacy of gabapentin for treatment of PTSD (Stein et al., 2007). Gabapentin has low to moderate adverse effects, is moderate cost, and has been shown to lack efficacy; thus, as quality evidence shows lack of efficacy, it is not recommended for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gabapentin, Neurontin, Anticonvulsants; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 18 articles in PubMed, 4 in CINAHL, 6 in Cochrane Library, 6870 in Google Scholar, and 0 from other sources\*. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## LAMOTRIGINE (LAMICTAL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of lamotrigine (Lamictal) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

There is no quality evidence for efficacy of lamotrigine for treatment of PTSD and thus there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Lamotrigine OR Lamictal; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 17 articles in PubMed, 0 in CINAHL, 8 in Cochrane Library, 2, 600 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **TOPIRAMATE (TOPAMAX) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## No Recommendation

There is no recommendation for the use of topiramate (Topamax) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

Quality studies substantially conflict regarding efficacy of topiramate for treatment of PTSD, with most studies suggesting lack of efficacy for PTSD treatment (Lindley, 2007, Tucker, 2007, Monga et al., 2023); thus, there is no recommendation.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: topiramate, topamax; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*,

randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 53 articles in PubMed, 2 in CINAHL, 8 in Cochrane Library, 9090 in Google Scholar, and 0 from other sources<sup>†</sup>. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **VALPROIC ACID FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Not Recommended**

Valproic acid is not recommended for the treatment of PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

#### Rationale

Two placebo-controlled trial found lack of efficacy of valproic acid for treatment of PTSD (Davis et al., 2008). Thus, with quality evidence documenting lack of efficacy, valproic acid is not recommended. However, there are other indications for valproic acid, such as seizures, that may co-exist in some patients with PTSD and thus would be indicated for select patients.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: valproic acid; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 15 articles in PubMed, 2 in CINAHL, 2 in Cochrane Library, 2710 in Google Scholar, and 0 from other sources<sup>†</sup>. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we

review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

TIAGABINE (GABATRIL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Tiagabine (Gabatril) is not recommended for the treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

There is one sizable placebo-controlled trial and it shows lack of efficacy of tiagabine (Davidson et al., 2007). There is one small trial suggesting a slight non-significant potential benefit for reducing relapse of PTSD symptoms (Connor et al., 2006). Tiagabine has low to moderate adverse effects, is moderate cost depending upon treatment duration, and has one sizable trial that showed lack of efficacy; thus, it is not recommended.

#### Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: tiagabine, Gabatril, post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 0 in CINAHL, 35 in Cochrane Library, 3, 410 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **ANTIPSYCHOTICS**

ARIPIPRAZOLE (ABILIFY) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of aripiprazole (Abilify) in the treatment of patients with PTSD.

# **Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There is no quality evidence of efficacy of aripiprazole for treatment of PTSD. In one study, the study was underpowered with a total of 12 patients (5 in the treatment group and 7 in the placebo group), so proven efficacy is not available (Naylor et al., 2015). A Cochrane review also concluded lack of evidence of efficacy (Williams et al., 2022). Aripiprazole has adverse effects, is low to moderate cost depending upon treatment duration, has no clear evidence of efficacy, and thus there is no recommendation.

#### Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: aripipirazole, abilify, Antipsychotic; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 33 articles in PubMed, 5 in CINAHL, 7 in Cochrane Library, 13800 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## QUETIAPINE (SEROQUEL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for or against quetiapine (Seroquel) for the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There is one trial of quetiapine that has high dropout rates that effectively preclude an assessment of efficacy for the treatment of PTSD (Villarreal et al., 2016). Quetiapine has low

to moderate adverse effects, is low to moderate cost depending upon treatment duration, has no clear evidence of efficacy, and thus there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: quetiapine, seroquel; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 33 articles in PubMed, 3 in CINAHL, 4 in Cochrane Library, 3470 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## RISPERIDONE (RISPERDAL) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of risperidone (Risperdal) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

The largest and highest-quality placebo-controlled RCT assessing risperidone for suggests lack of efficacy (Krystal JH et al., 2011), although a smaller study suggested possible efficacy. Thus, the quality data conflict regarding the efficacy of risperidone, with the strongest evidence indicating a lack of efficacy.

