AMERICAN COLLEGE OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

Posttraumatic Stress Disorder and Acute Stress Disorder

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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

Test/Procedure/Treatment	Details	Recommendation
Psychological / Psychiatric Evaluation	Psychological/Psychiatric Evaluation	Recommended, Insufficient Evidence (I)
PTSD Screening and Testing	PTSD Screening Tools	Recommended, Insufficient Evidence (I)
	Psychometric Testing	Recommended, Evidence (C)
	Pharmacogenomics Testing	No Recommendation, Insufficient Evidence (I)
	Functional MRI	Not Recommended, Insufficient Evidence (I)
Education and Exercise	Education: Trauma Affect Regulation (TARGET)	No Recommendation, Insufficient Evidence (I)
	Education: Educational Training	No Recommendation, Insufficient Evidence (I)
	Exercise	Moderately Recommended, Evidence (B)
	Yoga	Moderately Recommended, Evidence (B)
Psychological Interventions and Coping Strategies	Group Therapy	No Recommendation, Insufficient Evidence (I)
	Cognitive Behavioral Therapy	Moderately Recommended, Evidence (B)
	Computer-Assisted Cognitive Therapy	Moderately Recommended, Evidence (B)
	Cognitive Processing Therapy	Moderately Recommended, Evidence (B)
	Imagery Rehearsal Training	Moderately Recommended, Evidence (B)
	Narrative Exposure Therapy	Recommended, Evidence (C)
	Seeking Safety Therapy	No Recommendation, Insufficient Evidence (I)

Test/Procedure/Treatment	Details	Recommendation
	Dialectical Behavioral Therapy	No Recommendation, Insufficient Evidence (I)
	Stress Inoculation Training	No Recommendation, Insufficient Evidence (I)
	Acceptance and Commitment Therapy	No Recommendation, Insufficient Evidence (I)
	Brief Eclectic Therapy	No Recommendation, Insufficient Evidence (I)
	Mind/Body Interventions	
	Guided Imagery	Recommended, Insufficient Evidence (I)
	Mindfulness	Recommended, Insufficient Evidence (I)
	Music Therapy	No Recommendation, Insufficient Evidence (I)
	Art Therapy	No Recommendation, Insufficient Evidence (I)
	Spiritual-Based Interventions	No Recommendation, Insufficient Evidence (I)
	Deep Breathing Exercises	Recommended, Insufficient Evidence (I)
	Meditation	Recommended, Insufficient Evidence (I)
	Exposure Therapy and Prolonged Exposure Therapy	Moderately Recommended, Evidence (B)
	Virtual Reality	Moderately Recommended, Evidence (B)
	Individual Debriefing	No Recommendation, Insufficient Evidence (I)
	Group Debriefing	Not Recommended, Evidence (C)
	Critical Incident Stress Debriefing (CISD)	No Recommendation, Insufficient Evidence (I)
	Psychodynamic Psychotherapy	No Recommendation, Insufficient Evidence (I)
	Interpersonal Therapy	Recommended, Insufficient Evidence (I)
	Hypnotherapy	No Recommendation, Insufficient Evidence (I)
	Eye Movement Desensitization and Reprocessing	
	Eye Movement Component	Not Recommended, Insufficient Evidence (I)
	Exposure Therapy and Cognitive Behavioral Therapy Components	Recommended, Evidence (C)
	Tapping Techniques (Thought Field Therapy and Emotional Freedom Therapy)	No Recommendation, Insufficient Evidence (I)
	Emotional Freedom Techniques (EFT)	No Recommendation, Insufficient Evidence (I)

Test/Procedure/Treatment	Details	Recommendation
	Neurofeedback (Brain Computer Device and Interface)	No Recommendation, Insufficient Evidence (I)
	Animal-Assisted Therapy	No Recommendation, Insufficient Evidence (I)
Medications	Selective Serotonin Reuptake Inhibitors (SSRIs)	
	Sertraline	Moderately Recommended, Evidence (B)
	Paroxetine	Moderately Recommended, Evidence (B)
	Fluoxetine	Recommended, Insufficient Evidence (I)
	Fluvoxamine	No Recommendation, Insufficient Evidence (I)
	Escitalopram	Recommended, Insufficient Evidence (I)
	Citalopram	Recommended, Evidence (C)
	Vilazodone	Not Recommended, Evidence (C)
	Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs)	
	Venlafaxine	Moderately Recommended, Evidence (B)
	Tricyclic Antidepressants (TCAs)	
	Amitriptyline	No Recommendation, Insufficient Evidence (I)
	Desipramine	No Recommendation, Insufficient Evidence (I)
	Imipramine	No Recommendation, Insufficient Evidence (I)
	Nortriptyline	No Recommendation, Insufficient Evidence (I)
	Mirtazapine	Moderately Recommended, Evidence (B)
	Monoamine Oxidase Inhibitors (MAOIs)	
	Phenelzine	Recommended, Evidence (C)
	Atypical Antidepressants	
	Trazodone	No Recommendation, Insufficient Evidence (I)
	Nefazodone	Recommended, Evidence (C)
	Bupropion	Not Recommended, Evidence (C)
	Benzodiazepines	Not Recommended, Evidence (C)
	Anticonvulsants	

Test/Procedure/Treatment	Details	Recommendation
	Gabapentin	Not Recommended, Evidence (C)
	Lamotrigine	No Recommendation, Insufficient Evidence (I)
	Topiramate	No Recommendation, Insufficient Evidence (I)
	Valproic Acid	Not Recommended, Evidence (C)
	Tiagabine	Not Recommended, Evidence (C)
	Antipsychotics	
	Aripiprazole	No Recommendation, Insufficient Evidence (I)
	Quetiapine	Recommended, Insufficient Evidence (I)
	Risperidone	No Recommendation, Insufficient Evidence (I)
	Olanzapine	Recommended, Evidence (C)
	Adrenergic Inhibitors	
	Propranolol	No Recommendation, Insufficient Evidence (I)
	Prazosin	Recommended, Insufficient Evidence (I)
	Guanfacine	Not Recommended, Evidence (C)
	Clonidine	No Recommendation, Insufficient Evidence (I)
	Doxazosin	No Recommendation, Insufficient Evidence (I)
	Steroids	
	Hydrocortisone	No Recommendation, Insufficient Evidence (I)
	Alternative Therapies	
	Nutraceuticals	No Recommendation, Insufficient Evidence (I)
	Omega-3 Fatty Acids	No Recommendation, Insufficient Evidence (I)
	Marijuana, Cannabis, Cannabinoids, Cannabidiol	No Recommendation, Insufficient Evidence (I)
Neuromodulation Therapies	Transcranial Magnetic Stimulation (TMS) and Repetitive Transcranial Magnetic Stimulation (rTMS)	No Recommendation, Insufficient Evidence (I)
	Deep Brain Stimulation	Not Recommended, Insufficient Evidence (I)
	Vagal Nerve Stimulation	Not Recommended, Insufficient Evidence (I)
	Cranial Electrotherapy Stimulation	No Recommendation, Insufficient Evidence (I)

Test/Procedure/Treatment	Details	Recommendation
Allied Health Interventions	Massage	No Recommendation, Insufficient Evidence (I)
	Acupuncture	No Recommendation, Insufficient Evidence (I)

Related Terms

- Acute Stress Disorder
- Posttraumatic Stress Disorder (PTSD)
- Delayed stress disorder
- Delayed stress syndrome
- Shell shock
- Battle fatigue
- Combat neurosis

Introduction

Responses to trauma range widely [1], and include withdrawal, anxiety, posttraumatic growth, and the phenomenon that today is called posttraumatic stress disorder (PTSD). One of the first historical references to PTSD-like phenomena occurred in stories of the Trojan war contained in Homer's Iliad [2]. More recent conceptualizations of reactions to trauma include those described among World War I soldiers who were thought to suffer from "shell shock," while in World War II soldiers were thought to be suffering from "battle fatigue" [3].

Approximately 75% of the US population has been exposed to a life-threatening trauma [4]. In contrast, the cumulative prevalence of PTSD is reportedly 6.8% [5]. 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, 6, 24 months and 10 years respectively [6], although others report higher recovery rates [7, 8]. 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 6-92%, highlighting a relative lack of quality studies [1]. 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 [9].

PTSD and Types of Trauma

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 of these 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 2016, there were a total of 5,190 fatal work injuries recorded in the United States, with a fatal injury rate of 3.6 per 100,000 full-time equivalent (FTE) workers [10]. 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 17 percent of all work-related fatal occupational injuries in 2016 [10].

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. The prevalence of workplace injuries which could potentially precipitate PTSD are listed in Table 1.

Studies of trauma suggest that the risk of PTSD is associated with both the severity and the type of the trauma. One study of trauma severity found that “the prevalence of PTSD approached 100% when traumatic exposure reached extreme levels” [11]. Another study found that the types of trauma most likely to lead to PTSD were rape

followed by combat, with 65% of men and 46% of women who had reported being raped meeting criteria for rape-associated PTSD [12]. 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.

Table 1: Injury types that could potentially result in ASD/PTSD (incidence = per 10,000 full time workers)

Injury	Total private, state, and local government			Private industry		
	Number	*Incidence rate*	*Median days away from work*	*Number*	*Incidence rate*	*Median days away from work*
Amputations	5,700	0.5	22	5,360	0.6	26
Chemical burns and corrosions	3,490	0.3	3	3,200	0.3	3
Heat (thermal) burns	17,520	1.6	5	15,010	1.6	4
Multiple traumatic injuries	31,570	2.8	10	22,800	2.4	10
Violence and other injuries by persons or animals	75,720	6.8	5	38,440	4.0	4
Roadway incidents involving motorized land vehicles	44,490	4.0	8	31,130	3.2	10
Fires and explosions	1,850	0.2	9	1,270	0.1	11
Fall to lower level	60,490	5.5	18	50,490	5.3	19
Exposure to harmful substances or environment	51,650	4.7	4	40,250	4.2	3
Struck by object or equipment	157,490	14.2	5	135,280	14.1	5
Struck against object or equipment	59,010	5.3	5	50,160	5.2	5
Caught in or compressed by object or equipment	36,870	3.3	10	33,400	3.5	10
Total*	**1,153,490**	**104.0**	**8**	**902,160**	**93.9**	**8**

*Includes unlisted injuries.

Source: U.S. Department of Labor, Bureau of Labor Statistics. Nonfatal Occupational Injuries and Illnesses Requiring Days Away from Work, 2015. Available at: https://www.bls.gov/news.release/pdf/osh2.pdf.

The Prevalence of Sexual Assault

The most extensive studies of sexual assault in the workplace have been undertaken by the Department of Defense. According to the Department of Defense Fiscal Year 2016 Annual Report on Sexual Assault in the Military, 4.3% of active duty women and 0.6% of active duty men indicated that they had experienced a sexual assault within the previous 12 months [13]. Reported sexual assault in the military increased nearly 10% in 2017 [14], although the rise may be due to reduced barriers to reporting and other factors [15]. Sexual assault was defined in this survey as "a range of crimes, including rape, sexual assault, nonconsensual sodomy, aggravated sexual contact, abusive sexual contact, and attempts to commit these offenses" [16]. The degree to which Department of Defense data can be generalized to the population at large was examined. By way of comparison, the DOD's data indicating that 4.3% of active duty women are sexually assaulted each year is slightly lower than that of the CDC's estimate

that 5.2% of women living in the US experienced a sexual assault in the last 12 months [17, 18], and a similar Rand study estimate that 4.9% of women experienced a sexual assault in the last 12 month [19]. Thus, the prevalence of sexual assault in these three disparate studies was similar.

Studies of sexual assault prevalence are limited by several factors including the variable types of sexual assault which make precise definitions challenging, and the reluctance to report sexual assaults. A large Department of Defense study of 151,101 active duty Navy, Marines, Army, Air Force, and Coast Guard members estimated that the number of reported sexual assaults accounted for only 32 percent of the total assaults [20]. This finding within the military context appears consistent with patterns of under-reporting evident in the general US population: In a study of US civilians, reports to police were made by only 11.5% of college-aged women in the US who reported having been forced into nonconsensual oral, anal, or vaginal penetration [21].

The Department of Defense has also studied the reasons for not reporting sexual assault. Those who chose not to report a sexual assault most commonly cited reasons including they "wanted to forget about it and move on (68%), did not want more people to know (58%), or felt shamed or embarrassed (52%)." Male victims of sexual assault in the military population were less likely to formally report the incident to authorities or even disclose the assault to anyone at all as compared with female victims [13]. Additionally, 58% of female and 60% of male service members who reported to military officials that they had been sexual assaulted later indicated that they had experienced at least one form of retaliation (including professional reprisal, ostracism, and/or maltreatment) following their report of the assault [20].

Studies of workers are rare. One study of injured workers in Washington state in the 1980s examined the frequency of accepted worker compensation claims for workplace injuries attributed to rape and reported 1.5 workers compensation claims per 100,000 full-time equivalent female workers, with 4.4 worker compensation claims per 100,000 full-time equivalent female workers per year among high-risk job settings (e.g. taxi drivers, fast food, tavern workers) [22]. The Washington study also reported that in 30% of the reported cases, robbery was also involved, a weapon was used in 50%, was under 30 years of age in 73%, and in 85% the women were working alone when the rape occurred. However, the findings of this study included markedly lower prevalence rates of sexual assault than other studies, which generally reported prevalence rates about 1000 times higher [13, 17, 23, 24]. This may be attributable to the methods used including: 1) instead of all assaults, the authors reported the frequency with which women successfully opened a worker compensation claim for disabling physical injuries sustained during an act of rape in the workplace; 2) rape was defined as an accepted worker's compensation rape claim and were not opened unless the rape was sufficiently violent to produce a gynecological, orthopedic or other physical injury serious enough to produce disability, required time off of work and required medical intervention; 3) the physician's forms must have been coded with both an ICD9 diagnosis injury code, and a "Z16.2" system event code of "600" to indicate that the type of event leading to the injury was rape (no data were provided with regard to how often the Z16.2 event code system was used by practitioners in Washington); 4) claims involving PTSD without physical injury were disallowed regardless of involvement of a weapon, and there were no treatment benefits for psychological trauma; 5) 22% of these claims were denied by the payer and thus were not included; and 6) unlike the other prevalence studies, where information was obtained confidentially, treatment in the worker's compensation system had limited confidentiality. The limits of confidentiality, lack of available psychological treatments, frequency of which the perpetrator was a supervisor, and the challenges associated with opening a worker compensation claim necessitating both a physical and psychological injury likely reduced the frequency with which women could have successfully opened a worker's compensation claim for a sexual assault. These factors may help to explain the differences in prevalence rates among these studies.