The results of a third RCT assessing adjunctive use of risperidone in addition to sertraline suggested some efficacy, although the sample sizes are so small (n=9; n=11) that they preclude a robust conclusion (Rothbaum et al., 2008). Another study suggests that the addition of risperidone may improve PTSD symptoms (Bartzokis et al., 2005). Risperidone has low to moderate adverse effects, is of low to moderate cost depending upon treatment duration, but the strongest evidence suggests lack of efficacy as a treatment for PTSD. A

small study has suggested possible efficacy as adjunctive therapy to sertraline, but needs to be repeated in a larger study before a formal recommendation could be formed.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Risperidone; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2 articles in PubMed, 2 in CINAHL, 1 in Cochrane Library, 238 in Google Scholar, and 0 from other sources\*. We considered for inclusion 0 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## OLANZAPINE (ZYPREXA) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## Recommended

Olanzapine (Zyprexa) is selectively recommended for the treatment of patients with PTSD after multiple other interventions are trialed (e.g., CBT, exercise, prolonged/exposure therapy, cognitive processing therapy, SSRIs).

**Strength of evidence** Recommended, Evidence (C) **Level of confidence** Low

#### **Indications**

PTSD sufficient to require multiple first-line therapies such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, and SSRIs. May be especially used for flashbacks and nightmares. However, adverse effects suggest multiple other medications are generally indicated prior to trying olanzapine.

## **Benefits**

Improvements in PTSD symptoms.

#### Harms

Serious adverse effects are significantly limiting and include: allergic reaction, drug-induced parkinsonism, neuroleptic malignant syndrome, seizures, irregular heartbeat, orthostatic hypotension, somnolence, sedation, glucose dyscontrol, hyperlipidemia, dyskinesia, vision problems. Pregnancy risk category C. Less serious adverse effects include: altered mental status, constipation, cough, diarrhea, weight gain, rash, and anxiety.

Somnolence, weight gain, diabetes, extrapyramidal symptoms, QT interval prolongation, and hyperprolactinemia, extrapyramidal effects, pregnancy risk category C (Food et al., 2013, Food et al., 2017, Therapeutics, 2016).

# Frequency/Dose/Duration

Olanzapine 5 mg/day for one week and increased to 7. 5 mg/day for week two and then up to 10 mg/day for weeks three and four (Carey et al., 2012). Increased doses up to and above 20 mg/day may be utilized.

## Indications for discontinuation

Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication.

#### Rationale

There are three small moderate-quality, placebo-controlled trials, two of which suggest efficacy for olanzapine in treating PTSD, especially for treatment of flashbacks, nightmares, or PTSD refractory to first-line therapies (Stein et al., 2002, Carey et al., 2012). Olanzapine has moderate to quite significant adverse effects, is moderate cost depending upon treatment duration, but has some evidence of efficacy, and thus is selectively recommended as a second-line treatment for PTSD. However, because the adverse effects are considerable, multiple other treatments and medications are recommended to be trialed before olanzapine (e.g., CBT, exercise, prolonged/exposure therapy, cognitive processing therapy, SSRIs).

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Olanzapine; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 2 in CINAHL, 0 in Cochrane Library, 4, 840 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are

reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **ADRENERGIC INHIBITORS**

## PROPRANOLOL FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of propranolol in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There is conflicting quality evidence on the efficacy of propranolol for PTSD. Three studies showed lack of efficacy (Stein et al., 2007, Hoge et al., 2012, Roullet et al., 2021), but improvement in PTSD symptoms was reported in another study (Brunet et al., 2018) while some cognitive improvement was found in another study (Mahabir et al., 2016). Propranolol has moderate adverse effects, is low to moderate cost depending upon treatment duration, and has conflicting evidence of efficacy for PTSD; therefore, there is no recommendation.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Propranolol; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 9 articles in PubMed, 10 in CINAHL, 1 in Cochrane Library, 4, 050 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 2 randomized trials and 5 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# PRAZOSIN (MINIPRESS) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for prazosin (Minipress) for the treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There are multiple trials of prazosin for treatment of PTSD. The largest trial showed a lack of efficacy (Raskind et al., 2018). Smaller trials suggest efficacy for nightmares (Raskind et al., 2013), and alcohol dependence but not PTSD (Simpson et al., 2015). Another study also found lack of efficacy for PTSD (Petrakis et al., 2016). One other trial reported prazosin is not as effective as CBT, but better than placebo for sleep disturbances in military personnel (Germain et al., 2012). Prazosin has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, and has conflicting evidence of efficacy. Thus, there is no recommendation for PTSD. It may have some limited indications for treatment of nightmares associated with PTSD (Association, 2017).

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 31 articles in PubMed, 13 in CINAHL, 10 in Cochrane Library, 2400 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 6 articles considered for inclusion, 1 randomized trial and 5 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **GUANFACINE (INTUNIV) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## **Not Recommended**

Guanfacine (Intuniv) is not recommended for the treatment of patients with PTSD.

# **Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

#### Rationale

One moderate-quality, placebo-controlled study found lack of efficacy for guanfacine in the treatment of PTSD (Neylan et al., 2006). Guanfacine has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, has evidence of a lack of efficacy, and is thus not recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Guanfacine, Intuniv, Adrenergic alpha 2 receptor agonists, Adrenergic alpha-Agonists; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 2 in CINAHL, 3 in Cochrane Library, 1030 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **CLONIDINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

## No Recommendation

There is no recommendation for the use of clonidine in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

There are no quality studies using clonidine for PTSD. One small, low-quality study reported a potential benefit for hyperarousal symptoms (Ziegenhorn et al., 2009). Thus, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Clonidine, Catapres, Adrenergic alpha 2 receptor agonists, Adrenergic alpha-Agonists; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 14 articles in PubMed, 0 in CINAHL, 9 in Cochrane Library, 2910 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# DOXAZOSIN (CARDURA) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### **Not Recommended**

Doxazosin (Cardura) is not recommended for the treatment of PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## **Rationale**

One moderate-quality RCT suggested lack of efficacy (Back et al., 2023), although there is one low-quality trial suggesting potential efficacy (Rodgman et al., 2016), Doxazosin is not recommended.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Doxazosin, Adrenergic alpha-1 Receptor Antagonists, Cardura; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 19 articles in PubMed, 1 in CINAHL, 7 in Cochrane Library, 1010 in Google Scholar,

and 0 from other sources<sup>†</sup>. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **CANNABIS**

## CANNABINOIDS FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### **Not Recommended**

Cannabis is not recommended for treatment of patients with PTSD. See also the ACOEM Cannabis guideline.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

One high-quality placebo-controlled trial (n=80) found lack of efficacy of cannabis for the treatment of PTSD symptoms (Bonn-Miller et al., 2021). Another trial reported effects on threat processing but did not report effects on PTSD symptoms (Rabinak et al., 2020). A small trial of cannabinoids (n=10) reported significant adverse effects (Jetly et al., 2015). Systematic reviews did not find significant evidence of efficacy for routine use in the treatment of PTSD symptoms (Hindocha et al., 2020, Stanciu et al., 2021, Orsolini et al., 2019). Cannabinoids have significant adverse effects, have been shown to be ineffective, and thus are not recommended for the treatment of PTSD symptoms. See also the ACOEM Cannabis guideline.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Marijuana, cannabis, cannabinoids, cannabidiol; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 69 articles in PubMed, 40 in CINAHL, 62 in Cochrane Library, 15400 in Google Scholar, and 1 from other sources†. We considered for inclusion 7 from PubMed, 0 from CINAHL, 1 from Cochrane

Library, 1 from Google Scholar, and 1 from other sources. Of the 10 articles considered for inclusion, 4 randomized trials and 6 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **KETAMINE**

# **KETAMINE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### **Not Recommended**

Ketamine and ketamine-assisted psychotherapy is not recommended for treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