Risk Factors for Workplace Sexual Assault

A 2016 Department of Defense study identified a number of workplace culture factors that, when present, appear to increase the risk of sexual assault. Specifically, the study named, "high levels of workplace hostility, an unhealthy enlisted and officer climate with respect to sexual assault, quality of training, and low presence of female co-workers" [20]. For female service members who have been victims of sexual harassment, the risk of sexual assault is sixteen times greater that they will be sexually assaulted; for male service members, the risk is

fifty times higher. Additionally, 52% of men and 56% of women serving in the military who reported sexual assault also reported having been the target of sexual harassment or stalking before or after the assault occurred [13].

Sexual harassment, as defined in the Department of Defense WGRA study, is defined as, “a form of harassment that involves unwelcome sexual advances, requests for sexual favors, and other verbal or physical conduct of a sexual nature when: 1) Submission to such conduct is made either explicitly or implicitly a term or condition of a person’s job, pay, or career, or 2) Submission to or rejection of such conduct by a person is used as a basis for career or employment decisions affecting that person, or 3) Such conduct has the purpose or effect of unreasonably interfering with an individual’s work performance or creates an intimidating, hostile, or offensive environment” [25]. In contrast, a “healthy climate with low workplace hostility” appeared to have protective impact with regards to sexual assault occurrences in the workplace [20].

Still, the generalizability and applicability of prevalence rates of sexual assault among military studies to the general workplace is unclear.

The Nature of PTSD

The science of PTSD can be divided into two main directions, as some researchers tend to view PTSD differently [26]. In a review, Ross et al. concluded that “any contemporary neuroscience formulation of PTSD should include an understanding of fear conditioning, dysregulated circuits, memory reconsolidation, epigenetics, and genetic factors” [26]. This line of research suggests that PTSD may be associated with gene-environment interactions.

Alternately, the evolutionary biology model theorizes that PTSD is a syndrome that is associated with adaptations that increase the individual’s chances of survival. Thus, evolutionary biology suggests to think of PTSD not as disease or psychopathology, but rather as instinctual responses to extreme threat that improved the chances of survival [27-29].

Naturally, the argument that both views of PTSD (gene-environment interactions and evolutionary biology [27-29]) may have factual bases has arisen. Thus, this view maintains that it would be incorrect to think of PTSD as “a normative response to extreme stress” [30]. It may be better to view PTSD as originating in adaptive responses to extreme threat that can become distorted when genetic or epigenetic vulnerabilities are present. Including both perspectives may have treatment value [26, 27].

PTSD and Epigenetics.

From a psychiatric perspective, recent research suggests that it may be incorrect to think of PTSD as a purely learned behavioral condition. Instead, findings suggest that behavioral changes associated with PTSD may involve epigenetic modifications to DNA functioning. Further, this theory includes that these changes may be transmitted from parent to child, and also place the child at greater risk of developing PTSD. Perhaps the best example of epigenetic related behavior change is in the epigenetic version of the fight or flight response, which has been called the “spite then fight response.” The spite then fight response hypothesizes that if you spite the mother, you will fight her offspring [31]. Thus, a traumatized mother may respond with epigenetic changes, which increase the chances that she and her offspring will survive. These epigenetic changes may in essence “dial-up" her fight or flight response, which may increase her survivability. If the mother suffers from chronic hyperarousal, she is better prepared to run faster, and fight harder. She may also never sleep deeply, as this would place her in jeopardy of nocturnal threats. While these alterations may help her to survive, the chronic stress may also be associated with a shortened life span due to stress related disease. These epigenetic changes to her fight or flight response are due to modifications to her DNA functioning, and thus can be transmitted to her offspring. The traumatized mother may therefore produce more aggressive offspring, which may both defend her and have greater chances for survival in a dangerous environment themselves, at the cost of shortened lifespan. Consistent with this, one study found that pregnant women present near the World Trade Center on September 11, 2001 were observed to have altered cortisol levels, and later to have infants with greater distress in response to loud noises or strangers [32].

Micro-level epigenetic changes secondary to PTSD were illustrated in a recent study that identified 326 genes and 190 micro-RNA strands present in significantly different levels in the blood cells of PTSD patients [33]. Other studies have identified stress-related changes in genes associated with the regulation of serotonin, the amygdala and the hippocampus [34]. Additionally, microbial differences in the gut (decreased total abundance of 3 specific microbes) were noted in a recent study comparing subjects with PTSD and trauma exposure controls [35]. Advances in this science may make it possible to develop a blood test to identify soldiers in the battlefield who are developing PTSD [36-38].

Psychological Theories of PTSD

It has been proposed that any adequate theory of PTSD must address several matters. [39] From this point of view, an adequate theory of PTSD must account for the experiences of those suffering from PTSD, and the natural course of posttraumatic reactions. Further, any theory must account for different recovery trajectories (e.g. why do some who have been traumatized recover while others do not), and should offer a framework for understanding why certain psychological therapies are effective in reducing PTSD symptom severity [39]. Several theories of PTSD were found that meet these criteria and follow [36].

The Two-Factor Theory of Behavioral Conditioning

The most parsimonious theory of PTSD [40] involves the application of "two factor learning theory" [41]. Two factor theory is based solely on behavioral conditioning, and does not refer to subjective symptoms. According to two factor theory, PTSD initially develops in accordance with principles of classical conditioning, when neutral stimuli become associated with a trauma. In Pavlov's original experiment, a bell was rung before a dog was fed. Eventually, ringing the bell became associated with food, and bell ringing caused salivation. Similarly, after a traumatic motor vehicle accident, a stimulus such as sitting in a car may become associated with a near death experience. Due to this association, sitting in a car or seeing a highway now elicits feelings of terror. Studies have shown that the degree to which patients develop this conditioned response may be attributable to individual differences in "conditionability" secondary to genetic factors and/or prior trauma exposure.

Once this conditioned response has been established, the patient's behavior comes to be strongly influenced by avoidance behavior under operant conditioning. That is, the conditioned stimuli such as sitting in a car have come to produce a response so aversive that avoiding reminders of the traumatic experience is now rewarding or "reinforcing." The driver has now learned that anxiety can be reduced by avoiding cars and highways, and this may create marked behavioral changes. This avoidant behavior prevents learning that being in a car does not automatically result in an accident. As no contradictory evidence is encountered, this preserves the strength of the conditioned response.

The two-factor theory of PTSD has the advantage of being both parsimonious, and able to explain a variety of PTSD related behaviors. While this approach is powerful with regard to explaining behaviors associated with fear and anxiety, it is less able to explain the cognitive distortions known to be associated with PTSD, nor is it able to account for the other emotions associated with PTSD, such as the feelings of guilt and shame noted in the DSM-5 definition of PTSD [42].

Dual Representation Theory

A neuropsychological theory of PTSD is called dual representation theory [43, 44]. According to this theory, PTSD is associated with the formation of traumatic memories through two anatomically distinct neural pathways that operate in parallel. The nature of the traumatic memories created by each pathway are fundamentally different as a result of their unique neural activation routes.

Information about the trauma processed with the involvement of the hippocampus results in memories that are have a temporal and spatial context that is integrated within the patient's life, can be voluntarily retrieved from long-term memory, and can be easily communicated verbally.

In contrast, dual representation theory hypothesizes that some traumatic memories are sensation based, are non-verbal in nature, and cannot be voluntarily recalled. These memories could involve images, sounds, sensory experiences, or other aspects of the trauma which were encoded but not particularly attended to/recorded in the memory system described above. Information encoded by this second memory pathway can be triggered involuntarily by reminders of the trauma. These "sensory" memories lack temporal context, are difficult to revise, and are associated with intense emotion and sympathetic arousal. It is these memories that are responsible for the intense flashbacks in PTSD. At the level of neuroanatomy, these sensory-based memories are thought to involve the amygdala, insula, and parietal areas of the brain, but not the hippocampus.

Dual representation theory helps to explain why exposure therapy works for PTSD. According to the dual representation theory, exposure therapy effectively addresses PTSD symptoms not by altering the sensory memory but by creating a parallel competing verbal memory that is assigned a spatial and temporal context so the information no longer signals current danger. Once this verbal memory is rehearsed through repeated exposure therapy treatments, it can become the preferred version of the traumatic memory.

Schema theory

Another theory of PTSD is called schema theory. Accordingly, a person's schemas consist of the individual's core assumptions and beliefs about the world and life. Schema theory holds that most people assume the world is generally benevolent, people are trustworthy, there is meaning to life, and view themselves as being generally worthwhile and capable [45, 46].

According to schema theory, PTSD can occur when a traumatic event shatters these fundamental beliefs or assumptions. This has been termed by some the "loss of the assumptive world" [47]. Here, "assumptive world" refers to an individual's fundamental assumptions about life, self, others, safety and meaning, but these assumptions can be contradicted by a single traumatic experience. Thus, the perception of a workplace as safe, a coworker as trustworthy and oneself as nice-looking can be erased in an instant by a disfiguring injury caused by the careless act of another. Without a trusted conceptual framework that can be used to anticipate threat and ensure safety, the world appears to be far more unpredictable and dangerous. According to schema theory, effective therapy for PTSD must enable the individual to reconstruct an accurate way of perceiving the world, so that the individual can feel some assurance with regards to prediction of threat and safety, and adequacy of the self.

Cognitive Theory

In general, cognitive theories have explained emotional reactions as being attributable to cognitive appraisals of environmental events. Cognitive theory of PTSD holds that PTSD involves excessively negative cognitive appraisals of the world as being more dangerous than is objectively true, viewing the self as being more incompetent to maintain one's own safety than is objectively true, or both [48]. This causes PTSD sufferers to greatly overestimate the severity of a threat in the present environment, based on exposure to a traumatic event in the past [39]. From this point of view, psychopathology results from distorted cognitions [42].

Over time however, cognitive theories evolved into a more complex framework. In particular, it was hypothesized that in response to trauma, a network of associations would develop. This is because the trauma is extraordinarily significant, its unexpected nature violates previously held beliefs about danger and safety. Because of this, a network of associations may develop, linking objects in the environment, intense fear, intense physiological responses, behavioral responses such as running or self-defense actions, and belief systems. Finally, this network of association could be easily activated by a multitude of environmental cues [49]. The strength of these cognitive models was that they were able to explode provide an explanation for the cognitive processes observed in those who have been traumatized. This approach was also useful in developing effective treatment strategies for PTSD [42]. These therapeutic approaches focus on a patient's thoughts and beliefs, and the direct challenge of unrealistic beliefs through verbal discourse [48].

Emotional Processing Theory

A prominent theory of PTSD is based on Foa's emotional processing theory [50, 51], which is an expansion of Foa's earlier work on cognitive theories of PTSD [49]. This holds that emotions are organized as "emotion structures," which include emotions, images, recollections of events, cognitions and response tendencies. This theory hypothesizes that emotional disorders are based on an emotional structure which includes an intense or pathological emotion such as terror, which is associated with images of events related to this emotion, responses to the emotion and the cognitive meaning associated with these emotions, events, and responses [39].

According to emotional processing theory, emotion structures in PTSD can be readily activated when a person encounters something that serves as a reminder of some aspect of the emotion structure. This results in an activation of the entire emotion structure, producing cognitive, behavioral and physiological reactions. Accordingly, a healthy emotion structure can serve as a guideline for adaptive behavior. In contrast, a pathological emotion structure does not accurately present the world, and may erroneously associate harmless events with something that is terrifying [39, 50].

According to emotional processing theory, PTSD is thought to involve a number of neutral objects or events which are wrongly associated with terror, physiological arousal, and escape behaviors. Over time, an increasing number of objects or events can come to activate the emotion structure. Additionally, the associated perceptions of the person's behavior during the trauma can become associated with increased perceptions of vulnerability and inability to remain safe, this maintains the strength of PTSD avoidance behaviors. Accordingly, PTSD represents a failure to process the traumatic memory [39, 50].

Another premise of emotional processing theory is that successful treatment modifies the distorted information in the emotion structure. In order for this emotion structure to be modified, the emotion structure must be activated, and while activated, the information that is incompatible with the erroneous association must be available [39]. Overall, emotional processing theory has hypothesized about why exposure therapy works for PTSD, and seven proposed mechanisms have been identified. They are [50]:

1. Repeated reliving of the traumatic event would desensitize the patient to the trauma, and contradicts the belief that the traumatic anxiety was permanent.
2. Exposure to the trauma prevents avoidance, and the negative reinforcement of avoidance.
3. Recalling a traumatic memory in a safe therapeutic environment may reduce the perceived dangerousness of the trauma.
4. Recalling a traumatic memory can allow it to be seen as only one of many events that may be encountered in life, which can help the patient discriminate between the potential threats of various events in life.
5. Getting through and therapeutic exposure session reinforces the patient's self-perceptions of strength and mastery.
6. By reflecting on traumatic events in detail, the patients may be able to identify cognitions that are inconsistent with the evidence.
7. As traumatic memories tend to be fragmented, repeated reliving of the trauma helps to generate a more organized and realistic memory.

Consistent with emotional processing theory, exposure therapy for PTSD is effective in reducing PTSD symptoms.

PTSD and Evolutionary Biology.

PTSD is a condition that has been of particular interest to evolutionary biologists. This is because the central theoretical construct of biology is evolutionary theory and survival of the fittest, and PTSD is a condition that occurs in response to threats to existence. Although evolutionary theories are not commonly cited in psychology, discussions of the evolutionary psychology perspective of PTSD have been in the literature since 1988 [52], and in recent years this approach has been characterized as a major new theoretical perspective [53, 54]. From this point of view, PTSD likely exists because over the course of human history, PTSD reactions promoted human survival.

This offers an alternative paradigm for PTSD. Thus, as opposed to viewing PTSD as a sign of personal weakness, evolutionary biology views PTSD within the context of responses that increase the chances of survival. Thus, if a worker develops PTSD after a finger is traumatically amputated at work, hypervigilance around saws may reduce the risk of similar injuries in the future, and to some extent be adaptive. From this theoretical perspective, PTSD may be viewed as arising from a set of innate response tendencies that over the course of evolution have had survival value, as they attempt to correct for underestimates of environmental danger, or overestimates of one's personal abilities. These adaptations range in energy requirements from low to high, and may be applicable to the present environment or not. These inate mechanisms create an involuntary examination and reevaluation of the environment and the self until a new homeostasis is achieved. If successful, it allows the individual to adapt to environmental threats in a way that increases safety, while being minimally maladaptive.

In evolutionary biology, PTSD has been theorized to involve a set of innate survival mechanisms based on a one-trial method of learning after a close encounter with death or profound injury. Thus, if it takes the individual ten trials to learn how to escape from the lion, the individual is unlikely to survive the learning process. However, if the individual is fortunate enough to escape the first encounter with the lion, and later has 1000 intrusive flashback memories of the event, this provides the individual with extensive cognitive practice of escape behaviors. Thus, evolutionary biologists have characterized PTSD as "automatic learning following single exposure to novel threat [that] would have conferred survival value on the species" [29]. This innate mechanism creates a cognitive method for rehearsing traumatic memories following a single exposure to life-threatening trauma, can create enduring and even vivid memories of the threat, and generates a set of fear-based defensive behaviors. "Fear is the key emotion of posttraumatic stress disorder (PTSD). Fear's evolved function is motivating survival via defensive behaviours" [29]. Consistent with this conceptualization, patients with PTSD have numerous stress-related symptoms, including increased activity in their amygdala [55], reduced prefrontal cortex volume, thyroid abnormalities that reflect changes in maintenance of homeostatic functions, reduced GABA activity [56], and stress-related changes in the gut biome [57].

In addition to involving a novel type of one-trial learning, Cantor's 2009 review of evolutionary research hypothesized that the "fight or flight response" was too simple to account for the complexity of defense mechanisms associated with PTSD, and offered an alternative explanation based on ethology and evolutionary theory [28]. This model theorized that traumatic experiences trigger a hierarchy of six defensive responses that follow, which begin with defenses with low energy requirements, and progressing to defenses with high energy requirements.

Cantor theorized that the first and most basic defense triggered by trauma is *avoidance*. This is the most primitive defense, and involves a precognitive, fear-based avoidance of environmental reminders of the traumatic event. As this defense is the predominant one used by reptiles, it was hypothesized that in humans this defense would be associated with activity in the "reptilian" parts of the human brain [28]. In PTSD, environmental "cues" may trigger avoidance behavior.

The second defense is *attentive immobility*. Most herbivores, when sensing a potential predator, will become immobile so as not to be seen. This is associated with hypervigilance for potential threats, and readiness to flee. Hypervigilance is also a central feature of PTSD.

The third hypothesized defense is *withdrawal*: Flee to a refuge and do not leave the burrow until safe. In human behavior, this corresponds with agoraphobia.

The fourth hypothesized defense is *aggression*: the best defense is a good offense. As is seen with a bull pawing the ground, this may begin with displays of aggression to impress upon the predator that the cost of attack will be too high. Failing that, this may involve a fight to the death. In humans, PTSD is associated with verbal and physical aggression, sometimes with little provocation.

The fifth hypothesized defense is *appeasement*. This form of defense is seen only in higher life forms, and has been characterized as "flight to the source of threat." This form of defense is not believed to have arisen in response to

predation, but rather in response to aggression among members of the same species as seen in primates. In humans, an abused child may cling to the abuser, as appeasing the abuser may be the best means of survival [58]. In adults, this can be manifested in Stockholm syndrome among those who are kidnapped, yet bond with the aggressor [59], or in warfare, when surrender may be the only hope of survival [59].

The final hypothesized defense is *tonic immobility*: Tonic immobility is the most extreme of all defenses against existential threat. Tonic immobility has been defined as "an involuntary state of profound motor inhibition despite fully preserved consciousness, activated by extreme fear, perceived inescapable circumstances, usually involving an obviously more powerful predator or member of the same species.… It may promote survival through inhibition of predatory killing reflexes, [and] confusion of predators… [With members of the same species] its submissive aspects may also serve as appeasement to deter more serious assault" [28]. Tonic immobility has been shown to be associated with sexual assault [60], and with reduced injury from assault [61]. One study found that 42% of survivors of adult sexual assault reported significant immobility during the last assault, with 10% reporting extreme immobility [62]. Tonic immobility is also associated with dissociation [62-64] and with conversion paralysis [65, 66].

Overall, the biologically-based defenses associated with PTSD are believed to exist because over the course of time they have been associated with increased chances of survival. However, it is theorized that if these survival mechanisms are poorly regulated or over-generalized [67], coupled with overlearned survival responses [29], or are too strongly associated with fear circuits [26, 27, 68], this may create enduring habits which are expressed too readily or too intensely, and thus become dysfunctional [69]. PTSD could therefore be conceptualized as a "… mismatch between archaic biological mechanisms and novel cues in the modern environment [which] may play a role in triggering traumatic memories and associated fight and flight reactions" [29]. Using this conceptual framework, the underlying biological mechanisms that give rise to PTSD could be likened to the biological mechanisms associated with inflammation. The inflammatory response is essential to the immune system and the healing process, but can create inflammatory related disease when the inflammatory process is poorly regulated [70, 71].

PTSD, Adverse Childhood Experiences and Medical Unexplained Symptoms.

Numerous studies have explored the potential for adverse childhood experiences (neglect, discrimination, household dysfunction, or abuse) to act as epigenetic mechanisms predisposing individuals for later development of PTSD: "Adult PTSD may also reflect the biological continuation of a response to an earlier exposure to adversity" [72]. For example, McGowan and colleagues demonstrated that "epigenetic regulation of the glucocorticoid receptor gene is influenced by a history of child abuse"[73]. The resulting changes and individual differences in glucocorticoid receptors impact endocrine function, and thus may demonstrate that a history of child abuse or trauma results ultimately in a potential vulnerability to PTSD through epigenetic programming [30, 72, 74-76].

If PTSD is a condition that is part of an instinctual method of forming new memories and cognitions that promote safety, interpretations of adverse childhood experiences must take this into account. Those who suffer from psychological trauma may exhibit an alteration of the memory processes as noted above, including changes to autobiographical memories. One study found that autobiographical memory biases in PTSD include that recollections of trauma are more vivid, and associated with patients both dwelling on the traumatic thoughts more, while simultaneously trying to suppress them more. In contrast, patients with PTSD had less ability to recall nontrauma events, and their nontrauma recollections tended to be more general and vague in nature. Finally, individuals with PTSD reported that even pretrauma memories were related to the traumatic event, providing further evidence for the alterations in cognition and memory that may occur with PTSD [77].

One study examined the relationship between PTSD, recollections of abuse, and so-called "medically unexplained symptoms." This prospective study followed 676 individuals for which there was legal documentation of being sexually abused, physically abused or neglected in childhood. These subjects were compared to a demographically matched cohort of 520 subjects. When these two groups were compared in adulthood, the group abused in childhood was no more likely to report medically explained pain. However, adults who reported being abused as a child were more likely to report unexplained pain [78]. While the meaning is uncertain, the study suggests that a

patient's current report of PTSD–related physical symptoms should not be thought of as a direct product of the trauma, but may instead be more closely associated with current memories, cognitions and affect [79]. Thus, it is possible that some of the subjects who suffered from objective abuse no longer regarded the remote events as traumatic, while those who continued to have traumatic recollections were currently physically distressed. This is an important consideration given that while one cannot expunge a traumatic historical event, psychological treatment can potentially change cognitions and affect associated with that event, and facilitate a reinterpretation memories.

PTSD and Posttraumatic Growth

If PTSD defensive mechanisms exist because they increase the chances of survival, it seems in principle possible that these mechanisms may lead to personal growth. [80]. The idea of posttraumatic growth was been described in the literature as "perceiving positive self-change originating in the struggle with trauma" [81].

Studies of breast cancer survivors [82] and victims of violent crime [83] found that that women coping with the aftermath of violence or life-threatening disease are capable of experiencing posttraumatic growth. In another study, women who addressed the adversity of their health concerns had over-all higher levels of psychological adjustment [84].

The principles and constructs of posttraumatic growth may be applied to the intrusive symptoms inherent in PTSD. In theory, the intrusive recurring flashbacks associated with PTSD are thought to promote survival by stimulating one trial learning from a trauma. This begs the question, what does the individual learn? What distinguishes persons who exhibit posttraumatic growth? If the fear-based circuits in the brain dominate, the traumatized individual may seek to avoid the intrusive traumatic thoughts themselves. This may lead to a self-defeating vicious circle. One relevant study asked subjects to spend time "not thinking about a polar bear." Unfortunately, investing energy to not think about a polar bear paradoxically causes the individual to think about polar bears more [85]. As applied to PTSD, the effects of this phenomena may cause an individual with PTSD who is determined to not think about the trauma to paradoxically think about the trauma even more. In this manner, active avoidance of thinking about a trauma may paradoxically contribute to a self-defeating vicious circle, and chronic PTSD. If traumatized individuals are having intrusive thoughts, these thoughts need to be examined.

Potentially, intrusive PTSD ruminations can trigger intense cognitive scrutiny of environmental threats, and subsequently lead to: a) more accurate discriminations about what constitutes true environmental dangers, b) more accurate discriminations about when one is safe, and c) an increased level of adaptive behaviors. Over the course of time, overgeneralized fear-based PTSD defenses may be replaced by an improved cognitive ability to discriminate zones which are dangerous from ones which are safe. This can allow the unhelpful intrusive ruminations of PTSD to be replaced by intentional productive introspection about a life-changing event. Addressing trauma therapeutically may also lead to a greater appreciation of life and deepened spirituality [81].

Overview Summary

PTSD is a complex phenomenon that is increasingly theorized to have bases in evolutionary biology, epigenetics, and posttraumatic growth with a foundation in survival-driven responses to threats. Research supports recognition of PTSD not simply as a disease, a sign of pathology, or a universal response to trauma [30, 76]. Instead, PTSD can be understood to be a result of biological and epigenetic mechanisms that represent a dysregulated or overgeneralized variant of adaptive one-trial learning and defense mechanisms [27-29]. Current memories, cognitions, and affect related to an adverse event may also impact the development of PTSD symptoms [77].

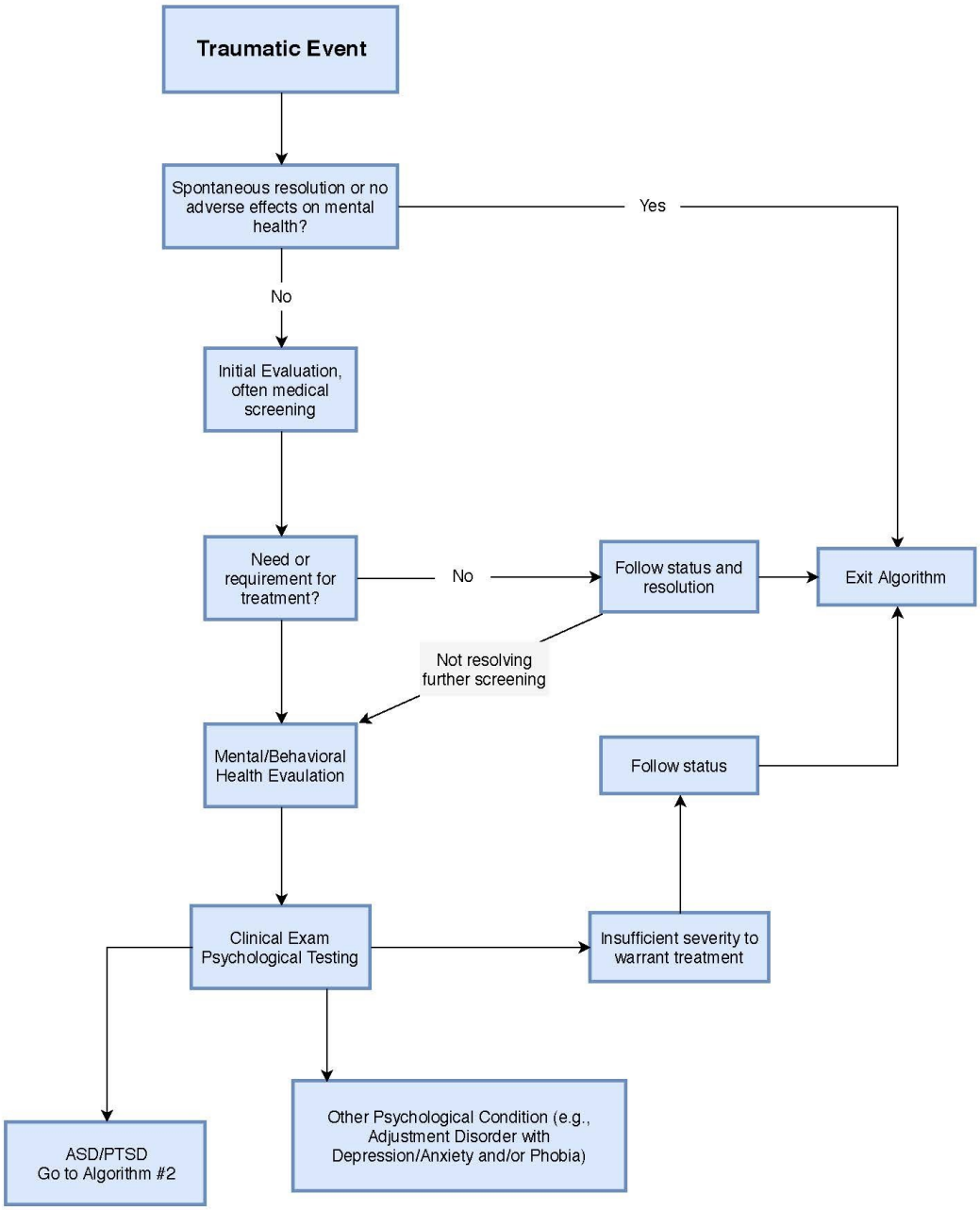
A neuroscience-informed approach to conceptualizing individuals with PTSD and developing effective interventions may help create greater consensus in previously disparate views of this phenomenon [26]. One manifestation of neuroscience informing our understanding of PTSD is illustrated in findings that indicate the presence of epigenetic changes that result from exposure to adverse life events. These adaptations have micro (intracellular level) and macro (behavioral level) repercussions [33], both of which can result in a "survival phenotype" [31] and predispose the same individual or subsequent generations to develop PTSD [74-76]. While the impact of PTSD on the lives of

the estimated nearly 22 million affected persons in the US [5] is significant, there is a notable body of evidence that indicates PTSD may be successfully treated using established, evidence-based methods to be discussed below. While treatment demands time and the development of skills for understanding and examining the biological and existential impact of the trauma, there is increasing recognition of the potential for individuals to experience significant personal growth (a sort of individualized sublimation response) in the wake of psychologically traumatic events [82, 84, 86, 87]. This final component of the discussion illustrates again the complex and multidimensional nature of PTSD.