One research group reported strong efficacy of ketamine (Feder et al., 2023, Feder et al., 2014). Another group reported lack of efficacy (Abdallah et al., 2022), while another reported equal (in)efficacy of ketamine with ketorolac (Dadabayev et al., 2020). A systematic review noted problems with biases and heterogeneity, with all control agents showing rapid acting effects such that placebo-responses and unblinding were concerns (Borgogna et al., 2024). Other systematic reviews concluded the evidence is low (Varker et al., 2021). One review concluded that based on the reported magnitudes of benefit, short duration of effects, and the need for multiple hospital visits for administrations, that ketamine would not supplant SSRIs or venlafaxine (Sicignano et al., 2024). Investigations for treatment-resistant PTSD are particularly felt to be needed (Liu et al., 2024). Ketamine is invasive, has adverse effects, is high cost, has conflicting evidence of efficacy, and thus is not recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: "esketamine"[Supplementary Concept] OR "esketamine"[All Fields] OR "ketamine"[All Fields] OR "ketamine"[MeSH Terms] OR "ketamin"[All Fields] OR "ketamine s"[All Fields] OR "ketamine"[Supplementary Concept] OR "esketamine"[All Fields] OR "ketamine"[All Fields] OR "ketamine"[MeSH Terms] OR "ketamin"[All Fields] OR "ketamine"[All Fields] OR "ketamines"[All Fields] OR "ketamine"[All Fields] OR "esketamine"[All Fields] OR "esketa

("ketamine"[All Fields] AND "hydrochloride"[All Fields]) OR "ketamine hydrochloride"[All Fields]) OR MeSH descriptor: [Ketamine] explode all trees OR ketalar OR Spravato OR ketajet; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 156 articles in PubMed, 31 in CINAHL, 133 in Cochrane Library, 12, 400 in Google Scholar, and 0 from other sources†. We considered for inclusion 33 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 10 from Google Scholar, and 0 from other sources. Of the 49 articles considered for inclusion, 14 randomized trials and 21 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **MDMA**

# MDMA FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against MDMA for treatment of PTSD symptoms in supervised, experimental research settings.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Harms

Memory problems, problems learning, changes in perception, confusion, anxiety, depression, paranoia, sleep problems, muscle tension, tremors, involuntary teeth clenching, muscle cramps, nausea, faintness, chills, sweating, and blurred vision (U. S. Department of Justice, 2020).

# Rationale

MDMA is a controlled substance that is classified as Schedule I under the Controlled Substances Act; it carries increased risks of memory problems, problems learning, changes in perception, confusion, anxiety, depression, paranoia, and sleep problems (U. S. Department of Justice, 2020). One RCT with multiple post-hoc analyses concluded there is evidence of efficacy (Mitchell et al., 2023, Mitchell et al., 2023, Nicholas et al., 2022, Van Der Kolk et al., 2024, Brewerton et al., 2022).

Other data are sparse and/or low quality. Two systematic reviews with meta-analyses concluded there were promising results; however, the evidence certainty was low due to small sample sizes, blinding, study heterogeneity and publication bias (Bahji et al., 2025, Velit-Salazar et al., 2024). Another review indicated that MDMA-assisted psychotherapy may improve PTSD symptoms, but problems with adverse effects and abuse risks hinder clinical applications (Yang et al., 2024). Several other systematic reviews concluded that MDMA is safe and effective (Bahji et al., 2020, Luoma et al., 2020, Shahrour et al., 2024, Smith et al., 2022, Tedesco et al., 2021). There is no recommendation for the use of MDMA in supervised, experimental research settings; it is not recommended in non-research settings.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: N-Methyl-3, 4-methylenedioxyamphetamine, MDMA, and Ecstasy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed articles in 106 PubMed, 39 in CINAHL, 28 in Cochrane Library, 17, 100 in Google Scholar, and 0 from other sources†. We considered for inclusion from 17 PubMed, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 19 articles considered for inclusion, 9 randomized trials and 8 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **NUTRACEUTICALS**

## **NUTRACEUTICALS FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### No Recommendation

There is no recommendation for the use of nutraceuticals in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

### Rationale

There is one moderate-quality study of inositol compared with placebo that reported a lack of efficacy (Kaplan et al., 1996) and no other trials. Nutraceuticals have unclear effects, are low to moderate to high cost depending upon type and treatment duration, have no proven efficacy, and have no standardization of dose. Therefore, there is no recommendation for nutraceuticals in the treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Nutraceuticals; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 15 articles in PubMed, 8 in CINAHL, 4 in Cochrane Library, 11000 in Google Scholar, and 1 from other sources†. We considered for inclusion 3 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 4 articles considered for inclusion, 3 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## OMEGA-3 FATTY ACIDS FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of omega-3 fatty acids in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There are few quality studies using omega-3 fatty acids. Studies to improve PTSD symptoms (Matsumura et al., 2016) or to secondarily prevent PTSD (Matsuoka Y, 2015) were inconclusive. Omega-3 fatty acids have low adverse effects, are low to moderate cost depending upon treatment duration, but have no clear evidence of efficacy. Thus, there is no recommendation for omega-3 fatty acids for PTSD.

#### Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: omega-3 fatty acids; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 0 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **OXYTOCIN**

# OXYTOCIN FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Intranasal oxytocin is not recommended for the treatment of PTSD symptoms.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

One trial of oxytocin in the emergency department for treatment of moderate to severe distress mostly related to accidents reported a failure to prevent PTSD symptoms (van Zuiden et al., 2017). Two sizable trials reported conflicting efficacy for amplifying the acquisition and consolidation of intrusive memories (Schultebraucks et al., 2022, Maslahati et al., 2023). Trials have assessed effects on cue-inducement among those with both alcohol use disorder and PTSD and reported no reductions in craving (Stauffer et al., 2019, Stauffer et al., 2022, Morrison et al., 2020, Flanagan et al., 2019). One systematic review reported the "results were mixed and insufficient to quantify the effectiveness of this intervention" (Giovanna et al., 2020), while another reported the sample sizes were quite small and "highly heterogeneous for clinical features" (Di Lorenzo et al., 2020). Intranasal oxytocin is not invasive, has low adverse effects, is moderate cost, has evidence that mostly suggests a lack of efficacy, and thus is not recommended for treatment of PTSD.

#### Evidence

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Oxytocin; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 37 articles in PubMed, 10 in CINAHL, 65 in Cochrane Library, 9, 910 in Google Scholar, and 0 from other sources\*. We considered for inclusion 19 from PubMed, 0 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 23 articles considered for inclusion, 21 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **STEROIDS**

## HYDROCORTISONE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## No Recommendation

There is no recommendation for the use of hydrocortisone in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There is limited evidence, with experimental trials and a few small RCTs. The higher quality RCTs suggest a lack of efficacy for treatment of PTSD (Lehrner et al., 2021, Ludäscher et al., 2015), although others suggest efficacy (Yehuda et al., 2015, Delahanty et al., 2013). Hydrocortisone has significant adverse effects, is low to moderate cost depending upon the duration of therapy, and there are conflicting studies; thus, there is no recommendation regarding its use for treatment of PTSD.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: TREATMENT TOPIC; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials,

randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 113 articles in PubMed, 36 in CINAHL, 31 in Cochrane Library, 2, 620 in Google Scholar, and 0 from other sources†. We considered for inclusion 7 from PubMed, 1 from CINAHL, 2 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 9 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **NEUROMUSCULAR THERAPIES**

# TRANSCRANIAL MAGNETIC STIMULATION

Transcranial magnetic stimulation, a noninvasive brain stimulation treatment, has been suggested for treatment of numerous neuropsychiatric conditions such as depression, anxiety or suicidal ideation (161-168), and PTSD (162, 164, 166, 169-177), although most data are for depression. There are no good data for use in PTSD.

# TRANSCRANIAL MAGNETIC STIMULATION (TMS/RTMS) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of transcranial magnetic stimulation (TMS) or repetitive transcranial magnetic stimulation (rTMS) in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

The highest quality study compared TMS + brief exposure imagery vs. sham TMS + brief exposure imagery and found the sham plus brief exposure group was significantly better suggesting lack of efficacy (Isserles, 2021, Guzick et al., 2024). The next highest quality study compared rTMS to sham added in both arms to CPT and reported evidence of efficacy (Kozel et al., 2018). The remaining quality RCTs were all small and heterogeneous studies of TMS for PTSD, and some of these suggest some potential efficacy compared to sham (Nam et al., 2013, Cohen et al., 2004, Isserles et al., 2013, Watts et al., 2012, Boggio et al., 2010). Meta-analysis shows significant effect size on PTSD symptoms that may be correlated with total number of stimulations (C. A. f. D. a. T. i, 2014). A Cochrane review concluded there was moderate certainty that rTMS makes little to no difference in PTSD severity compared with

sham (Brown et al., 2024). TMS is not invasive, has low to moderate adverse effects, is moderate to high cost depending upon duration of treatment, and has conflicting evidence of efficacy; thus, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Transcranial Magnetic Stimulation); post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 105 articles in PubMed, 23 in CINAHL, 35 in Cochrane Library, 9, 990 in Google Scholar, and 0 from other sources\*. We considered for inclusion 8 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 5 randomized trials and 4 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# TRANSCRANIAL DIRECT CURRENT STIMULATION

TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against transcranial direct current stimulation for the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

The only sizable sham-controlled trial of a mixed patient population of PTSD, anxiety, and impulse aggression reported tDCS to be ineffective (Smits et al., 2022). Another sham-controlled trial of tDCS found some evidence of potential efficacy (van 't Wout-Frank et al., 2024), while another found differences at immediate follow-up that did not persist (Ahmadizadeh et al., 2019). There are other small and low-quality studies. Transcranial direct current stimulation is not invasive, has low adverse effects, is high cost, and has conflicting evidence of efficacy; thus, there is no recommendation.

### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Transcranial direct current stimulation, tDCS; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 41 articles in PubMed, 10 in CINAHL, 9 in Cochrane Library, 13, 900 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **DEEP BRAIN STIMULATION**

## DEEP BRAIN STIMULATION FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Deep brain stimulation is not recommended for the treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Evidence (C) **Level of confidence** Low

## Rationale

There is no quality evidence to support the use of deep brain stimulation for PTSD. Deep brain stimulation is invasive, has moderate to severe adverse effects (including but not limited to hemorrhage and psychological sequelae), is high cost, and, in the absence of efficacy, is not recommended for treatment of PTSD.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Deep brain stimulation; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 1 in CINAHL, 1 in

Cochrane Library, 1 in Google Scholar, and 0 from other sources<sup>†</sup>. We considered for inclusion 0 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **VAGAL NERVE STIMULATION**

## **VAGAL NERVE STIMULATION FOR POSTTRAUMATIC STRESS DISORDER (PTSD)**

#### **Not Recommended**

Vagal nerve stimulation is not recommended for the treatment of patients with PTSD.

**Strength of evidence** Not Recommended, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

Published studies are only of small sample sizes (Bremner et al., 2021, Wittbrodt et al., 2021). There is no quality evidence for vagal nerve stimulation for the treatment of PTSD symptoms, although it has been used for refractory epilepsy and depression. Vagal nerve stimulation is invasive, has adverse effects (lead problems, infections, facial weakness, cough, hoarseness, chest pain, difficulty swallowing, breathing, and headache), and is high cost. In the absence of quality evidence of efficacy, it is not recommended.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Vagal nerve stimulation; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 26 articles in PubMed, 2 in CINAHL, 10 in Cochrane Library, 17, 200 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we

review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **CRANIAL ELECTROTHERAPY STIMULATION**

## CRANIAL ELECTROTHERAPY STIMULATION FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of cranial electrotherapy stimulation in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There is no quality evidence showing efficacy (or lack thereof) for cranial electrotherapy stimulation. A systematic review concluded the available studies are at high risk of bias and the evidence was insufficient to support that cranial electrical stimulation was effective (Shekelle et al., 2018). Thus, there is no recommendation.

## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cranial electrical stimulation, CES, Cranial electrotherapy stimulation, Transcranial direct current stimulation; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 58 articles in PubMed, 28 in CINAHL, 75 in Cochrane Library, 16100 in Google Scholar, and 0 from other sources†. We considered for inclusion 6 from PubMed, 1 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 10 articles considered for inclusion, 6 randomized trials and systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

# **ALLIED HEALTH INTERVENTIONS**

# MASSAGE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of massage in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