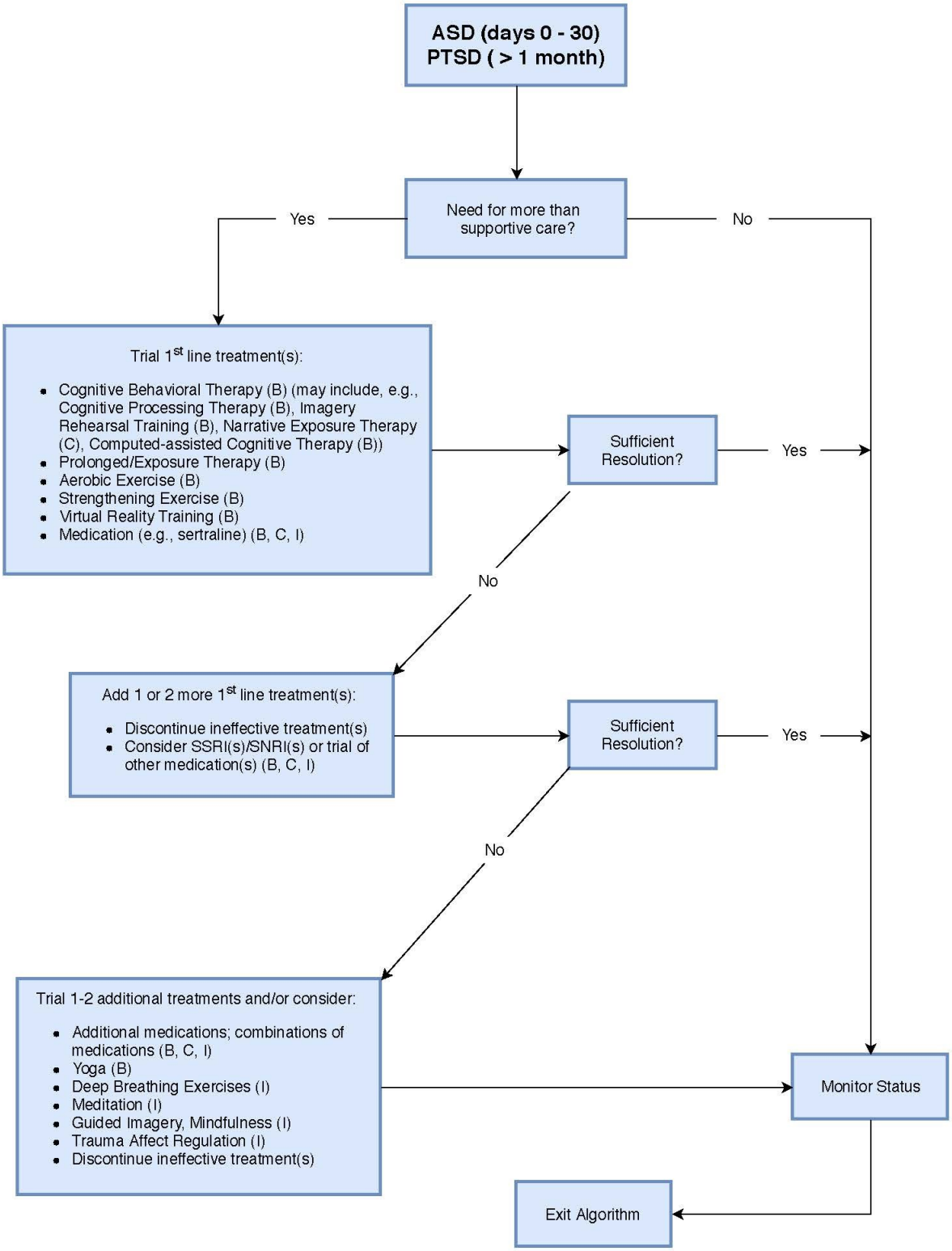
Despite the complexities of PTSD, the prognosis is good with the vast majority of people recovering to lead productive lives. A minority (approximately 4-22%) develop chronic PTSD [5, 6, 88-91].

Algorithms

PTSD Algorithm #1



PTSD Algorithm #2



Treatment Overview

PTSD: Prevention

There are few quality data addressing prevention of PTSD/ASD. To date, there is an absence of quality data showing efficacy of interventions including debriefing and counseling after events have occurred, and some RCT data suggest potential harm, especially from critical incidence stress debriefing or psychological debriefing [92]. There also is no clear evidence of efficacy of resilience training. The other areas of potential prevention would naturally include prevention of high-stress inciting events. However, there are no quality data addressing efficacy to prevent PTSD using preventive programs.

Ptsd: Psychological Management

The primary initial intervention is 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.

PTSD: Pharmacological And Other Management

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.

Risk and Causation

See the Introduction of the Workplace Mental Health Guideline.

Symptoms and Signs

There are many symptoms of PTSD and ASD [DSM 5]. Symptoms are common, but the diagnosis of PTSD is relatively rare. These symptoms include the following [93]:

- Re-experiencing or flashbacks of event
- Unwanted, or intrusive memories
- Nightmares, or bad dreams
- Frightening thoughts
- Avoidance of settings that remind of the event(s) or experience(s)
- Avoiding thoughts or feelings of the event(s)
- Restlessness
- Being easily startled, hyperarousal
- Hypervigilance
- Feeling tense or on edge
- Feeling stressed
- Difficulty with sleeping
- 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:

- Tachycardia
- Tachypnea
- Sweating while re-experiencing the event or telling of it.
- Signs of fatigue and lack of sleep
- Ease of startle

History and Psychological/Psychiatric Examination

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 death, serious injury or sexual violence [DSM5]. Evaluation of topics such as current living situation, employment, education, social interaction levels, substance use, and childhood experience should all be considered. Assessment of and testing for secondary gain factors and potential malingering is often required in occupational settings (see also Psychometric Testing: Acute Stress Disorder and PTSD). A thorough examination of both physical and mental symptoms is also required in order to differentiate between PTSD andASD (which differ by duration of > or < 30 days duration) from another psychological disorder.

Medical History Questionnaire

See the Introduction to the Workplace Mental Health guideline.

Types Of Measures For PTSD Assessment

There are at least three types of psychological measures, screening tools, outcome measures and psychological inventories. In most cases, a screen 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.

The Psychological Examination of PTSD

The Nature of Psychological Trauma

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 [94-96]. A traumatic event is one that in an instant can invalidate all of these cognitive assumptions, leaving the patient feeling profound disorientation. A traumatic event is also one that elicits profound emotions, including overwhelming feelings of loss, terror, horror, rage, or guilt.

For example, a patient's assumptive world may include beliefs and assumptions such as "I have a stable and secure family life," "I will work at this job until I retire," "I am financially secure," "I will continue playing on the softball team," and "I am a normal (perhaps good) looking person." In an instant, an event such as a traumatic amputation of a hand can void all of those assumptions. A traumatic event such as this disrupts the sense of identity, personal security, causes the patient to reassess his or her own mortality, and requires the patient to identify a new plan for survival and functioning in a world that is now viewed very differently. PTSD is a condition which, when present, is associated with a traumatic disruption to an individual's sense of personal security.

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/Biopsychosocial Assessment of PTSD

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 elsewhere in this guideline (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 medical providers. 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?

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 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 his 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, 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

The DSM5 states that 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 [97].
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 [23]. 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 [98].

Diagnosis

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 [DSM5]. After ruling out malingering or secondary gain, the diagnosis of PTSD is based primarily on symptoms [DSM5], 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 [DSM5]) is the *essential condition* for PTSD to develop, the stressor alone may not be sufficient to generate PTSD [30]. 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 [30, 76]. While this was the most prevalent view of the diagnosis since it was first specified in the DSM-III in 1980 [99], 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 [27].

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

> "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:

1. Depersonalization: Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly).
2. Derealization: Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted).

Note: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (e.g., blackouts, behavior during alcohol intoxication) or another medical condition (e.g., complex partial seizures).

Specify if:

With delayed expression: If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate)." (American Psychiatric Association, 2013)

ICD-10 criteria (F43.1) include requirements that there is:

- Exposure to one or more traumatic events (e.g., sexual assault, warfare, traffic collisions, terrorism or other life-threatening events).
- Symptoms include disturbing recurring flashbacks, avoidance or numbing of memories of the event, and hyperarousal, and
- Symptoms lasting over one month after the event.

Classification

Acute Stress Disorder (ASD) occurs within the first month after a traumatic event. PTSD is not diagnosed until greater than one month after a traumatic event. PTSD (and ASD) are generally not classified per se. However, they occasionally can be categorized based on mechanism (e.g., war-related trauma, death, trauma). It may also be classified by severity (e.g., disabled, partially disabled, not disabled).

Summary of Diagnostic Divergence

There are multiple diagnostic definitions of PTSD, which are similar yet distinct. The DSM-5 and ICD-10 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 have considerable overlap, there are noteworthy differences between them. It should be noted that although the DSM-5 definition of PTSD is probably the most accepted one in the United States and ICD-10 is the standard elsewhere, the vast majority of moderate- and high-quality PTSD research reviewed in this guideline is based on older DSM-IV diagnostic criteria. Knowledge of the differences between these definitions may be helpful in interpreting some research findings.

1. In comparison to other PTSD definitions, DSM5 has an expanded definition of trauma, especially with regard to first responders and law enforcement officers.
2. DSM-5 Acute Stress Disorder adopts the DSM5 has an expanded definition of trauma. It lists 14 symptoms in the categories of intrusive symptoms such as flashbacks or nightmares, negative mood, dissociation, avoidance, and arousal. The presence of nine or more of these 14 systems confirms a diagnosis of acute stress disorder.
3. In DSM-III and DSM-IV PTSD was categorized as an anxiety disorder. However, DSM-5, ICD-10 and ICD-11 all classify PTSD as a stress and trauma related disorder. This stresses the distinction that PTSD is a condition precipitated by a trauma, which distinguishes it from anxiety which can be part of an individual's inherited temperament.
4. The DSM-IV definition of PTSD excludes criteria D and H above
5. The DSM-III definition of PTSD excludes criteria D, G, and H above. Note that Acute Stress Disorder was not a recognized diagnosis in DSM-III.
6. The ICD-10 definition of PTSD generally follows DSM-IV, although the ICD-10 diagnostic criteria have less specificity. An important difference is that ICD-10 distinguishes between acute PTSD (1-3 months) and chronic PTSD (more than 3 months).

7. ICD-11 drops the distinction between acute and chronic PTSD, and replaces this with PTSD and Complex PTSD. PTSD is defined by core symptoms A, B, C, E and G above
8. ICD-11 adds Complex PTSD, which is defined by the presence of the core symptoms, but requires exposure to recurring traumatic events from which escape is difficult if not impossible (e.g. torture, prolonged domestic violence, or repeated childhood abuse). In addition to the core symptoms of PTSD, complex PTSD includes the following:
    a. Severe and pervasive problems with affect regulation
    b. Persistent beliefs about oneself as worthless and accompanied by pervasive feelings of shame, guilt or failure related to the traumatic event
    c. Persistent difficulties in sustaining relationships and feeling close to others.

Screening and Testing Recommendations

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

Recommended.

Psychological/psychiatric evaluation is recommended for all patients with potential acute stress disorder or post-traumatic stress disorder.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – **Low**

Indications:	Evaluation of all patients with potential ASD or PTSD. Evaluation should especially include focus on ASD, PTSD, anxiety disorder(s), depression, substance use disorder(s) and risk of suicide.
Benefits:	Make and/or confirm diagnosis after analyses of screening, test results and interview.
Harms:	N/A
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, thus there is high confidence that they are needed. They also set the stage for subsequent treatment plans.

There are various posttraumatic stress disorder screening tools. The Posttraumatic Adjustment scale is a 10-item symptom based screening tool used to detect PTSD or major depressive episodes [100-102]. A PTSD checklist has been developed [103]. Other screening tools (e.g., anxiety, depression, substance use, suicidality) are reviewed in other guidelines.

PTSD Screening Tools

Recommended.

PTSD screening tools are recommended for the evaluation of patients at risk of post-traumatic stress disorder.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
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 disorder(s), depression, substance use disorder(s) 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 in the absence of confirmatory analyses.
Frequency/Dose/Duration:	Generally only one administration
Rationale:	There are relatively few quality studies for most of the PTSD screening tools. Screening tools include: PTSD Checklist, Primary Care PTSD Screen, and the Posttraumatic Adjustment scale. PTSD screening tools are efficient, low cost and are recommended.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: posttraumatic adjustment scale, PAS; Acute Stress Disorder, Traumatic Stress Disorder, Acute Traumatic Stress, Posttraumatic Stress Disorder, Post Traumatic Stress, PTSD; psychometric, psychological, trauma test, screening, inventory. We found and reviewed 2 articles in PubMed, 3248 in Scopus, 7 in CINAHL, 28 in Cochrane Library, 23 in Google Scholar and 0 from other sources[†]. We considered for inclusion 0 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Visual analogue pain scale, VAS, Pain measurements; Acute Stress Disorder, Traumatic Stress Disorder, Acute Traumatic Stress, Posttraumatic Stress Disorder, Post Traumatic Stress, PTSD; psychometric, validity, reliability, disability index, questionnaire. We found and reviewed 148 articles in PubMed, 542 in Scopus, 29 in CINAHL, 14 in Cochrane Library, 16700 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar and 0 from other sources. Zero articles met the inclusion criteria. A comprehensive literature search was conducted using PubMed without date limits using the following terms: SPAN, SPIRIT, primary

care PTSD screen, trauma screening questionnaire, PTSD checklist, diagnostic interview; posttraumatic adjustment scale, PAS; Acute Stress Disorder, Traumatic Stress Disorder, Acute Traumatic Stress, Post-traumatic Stress Disorder, Post Traumatic Stress, PTSD; psychometric, psychological, trauma test, screening, inventory. We found and reviewed 5232 articles in PubMed†. We considered for inclusion 34 from PubMed and 0 from other sources. Of the 34 articles considered for inclusion, 34 diagnostic studies and 0 systematic studies 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.

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 [104-112]. Tests for malingering are also commonly viewed as necessary in testing patients with PTSD.

Psychometric Testing: Acute Stress Disorder and PTSD

Recommended.

Psychometric tests is recommended for individuals presenting with signs and symptoms consistent with acute stress disorder or post-traumatic stress disorder.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – **High**

Indications:	For individuals presenting with signs and symptoms consistent with Acute Stress Disorder or PTSD. Evaluation should especially include focus on ASD, PTSD, anxiety disorder(s), depression, substance use disorder(s), and risk of suicide. Tests to detect malingering 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 over-reliance 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 [109, 110, 113].
Rationale:	There are moderate quality studies that suggest utility for the screening of ASD [114, 115] and PTSD [104, 109, 110, 113, 116-119]. 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, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: acute stress disorder scale; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, post traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, efficiency. We found and reviewed 19 articles in PubMed, 168 in Scopus, 5 in CINAHL, 3 in Cochrane Library, 400 in Google Scholar, and 2 from other sources[†]. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 3 articles considered for inclusion, 3 diagnostic studies and 0 systematic reviews met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Clinically administered PTSD Scale, clinician administered PTSD Scale; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, posttraumatic stress, PTSD; diagnosis,

diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, efficiency. We found and reviewed 654 articles in PubMed, 1989 in Scopus, 74 in CINAHL, 283 in Cochrane Library, 24400 in Google Scholar, and 0 from other sources†. We considered for inclusion 13 from PubMed, 0 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 14 articles considered for inclusion, 7 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.

Pharmacogenomics Testing

No Recommendation.

There is no recommendation for the use of pharmacogenomic testing in the evaluation of post-traumatic stress disorder.

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, and thus is not recommended [122].

Evidence: A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: pharmacogenomics testing; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, post traumatic stress, PTSD; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, efficiency. We found and reviewed 0 articles in PubMed, 0 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 945 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 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.

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 [123-129].

Functional MRI

Not Recommended.

Functional MRI is not recommended for the diagnosis of post-traumatic stress disorder.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale:	There are no quality studies assessing Functional MRI for diagnosis of PTSD or studies showing it alters the clinical course (see also ACOEM TBI Guideline). Thus, it is not recommended for the diagnosis of PTSD [123].

Treatment Recommendations

Treatment recommendations follow. Recommendations are based on the available quality evidence [130]. An algorithm was also developed to assist healthcare providers. 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.

Education and Exercise

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 [131, 132]. Affect regulation teaches a specific set of skills called "FREEDOM" to help patients deal with emotional and physical reactivity to specific traumatic stimuli [131, 132]. FREEDOM stands for focusing, recognizing triggers, emotion awareness, evaluating thoughts, defining goals, choosing options, and making a positive contribution to the world by regulation emotions [131, 132].

Education: Trauma Affect Regulation (TARGET)

No Recommendation.

There is no recommendation for the use of TARGET as an adjunct treatment for patients with 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 [131].
Frequency/Dose/Duration:	12- 75 minute sessions for as long as necessary [131, 133]. Consists of three core TARGET components: education, teaching and guided practice of FREEDOM skill sequence, and experiential exercise [131, 133].
Indications for Discontinuation:	Resolution of symptoms, non-compliance, lack of efficacy or adverse effect
Rationale:	There is sparse quality evidence for the use of TARGET for PTSD. The largest trial suggested efficacy, but enrolled minority 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 [132]. One study compared TARGET to Supportive Group Therapy and both groups showed decreased PTSD symptom severity with the TARGET group showing improvement in forgiveness [131]. TARGET has low adverse effects, of low to moderate cost depending upon treatment duration, has some evidence to support efficacy, but the study population is not clearly generalizable to a population of workers 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: Guide for Education and Therapy (TARGET), Educational and therapeutic intervention, Trauma Affect Regulation; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 26 articles in PubMed, 124 in Scopus, 1 in CINAHL, 56 in Cochrane Library, 14300 in Google Scholar, and 1 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 4 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.

Education: Educational Training

No Recommendation.

There is no recommendation for the use of educational training for patients with 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 with some studies showing an overall lack of efficacy [137], and one study showing efficacy [135]. Clearly, education about a particular condition remains warranted; however, education as a stand-alone treatment strategy is low cost, has inconclusive 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: Education; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 28 in Scopus, 837 in CINAHL, 231 in Cochrane Library, 2060 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 6 from PubMed, 4 from Scopus, 0 from CINAHL, 5 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 15 articles considered for inclusion, 4 randomized trials and 1 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

Moderately Recommended.

Exercise is moderately recommended for the treatment of patients with 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, and SSRIs.
Benefits:	Improvement in PTSD symptoms and overall well being
Harms:	Negligible
Frequency/Dose/Duration:	Aerobic exercise (treadmill, walking, biking, etc.) for at least 3 times per week and resistance training (weights) at least 2 times per week [148, 149].
Indications for Discontinuation:	Resolution of PTSD symptoms, non-compliance. or unanticipated adverse event
Rationale:	Several moderate quality studies consistently suggest efficacy for both aerobic exercise as well as resistance training [148-151]. In [151], all 3 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 [148, 149]. Exercise has low adverse effects, is of low to moderate cost depending upon whether achieved in group sessions or via a personal trainer, 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: exercise; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 1,677 in Scopus, 16 in CINAHL, 18 in Cochrane Library, 127,000 in Google Scholar, and 0 from other sources†. We considered for inclusion 5 from PubMed, 2 from Scopus, 0 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.

Yoga

Moderately Recommended.

Yoga 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 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, posture, 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 [166], although other studies have reported efficacy with more intense interventional hours 22 hours, but shorter overall duration (5 days) [167].
Indications for Discontinuation:	Lack of PTSD symptom improvement or sufficient improvement to not warrant further sessions; non-compliance; intolerance.
Rationale:	Several moderate quality studies consistently suggest yoga improves PTSD symptoms [166-169]. Some studies show sustained improvements for up to 6 months [167] and one study suggests symptom improvement up to 18 months [170]. Yoga has negligible adverse effects, is low to moderate cost (depending on whether self-directed or supervised), has some evidence of efficacy, and therefore yoga is recommended for adjunctive use in select patients with PTSD.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Yoga; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 208 in Scopus, 52 in CINAHL, 28 in Cochrane Library, 2130 in Google Scholar, and 0 from other sources†. We considered for inclusion 8 from PubMed, 4 from Scopus, 8 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 22 articles considered for inclusion, 9 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.

Psychological Interventions and Coping Strategies

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 [171, 172]. Group therapy has been suggested to be effective in helping patients with PTSD address interpersonal relationship problems and improve self-esteem [171-173]. A few studies have examined using couple's therapy as a form of group therapy to help patients manage PTSD symptoms [173, 174].

Group Therapy

No Recommendation.

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

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Rationale:

There is limited evidence assessing the use of group therapy for PTSD. One study showed that couples-based group therapy was effective in in improving PTSD symptoms versus education [174]. However, another study with usual care bias showed comparable efficacy between groups which compared mindfulness theory to usual care [175]. Group compared with individual cognitive processing therapy has also reportedly found better treatment gains in the individual sessions [176]. Group therapy has low adverse effects, is moderate cost depending upon treatment duration, and has conflicting evidence of efficacy; thus, there is no recommendation for PTSD. However, the threshold for using group therapy should be low as it is generally low to modest cost.

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, Group Psychotherapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 196 articles in PubMed, 404 in Scopus, 82 in CINAHL, 140 in Cochrane Library, 19800 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 0 from Scopus, 3 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 8 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.

Behavioral and Psychological Interventions

Cognitive behavioral therapy (CBT) has been used to treat PTSD [177-180]. It includes a variety of component therapies including cognitive 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 [181], 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

Moderately Recommended.

The use of cognitive behavioral therapy is moderately 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**

Cognitive Behavioral Therapy Component: Computer-Assisted Cognitive Therapy

Moderately Recommended.

The use of computer-assisted cognitive therapy as a component of cognitive behavioral therapy is moderately recommended for the treatment of PTSD.

Strength of Evidence – **Moderately Recommended, Evidence (B)**
Level of Confidence – **Moderate**

Cognitive Behavioral Therapy Component: Cognitive Processing Therapy

Moderately Recommended.

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

Strength of Evidence – **Moderately Recommended, Evidence (B)**
Level of Confidence – **Moderate**

Cognitive Behavioral Therapy Component: Imagery Rehearsal Training

Moderately Recommended.

The use of imagery rehearsal training as a component of cognitive behavioral therapy is moderately recommended for the treatment of PTSD.

Strength of Evidence – **Moderately Recommended, Evidence (B)**
Level of Confidence – **Moderate**

Cognitive Behavioral Therapy Component: Narrative Exposure Therapy

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**

Cognitive Behavioral Therapy Component: Seeking Safety

No Recommendation.

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

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Cognitive Behavioral Therapy Component: Dialectical Behavioral Therapy

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**

Cognitive Behavioral Therapy Component: Brief Eclectic Therapy

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**

Cognitive Behavioral Therapy Component: Stress Inoculation Training

No Recommendation.

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

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Cognitive Behavioral Therapy Component: Acceptance and Commitment Therapy

No Recommendation.

There is no recommendation for the use of acceptance and commitment 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**

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 [182, 183] 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 min., generally a minimum of 6 weeks and up to 3 months [184-188].
Indications for Discontinuation:	Resolution of PTSD symptoms, non-compliance, lack of efficacy, or adverse effects
Rationale:	Many moderate quality studies consistently suggest efficacy of CBT for PTSD (e.g.,[182-184, 186-195]). Many studies report improved sleep, fewer nightmares, less depression, and less anxiety with CBT [185, 207, 215], and some studies suggest combination therapy such as Cognitive Restructuring and Exposure Therapy is superior to Cognitive Behavioral Therapy alone [183]. Treatment gains have been reportedly maintained up to one year [216]. There are many different components or types of CBT. Quality evidence for any specific CBT component is currently variable, ranging from adequate to sparse. Examples of CBT components with quality evidence allowing evidence-based guidance include Computer-Assisted Cognitive Therapy, Cognitive Processing Therapy, Narrative Exposure Therapy, and Imagery Rehearsal Training. Evidence is weak for Seeking Safety Therapy, Dialectical Behavioral Therapy, Acceptance and Commitment Therapy, Stress Inoculation Training, and Brief Eclectic Therapy, CBT has low adverse effects, is moderate cost depending upon treatment duration, has broad and consistent evidence of efficacy for the treatment of PTSD, and thus, CBT 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: Seeking Safety Therapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 56 in Scopus, 4 in CINAHL, 1 in Cochrane Library, 14300 in Google Scholar, and 1 from other sources†. We considered for inclusion 10 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of

the 12 articles considered for inclusion, 5 randomized trials and 2 systematic reviews met the inclusion criteria.
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cognitive therapy, cognitive behavioral therapy, CBT; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 949 articles in PubMed, 6492 in Scopus, 882 in CINAHL, 93 in Cochrane Library, 44600 in Google Scholar, and 1 from other sources†. We considered for inclusion 120 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 121 articles considered for inclusion, 51 randomized trials and 34 systematic reviews met the inclusion criteria.

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, Therapy, Computer-Assisted; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 43 articles in PubMed, 2 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 5270 in Google Scholar, and 19 from other sources†. We considered for inclusion 5 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 19 from other sources. Of the 26 articles considered for inclusion, 14 randomized trials and 1 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cognitive Processing Therapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 644 articles in PubMed, 1 in Scopus, 33 in CINAHL, 8 in Cochrane Library, 1950 in Google Scholar, and 5 from other sources†. We considered for inclusion 22 from PubMed, 0 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 5 from other sources. Of the 30 articles considered for inclusion, 11 randomized trials and 3 systematic reviews met the inclusion criteria.

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 (DBT); acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 12 articles in PubMed, 12 in Scopus, 3 in CINAHL, 1 in Cochrane Library, 1,610 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 0 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 12 articles in PubMed, 784 in Scopus, 3 in CINAHL, 53 in Cochrane Library, 26300 in Google Scholar, and 3 from other sources†. We considered for inclusion 4 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Zero articles met the inclusion criteria.

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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 23 articles in PubMed, 721 in Scopus, 20 in CINAHL, 32 in Cochrane Library, 5830 in Google Scholar, and 0 from other sources†. We considered for inclusion 5 from PubMed, 0 from Scopus, 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.
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, IRT; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 239 in Scopus, 0 in CINAHL, 13 in Cochrane Library, 5690 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 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.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Brief Eclectic Psychotherapy, Brief Eclectic Therapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 13 articles in PubMed, 11 in Scopus, 11 in CINAHL, 9 in Cochrane Library, 569 in Google Scholar, and 1 from other sources†. We considered for inclusion 7 from PubMed, 0 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 13 articles considered for inclusion, 5 randomized trials and 5 systematic reviews met the inclusion criteria.

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, NET; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 65 articles in PubMed, 1549 in Scopus, 19 in CINAHL, 88 in Cochrane Library, 19500 in Google Scholar, and 1 from other sources†. We considered for inclusion 8 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 9 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.

Mind/Body Interventions: Guided Imagery

Recommended.

The mind/body intervention of guided imagery is recommended for the treatment of patients with PTSD.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – **Low**

Mind/Body Interventions: Mindfulness

Recommended.

The mind/body intervention of mindfulness is recommended for the treatment of patients with PTSD.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – **Low**

Mind/Body Interventions: Music Therapy

No Recommendation.

There is no recommendation for the use of the mind/body intervention of music therapy in the treatment of patients with PTSD.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Mind/Body Interventions: Art Therapy

No Recommendation.

There is no recommendation for the use of the mind/body intervention of art therapy in the treatment of patients with PTSD.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Mind/Body Interventions: Spiritual-based Interventions

No Recommendation.