#### Rationale

There are no quality studies involving the use of massage for PTSD and thus there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Massage; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 11 in CINAHL, 11 in Cochrane Library, 9, 960 in Google Scholar, and 0 from other sources†. Zero articles met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### ACUPUNCTURE FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for the use of acupuncture in the treatment of patients with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There are three moderate-quality studies of acupuncture for PTSD (Engel et al., 2014, Hollifield et al., 2024, Prisco, 2013), but these studies have considerable methodological

issues. One trial attempted a sham, but treated the two groups substantially differently regarding stimulation and elicitation of deqi, while also failing to report the success of blinding and/or degree of unblinding that did or did not occur (Hollifield et al., 2024). One trial was subject to usual care bias (Engel et al., 2014) and the other trial had small samples and included a sham for auricular acupuncture with reported inconsistent results between groups and over time (Prisco, 2013). Acupuncture is minimally invasive, has low to moderate adverse effects, and is moderate cost depending upon treatment duration. However, in the absence of quality evidence of efficacy, there is no recommendation.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Acupuncture; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 51 articles in PubMed, 23 in CINAHL, 35 in Cochrane Library, 9, 380 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **INJECTION THERAPIES**

# STELLATE GANGLION BLOCK FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

## **Not Recommended**

Stellate ganglion blocks are not recommended for treatment of PTSD.

**Strength of evidence** Not Recommended, Insufficient Evidence (I) **Level of confidence** Low

#### **Rationale**

Two sham-controlled RCTs conflict regarding whether there was lack of efficacy (Hanling et al., 2016) or efficacy in two reports of one trial (Rae Olmsted et al., 2020, Blakey et al., 2024) of stellate ganglion blocks. A systematic review noted these conflicting studies (Kerzner et

al., 2021). Stellate ganglion blocks are invasive, have adverse effects, are high cost and with conflicting evidence of efficacy are not recommended.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Stellate Ganglion bock; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 18 articles in PubMed, 10 in CINAHL, 14 in Cochrane Library, 2, 500 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 3 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

## **DEVICES**

## WEARABLE DEVICES FOR POSTTRAUMATIC STRESS DISORDER (PTSD)

#### No Recommendation

There is no recommendation for or against wearable devices for sleep disturbance associated with PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## **Rationale**

There is one industry-sponsored trial of the NightWare system that suggests efficacy compared with sham (Davenport et al., 2023). More data are needed to develop supportive guidance for this moderately costly technology.

#### **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Active system, Wearable electronic device, Wearable device; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD;

controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 9 articles in PubMed, 1 in CINAHL, 8 in Cochrane Library, 1140 in Google Scholar, and 0 from other sources\*. We considered for inclusion 2 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### MORNING BLUE LIGHT THERAPY FOR PTSD

#### No Recommendation

There is no recommendation for or against morning blue light therapy for treatment of PTSD.

**Strength of evidence** No Recommendation, Insufficient Evidence (I) **Level of confidence** Low

## Rationale

A moderate-quality RCT found longer sleep duration among those exposed to morning blue light treatment (Killgore et al., 2022, Vanuk et al., 2022). Another RCT found favorable impacts regarding PTSD symptoms but failed to find effects on sleep (Youngstedt et al., 2021). A systematic review concluded the data are sparse (Millot et al., 2024). Blue light therapies have few trials and somewhat conflicting evidence regarding potential efficacy. Thus, there is no recommendation.

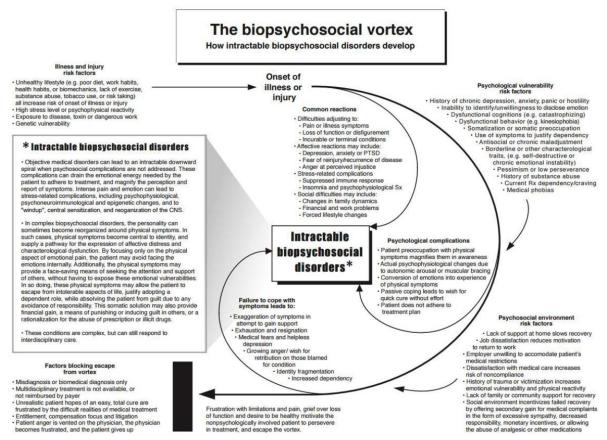
## **Evidence**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Morning light therapy; post-traumatic stress disorder, acute stress disorder, traumatic stress disorder, acute traumatic stress, post-traumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 41 articles in PubMed, 2 in CINAHL, 35 in Cochrane Library, 17, 900 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

#### **FIGURES**

# FIGURE 1. THE BIOPSYCHOSOCIAL VORTEX



Biopsychosocial Vortex © 2016 by Daniel Bruns, PsyD and John Mark Disorbio, EdD. All Rights Reserved. Reprinted with permission

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