There is no recommendation for the use of spiritual-based mind/body interventions in the treatment of patients with PTSD.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Indications:	Individuals with PTSD
Benefits:	Improvement in PTSD symptoms.
Harms:	Negligible
Frequency/Dose/Duration:	Weekly 2.5-hour sessions of Mindfulness therapy. (See other guidance for components of this intervention)
Indications for Discontinuation:	Symptom resolution or lack of efficacy
Rationale:	There are multiple moderate quality studies of mind/body interventions that suggest efficacy, although many trials had numerous co-interventions. One study showed improvement in PTSD symptoms in combat veterans using Mind/Body Interventions over Present Centered Group Therapy [225]. Another study suggested improvement in PTSD symptoms and sleep quality but no improvement in depressive symptoms or overall quality of life [226]; in [623], self-efficacy improved. However, one study found lack of efficacy [227] but the other quality studies show improvement in PTSD symptoms. Mind/Body Interventions have low adverse effects, are moderately costly depending upon treatment duration, have some evidence of efficacy, and thus are recommended for PTSD. There is no recommendation for art therapy, music therapy, or spiritual-based interventions, as there is no quality evidence of efficacy.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Mind body interventions, mind body therapies, guided imagery, meditation, hypnosis, art therapy, music therapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 214 articles in PubMed, 8659 in Scopus, 191 in CINAHL, 122 in Cochrane Library, 28200 in Google Scholar, and 49 from other sources†. We considered for inclusion 14 from PubMed, 0 from Scopus, 9 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 5 from other sources. Of the 30 articles considered for inclusion, 11 randomized trials and 6 systematic reviews met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Relaxation, Relaxation therapy, Relaxation techniques, Relaxation technics; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 133 articles in PubMed, 3405 in Scopus, 152 in CINAHL, 4 in Cochrane Library, 17300 in Google Scholar, and 0 from other sources†. We considered for inclusion 5 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 3 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.

Deep Breathing Exercises

Recommended.

The use of deep breathing exercises is recommended for the treatment of patients with PTSD.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – **Low**

Indications:	Patients with PTSD symptoms typically used as adjunctive rather than first-line therapy (e.g., CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, SSRI/SNRIs).
Benefits:	Improvements in PTSD symptoms
Harms:	Negligible
Frequency/Dose/Duration:	As often as needed for improvement of symptoms, several times a day.
Indications for Discontinuation:	Resolution of symptoms or lack of efficacy
Rationale:	There is limited evidence for Deep Breathing and PTSD with some evidence of efficacy [181, 228]. Often, these deep breathing techniques are used in conjunction with yoga (see Yoga) and/or meditation, resulting in difficulty ascertaining an independent benefit from deep breathing. Deep Breathing has negligible adverse effects, is negligible cost, has some limited evidence of efficacy, and is therefore recommended for adjunct PTSD therapy.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: deep breathing exercise; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 1 articles in PubMed, 12 in Scopus, 5 in CINAHL, 4 in Cochrane Library, 2070 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 1 from Scopus, 1 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.

Meditation

Recommended.

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

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:	As often as individual requires (self-administered)
Indications for Discontinuation:	Resolution of symptoms or lack of efficacy
Rationale:	There is limited evidence for meditation and PTSD and often meditation is used in tandem with Deep Breathing and Yoga (see Yoga) [228]. Meditation has negligible adverse effects, is of minimal cost (if any), has some efficacy and is therefore recommended for PTSD as adjunct therapy.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: meditation; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 34 articles in PubMed, 1 in Scopus, 50 in CINAHL, 79 in Cochrane Library, 70 in Google Scholar, and 0 from other sources†. We considered for inclusion 15 from PubMed, 0 from Scopus, 6 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 24 articles considered for inclusion, 1 randomized trials and 12 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 and Prolonged Exposure Therapy

Moderately Recommended.

The use of exposure therapy and prolonged exposure therapy is moderately 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 [186].
Benefits:	Improvement in PTSD symptoms and reduce emotional response to traumatic stimuli and to help emotionally process a traumatic experience [237, 238].
Harms:	Increased symptoms, intolerance
Frequency/Dose/Duration:	Weekly 90-minute sessions for 10 weeks [243]. This often includes: 1) introducing the visual confrontation of the trauma and 2) repeatedly visiting the trauma memory [238, 239].
Indications for Discontinuation:	Resolution of symptoms, non-compliance, 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. One study compared Prolonged Exposure Therapy to Present Centered Therapy in female veterans with PTSD showing significant improvement in PTSD symptoms [243]. Other studies compared Exposure Therapy or Prolonged Exposure therapy to Interpersonal Psychotherapy and found comparable efficacy between both interventions [244]; Bryant et al. [627] suggested 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 [245]. Exposure Therapy/Prolonged Exposure has low adverse effects, is moderate cost depending upon treatment duration, has many studies suggesting efficacy 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: Exposure therapy, implosive therapy, flooding therapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 849 articles in PubMed, 13512 in Scopus, 1157 in CINAHL, 129 in Cochrane Library, 57100 in Google Scholar, and 396 from other sources†. We considered for inclusion 43 from PubMed, 0 from Scopus, 3 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of

the 47 articles considered for inclusion, 15 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.

Virtual Reality Exposure Therapy

Moderately Recommended.

The use of virtual reality exposure therapy 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.
Benefits:	Improvement in PTSD symptoms
Harms:	Increased symptoms, intolerance
Frequency/Dose/Duration:	Once to twice weekly 90 minutes sessions for 5 weeks [249, 251].
Indications for Discontinuation:	Resolution of symptoms, non-compliance, adverse effects or lack of efficacy for PTSD
Rationale:	There are multiple moderate quality studies showing evidence of efficacy for virtual reality [249, 252-258]. Virtual reality has low adverse effects, is low 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, virtual reality exposure therapy, VR; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 8 articles in PubMed, 732 in Scopus, 5 in CINAHL, 27 in Cochrane Library, 3,300 in Google Scholar, and 3 from other sources†. We considered for inclusion 4 from PubMed, 3 from Scopus, 1 from CINAHL, 5 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 16 articles considered for inclusion, 10 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.

Individual Debriefing

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 [137], and one shows efficacy [259]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 396 articles in PubMed, 97 in Scopus, 1 in CINAHL, 4 in Cochrane Library, 4,730 in Google Scholar, and 5 from other sources†. We considered for inclusion 9 from PubMed, 2 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 5 from other sources. Of the 18 articles considered for inclusion, 3 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.

Group Debriefing

Not Recommended.

The use of group debriefing is not recommended for the treatment of patients with PTSD.

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence – **Moderate**

Rationale: There is one moderate quality study showing lack of efficacy [260]. Group Debriefing has moderate adverse effects, of low to moderate cost depending upon treatment duration, has evidence of 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 56 articles in PubMed, 1136 in Scopus, 10 in CINAHL, 52 in Cochrane Library, 7480 in Google Scholar, and 8 from other sources†. We considered for inclusion 7 from PubMed, 0 from Scopus, 0 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.

Critical Incident Stress Debriefing (CISD)

No Recommendation.

There is no recommendation of the use of critical incident stress debriefing (CISD) in the treatment of patients with PTSD.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Rationale: There are 3 quality studies [259, 260, 621] that conflict, and 2 of them [260, 621] suggest lack of efficacy; thus, there is no recommendation. There are many additional low-quality studies.

Evidence: A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: crisis intervention, critical incident stress debriefing; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, post-traumatic stress disorders, 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 135 articles in PubMed, 118 in Scopus, 104 in CINAHL, 28 in Cochrane Library, 28,400 in Google Scholar, and 9 from other sources†. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 9 from other sources. Of the 12 articles considered for inclusion, 9 randomized trials and 3 systematic studies 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

No Recommendation.

There is no recommendation for 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 (in)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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 101 in Scopus, 5 in CINAHL, 11 in Cochrane Library, 5200 in Google Scholar, and 1 from other sources†. We considered for inclusion 4 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 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.

Interpersonal therapy has been used to treat PTSD [244].

Interpersonal Therapy

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 [244].
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 [244].
Indications for Discontinuation:	Completion of a course of treatment, sufficient resolution of symptoms and/or non-compliance.
Rationale:	The highest quality study suggested comparable efficacy to exposure therapy [244]; 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, Interpersonal Psychotherapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, post-traumatic stress disorders, 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, 3 in Scopus, 29 in CINAHL, 5 in Cochrane Library, 90 in Google Scholar, and 1 from other sources†. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 1 article considered for inclusion, 1 randomized trials and 0 systematic studies 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

No Recommendation.

There is no recommendation for 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 [275, 276]. Another study compared hypnotherapy to Zolpidem and found comparable (in)efficacy [277]. In [278], 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: hypnosis; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 77 in Scopus, 12 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 0 from other sources†. We considered for inclusion 9 from PubMed, 1 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 13 articles considered for inclusion, 4 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.

Eye Movement Desensitization and Reprocessing: Eye Movement Component of Treatment

Not Recommended.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – **Low**

Eye Movement Desensitization and Reprocessing: Exposure Therapy and Cognitive Behavioral Therapy Components of Treatment

Recommended.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – **Low**

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.

There are a few moderate quality studies for EMDR [222, 224, 287-292], but the highest quality study, also the only sham-controlled trial, found a lack of efficacy [287] regarding the eye-movement component; thus, there are no other trials able to document efficacy of the eye-movement components of these heterogeneous EMDR treatments. EMDR has been reported to be equivalent to prolonged/exposure [285, 622], worse than exposure [224], equivalent to emotional freedom training [290], superior to biofeedback, and equivalent to brief eclectic therapy [289]. These results raise questions of response biases. EMDR has low adverse effects, is moderate cost depending upon duration of treatment, but has evidence of inefficacy compared with sham and thus the eye-component part of this therapy is not recommended. The parts of this treatment with proven efficacy (see, e.g., Cognitive Behavioral Therapy and Exposure Therapy) are continued to be recommended.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Eye Movement Desensitization Reprocessing, EMDR; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 6 in Scopus, 48 in CINAHL, 0 in Cochrane Library, 2390 in Google Scholar, and 2 from other sources[†]. We considered for inclusion 14 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 2 from other sources. Of the 20 articles considered for inclusion, 11 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.

Tapping Techniques (Thought Field Therapy and Emotional Freedom Therapy)

No Recommendation.

There is no recommendation for 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 wait-list control bias [293]. 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: Thought Field Therapy, TFT; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 7 articles in PubMed, 25 in Scopus, 1 in CINAHL, 1 in Cochrane Library, 150 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the seven 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.

Emotional Freedom Techniques (EFT)

No Recommendation.

There is no recommendation for 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 wait-list control biases [299]. 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 Techniques; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 12 articles in PubMed, 19 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 9 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 0 from Scopus, 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 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.

Neurofeedback (Brain-Computer Device and Interface)

No Recommendation.

There is no recommendation for 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 waitlisted control [222]. 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: brain-computer interface, brain computer device; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 1 articles in PubMed, 2 in Scopus, 1 in CINAHL, 1 in Cochrane Library, 625 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from Scopus, 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.

Animal-Assisted Therapy

No Recommendation.

There is no recommendation for 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: There is no quality evidence for efficacy of animal therapy for PTSD [308], 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: Animal assisted therapy, animal facilitated therapy, pet assisted therapy, pet facilitated therapy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 7 articles in PubMed, 2151 in Scopus, 2 in CINAHL, 50 in Cochrane Library, 16400 in Google Scholar, and 16 from other sources†. We considered for inclusion 3 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 4 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.

Medications

There are few medications with FDA indications for PTSD. These recommendations are based upon the available quality data [130]. 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.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Sertraline (Zoloft) is an SSRI anti-depressant that has been used for treatment of PTSD [312-319].

SERTRALINE

Moderately 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) [320].
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 [319, 321, 322, 323]. Fast escalations in dose are often not tolerated.

Indications for Discontinuation:	Lack of efficacy, adverse effects, resolution of PTSD sufficiently to not require medication.
Rationale:	Multiple moderate quality studies suggest efficacy of sertraline compared with placebo for treatment of PTSD [316, 321-325] and only one lower quality study showed lack of efficacy [326]. One study reported [324] sustained results with patients reporting improved quality of life and less relapse. 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: Sertraline, Zoloft; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 102 articles in PubMed, 116 in Scopus, 92 in CINAHL, 2 in Cochrane Library, 150 in Google Scholar, and 2 from other sources†. We considered for inclusion 15 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 17 articles considered for inclusion, 15 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.

PAROXETINE

Moderately 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, 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) [320].
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
Rationale:	All sufficiently-sized placebo-controlled quality studies suggest efficacy [335-338]. Some reporting greater efficacy with prolonged exposure or lack of additive benefit of paroxetine to prolonged exposure [339, 340]. One study compared paroxetine to mirtazapine and found paroxetine non-superior to mirtazapine [341]. 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, Paxil, Pexeva, Brisdelle; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 60 articles in PubMed, 28 in Scopus, 98 in CINAHL, 45 in Cochrane Library, 2 in Google Scholar, and 3 from other sources[†]. We considered for inclusion 9 from PubMed, 0 from Scopus, 4 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 17 articles considered for inclusion, 9 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.

FLUOXETINE

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 C, allergic reactions, irregular heartbeat, hyponatremia, bleeding, suicidal ideation, and suicide attempts. 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 Fluoxetine 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. 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) [320].
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
Rationale:	There are multiple moderate quality studies that substantially conflict regarding efficacy of fluoxetine [350-353]. The largest study is statistically negative [352]. However, there are two studies suggesting that fluoxetine may have some efficacy in PTSD symptom maintenance preventing relapse [349, 351]. 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, Prozac, Sarafem; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 57 articles in PubMed, 50 in Scopus, 49 in CINAHL, 60 in Cochrane Library, 4200 in Google Scholar, and 0 from other sources†. We considered for inclusion 7 from PubMed, 1 from Scopus, 1 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 6 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.

FLUVOXAMINE

No Recommendation.

There is no recommendation for 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 placebo-controlled trials. One moderate-quality RCT showed comparable efficacy between fluvoxamine and reboxetine in MVA PTSD survivors [359]. 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 [360]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 4 articles in PubMed, 85 in Scopus, 10 in CINAHL, 37 in Cochrane Library, 1460 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 1 from Scopus, 4 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 1 randomized trial 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.

ESCITALOPRAM

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 [318].
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) [320].
Frequency/Dose/Duration:	Escitalopram 10-20 mg/day with flexible daily doses increased at varying intervals per responses [365].
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 [8, 365]. Yet, the enantiomer citalopram has a moderate quality study suggesting superiority to placebo but inferiority to sertraline (see below). Escitalopram has low adverse effects, is moderate cost, has evidence of lacking efficacy, whereas 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: lexapro, escitalopram; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 28 articles in PubMed, 24 in Scopus, 1 in CINAHL, 78 in Cochrane Library, 50 in Google Scholar, and 0 from other sources†. We considered for inclusion 9 from PubMed, 2 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 17 articles considered for inclusion, 3 randomized trials and 14 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

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 [318].
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) [320].
Frequency/Dose/Duration:	Citalopram 20-50 mg/day with flexible daily doses increased at varying intervals per responses [318].
Indications for Discontinuation:	Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication
Rationale:	There is one moderate quality study comparing citalopram to sertraline and placebo and found sertraline superior to citalopram but both medications superior to placebo [318]. One study added baclofen but had a significant dropout rate [368]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 29 articles in PubMed, 20 in Scopus, 1 in CINAHL, 8 in Cochrane Library, 2110 in Google Scholar, and 1 from other sources†. We considered for inclusion 4 from PubMed, 1 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 9 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.

VILAZODONE

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**

Rationale: There is little quality evidence assessing vilazodone for PTSD. There is one study showing apparent lack of efficacy compared to placebo [372]. 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, viibryd; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 1 articles in PubMed, 60 in Scopus, 1 in CINAHL, 7 in Cochrane Library, 201 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 3 articles 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 is a serotonin-norepinephrine reuptake inhibitor antidepressant that has been utilized for the treatment of PTSD and other stress disorders [373-376].

VENLAFAXINE
Moderately 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 [320].
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/d 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, 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, effexor; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 13 articles in PubMed, 78 in Scopus, 42 in CINAHL, 7 in Cochrane Library, 2390 in Google Scholar, and 4 from other sources†. We considered for inclusion 5 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 11 articles considered for inclusion, 2 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.

Tricyclic Antidepressants (TCAs)

Amitriptyline is a tricyclic antidepressant that has been used for treatment of PTSD [377, 378].

AMITRIPTYLINE

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 [379]. Other studies of TCAs conflict (see 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 15 in Scopus, 0 in CINAHL, 10 in Cochrane Library, 1450 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 5 articles 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.

DESIPRAMINE

No Recommendation.

There is no recommendation for the use of desipramine 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 [382]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 13 articles in PubMed, 10 in Scopus, 2 in CINAHL, 3 in Cochrane Library, 1190 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 1 from PubMed, 0 from Scopus, 1 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.

IMIPRAMINE

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 [384]. In another study, there were exposure differences, which likely biased the study outcomes and high dropout rates [388]. 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 [387]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 13 articles in PubMed, 28 in Scopus, 17 in CINAHL, 30 in Cochrane Library, 2120 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 4 from PubMed, 2 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 9 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.

NORTRIPTYLINE

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, Sensoval, Aventyle, Pamelor, Norpress, Allegron, Noritren, Nortilen; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 28 in Scopus, 1 in CINAHL, 1 in Cochrane Library, 180 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 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.

Mirtazapine (Remeron) is an antidepressant used for PTSD treatment [394, 395], as well as for treatment of anxiety [341, 396-398].

Mirtazapine

Moderately Recommended.

Mirtazapine (Remeron) is moderately 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 such as CBT, prolonged/exposure therapy, aerobic exercise, strengthening exercise, or SSRIs. Mirtazapine may be used after CBT and PE or in combination with an SSRI. Generally, sertraline, venlafaxine and paroxetine would all be preferable initial medicine recommendations.
Benefits:	Improvements in PTSD symptoms
Harms:	More severe adverse effects include suicidal ideation, increased depression, rash, blisters, racing or uneven heartbeat, hyponatremia, sudden rigidity, high fever, hallucinations, tremors, profuse sweating and confusion. More common adverse effects include; drowsiness, dizziness, vision changes, (including blurred vision), constipation, weight gain, and dry mouth.
Frequency/Dose/Duration:	Mirtazapine 7.5-45 mg/d 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 a few moderate-quality studies using mirtazapine for PTSD. However, one shows greater efficacy for paroxetine [341]. There is evidence of efficacy versus placebo in two moderate-quality trials [396, 398]. Mirtazapine has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, and has some demonstrated efficacy. Therefore, mirtazapine 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: mirtazapine; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, posttraumatic stress, PTSD; controlled clinical trial, controlled trials, randomized controlled trial, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 19 articles in PubMed, 1127 in Scopus, 5 in CINAHL, 40 in Cochrane Library, 1370 in Google Scholar, and 1 from other sources†. We considered for inclusion 4 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 6 articles considered for inclusion, 4 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.

Monoamine Oxidase Inhibitors (MAOIs)

Phenelzine (Nardil) is an MAOI [388, 399] that has been used to treat depression and anxiety disorders [388, 399-404].

PHENELZINE

Recommended.

Phenelzine (Nardil) is recommended as a treatment for patients with PTSD.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – **Low**

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. 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 [384].
Indications for Discontinuation:	Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication
Rationale:	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 [384]. In another study, there were exposure differences that likely biased the study outcomes and high dropout rates [388]. 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 [387]). 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.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Phenelzine, Beta-Phenylethylhydrazine, Monoamine Oxidase Inhibitor, Energy; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 36 articles in PubMed, 270 in Scopus, 3 in CINAHL, 18 in Cochrane Library, 209 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 3 from Scopus, 0 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.

Atypical Antidepressants

Trazodone is an antidepressant [405-407] that has been used to treat insomnia and nightmares associated with PTSD [408, 409].

TRAZODONE

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**

Rationale:	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, Oleptro; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 860 in Scopus, 9 in CINAHL, 48 in Cochrane Library, 4580 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from Scopus, 1 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.

Nefazodone is a serotonin-2 (5-HT2) selective antagonist that inhibits both serotonin and norepinephrine reuptake [410, 411]. It is used as an antidepressant [411] and has been used to treat PTSD [355, 412-414].

NEFAZODONE

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 as 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 [320].
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 [413]. Another trial showed nefazodone had comparable efficacy to sertraline [414], 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, Serzone, dutonin; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 943 in Scopus, 14 in CINAHL, 19 in Cochrane Library, 3110 in Google Scholar, and 10 from other sources. We considered for inclusion 8 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 11 articles considered for inclusion, 2 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.

BUPROPION

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 [422]. 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, Bupropion, Zyban, Aplenzin, Wellbutrin, bupropion hydrochloride; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 12 articles in PubMed, 34 in Scopus, 15 in CINAHL, 7 in Cochrane Library, 1690 in Google Scholar, and 1 from other sources†. We considered for inclusion 2 from PubMed, 1 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 3 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.

Benzodiazepines

Anxiety, irritability, and insomnia associated with PTSD have been treated with benzodiazepines, although the risks associated with benzodiazepines have been generally thought to outweigh any short-term benefits [423, 424]. They are used to treat other anxiety disorders [425-435] but some have reportedly been used to treat PTSD [436-441].

BENZODIAZEPINES

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 [436], and another of temazepam [442] showing a lack of efficacy. One trial of alprazolam as a co-intervention found no clear evidence of the utility of alprazolam [255]. 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: alprazolam; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 12 articles in PubMed, 1451 in Scopus, 12 in CINAHL, 10 in Cochrane Library, 1820 in Google Scholar, and 2 from other sources[†]. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 4 articles considered for inclusion, 2 randomized trials and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: clonazepam; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 934 in Scopus, 4 in CINAHL, 1 in Cochrane Library, 1430 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from

Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Temazepam; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 3 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 480 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Diazepam; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 2160 in Scopus, 4 in CINAHL, 37 in Cochrane Library, 11600 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 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.

Anticonvulsants

Gabapentin (Neurontin) is an antiepileptic, is used to treat neuropathic pain, and has been used to treat PTSD [383, 443-445].

GABAPENTIN

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 [446]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 16 articles in PubMed, 15 in Scopus, 4 in CINAHL, 8 in Cochrane Library, 1300 in Google Scholar, and 1 from other sources†. We considered for inclusion 1 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 4 articles 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.

LAMOTRIGINE

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**

Rationale:	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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 1330 in Scopus, 17 in CINAHL, 20 in Cochrane Library, 5750 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 articles 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.

TOPIRAMATE

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; 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 16 articles in PubMed, 1316 in Scopus, 36 in CINAHL, 43 in Cochrane Library, 4400 in Google Scholar, and 0 from other sources†. We considered for inclusion 5 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 6 articles considered for inclusion, 4 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.

VALPROIC ACID

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 [462]. 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 PTSD patients and thus 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, Valproate; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 7 in Scopus, 1 in CINAHL, 3 in Cochrane Library, 903 in Google Scholar, and 0 from other sources†. We considered for inclusion 8 from PubMed, 0 from Scopus, 1 from CINAHL, 4 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 17 articles considered for inclusion, 3 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.

TIAGABINE

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 [465]. There is one small trial suggesting a slight non-significant potential benefit for reducing relapse of PTSD symptoms [463]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 494 in Scopus, 8 in CINAHL, 14 in Cochrane Library, 1180 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 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.

Antipsychotics

Aripiprazole (Abilify) is an anti-psychotic used for treatment of PTSD, bipolar, and other stress disorders [467, 468] as well as for sleep disturbances [469, 470].

ARIPIPRAZOLE

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 [471]. 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: aripiprazole; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 8 articles in PubMed, 801 in Scopus, 16 in CINAHL, 2 in Cochrane Library, 1080 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 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.

QUETIAPINE

Recommended.

Quetiapine (Seroquel) 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. Generally, other treatments are trialed before quetiapine for PTSD as its evidence of efficacy is relatively weak.
Benefits:	Improvements in PTSD symptoms
Harms:	Quetiapine adverse effects include: severe allergic reaction, neuroleptic malignant syndrome, seizures, hyperlipidemia, glucose dyscontrol, somnolence, sedation, dry mouth, muscle rigidity, tremors, blurred vision, difficulty swallowing, speech problems, increased thirst, fever, confusion, nausea and vomiting, constipation, dizziness, orthostatic hypotension, fatigue, weight gain. Pregnancy risk category C. Somnolence, weight gain, diabetes, extrapyramidal symptoms, QT interval prolongation, and hyperprolactinemia, extrapyramidal effects, pregnancy risk category C [478-480]
Frequency/Dose/Duration:	Quetiapine 25 mg/day to start and increased to a maximum of 800 mg/day (dosing typically ranges from 50-800 mg/day) [475].
Indications for Discontinuation:	Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication
Rationale:	There is one moderate-quality trial of quetiapine suggesting efficacy for the treatment of PTSD [475], although the dropout rates were high due to mostly adverse effects (dry mouth, somnolence, sedation) in the drug arm and lack of efficacy in the placebo arm. Quetiapine has low to moderate adverse effects, is low to moderate cost depending upon treatment duration, has some evidence of efficacy, and is therefore 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: Quetiapine, Seroquel; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 1544 in Scopus, 19 in CINAHL, 6 in Cochrane Library, 2690 in Google Scholar, and 3 from other sources†. We considered for inclusion 6 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 8 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.

RISPERIDONE

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 [483], 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 [485]. Another study suggests that the addition of risperidone may improve PTSD symptoms [484]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 44 articles in PubMed, 2141 in Scopus, 4 in CINAHL, 26 in Cochrane Library, 7510 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 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.

OLANZAPINE

Recommended.

Olanzapine (Zyprexa) is 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. 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 [478-480].
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 [492]. 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 [488, 492]. Olanzapine has moderate to quite significant adverse effects, is moderate cost depending upon treatment duration, but has some evidence of efficacy, and thus is recommended as a second-line treatment for PTSD. However, because the adverse effects are considerable, multiple other medications are recommended to be trialed before olanzapine.
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Olanzapine; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 26 articles in PubMed, 2134 in Scopus, 21 in CINAHL, 36 in Cochrane Library, 8420 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 4 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 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.

Adrenergic Inhibitors

Propranolol is a beta-blocker [383, 494, 495] that has been used for the treatment of PTSD [446, 495-501].

PROPRANOLOL

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. Two studies showed lack of efficacy [446, 502], but some cognitive improvement was found in another study [498]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 35 articles in PubMed, 23 in Scopus, 10 in CINAHL, 37 in Cochrane Library, 1780 in Google Scholar, and 0 from other sources†. We considered for inclusion 15 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 4 randomized trials and 10 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

Sometimes Recommended.

Prazosin (Minipress) is selectively recommended for the treatment of patients with PTSD, particularly for nightmares and/or sleep disturbances.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – **Low**

Indications:	PTSD with prominent nightmares and/or sleep disturbances [473, 479 ,517]
Benefits:	Reduced nightmares and/or sleep disturbances
Harms:	Tachycardia, postural hypotension, increased incidence of heart failure, stroke, and combined cardiovascular disease (coronary heart disease death, nonfatal myocardial infarction, stroke, angina, coronary revascularization, congestive heart failure, and peripheral arterial disease), stress incontinence [516].
Frequency/Dose/Duration:	Titrated based on nightmare response over 6 weeks to a possible maximum dose of 5 mg midmorning and 20 mg at bedtime for men and 2 mg midmorning and 10 mg at bedtime for women [517].
Indications for Discontinuation:	Lack of efficacy, adverse effects, non-compliance, resolution of PTSD sufficiently to not require medication
Rationale:	There are multiple trials of prazosin for treatment of PTSD. The highest quality placebo-controlled trial suggests efficacy for nightmares [517]. One trial suggested benefits for alcohol dependence but not PTSD [513], while another in a similar population also found lack of efficacy for PTSD [515]. One other trial reported prazosin is not as effective as CBT, but better than placebo for sleep disturbances in military personnel [510]. Prazosin has low-moderate adverse effects, is low to moderate cost depending upon treatment duration, and has somewhat conflicting evidence of efficacy; however, the highest quality placebo-controlled trial found efficacy. Thus, it is selectively recommended, particularly for treatment of nightmares associated with PTSD [518].
Evidence:	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms; Prazosin, alpha-1 blockers, Terazosin, doxazosin, acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 78 articles in PubMed, 11 in Scopus, 105 in CINAHL, 4 in Cochrane Library, 60 in Google Scholar, and 0 from other sources†. We considered for inclusion 18 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 19 articles considered for inclusion, 5 randomized trials and 11 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

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 [523]. 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, guanfacine hydrochloride; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 9 in Scopus, 3 in CINAHL, 5 in Cochrane Library, 627 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 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.

CLONIDINE

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; 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, Kapvay, Catapres-TTS-1; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 502 in Scopus, 15 in CINAHL, 6 in Cochrane Library, 7260 in Google Scholar, and 1 from other sources†. We considered for inclusion 3 from PubMed, 5 from Scopus, 3 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 13 articles considered for inclusion, 0 randomized trials and 10 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.

Doxazosin (Cardura) is a long-acting α1-antagonist [536, 537] that has been used to treat prostatic hyperplasia [536, 538], sleep disturbances, and nightmares associated with PTSD [539, 540].

DOXAZOSIN

No Recommendation.

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

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Rationale: There are no sizable trials and only one small study that suggested potential efficacy [540]. Doxazosin has low to moderate adverse effects, is low to moderate cost, but has no sufficiently sizable study; 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: Doxazosin; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 88 in Scopus, 2 in CINAHL, 1 in Cochrane Library, 793 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 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 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.

Steroids

Low-dose hydrocortisone has been used to attempt to reduce risk of PTSD after trauma [541-551].

HYDROCORTISONE

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 only one small RCT, with the RCT suggesting modest improvements in depressive symptoms [541]; yet, steroids would tend to produce those symptom reductions. Hydrocortisone has significant adverse effects, is low to moderate cost depending upon the duration of therapy, and shows insufficient evidence of efficacy, especially given the significant adverse effects; 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: hydrocortisone; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 154 articles in PubMed, 2292 in Scopus, 173 in CINAHL, 8 in Cochrane Library, 7430 in Google Scholar, and 0 from other sources†. We considered for inclusion 10 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 10 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.

Alternative Therapies

Nutraceuticals (pharmaconutrients) are used to attempt to prevent or treat diseases [552, 553] and have occasionally been used to treat PTSD [553].

NUTRACEUTICALS

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 [553] and no other trials. Nutraceuticals have unclear effects, are of 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 25 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 165 in Google Scholar, and 2 from other sources†. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 4 articles considered for inclusion, 1 randomized trial 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.

OMEGA-3 FATTY ACIDS

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 to improve PTSD symptoms, and this evidence is 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 18 in Scopus, 4 in CINAHL, 10 in Cochrane Library, 635 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 3 from PubMed, 0 from Scopus, 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 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.

Marijuana, Cannabis, Cannabinoids, and Cannabidiol

No Recommendation.

There is no recommendation for the use of marijuana, cannabis, cannabinoids, and cannabidiol in the treatment of patients with PTSD.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – **Low**

Rationale:	There is only one underpowered trial of cannabinoids for treatment of PTSD, which reported significant adverse effects [570]. Cannabinoids have significant adverse effects; in the absence of 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: Marijuana, cannabis, cannabinoids, Cannabidiol; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 48 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 4200 in Google Scholar, and 1 from other sources†. We considered for inclusion 4 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 5 articles considered for inclusion, 1 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.

Neuromodulation Therapies

Transcranial magnetic stimulation, a non-invasive brain stimulation treatment, has been suggested for treatment of numerous neuropsychiatric conditions such as depression, anxiety suicidal ideation [571-578], and PTSD [572, 574, 576, 579-587], although most data are for depression.

Transcranial Magnetic Stimulation (TMS) and Repetitive Transcranial Magnetic Stimulation (rTMS)

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:

All trials involving TMS for PTSD have relatively small sample sizes. There are moderate quality heterogeneous studies of TMS for PTSD, and some of these suggest some potential efficacy compared to sham [577, 584, 585, 588, 589]. In one review [579], eight studies suggested effectiveness of TMS for PTSD, yet with no clear advantage of low versus high frequency; similar findings were reported in a systematic review [590]. Meta-analysis shows significant effect size on PTSD symptoms that may be correlated with total number of stimulations [591]. TMS is not invasive, has low to moderate adverse effects, is moderate to high cost depending upon duration of treatment, and has only preliminary evidence for possible efficacy in small studies for adjunct therapy for PTSD. 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; acute stress disorders, traumatic stress disorders, acute traumatic stress, posttraumatic stress disorders, 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 33 articles in PubMed, 1 in Scopus, 1 in CINAHL, 0 in Cochrane Library, 50 in Google Scholar, and 1 from other sources[†]. We considered for inclusion 6 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 1 from other sources. Of the 13 articles considered for inclusion, 1 randomized trial and 6 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Repetitive Transcranial Magnetic Stimulation, rTMS; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 23 articles in PubMed, 75

in Scopus, 9 in CINAHL, 10 in Cochrane Library, 442 in Google Scholar, and 5 from other sources†. We considered for inclusion 10 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 5 from other sources. Of the 21 articles considered for inclusion, 6 randomized trials and 16 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.

Deep Brain Stimulation

Not Recommended.

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

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
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, DBS; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 4 articles in PubMed, 44 in Scopus, 1 in CINAHL, 2 in Cochrane Library, 297 in Google Scholar, and 1 from other sources†. We considered for inclusion 0 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 0 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.

Vagal nerve stimulation (VNS) is designed to deliver electrical pulses directly to the vagus nerve through an implanted device and has been mainly used for treatment of epilepsy and depression [608-610].

Vagal Nerve Stimulation

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: 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), is high cost, and in the absence of quality evidence of efficacy, 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, VNS; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 2 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 193 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from Scopus, 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 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 uses low-intensity microcurrent waveforms with different frequencies to stimulate and alter electrical activity of the brain [611-613] and has been used for treatment of anxiety, depression, and PTSD [610, 611, 613].

Cranial Electrotherapy Stimulation

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. 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 Electrotherapy Stimulation; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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, 5 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 1,070 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 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.

Allied Health Interventions

Massage therapy has been used for the treatment of anxiety, depression [614, 615], and PTSD [616].

Massage

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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 Scopus, 0 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Acupuncture involves the insertion and manipulation of thin solid needles into specific chosen points and has been used for many disorders, including PTSD [617, 618].

Acupuncture

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 a few moderate-quality studies of acupuncture for PTSD, but these studies have considerable methodological issues. One trial was subject to usual care bias [619] and the other trial had small samples and included a sham for auricular acupuncture with reported inconsistent results between groups and over time [620]. 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; acute stress disorders, traumatic stress disorders, acute stress disorder, acute traumatic stress, posttraumatic stress disorders, 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 34 articles in PubMed, 43 in Scopus, 42 in CINAHL, 1 in Cochrane Library, 1840 in Google Scholar, and 2 from other sources†. We considered for inclusion 6 from PubMed, 1 from Scopus, 2 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 12 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.

Appendix 1: PICO Questions

Screening and Testing:

P- Workers and/or patients with PTSD
I-Psychological/Psychiatric Evaluation
C-What is the quality evidence supporting a Psychological/Psychiatric Evaluation?
O-Identification of PTSD and/or associated symptoms

P- Workers and/or patients with PTSD
I-PTSD Screening Tools
C-Are PTSD Screening Tools superior to other screening and testing tools?
O-Identification of PTSD and/or associated symptoms

P- Workers and/or patients with PTSD
I- Psychometric Testing
C-What is the quality evidence supporting Psychometric Testing?
O-Identification of PTSD and/or associated symptoms

P- Workers and/or patients with PTSD
I-Pharmacogenomics
C-What is the quality evidence supporting the use of Pharmacogenomic testing?
O-Identification of PTSD and/or associated symptoms

P- Workers and/or patients with PTSD
I-Functional MRI
C-Is Functional MRI superior to other screening and testing tools?
O-Identification of PTSD and/or associated symptoms

Education:

P- Workers and/or patients with PTSD
I-Trauma Affect Regulation
C-Is Trauma Affect Regulation superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with Post-Traumatic Stress Disorder (PTSD)
I-Education
C-Is Education superior to sham, or equivalent to other effective treatments?
O- PTSD and associated symptoms

Exercise:

P- Workers and/or patients with PTSD
I-Exercise
C-Is Exercise superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Yoga
C-Is Yoga superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Coping Strategies:

P- Workers and/or patients with PTSD
I-Group Therapy

C-Is Group Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Behavioral and Psychological Interventions:

Cognitive Behavioral Therapy:

P- Workers and/or patients with PTSD
I-Cognitive Behavioral Therapy (CBT)
C-Is CBT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Computer-assisted Cognitive Therapy
C-Is Computer-assisted Cognitive Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Cognitive Processing Therapy (CPT)
C-Is CPT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Imagery Rehearsal Training (IRT)
C-Is IRT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Narrative Exposure Therapy
C-Is Narrative Exposure Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Seeking Safety Therapy
C-Is Seeking Safety Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Dialectical Behavior Therapy (DBT)
C-Is DBT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Brief Eclectic Therapy
C-Is Brief Eclectic Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Stress Inoculation Training (SIT)
C-Is SIT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Acceptance and Commitment Theory (ACT)
C-Is ACT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Other Psychological Interventions:

P- Workers and/or patients with PTSD
I-Mind/Body Interventions for Stress Relief
C-Are Mind/Body Interventions superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Relaxation
C-Is Relaxation superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Deep Breathing Exercises
C-Are Deep Breathing Exercises superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Meditation
C-Is Meditation superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Exposure Therapy (ET)
C-Is ET superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Prolonged Exposure Therapy (PE)
C-Is PE superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Virtual Reality
C-Is Virtual Reality superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Individual Debriefing
C-Is Individual Debriefing superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Group Debriefing
C-Is Group Debriefing superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Critical Incident Stress Debriefing
C-Is Critical Incident Stress Debriefing superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Psychodynamic Psychotherapy
C-Is Psychodynamic Psychotherapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Interpersonal Therapy
C-Is Interpersonal Therapy superior to sham, or equivalent to other effect treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Hypnotherapy
C-Is Hypnotherapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Eye Movement Desensitization and Reprocessing (EMDR)
C-Is EMDR superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Thought Field Therapy
C-Is Thought Field Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Emotional Freedom Techniques (EFT/Tapping Techniques)
C-Is EFT superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P-Workers and/or patients with PTSD
I- Neurofeedback
C-Is Neurofeedback superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Animal-Assisted Therapy
C-Is Animal-Assisted Therapy superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Medications:

SSRIs:

P- Workers and/or patients with PTSD
I-Selective Serotonin Reuptake Inhibitors (SSRIs)

C-Are SSRIs (as a class) superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Sertraline (Zoloft)
C-Is sertraline superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Paroxetine (Paxil, Pexeva, Brisdelle)
C-Is Paxil superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Fluoxetine (Prozac)
C-Is Prozac superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Fluvoxamine (Luvox)
C-Is Fluvoxamine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Escitalopram (Lexapro)
C-Is Escitalopram superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Citalopram (Celexa)
C-Are Nutraceuticals superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Vilazodone (viibryd)
C-Is Vilazodone superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

SNRIs:

P- Workers and/or patients with PTSD
I-Serotonin-norepinephrine Reuptake Inhibitors
C-Are SNRIs (as a class) superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Venlafaxine (Effexor)
C-Is Venlafaxine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

TCAs:

P- Workers and/or patients with PTSD
I-Tricyclic Antidepressants (TCAs)
C-Are TCAs (as a class) superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Amitriptyline (Elavil)
C-Is Amitriptyline superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Desipramine (Norpramin)
C-Is Desipramine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Imipramine (Tofranil, Tofranil-pm)
C-Is Imipramine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Nortriptyline (Pamelor)
C-Is Nortriptyline superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Mirtazapine (Remeron, Remeronsoltab)
C-Is Mirtazapine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

MAOIs:

P- Workers and/or patients with PTSD
I-Monoamine Oxidase Inhibitors (MAOIs)
C-Are MAOIs (as a class) to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Phenelzine (Nardil, Nardelzine)
C-Is Phenelzine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Atypical Antidepressants:

P- Workers and/or patients with PTSD
I-Trazodone (Desyrel, Oleptro)
C-Is Trazodone superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Nefazodone (Serzone)
C-Is Nefazodone superior to placebo, or equivalent to other effective treatments?

O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Bupropion (Wellbutrin, Zyban, Aplenzin, Bupropan, Budeprion)
C-Is Bupropion superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Benzodiazepams:

P- Workers and/or patients with PTSD
I-Benzodiazepams
C-Are Benzodiazepams (as a class) superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Alprazolam
C-Is Alprazolam superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Clonazepam
C-Is Clonazepam superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Temazepam
C-Temazepam superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Anticonvulsants:

P- Workers and/or patients with PTSD
I-Gabapentin (Neurontin)
C-Is Gabapentin superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Anticonvulsants:

P- Workers and/or patients with PTSD
I-Lamotrigine (Lamictal)
C-Is Lamotrigine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Topiramate (Topamax, Quedexy)
C-Is Topiramate superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Valproic Acid (Valproate, Divalproex Sodium, Depakote)
C-Is Valproic Acid superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Tiagabine (Gabatril)
C-Are Nutraceuticals superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Anti-psychotics:

P- Workers and/or patients with PTSD
I-Aripiprazole (Abilify)
C-Is Aripiprazole superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Quetiapine (Seroquel, Seroquel-XR)
C-Is Quetiapine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Risperidone (Risperdal)
C-Is Risperidone superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Olanzapine (Zyprexa)
C-Is Olanzapine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Adrenergic Inhibitors:

P- Workers and/or patients with PTSD
I-Propranolol
C-Is Propranolol superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Prazosin (Minipress, Vasoflex, Lentopres, Hypovase)
C-Is Prazosin superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Guanfacine (Intuniv, Tenex)
C-Are Nutraceuticals superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Clonidine (Klonopin)
C-Is Clonidine superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Doxazosin (Cardura)
C-Is Doxazocin superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Steroids:

P- Hydrocortisone
I-Hydrocortisone
C-Is Hydrocortisone superior to placebo, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Alternative Therapies:

P- Workers and/or patients with PTSD
I-Nutraceuticals
C-Are Nutraceuticals superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Omega-3 Fatty Acids
C-Are Omega-3 Fatty Acids superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Marijuana
C-Is Marijuana superior to shame, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Alternative Therapies:

P- Workers and/or patients with PTSD
I-Transcranial Magnetic Stimulation (TMS)
C-Is TMS superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Repetitive Transcranial Magnetic Stimulation (rTMS)
C-Is rTMS superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Deep Brain Stimulation (DBS)
C-Is DBS superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Vagal Nerve Stimulation (VNS)
C-Is VNS superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Cranial Electrotherapy Stimulation (CES)
C-Is CES superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

Allied Health Interventions:

P-Workers and/or patients with PTSD
I- Acupuncture
C-Is Acupuncture superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

P- Workers and/or patients with PTSD
I-Massage
C-Is Massage superior to sham, or equivalent to other effective treatments?
O-PTSD and associated symptoms

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